STEP THERAPY POLICY

POLICY: Alzheimer's – Namenda/Namenda XR Step Therapy Policy
- Namenda® (memantine tablets and oral solution – Allergan, generic)
- Namenda XR® (memantine extended-release capsules – Allergan)

REVIEW DATE: 12/04/2024

OVERVIEW

Memantine tablets, memantine oral solution, and Namenda XR, N-methyl-D-aspartate (NMDA) receptor antagonists, are indicated for the **treatment of moderate to severe dementia of the Alzheimer's type**.[1,2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Generic memantine extended-release capsules are not included in either Step 1 or Step 2 of this program. This policy does not include Namzaric® (memantine extended-release and donepezil capsules); the *Alzheimer's Disease Step Therapy* policy, which addresses the acetylcholinesterase inhibitors (ChIs) [donepezil, rivastigmine, galantamine], includes Namzaric.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic memantine tablets, generic memantine oral solution

Step 2: Namenda tablets, Namenda oral solution, Namenda XR

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Namenda® tablets and oral solution [prescribing information]. Madison, NJ: Allergan; November 2018.
2. Namenda XR® extended-release capsules [prescribing information]. Madison, NJ: Allergan; November 2019.
3. Namzaric® capsules [prescribing information]. Madison, NJ: Allergan; July 2019.

STEP THERAPY POLICY

POLICY: Alzheimer's Disease Step Therapy Policy

- Adlarity® (donepezil transdermal system – Corium)
- Aricept®, Aricept® ODT (donepezil tablets and orally disintegrating tablets – Pfizer/Eisai, generic)
- Exelon® (rivastigmine capsules – Novartis, generic)
- Exelon® Patch (rivastigmine transdermal system – Novartis, generic)
- Namzaric® (memantine extended-release and donepezil capsules – Forest)
- Razadyne® (galantamine tablets and oral solution – Janssen, generic)
- Razadyne® ER (galantamine extended-release capsules – Janssen, generic)

REVIEW DATE: 12/04/2024

OVERVIEW

The acetylcholinesterase inhibitors (ChIs) [donepezil, rivastigmine, galantamine] and the *N*-methyl-D-aspartate (NMDA) antagonist memantine are indicated for the **treatment of Alzheimer's disease** (AD).[1-9]

- Adlarity, donepezil, and transdermal rivastigmine are the only agents approved for **all degrees of AD [mild, moderate, and severe]**.
- Galantamine/galantamine extended-release (ER) and oral rivastigmine are approved for **mild to moderate AD**.
- Oral and transdermal rivastigmine are also indicated for the **treatment of mild to moderate dementia associated with Parkinson's disease (PD)**.
- Namzaric is indicated for the **treatment of moderate to severe dementia of the Alzheimer's type in patients stabilized on donepezil 10 mg once daily**.

Namzaric is a fixed-dose combination containing donepezil and memantine ER.[8]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 (A or B) Product prior to the use of a Step 2 (A or B) Product. If the Step Therapy rule is not met for the Step 2 (A or B) Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: This program has two separate components: one for **generic acetylcholinesterase inhibitor products** (does NOT include donepezil 23 mg tablets) and one for the **Aricept 23 mg strength products (brand or generic)**. This policy does not include the single-agent NMDA antagonists.

Automation: A patient with a of one Step 1 (A or B) Product within the 130-day look-back period is excluded from Step Therapy.

Generic acetylcholinesterase inhibitor:

Step 1A: generic donepezil tablets and orally disintegrating tablets (does NOT include donepezil 23 mg tablets), generic galantamine tablets or oral solution, generic galantamine extended-release capsules, generic rivastigmine capsules, generic rivastigmine transdermal system

Step 2A: Adlarity, Aricept 5 and 10 mg tablets, Aricept ODT, Exelon, Exelon Patch, Namzaric, Razadyne, Razadyne ER

Aricept 23 mg strength (brand or generic):

Step 1B: Aricept 10 mg tablets (brand or generic), Aricept ODT 10 mg (brand or generic)

Step 2B: Aricept 23 mg tablets (brand or generic)

CRITERIA

Generic acetylcholinesterase inhibitor criteria

1. If the patient has tried one Step 1A Product, approve a Step 2A Product.
2. No other exceptions are recommended.

Aricept 23 mg strength (brand or generic) criteria

1. If the patient has tried one Step 1B Product, approve a Step 2B Product.
2. No other exceptions are recommended.

REFERENCES

1. Aricept® tablets/Aricept® ODT (orally disintegrating tablets) [prescribing information]. Woodcliff Lake, NJ: Eisai; December 2018.
2. Razadyne® tablets [prescribing information]. Titusville, NJ: Janssen; August 2021.
3. Razadyne® ER extended-release capsules [prescribing information]. Titusville, NJ: Janssen; September 2022.
4. Exelon® capsules [prescribing information]. East Hanover, NJ: Novartis; December 2018.
5. Exelon® patch [prescribing information]. East Hanover, NJ: Novartis; May 2024.
6. Namenda® tablets and oral solution [prescribing information]. Madison, NJ: Allergan; November 2018.
7. Namenda XR® extended-release capsules [prescribing information]. Madison, NJ: Allergan; November 2019.
8. Namzaric® capsules [prescribing information]. Madison, NJ: Allergan; July 2019.
9. Adlarity® transdermal system [prescribing information]. Grand Rapids, MI: Corium; March 2022.

STEP THERAPY POLICY

POLICY: Angiotensin Receptor Blocker Step Therapy Policy

Single-Entity Products

- Atacand® (candesartan tablets – AstraZeneca/Ani, generic)
- Avapro® (irbesartan tablets – sanofi-aventis, generic)
- Benicar® (olmesartan tablets – Cosette, generic)
- Cozaar® (losartan tablets – Organon, generic)
- Diovan® (valsartan tablets – Novartis, generic)
- Edarbi® (azilsartan tablets – Takeda/Azurity)
- eprosartan tablets – generic
- Micardis® (telmisartan tablets – Boehinger-Ingelheim, generic)

Combination Products

- Atacand HCT® (candesartan/hydrochlorothiazide tablets – AstraZeneca, generic)
- Avalide® (irbesartan/hydrochlorothiazide tablets – sanofi-aventis, generic)
- Azor® (olmesartan/amlodipine tablets – Cosette, generic)
- Benicar HCT® (olmesartan/hydrochlorothiazide tablets – Cosette, generic)
- Diovan HCT® (valsartan/hydrochlorothiazide tablets – Novartis, generic)
- Edarbyclor® (azilsartan/chlorthalidone tablets – Takeda/Arbor)
- Exforge® (valsartan/amlodipine tablets – Novartis, generic)
- Exforge HCT® (valsartan/amlodipine/hydrochlorothiazide tablets – Novartis, generic)
- Hyzaar® (losartan/hydrochlorothiazide tablets – Merck, generic)
- Micardis® HCT (telmisartan/hydrochlorothiazide tablets – Boehringer Ingelheim, generic)
- Tribenzor® (olmesartan/amlodipine/hydrochlorothiazide tablets – Cosette, generic)
- Twynsta® (telmisartan/amlodipine tablets – Boehringer Ingelheim, generic)
- Valsartan oral solution (generic)

REVIEW DATE: 10/02/2024

OVERVIEW

Angiotensin receptor blockers (ARBs) [also known as angiotensin II receptor antagonists] are all indicated for the treatment of adults with **hypertension**; selected agents are also indicated for use in pediatric patients.[1-8] Some ARBs have other indications as well. Several clinical outcome trials with ARBs have shown positive results. All ARBs, except Edarbi, are also available as combination products with hydrochlorothiazide (HCTZ).[9-14] Edarbi is available as a combination product containing chlorthalidone (Edarbyclor).[15] There are several products that combine an ARB with amlodipine (plus or minus HCTZ); these products are indicated for the treatment of hypertension.[16-20]

Prexxartan, an oral solution containing valsartan, is indicated for the following uses:[21]

- Treatment of **hypertension** in adults and children ≥ 6 years of age, to lower blood pressure.
- Management of **heart failure** (New York Heart Association [NYHA] Class II to IV) to reduce the risk of hospitalization for heart failure in patients who are unable to swallow valsartan tablets.
- **Reduce the risk of cardiovascular death** in clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction in patients who are unable to swallow valsartan tablets.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: candesartan, candesartan/HCTZ, eprosartan, irbesartan, irbesartan/HCTZ, losartan, losartan/HCTZ, olmesartan, olmesartan/amlodipine, olmesartan/HCTZ, olmesartan/amlodipine/HCTZ, telmisartan, telmisartan/amlodipine, telmisartan/HCTZ, valsartan, valsartan/amlodipine, valsartan/HCTZ, valsartan/amlodipine/hydrochlorothiazide

Step 2: Atacand, Atacand HCT, Avalide, Avapro, Azor, Benicar, Benicar HCT, Cozaar, Diovan, Diovan HCT, Edarbi, Edarbyclor, Exforge, Exforge HCT, Hyzaar, Micardis, Micardis HCT, Tribenzor, Twynsta, valsartan oral solution

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. Approve a Step 2 Product if the patient meets the following (A, B, and C):
- **A)** The generic equivalent is not available in Step 1; AND
- **B)** Patient was hospitalized and discharged within the previous 30 days for a cardiovascular event; AND
  Note: Examples of a cardiovascular event include a myocardial infarction, a hypertensive emergency, and decompensated heart failure.
- **C)** Patient has been started and stabilized on the Step 2 Product.

3. If the patient cannot swallow or has difficulty swallowing tablets, approve valsartan oral solution.

4. No other exceptions are recommended.

REFERENCES

1. Diovan® tablets [prescribing information]. East Hanover, NJ: Novartis; April 2021.
2. Avapro® tablets [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2021.
3. Cozaar® tablets [prescribing information]. Jersey City, NJ: Organon; October 2021.
4. Atacand® tablets [prescribing information]. Baudette, MN and Sodertalje, Sweden: ANI and AstraZeneca; December 2022.
5. Micardis® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; December 2022.
6. Teveten® tablets [prescribing information]. North Chicago, IL: AbbVie; June 2018.
7. Benicar® tablets [prescribing information]. South Plainfield, NJ: Cosette; February 2022.
8. Edarbi® tablets [prescribing information]. Woburn, MA: Takeda and Azurity; January 2024.
9. Hyzaar® tablets [prescribing information]. Jersey City, NJ: Organon; March 2023.
10. Diovan® HCT tablets [prescribing information]. East Hanover, NJ: Novartis; August 2020.
11. Avalide® tablets [prescribing information]. Bridgewater, NJ: sanofi-aventis; September 2021.
12. Atacand HCT® tablets [prescribing information]. Baudette, MN and Sodertalje, Sweden: ANI and AstraZeneca; August 2020.
13. Micardis HCT® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; December 2022.
14. Benicar HCT® tablets [prescribing information]. South Plainfield, NJ: Cosette; February 2022.
15. Edarbyclor® tablets [prescribing information]. Osaka, Japan and Atlanta, GA: Takeda and Arbor; March 2020.
16. Exforge® tablets [prescribing information]. East Hanover, NJ: Novartis; April 2021.
17. Exforge® HCT tablets [prescribing information]. East Hanover, NJ: Novartis; February 2021.
18. Azor® tablets [prescribing information]. South Plainfield, NJ: Cosette; February 2022.

19. Twynsta® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; November 2018.
20. Tribenzor® tablets [prescribing information]. South Plainfield, NJ: Cosette; February 2022.
21. Valsartan oral solution [prescribing information]. New Brunswick, NJ: Lifsa Drugs; April 2022.

STEP THERAPY POLICY

POLICY: Antidepressants – Bupropion Long-Acting Step Therapy Policy

- Aplenzin® (bupropion hydrobromide extended-release tablets – Bausch Health)
- Auvelity™ (dextromethorphan hydrobromide and bupropion hydrochloride extended-release tablets – Axsome)
- Forfivo XL (bupropion hydrochloride extended-release tablets – Almatica)
- Wellbutrin SR® (bupropion hydrochloride sustained-release tablets – GlaxoSmithKline, generic)
- Wellbutrin XL® (bupropion hydrochloride extended-release tablets – Bausch Health, generic)

REVIEW DATE: 04/03/2024

OVERVIEW

Aplenzin, Auvelity, Forfivo XL, bupropion hydrochloride (HCl) sustained-release (SR) tablets, and bupropion HCl extended-release (ER) tablets are indicated for the **treatment of depression**.[1-5] Bupropion HCl ER tablets and Aplenzin are also indicated for the prevention of seasonal major depressive episodes in patients with seasonal affective disorder.[2,3]

Aplenzin contains bupropion hydrobromide (HBr). Of note, 174 mg/day of bupropion HBr is equivalent to 150 mg/day of bupropion HCl.[3] Therefore, when switching patients from bupropion HCl SR or ER tablets to Aplenzin (or vice versa), it is possible to give equivalent daily doses. Aplenzin is bioequivalent to bupropion HCl ER tablets, which has been demonstrated to have similar bioavailability to both the immediate-release and the SR formulations of bupropion. Forfivo XL is available as 450 mg ER tablets, while the other bupropion HCl ER tablets are available as 150 mg or 300 mg.[2,4]

Auvelity contains a combination of dextromethorphan HBr, an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist, and bupropion HCl, an aminoketone and cytochrome P450 (CYP)2D6 inhibitor.[5] Each tablet contains 45 mg dextromethorphan HBr (equivalent to 32.98 mg dextromethorphan base) in an immediate-release formulation and 105 mg bupropion HCl (equivalent to 91.14 mg bupropion base) in an ER formulation.

Zyban® (bupropion HCl SR, generic only) contains the same active ingredient as bupropion HCl SR and ER tablets and Forfivo XL; however, Zyban is indicated as an aid to smoking cessation treatment.[6] Because of the different indication for use, Zyban is not included in this policy.

Table 1. Available Long-Acting Bupropion-Containing Products.[1-5]

Table 1 (continued). Available Long-Acting Bupropion-Containing Products.[1-5]
HBr – Hydrobromide; HCl – Hydrochloride; ER – Extended-release; CYP – Cytochrome P450; SR – Sustained-release.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic bupropion extended-release tablets, generic bupropion sustained-release tablets

Step 2: Aplenzin, Auvelity, Forfivo XL, Wellbutrin SR, Wellbutrin XL

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: If the patient has tried bupropion immediate-release tablets, they must still try a generic sustained- or extended-release tablet before receiving authorization for a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Wellbutrin SR® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2022.
2. Wellbutrin XL® extended-release tablets [prescribing information]. Bridgewater, NJ: Bausch Health; March 2022.
3. Aplenzin® extended-release tablets [prescribing information]. Bridgewater, NJ: Bausch Health; March 2022.
4. Forfivo XL extended-release tablets [prescribing information]. Pine Brook, NJ: Almatica; December 2019.
5. Auvelity™ extended-release tablets [prescribing information]. New York, NY: Axsome; August 2022.
6. Zyban® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.

STEP THERAPY POLICY

POLICY: Antidepressants – Selective Serotonin Reuptake Inhibitors Step Therapy Policy

- Brisdelle® (paroxetine mesylate 7.5 mg capsules – Sebela [brand discontinued 5/2022], generic)
- Celexa® (citalopram tablets and oral solution – Allergan, generic)
- Citalopram capsules – Almatica
- Fluoxetine capsules (generic to discontinued Sarafem® capsules [brand discontinued 12/2021])
- Fluoxetine delayed-release capsules (generic to discontinued Prozac® Weekly™)
- Fluoxetine tablets (generic only)
- Fluvoxamine extended-release capsules (generic only)
- Fluvoxamine tablets (generic only)
- Lexapro® (escitalopram tablets and oral solution – Allergan, generic)
- Paxil® (paroxetine hydrochloride tablets and oral suspension – Apotex, generic)
- Paxil CR® (paroxetine hydrochloride controlled-release tablets – Apotex, generic)
- Pexeva® (paroxetine mesylate tablets – Sebela [discontinued 5/2023])
- Prozac® (fluoxetine capsules, tablets, and oral solution – Lilly, generic)
- Sertraline capsules – Almatica/Viking
- Trintellix™ (vortioxetine tablets – Takeda)
- Viibryd® (vilazodone hydrochloride tablets – Allergan, generic)
- Zoloft® (sertraline tablets and oral solution – Pfizer, generic)

REVIEW DATE: 03/13/2024

OVERVIEW

The selective serotonin reuptake inhibitors (SSRIs) comprise a pharmacologic class of agents with antidepressant action and efficacy in the treatment of a wide range of mood and anxiety disorders (see Table 1).[1-14]

Table 1. FDA-Approved Indications.[1-14]

Table 1 (continued). FDA-Approved Indications.[1-14]

MDD – Major Depressive Disorder; OCD – Obsessive compulsive disorder; PTSD – Posttraumatic stress disorder; SAD – Social anxiety disorder; GAD – Generalized anxiety disorder; PMDD – Premenstrual dysphoric disorder; VMS – Vasomotor symptoms; * Approved for the prevention of relapse during the continuation treatment phase of depression; † FDA-approved indication includes children and adolescents; α FDA-approved indication includes adolescents 12 to 17 years of age; ^ FDA-approved indication includes children and adolescents 7 to 17 years of age; CR – Controlled release; HCl – Hydrochloride.

POLICY STATEMENT

This program has been developed to encourage the use of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) prior to the use of a Step 2 Product in adults. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) within the 130-day look-back period is excluded from Step Therapy. Patients > 18 years of age are targeted in this Step Therapy program.

Step 1: generic citalopram tablets, generic citalopram oral solution, generic escitalopram tablets, generic fluoxetine immediate-release capsules, generic fluoxetine oral solution, generic fluvoxamine immediate-release tablets, generic paroxetine HCl immediate-release tablets, generic sertraline tablets, generic sertraline oral solution

Step 2: Brisdelle, Celexa, citalopram capsules (brand product), generic escitalopram oral solution, generic fluoxetine delayed-release 90 mg capsule, generic fluoxetine immediate-release tablets, generic fluvoxamine extended-release capsules, generic paroxetine HCl controlled-release (CR)/extended-release (ER) tablets, generic paroxetine HCl oral suspension, generic paroxetine mesylate capsules, generic vilazodone hydrochloride tablets, Lexapro, Paxil, Paxil CR, Pexeva, Prozac, Sarafem, sertraline capsules (brand product), Trintellix, Viibryd, Zoloft

STANDARD CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient is currently taking or has taken Pexeva, Viibryd, or Trintellix at any time in the past and discontinued its use, approve the Product that they have used.

3. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve generic escitalopram oral solution or generic paroxetine HCl oral suspension.

4. If the patient has suicidal ideation, approve Pexeva, Viibryd, or Trintellix.

HIGH IMPACT CRITERIA

1. If the patient has tried two Step 1 Products, approve a Step 2 Product.

2. If the patient is currently taking or has taken Pexeva, Viibryd, or Trintellix at any time in the past and discontinued its use, approve the Product that they have used.

3. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve generic escitalopram oral solution or generic paroxetine HCl oral suspension.

4. If the patient has suicidal ideation, approve Pexeva, Viibryd, or Trintellix.

REFERENCES

1. Prozac® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
2. Paxil® tablets and oral suspension [prescribing information]. Weston, FL: Apotex; August 2023.
3. Zoloft® tablets, oral concentrate [prescribing information]. New York, NY: Pfizer; August 2023.
4. Celexa® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
5. Paxil CR® controlled-release tablets [prescribing information]. Weston, FL: Apotex; February 2024.
6. Lexapro® tablets/oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
7. Pexeva® paroxetine mesylate tablets [prescribing information]. Roswell, GA: Sebela; August 2023.
8. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI: August 2023.
9. Fluvoxamine extended-release capsules [prescribing information]. Chestnut Ridge, NY: Par; October 2023.
10. Viibryd® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.
11. Trintellix™ tablets [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; August 2023.
12. Brisdelle® capsules [prescribing information]. Roswell, GA: Sebela; August 2023.
13. Sertraline capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
14. Citalopram capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.

STEP THERAPY POLICY

POLICY: Antidepressants – Serotonin and Norepinephrine Reuptake Inhibitors Step Therapy Policy

- Cymbalta® (duloxetine HCl delayed-release capsules – Lilly, generic)
- Desvenlafaxine extended-release tablets (Alembic /Ranbaxy [brand product])
- Drizalma Sprinkle™ (duloxetine delayed-release capsules – Sun Pharma)
- Effexor® XR (venlafaxine HCl extended-release capsules – Wyeth, generic)
- Fetzima® (levomilnacipran HCl extended-release capsules – Forest)
- Pristiq® (desvenlafaxine succinate extended-release tablets – Wyeth, generic)
- Savella® (milnacipran HCl tablets – Forest)
- Venlafaxine besylate extended-release tablets (Almatica)
- Venlafaxine HCl tablets (generic only)
- Venlafaxine HCl extended-release tablets (generic)

REVIEW DATE: 03/13/2024

OVERVIEW

Desvenlafaxine, duloxetine, Fetzima, and venlafaxine are serotonin and norepinephrine reuptake inhibitors (SNRIs) indicated for the **treatment of depression**.[1-9] In addition, venlafaxine is indicated for the treatment of generalized anxiety disorder (GAD), social anxiety disorder, and panic disorder. Duloxetine delayed-release capsules are indicated for the treatment of GAD, the management of neuropathic pain associated with diabetic peripheral neuropathy, the management of fibromyalgia, and the management of chronic musculoskeletal pain. Savella is only indicated for the management of fibromyalgia.[10] While Savella is approved outside the US for major depressive disorder (MDD), it is not in development for this or any other indication in the US.

A venlafaxine *hydrochloride* (HCl) extended-release tablet formulation and a venlafaxine *besylate* extended-release tablet are also available.[5,6] These formulations do not carry the same indications as the capsule formulation (Effexor XR, generic). Venlafaxine HCl extended-release tablets are indicated for MDD and social anxiety disorder.[5] Equal doses of venlafaxine HCl extended-release tablets are bioequivalent to venlafaxine extended-release *capsules* (Effexor XR, generic) when administered under fed conditions; however, these products are not AB-rated to each other. Venlafaxine besylate extended-release tablets are indicated for MDD and GAD, and they are only available in a 112.5 mg strength.[6] Venlafaxine besylate extended-release tablets cannot be used to initiate venlafaxine treatment, titrate by doses less than 112.5 mg, or taper treatment.

Similarly, in addition to desvenlafaxine *succinate* extended-release tablets (Pristiq, generic), branded Desvenlafaxine is available.[4,8] Desvenlafaxine and desvenlafaxine succinate are available in the same strength extended-release tablets, and share the same indication (treatment of MDD). Desvenlafaxine, Desvenlafaxine fumarate (discontinued), and desvenlafaxine succinate are not AB-rated to each other. However, efficacy studies conducted with desvenlafaxine succinate are cited in the Desvenlafaxine product information. Drizalma Sprinkle relied on clinical efficacy studies for Cymbalta for approval and has the same indications as Cymbalta with the exception of a fibromyalgia indication.[1,9]

The selective serotonin reuptake inhibitors (SSRIs) are a pharmacologic class of agents with antidepressant action and efficacy in the treatment of a wide range of mood and anxiety disorders that include obsessive compulsive disorder (OCD), panic disorder, social anxiety disorder (social phobia), posttraumatic stress disorder (PTSD), bulimia-nervosa, and GAD.[11] There are many off-label uses for the SSRIs and SNRIs in

a wide variety of psychiatric, as well as nonpsychiatric, conditions. Of note, some patients may have a primary disorder, such as depression, and a comorbid condition, such as anxiety or sleep disorder, which may or may not affect response or the ability to tolerate adverse events (AEs).

INDICATIONS

All of the SNRIs (with the exception of Savella) are indicated for the treatment of MDD. Some of the SNRIs carry additional indications (Table 1). Table 2 provides the approved indications for the available SSRIs.

Table 1. FDA-Approved Indications for the SNRIs in Adults.[1-10]

SNRI – Serotonin norepinephrine reuptake inhibitor; MDD – Major depressive disorder; GAD – Generalized anxiety disorder; SAD – Social Anxiety Disorder; DPN – Diabetic peripheral neuropathy; ^ Efficacy studied in patients $\underline{\geq}$ 7 years of age with GAD; * Approved for use in patients ≥ 13 years of age; HCl – Hydrochloride.

Table 2. FDA-Approved Indications for the SSRIs.[12-24]

Table 2 (continued). FDA-Approved Indications for the SSRIs.[12-24]
MDD – Major Depressive Disorder; OCD – Obsessive compulsive disorder; PTSD – Posttraumatic stress disorder; SAD – Social anxiety disorder; GAD – Generalized anxiety disorder; PMDD – Premenstrual dysphoric disorder; VMS – Vasomotor symptoms; * Approved for the prevention of relapse during the continuation treatment phase of depression; † FDA-approved indication includes children and adolescents; ᵅ FDA-approved indication includes adolescents 12 to 17 years of age; ^ FDA-approved indication includes children and adolescents 7 to 17 years of age; CR – Controlled release; HCl – Hydrochloride.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy. Patients > 18 years of age are targeted in this Step Therapy program.

Step 1: citalopram tablets (Celexa, generic), generic citalopram oral solution, generic duloxetine delayed-release 20 mg, 30 mg, 60 mg capsules, escitalopram tablets (Lexapro, generic), escitalopram oral solution (Lexapro, generic), fluoxetine immediate-release capsules and tablets (Prozac, Sarafem, generic), generic fluoxetine oral solution, generic fluoxetine delayed-release capsules, generic fluvoxamine immediate-release tablets, generic fluvoxamine extended-release capsules, paroxetine HCl immediate- and controlled-release tablets (Paxil, Paxil CR, generic), paroxetine oral suspension (Paxil, generic), Pexeva, sertraline tablets (Zoloft, generic), sertraline oral solution (Zoloft, generic), Trintellix (formerly Brintellix), Viibryd, generic venlafaxine immediate-release tablets, generic venlafaxine extended-release capsules

Step 2: Cymbalta, Desvenlafaxine extended-release tablets (brand product), Drizalma Sprinkle, Effexor XR, Fetzima, Pristiq, Savella, generic desvenlafaxine succinate extended-release tablets, generic duloxetine 40 mg delayed-release capsules, generic venlafaxine HCl extended-release tablets, venlafaxine besylate extended-release tablets

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient is currently taking or has taken brand name Desvenlafaxine extended-release tablets, desvenlafaxine succinate extended-release tablets (Pristiq or generics), or Fetzima at any time in the past and discontinued its use, approve the Product that they have used.

3. If the patient has suicidal ideation, approve Desvenlafaxine extended-release tablets, desvenlafaxine succinate extended-release tablets (Pristiq or generics), or Fetzima.

REFERENCES

1. Cymbalta® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
2. Effexor XR® extended-release capsules [prescribing information]. Morgantown, WV: Viatris; August 2023.
3. Venlafaxine hydrochloride tablets [prescribing information]. Parsippany, NJ: Teva; August 2023.
4. Pristiq® extended-release tablets [prescribing information]. Philadelphia, PA: Wyeth; August 2023.
5. Venlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; September 2023.
6. Venlafaxine besylate extended-release tablets [prescribing information]. Morristown, NJ: Almatica; August 2023.
7. Fetzima® extended-release capsules [prescribing information]. North Chicago, IL: AbbVie; August 2023.
8. Desvenlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; August 2023.

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10. Savella® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.
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12. Prozac® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
13. Paxil® tablets and oral suspension [prescribing information]. Weston, FL: Apotex; August 2023.
14. Zoloft® tablets, oral concentrate [prescribing information]. New York, NY: Pfizer; August 2023.
15. Celexa® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
16. Paxil CR® controlled-release tablets [prescribing information]. Westin, FL: Apotex; February 2024.
17. Lexapro® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
18. Pexeva® tablets [prescribing information]. Roswell, GA: Sebela; August 2023.
19. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI; August 2023.
20. Sarafem® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
21. Fluvoxamine extended-release capsules [prescribing information]. Chestnut Ridge, NY: Par; October 2023.
22. Viibryd® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.
23. Trintellix™ (formerly Brintellix® tablets) [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; August 2023.
24. Brisdelle® capsules [prescribing information]. Roswell, GA: Sebela; August 2023.

STEP THERAPY POLICY

POLICY: Antidepressants Step Therapy Policy

REVIEW DATE: 05/29/2024; effective 07/01/2024

OVERVIEW

Bupropion Products

Aplenzin, Auvelity, Forfivo XL (authorized generics), bupropion hydrochloride (HCl) sustained-release (SR) tablets, and bupropion HCl extended-release (ER) tablets are indicated for the **treatment of depression**.[1-5] Bupropion HCl ER tablets and Aplenzin are also indicated for the prevention of seasonal major depressive episodes in patients with seasonal affective disorder.[2,3] Table 1 lists the available bupropion-containing products.

Table 1. Available Long-Acting Bupropion-Containing Products.[1-5]

HBr – Hydrobromide; HCl – Hydrochloride; ER – Extended-release; CYP – Cytochrome P450; SR – Sustained-release.

Aplenzin contains bupropion hydrobromide (HBr). Of note, 174 mg/day of bupropion HBr is equivalent to 150 mg/day of bupropion HCl.[3] Therefore, when switching patients from bupropion HCl SR or ER tablets to Aplenzin (or vice versa), it is possible to give equivalent daily doses. Aplenzin is bioequivalent to bupropion HCl ER tablets, which has been demonstrated to have similar bioavailability to both the immediate-release and the SR formulations of bupropion. Forfivo XL (authorized generics) is available as 450 mg ER tablets, while the other bupropion HCl ER tablets are available as 150 mg or 300 mg.[2,4]

Auvelity contains a combination of dextromethorphan HBr, an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist, and bupropion HCl, an aminoketone and cytochrome P450 (CYP)2D6 inhibitor.[5] Each tablet contains 45 mg dextromethorphan HBr (equivalent to 32.98 mg dextromethorphan base) in an immediate-release formulation and 105 mg bupropion HCl (equivalent to 91.14 mg bupropion base) in an ER formulation.

Zyban® (bupropion HCl SR, generic only) contains the same active ingredient as bupropion HCl SR and ER tablets and Forfivo XL (authorized generics); however, Zyban is indicated as an aid to smoking cessation treatment.[6] Because of the different indication for use, Zyban is not included in this policy.

Selective Serotonin Reuptake Inhibitor (SSRI) Products

The SSRIs comprise a pharmacologic class of agents with antidepressant action and efficacy in the treatment of a wide range of mood and anxiety disorders (see Table 2).[7-21]

Table 2. FDA-Approved Indications for the SSRIs.[7-21]

Table 2 (continued). FDA-Approved Indications for the SSRIs.[7-21]

SSRIs – Selective serotonin reuptake inhibitors; MDD – Major depressive disorder; OCD – Obsessive compulsive disorder; PTSD – Posttraumatic stress disorder; SAD – Social anxiety disorder; GAD – Generalized anxiety disorder; PMDD – Premenstrual dysphoric disorder; VMS – Vasomotor symptoms; * Approved for the prevention of relapse during the continuation treatment phase of depression; † FDA-approved indication includes children and adolescents; α FDA-approved indication includes adolescents 12 to 17 years of age; ^ FDA-approved indication includes children and adolescents 7 to 17 years of age; CR – Controlled release; HCl – Hydrochloride.

Serotonin and Norepinephrine Reuptake Inhibitor (SNRI) Products

Desvenlafaxine, duloxetine, Fetzima, and venlafaxine are SNRIs indicated for the **treatment of depression**.[22-31] Additional indications vary by product. Table 3 provides the approved indications for the

available SSRIs. While Savella is approved outside the US for major depressive disorder (MDD), it is not in development for this indication in the US.

A venlafaxine *hydrochloride* (HCl) extended-release tablet formulation and a venlafaxine *besylate* extended-release tablet are also available.[26,27] These formulations do not carry the same indications as the capsule formulation (Effexor XR, generic). Venlafaxine HCl extended-release tablets are indicated for MDD and social anxiety disorder.[26] Equal doses of venlafaxine HCl extended-release tablets are bioequivalent to venlafaxine extended-release *capsules* (Effexor XR, generic) when administered under fed conditions; however, these products are not AB-rated to each other. Venlafaxine besylate extended-release tablets are indicated for MDD and GAD, and they are only available in a 112.5 mg strength.[27] Venlafaxine besylate extended-release tablets cannot be used to initiate venlafaxine treatment, titrate by doses less than 112.5 mg, or taper treatment.

Similarly, in addition to desvenlafaxine *succinate* extended-release tablets (Pristiq, generic), branded Desvenlafaxine is available.[25,29] Desvenlafaxine and desvenlafaxine succinate are available in the same strength extended-release tablets, and share the same indication (treatment of MDD). Desvenlafaxine, Desvenlafaxine fumarate (discontinued), and desvenlafaxine succinate are not AB-rated to each other. However, efficacy studies conducted with desvenlafaxine succinate are cited in the Desvenlafaxine product information. Drizalma Sprinkle relied on clinical efficacy studies for Cymbalta for approval and has the same indications as Cymbalta with the exception of a fibromyalgia indication.[22,30]

Table 3. FDA-Approved Indications for the SNRIs in Adults.[22-31]
SNRI – Serotonin norepinephrine reuptake inhibitor; MDD – Major depressive disorder; GAD – Generalized anxiety disorder; SAD – Social anxiety disorder; DPN – Diabetic peripheral neuropathy; ^ Efficacy studied in patients ≥ 7 years of age with GAD; * Approved for use in patients ≥ 13 years of age; HCl – Hydrochloride.

POLICY STATEMENT

This program has been developed to encourage the use of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) prior to the use of a Step 2 Product in adults. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) within the 130-day look-back period is excluded from Step Therapy. Patients > 18 years of age are targeted in this Step Therapy program.

Step 1: generic bupropion extended-release tablets, generic bupropion sustained-release tablets, generic citalopram oral solution, generic citalopram tablets, generic duloxetine delayed-release (20 mg, 30 mg, 60 mg) capsules, generic escitalopram tablets, generic fluoxetine immediate-release capsules, generic fluoxetine oral solution, generic fluvoxamine immediate-release tablets, generic paroxetine HCl immediate-release tablets, generic sertraline oral solution, generic sertraline tablets, generic venlafaxine extended-release capsules, generic venlafaxine immediate-release tablets

Step 2: Aplenzin, Auvelity, Brisdelle, Bupropion XL tablets (authorized generics to Forfivo XL), Celexa, Citalopram capsules (brand), Cymbalta, Desvenlafaxine extended-release tablets (brand), generic desvenlafaxine succinate extended-release tablets, generic duloxetine 40 mg delayed-release capsules, Drizalma Sprinkle, Effexor XR, generic escitalopram oral solution, Fetzima, generic fluoxetine delayed-release 90 mg capsule, generic fluoxetine immediate-release tablets, generic fluvoxamine extended-release capsules, Forfivo XL, Lexapro, Paxil, Paxil CR, generic paroxetine HCl controlled-release (CR)/extended-release (ER) tablets, generic paroxetine HCl oral suspension, generic paroxetine mesylate capsules, Pexeva, Pristiq, Prozac, Sarafem, Savella, Sertraline capsules (brand), Trintellix, Venlafaxine besylate extended-release tablets (brand), generic venlafaxine HCl extended-release tablets, generic vilazodone hydrochloride tablets, Viibryd, Wellbutrin SR, Wellbutrin XL, Zoloft

STANDARD CRITERIA

5. If the patient has tried one Step 1 Product, approve a Step 2 Product.

6. If the patient is currently taking or has taken Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (Pristiq or generics), Fetzima, Pexeva, vilazodone hydrochloride tablets (Viibryd or generics), or Trintellix at any time in the past and discontinued its use, approve the Product that they have used.

7. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve generic escitalopram oral solution or generic paroxetine HCl oral suspension.

8. If the patient has suicidal ideation, approve Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (Pristiq or generics), Fetzima, Pexeva, vilazodone hydrochloride tablets (Viibryd or generics), or Trintellix.

HIGH IMPACT CRITERIA

5. If the patient has tried two Step 1 Products, approve a Step 2 Product.

6. If the patient is currently taking or has taken Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (Pristiq or generics), Fetzima, Pexeva, vilazodone hydrochloride tablets (Viibryd or generics), or Trintellix at any time in the past and discontinued its use, approve the Product that they have used.

7. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve generic escitalopram oral solution or generic paroxetine HCl oral suspension.

8. If the patient has suicidal ideation, approve Desvenlafaxine extended-release tablets (brand product), desvenlafaxine succinate extended-release tablets (Pristiq or generics), Fetzima, Pexeva, vilazodone hydrochloride tablets (Viibryd or generics), or Trintellix.

REFERENCES

15. Wellbutrin SR® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2022.
16. Wellbutrin XL® extended-release tablets [prescribing information]. Bridgewater, NJ: Bausch Health; March 2022.
17. Aplenzin® extended-release tablets [prescribing information]. Bridgewater, NJ: Bausch Health; March 2022.
18. Forfivo XL extended-release tablets [prescribing information]. Pine Brook, NJ: Almatica; December 2019.
19. Auvelity™ extended-release tablets [prescribing information]. New York, NY: Axsome; August 2022.
20. Zyban® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.
21. Prozac® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
22. Paxil® tablets and oral suspension [prescribing information]. Weston, FL: Apotex; August 2023.
23. Zoloft® tablets, oral concentrate [prescribing information]. New York, NY: Pfizer; August 2023.
24. Celexa® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
25. Paxil CR® controlled-release tablets [prescribing information]. Weston, FL: Apotex; February 2024.
26. Lexapro® tablets/oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
27. Pexeva® paroxetine mesylate tablets [prescribing information]. Roswell, GA: Sebela; August 2023.
28. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI: August 2023.
29. Fluvoxamine extended-release capsules [prescribing information]. Chestnut Ridge, NY: Par; October 2023.
30. Sarafem® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
31. Viibryd® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.
32. Trintellix™ tablets [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; August 2023.
33. Brisdelle® capsules [prescribing information]. Roswell, GA: Sebela; August 2023.
34. Sertraline capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
35. Citalopram capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
36. Cymbalta® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
37. Effexor XR® extended-release capsules [prescribing information]. Morgantown, WV: Viatris; August 2023.
38. Venlafaxine hydrochloride tablets [prescribing information]. Parsippany, NJ: Teva; August 2023.
39. Pristiq® extended-release tablets [prescribing information]. Philadelphia, PA: Wyeth; August 2023.
40. Venlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; September 2023.
41. Venlafaxine besylate extended-release tablets [prescribing information]. Morristown, NJ: Almatica; August 2023.
42. Fetzima® extended-release capsules [prescribing information]. North Chicago, IL: AbbVie; August 2023.
43. Desvenlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; August 2023.
44. Drizalma Sprinkle™ delayed-release capsules [prescribing information]. Cranbury, NJ: Sun; August 2023.
45. Savella® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.

STEP THERAPY POLICY

POLICY: Antifungals for Vulvovaginal Candidiasis Step Therapy Policy

- Brexafemme® (ibrexafungerp tablets – Scynexis)
- Diflucan® (fluconazole tablets – Pfizer, generic)
- Miconazole vaginal suppository (100 mg, 200 mg, or 1,200 mg) [over-the-counter]
- Terconazole vaginal cream 0.4% (generic only)
- Terconazole vaginal cream 0.8% (generic only)
- Terconazole vaginal suppository 80 mg (generic only)

REVIEW DATE: 09/18/2024

OVERVIEW

The listed vaginal antifungals, oral fluconazole, and Brexafemme are indicated for the **treatment of vulvovaginal candidiasis**.[1-4] Brexafemme is also indicated to reduce the incidence of recurrent vulvovaginal candidiasis in adults and post-menarchal pediatric females.[1] Many of the vaginal antifungals are available as over-the-counter (OTC) products.[3,4]

Guidelines

Brexafemme is not addressed in the guidelines. The Centers for Disease Control and Prevention (CDC) Sexually Transmitted Infections Treatment Guidelines (2021) recommend an intravaginal product (e.g., miconazole, tioconazole) or oral fluconazole for the treatment of vulvovaginal candidiasis.[5] Treatment with an azole antifungal typically results in relief of symptoms and negative cultures in 80% to 90% of patients who complete treatment. There are no data to show superiority of one intravaginal product over another.[6] The efficacy of oral fluconazole and intravaginal antifungals is similar.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic fluconazole 150 mg tablets, miconazole vaginal suppository (over-the-counter kits that include miconazole vaginal suppository are also included), generic terconazole vaginal cream, generic terconazole vaginal suppository

Step 2: Brexafemme

CRITERIA

3. If the patient has tried one Step 1 Product, approve a Step 2 Product.

4. No other exceptions are recommended.

REFERENCES

7. Brexafemme® tablets [prescribing information]. Jersey City, NJ: Scynexis; November 2022.
8. Diflucan® tablets and powder for oral suspension [prescribing information]. New York, NY: Pfizer, February 2024.
9. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: http://fco.factsandcomparisons.com/lco/action/home. Accessed on September 11, 2024. Search terms: fluconazole, miconazole, terconazole.
10. Clinical Pharmacology [database online]. Elsevier Inc. © 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed on September 11, 2024. Search terms: fluconazole, miconazole, terconazole.
11. Workowski KA, Bachmann LH, Chan PA, et al. Sexually transmitted infections treatment guidelines 2021. *MMWR Recomm Rep*. 2021;70(4):1-187.
12. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4):e1-50.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Divalproex Sodium/Valproic Acid Step Therapy Policy

- Depakote® (divalproex sodium delayed-release tablets – AbbVie, generic)
- Depakote® Sprinkle Capsules (divalproex sodium delayed-release capsules – AbbVie, generic)
- Depakote® ER (divalproex sodium extended-release tablets – AbbVie, generic)
- Valproic acid capsules and oral solution (generic to discontinued Depakene®)

REVIEW DATE: 08/07/2024

OVERVIEW

All of these products are indicated for the following uses:[1-4]

- As monotherapy and adjunctive therapy in the treatment of patients with **complex partial seizures** and **simple and complex absence seizures**.
- Adjunctively in patients with multiple seizure types that include **absence seizures**.
- In addition, divalproex sodium tablets (Depakote, generic) and divalproex sodium extended-release tablets (Depakote ER, generic) are also indicated for **prophylaxis of migraine headaches** and treatment of **bipolar disorder**.[1,3]

Divalproex sodium and valproic acid are antiseizure medications.[1-4] Divalproex sodium is comprised of sodium valproate and valproic acid.[1] Divalproex sodium and valproic acid each dissociate to the valproate ion in the gastrointestinal (GI) tract.[1-4] Equivalent oral doses of divalproex sodium products (Depakote, generic) and valproic acid products deliver equivalent quantities of valproate ion systemically. Although the rate of valproate ion absorption may vary with the formulation administered (liquid, solid, or sprinkle), conditions of use (e.g., fasting or postprandial) and the method of administration (e.g., whether the contents of the capsule are sprinkled on food or the capsule is taken intact), these differences should be of minor clinical importance under the steady state conditions achieved in chronic use in the treatment of epilepsy. Experience administering dosing regimens from once daily to four times daily indicate that total daily systemic bioavailability (extent of absorption) is the primary determinant of seizure control and differences in the ratios of plasma peak to trough concentrations between valproate formulations are inconsequential from a practical clinical standpoint.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic divalproex sodium capsules, generic divalproex sodium delayed-release tablets, generic divalproex sodium extended-release tablets, generic valproic acid capsules, generic valproic acid oral solution

Step 2: Depakote, Depakote ER/EC/DR, Depakote Sprinkle

CRITERIA

5. If the patient has tried one Step 1 Product, approve a Step 2 Product.

6. No other exceptions are recommended.

REFERENCES

13. Depakote® delayed-release tablets [prescribing information]. North Chicago, IL: AbbVie; March 2024.
14. Depakote® Sprinkle Capsules delayed-release capsules [prescribing information]. North Chicago, IL: AbbVie; March 2024.
15. Depakote® ER extended-release tablets [prescribing information]. North Chicago, IL: AbbVie; March 2024.
16. Depakene® capsules and oral solution [prescribing information]. North Chicago, IL: AbbVie; May 2020.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Lacosamide Step Therapy Policy
- Motpoly XR™ (lacosamide extended-release capsules – Aucta)
- Vimpat® (lacosamide tablets and oral solution – UCB, generic)

REVIEW DATE: 03/13/2024

OVERVIEW

Lacosamide (Vimpat, generic) is indicated for the following:[1]
- **Treatment of partial-onset seizures** in patients ≥ 1 month of age.
- **Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures** in patients ≥ 4 years of age.

Motpoly XR is indicated for the **treatment of partial-onset seizures** in adults and in pediatric patients weighing ≥ 50 kg.[2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic lacosamide tablets, generic lacosamide oral solution

Step 2: Motpoly XR, Vimpat tablets, Vimpat oral solution

CRITERIA

3. If the patient has tried one Step 1 Product, approve a Step 2 Product.

4. No other exceptions are recommended.

REFERENCES

4. Vimpat® tablets and oral solution [prescribing information]. Smyrna, GA: UCB; October 2023.
5. Motpoly XR™ extended-release capsules [prescribing information]. Piscataway, NJ: Aucta; May 2023.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Lamotrigine Step Therapy Policy

- Lamictal® (lamotrigine tablets and chewable dispersible tablets – GlaxoSmithKline, generic)
- Lamictal ODT® (lamotrigine orally disintegrating tablets – GlaxoSmithKline, generic)
- Lamictal® XR™ (lamotrigine extended-release tablets – GlaxoSmithKline, generic)

REVIEW DATE: 11/13/2024

OVERVIEW

The immediate-release formulations of lamotrigine (tablets, chewable dispersible tablets, and orally disintegrating tablets [Lamictal, Lamictal ODT, generic]), an antiseizure medication (ASM) of the phenyltriazine class, are indicated for the following:[1]

- Adjunctive therapy in patients ≥ 2 years of age with **partial seizures, primary generalized tonic-clonic seizures, and generalized seizures of Lennox-Gastaut syndrome**.
- Monotherapy in patients ≥ 16 years of age with **partial seizures** who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single ASM.
- **Maintenance treatment of bipolar I disorder** to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy.

Lamotrigine extended-release tablets (Lamictal XR, generic) are indicated for the following:[2]

- Adjunctive therapy for **primary generalized tonic-clonic seizures and partial onset seizures** with or without secondary generalization in patients ≥ 13 years of age.
- **Conversion to monotherapy** in patients ≥ 13 years of age with **partial seizures** who are receiving treatment with a single ASM.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic lamotrigine tablets, generic lamotrigine chewable dispersible tablets, generic lamotrigine extended-release tablets, and generic lamotrigine orally disintegrating tablets

Step 2: Lamictal tablets, Lamictal chewable dispersible tablets, Lamictal XR, Lamictal ODT

CRITERIA

7. If a patient has tried one Step 1 product, approve a Step 2 Product.

8. No other exceptions are recommended.

REFERENCES

17. Lamictal® tablets, chewable dispersible tablets, and Lamictal ODT® [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.
18. Lamictal® XR™ extended-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Levetiracetam, Brivaracetam Step Therapy Policy

- Briviact® (brivaracetam tablets and oral solution – UCB)
- Elepsia™ XR (levetiracetam extended-release tablets – Tripoint)
- Keppra® (levetiracetam tablets and oral solution – UCB, generic)
- Keppra XR® (levetiracetam extended-release tablets – UCB, generic)
- Roweepra® (levetiracetam tablets – OWP [branded generic])
- Roweepra XR™ (levetiracetam extended-release tablets – OWP [branded generic])
- Spritam® (levetiracetam tablets for oral suspension – Prasco)

REVIEW DATE: 06/26/2024

OVERVIEW

Levetiracetam is an antiseizure medication (ASM); the immediate-release tablets and oral solution (Keppra, generic) are indicated for the treatment of:[1]

- **Partial-onset seizures** in patients ≥ 1 month of age.
- **Myoclonic seizures**, as adjunctive therapy in patients ≥ 12 years of age with juvenile myoclonic epilepsy.
- **Primary generalized tonic-clonic seizures**, as adjunctive therapy in patients ≥ 6 years of age with idiopathic generalized epilepsy.

Levetiracetam extended-release tablets (Keppra XR, generic; Elepsia XR) are indicated for the treatment of **partial-onset seizures** in patients ≥ 12 years of age.[2,7]

Spritam is indicated as adjunctive therapy in the treatment of:[3]

- **Partial-onset seizures** in patients ≥ 4 years of age and weighing > 20 kg with epilepsy.
- **Myoclonic seizures**, as adjunctive therapy in patients ≥ 12 years of age with juvenile myoclonic epilepsy.
- **Primary generalized tonic-clonic seizures**, as adjunctive therapy in patients ≥ 6 years of age with idiopathic generalized epilepsy.

Roweepra (levetiracetam tablets) and Roweepra XR (levetiracetam extended-release tablets) are branded generics to Keppra tablets and Keppra XR, respectively, with the same indications.[4,5]

Briviact is an ASM that is indicated for the treatment of **partial-onset seizures** in patients ≥ 1 month of age.[6] Briviact has a similar mechanism of action as that of levetiracetam.[1,6] Both ASMs display a high and selective affinity for synaptic vesicle protein 2A (SV2A) in the brain, which may contribute to their anticonvulsant effect by modulating neurotransmitter release into the synapse. Unlike levetiracetam, Briviact is a controlled substance (C-V).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic carbamazepine (tablets, chewable tablets, ER tablets, ER capsules, oral suspension), generic divalproex (DR capsules, DR tablets, ER tablets), generic ethosuximide (capsules, oral solution), generic felbamate (tablets, oral solution), generic gabapentin (capsules, tablets, oral solution), generic lamotrigine (tablets, chewable tablets, ER tablets, ODT tablets), generic levetiracetam (tablets, ER tablets, oral solution), generic oxcarbazepine (tablets, oral suspension), generic phenytoin (ER capsules, chewable tablets, oral suspension), generic pregabalin (capsules, oral solution), generic rufinamide oral suspension, generic tiagabine tablets, generic topiramate (capsules, ER capsules, tablets), generic valproic acid (capsules, DR capsules, oral solution), generic vigabatrin (tablets, powder for oral solution), generic zonisamide capsules, Roweepra, Roweepra XR
Note: ER – Extended-release; DR – Delayed –release; ODT – Orally-disintegrating tablet.

Step 2: Briviact, Elepsia XR, Keppra, Keppra XR, Spritam

CRITERIA

9. If the patient has tried one Step 1 Product, approve a Step 2 Product.

10. If the patient is currently taking or has taken Briviact at any time in the past and discontinued its use, approve Briviact.

11. No other exceptions are recommended.

REFERENCES

19. Keppra® tablets and oral solution [prescribing information]. Smyrna, GA: UCB; March 2024.
20. Keppra XR® extended-release tablets [prescribing information]. Smyrna, GA: UCB; March 2024.
21. Spritam® tablets for oral suspension [prescribing information]. Mason, OH: Prasco; June 2024.
22. Roweepra® tablets [prescribing information]. Naperville, IL: OWP; April 2024.
23. Roweepra XR™ extended-release tablets [prescribing information]. Naperville, IL: OWP; October 2020.
24. Briviact® tablets, oral solution, and injection [prescribing information]. Smyrna, GA: UCB; May 2023.
25. Elepsia™ XR extended-release tablets [prescribing information]. Westfield, NJ: Tripoint; March 2024.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Oxcarbazepine Step Therapy Policy

- Oxtellar XR® (oxcarbazepine extended-release tablets – Supernus, generic)
- Trileptal® (oxcarbazepine tablets and oral suspension – Novartis, generic)

REVIEW DATE: 04/03/2024; selected revision 9/18/2024

OVERVIEW

Oxcarbazepine tablets and oral suspension are indicated for use as monotherapy or adjunctive therapy in the treatment of **partial seizures** in adults, as monotherapy in the treatment of partial seizures in patients ≥ 4 years of age with epilepsy, and as adjunctive therapy in the treatment of partial seizures in patients ≥ 2 years of age.[1] Oxcarbazepine extended-release (XR) is indicated for the treatment of partial seizures in patients ≥ 6 years of age.[2]

Oxcarbazepine is an antiseizure medication available in immediate- and XR formulations.[1,2] Oxcarbazepine XR administered as a once daily dose is not bioequivalent to the same total dose of the immediate-release formulation given twice daily at steady state.[2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic oxcarbazepine tablets, generic oxcarbazepine oral suspension

Step 2: Oxtellar XR (brand and generic), Trileptal tablets and oral suspension

CRITERIA

12. If a patient has tried one Step 1 Product, approve a Step 2 Product.

13. No other exceptions are recommended.

REFERENCES

26. Trileptal® tablets and oral suspension [prescribing information]. East Hanover, NJ: Novartis; January 2019.
27. Oxtellar XR® extended-release tablets [prescribing information]. Rockville, MD: Supernus; December 2018.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Topiramate Step Therapy Policy
- Eprontia® (topiramate oral solution – Azurity)
- Qudexy® XR (topiramate extended-release capsules – Upsher-Smith, generic, including an authorized generic)
- Topamax® (topiramate tablets and sprinkle capsules – Ortho-McNeil, generic)
- Trokendi XR® (topiramate extended-release capsules – Supernus, generic)

REVIEW DATE: 12/04/2024

OVERVIEW

Topiramate and topiramate extended-release (XR) are indicated for the following uses:[1,3]
- Initial monotherapy for the treatment of **partial onset or primary generalized tonic-clonic seizures** in patients ≥ 2 years of age.
- Adjunctive therapy for the treatment of **partial onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut Syndrome** in patients ≥ 2 years of age.
- Preventive treatment of **migraine headache** in patients ≥ 12 years of age.

Trokendi XR (brand and generic) is indicated for the following uses:[2]
- Initial monotherapy for the treatment of **partial onset or primary generalized tonic-clonic seizures** in patients ≥ 6 years of age.
- Adjunctive therapy for the treatment of **partial onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut syndrome** in patients ≥ 6 years of age.
- Prophylaxis of **migraine headache** in patients ≥ 12 years of age.

Eprontia is indicated for the following uses:[4]
- Initial monotherapy for the treatment of **partial onset or primary generalized tonic-clonic seizures** in patients ≥ 2 years of age.
- Adjunctive therapy for the treatment of **partial onset seizures, primary generalized tonic-clonic seizures, and seizures associated with Lennox-Gastaut Syndrome** in patients ≥ 2 years of age.

Topiramate sprinkle capsules may be swallowed whole or may be administered by sprinkling the entire contents of a capsule on a small amount (teaspoon) of soft food.[1]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic topiramate tablets, generic topiramate sprinkle capsules

Step 2: Eprontia, Qudexy XR (brand and generic), Topamax tablets, Topamax Sprinkle Capsules, Trokendi XR (brand and generic), Topiramate ER capsules (branded product)

CRITERIA

5. If the patient has tried one Step 1 Product, approve a Step 2 Product.

6. No other exceptions are recommended.

REFERENCES

6. Topamax® tablets, sprinkle capsules [prescribing information]. Titusville, NJ: Janssen; May 2023.
7. Trokendi XR® extended-release capsules [prescribing information]. Rockville, MD: Supernus; January 2024.
8. Qudexy® XR extended-release capsules [prescribing information]. Maple Grove, MN: Upsher-Smith; March 2024.
9. Eprontia® oral solution [prescribing information]. Woburn, MA: Azurity; May 2024.

STEP THERAPY POLICY

POLICY: Antiseizure Medications – Zonisamide Step Therapy Policy

- Zonegran® (zonisamide capsules – Concordia, generic)
- Zonisade™ (zonisamide oral suspension – Azurity)

REVIEW DATE: 11/13/2024

OVERVIEW

All of these products are indicated as adjunctive therapy for the treatment of partial-onset seizures in adults and pediatric patients ≥ 16 years of age with epilepsy.[1,2]

Zonisamide capsules are available in 25 and 100 mg strengths and should be swallowed whole.[1] Zonisade is available as a 100 mg/5 mL strawberry flavored oral suspension.[2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic zonisamide capsules

Step 2: Zonisade, Zonegran (brand)

CRITERIA

14. If the patient has tried one Step 1 Product, approve a Step 2 Product.

15. If the patient cannot swallow or has difficulty swallowing solid oral dosage forms, approve Zonisade.

16. No other exceptions are recommended.

REFERENCES

28. Zonisade™ oral suspension [prescribing information]. Wilmington, MA: Azurity; July 2022.
29. Zonegran® capsules [prescribing information]. Overland Park, KS: Concordia; April 2020.

STEP THERAPY POLICY

POLICY: Attention Deficit Hyperactivity Disorder Non-Stimulant Medications Step Therapy Policy

- Intuniv® (guanfacine extended-release tablets – Shire)
- Kapvay® (clonidine hydrochloride extended-release tablets – Concordia)
- Onyda™ XR (clonidine hydrochloride extended-release oral suspension – Tris)
- Strattera® (atomoxetine capsules – Lilly, generic)
- Qelbree® (viloxazine extended-release capsules – Supernus)

REVIEW DATE: 06/12/2024; selected revision 10/02/2024

OVERVIEW

The non-stimulant medications are indicated for the **treatment of attention deficit hyperactivity disorder** (ADHD) in children and adolescents 6 to 17 years of age.[1-5]

- Atomoxetine capsules (Strattera, generic) and Qelbree are also indicated for the treatment of ADHD in adults.[1,4]

Numerous stimulants are approved for the treatment of ADHD in children and adolescents, as well as adults.[6-8]

GUIDELINES

The American Academy of Pediatrics clinical practice guideline for the diagnosis, evaluation, and treatment of ADHD in children and adolescents (2019) indicates that stimulants have the most evidence for efficacy and safety in the treatment of ADHD, and remain the first choice of medication treatment.[9] The evidence is particularly strong for stimulant medications and sufficient but less strong for atomoxetine, extended-release guanfacine, and extended-release clonidine (in that order) [strong recommendation]. Qelbree is not addressed in the guideline.

A meta-analysis of 133 double-blind, randomized, controlled trials (published in 2018) found that all included medications (amphetamines, methylphenidate, atomoxetine, bupropion, clonidine, guanfacine, and modafinil) were superior to placebo for clinicians' ratings of ADHD core symptoms in children and adolescents.[10] When evaluating teachers' ratings, only methylphenidate and modafinil were more efficacious than placebo. In clinicians' ratings of adults, amphetamines, methylphenidate, bupropion, and atomoxetine, but not modafinil, demonstrated improvements over placebo. With respect to tolerability, amphetamines were inferior to placebo in children, adolescents, and adults; guanfacine was inferior to placebo in children and adolescents only; and atomoxetine, methylphenidate, and modafinil were less well-tolerated than placebo in adults only. In head-to-head comparisons, differences in efficacy (based on clinicians' ratings) were found that favored amphetamines over modafinil, atomoxetine, and methylphenidate in children, adolescents, and adults. Taking into account both efficacy and safety, evidence from this meta-analysis supports the use of methylphenidate in children and adolescents and amphetamines in adults, as preferred first-line medications for treatment of ADHD.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: Generic guanfacine extended-release tablets and generic clonidine extended-release tablets are not included in either Step 1 or Step 2 of this program.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic atomoxetine capsules, stimulant medications (amphetamine and methylphenidate/dexmethylphenidate products)

Amphetamines (Note: This is not an all-inclusive list.)

- Amphetamine sulfate tablets (Evekeo™)
- Amphetamine extended-release orally disintegrating tablets (Adzenys XR-ODT™)
- Amphetamine extended-release oral suspension (Dyanavel™ XR, Adzenys ER™)
- Mixed amphetamine salts [dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine sulfate, amphetamine aspartate] immediate-release tablets (Adderall®, generic)/ extended-release capsules (Adderall XR®, generic)
- Dextroamphetamine immediate release tablets (Dexedrine®, Zenzedi®, generic)/sustained-release capsules (Dexedrine® Spansules®, generic)
- Dextroamphetamine sulfate oral solution (ProCentra®, generic)
- Methamphetamine tablets (Desoxyn®, generic)
- Lisdexamfetamine capsules and chewable tablets (Vyvanse®, generic)

Methylphenidate/dexmethylphenidate (**Note: This is not an all-inclusive list.**)

- methylphenidate extended-release tablets or capsules (Adhansia XR™, Aptensio XR™, Concerta®, Metadate® CD, Metadate® ER, Ritalin® LA, Ritalin-SR®, generic)
- methylphenidate immediate release tablets, oral solution, and chewable tablets (Ritalin®, Methylin®, Methylin® Chewable, generic)
- dexmethylphenidate immediate-release tablets (Focalin®, generic)
- dexmethylphenidate extended-release capsules (Focalin XR®, generic)
- methylphenidate transdermal system (Daytrana®)
- methylphenidate extended-release oral suspension (Quillivant™ XR, QuilliChew ER™)

Step 2: Strattera (brand), Intuniv (brand), Kapvay (brand), Onyda XR, Qelbree

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient is unable to take a stimulant medication and unable to swallow whole capsules and tablets according to the prescriber, approve Qelbree or Onyda XR.

3. No other exceptions are recommended.

REFERENCES

1. Strattera® capsules [prescribing information]. Indianapolis, IN: Lilly; January 2022.
2. Intuniv® extended-release tablets [prescribing information]. Lexington, MA: Shire; December 2019.
3. Kapvay® extended-release tablets, oral [prescribing information]. Overland Park, KS: Concordia; February 2020.
4. Qelbree® extended-release capsules [prescribing information]. Rockville, MD: Supernus; April 2022.

5. Onyda™ XR extended-release oral suspension [prescribing information]. Monmouth Junction, NJ: Tris; May 2024.
6. Clinical Pharmacology [database online]. Philadelphia, PA: Elsevier, Inc.; 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed on June 5, 2024. Search terms: amphetamine, methylphenidate, and lisdexamfetamine.
7. Concerta® extended-release tablets [prescribing information]. Titusville, NJ: Janssen; October 2023.
8. Adderall XR® extended-release capsules [prescribing information]. Lexington, MA: Takeda; October 2023.
9. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2019;144(4):e20192528.
10. Cortese S, Adamo N, Del Giovane C, et al. Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis. *Lancet Psychiatry*. 2018;5(9):727-738.

STEP THERAPY POLICY

POLICY: Attention Deficit Hyperactivity Disorder Stimulant Medications Step Therapy Policy

- Adderall XR® (mixed amphetamine salts [dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine sulfate, amphetamine aspartate] extended-release capsules – Shire, generic)
- Adhansia XR® (methylphenidate extended-release capsule – Purdue)
- Adzenys ER™ (amphetamine extended-release oral suspension – Neos Therapeutics)
- Adzenys XR-ODT™ (amphetamine extended-release orally disintegrating tablets – Neos Therapeutics)
- Aptensio XR® (methylphenidate extended-release capsules – Rhodes, generic)
- Azstarys™ (serdexmethylphenidate and dexmethylphenidate capsules – Corium)
- Concerta® (methylphenidate extended-release tablets – McNeil, generic)
- Cotempla XR-ODT™ (methylphenidate extended-release orally disintegrating tablets – Neos Therapeutics)
- Daytrana® (methylphenidate transdermal system – Noven, generic)
- Dexedrine® Spansules® (dextroamphetamine sustained-release capsules – Amedra, generic)
- Dyanavel® XR (amphetamine extended-release tablets and oral suspension – Tris)
- Focalin® XR (dexmethylphenidate extended-release capsules – Novartis, generic)
- Jornay PM® (methylphenidate hydrochloride extended-release capsules – Ironshore)
- Metadate® CD (methylphenidate extended-release capsules – UCB, generic)
- Metadate® ER (methylphenidate sustained-release tablets – UCB, generic only)
- Methylphenidate extended-release capsules (generic to discontinued Methylin™ ER)
- Mydayis® (mixed salts of a single-entity amphetamine product extended-release capsules – Shire, generic)
    - QuilliChew ER® (methylphenidate extended-release chewable tablets – Pfizer)
- Quillivant® XR (methylphenidate extended-release oral suspension – NextWave)
- Relexxii® (methylphenidate extended-release tablets – Vertical, authorized generic)
- Ritalin® LA (methylphenidate extended-release capsules – Novartis, generic)
- Methylphenidate sustained-release tablets (generic to discontinued Ritalin-SR®)
- Vyvanse® (lisdexamfetamine dimesylate capsules and chewable tablets – Shire, generic)
- Xelstrym® (dextroamphetamine transdermal system – Noven)

REVIEW DATE: 04/19/2024

OVERVIEW

All of the long-acting stimulants are indicated for the treatment of **attention-deficit hyperactivity disorder (ADHD)**.[1-24] Refer to Table 1 for a summary of indications.

- Some products are also indicated for the treatment of **narcolepsy**.
- Vyvanse is the only stimulant medication that is also indicated for the treatment of **binge eating disorder**.[11]

All of these products have abuse potential and are Schedule II controlled substances.[1-24]

Table 1. FDA-Approved Indications for Long-Acting Stimulants.[1-24]
ADHD – Attention-deficit hyperactivity disorder.

GUIDELINES

The American Academy of Pediatrics (AAP) clinical practice guideline for the diagnosis, evaluation, and treatment of ADHD in children and adolescents was updated in 2019, and incorporates many of the findings from the Multimodal Treatment Study of Children With ADHD (MTA).[25] The AAP recommendations for treatment of children and youth with ADHD vary depending on the patient's age. For preschool-aged children (4 to 5 years of age), parent- and/or teacher-administered behavior therapy should be prescribed as first-line treatment; methylphenidate may be prescribed if behavior interventions do not provide significant improvement and disturbance of function continues. For elementary school-aged children (6 to 11 years of age), an FDA-approved medication for ADHD (and/or behavior therapy, but preferably both) should be prescribed. Evidence is particularly strong for stimulant medications, and sufficient but less strong for atomoxetine, guanfacine extended-release (ER) tablets, and clonidine ER tablets (in that order). For adolescents (12 to 18 years of age), an FDA-approved medication for ADHD (and/or behavior therapy, but preferably both) should be prescribed with the assent of the adolescent. The dose of medication should be titrated to achieve maximum benefit with minimum adverse events (AEs). The findings from the MTA study suggested that more than 70% of children and youth with ADHD respond to one of the stimulant medications at an optimal dose when a systematic trial is used. Titration to maximum doses that control symptoms without AEs is recommended instead of titration strictly on a mg-per-kg basis.

Methylphenidate and amphetamine formulations have similar effects and AEs, and remain the first choice of medication treatment.[25] Some patients will respond better to or display more AEs with one compound vs. another; however, these effects cannot be predetermined. Therefore, if a trial with one group is unsuccessful (poor efficacy or AEs), a trial on a medication from the other group should be undertaken. At least half of the patients whose symptoms fail to respond to one stimulant medication may have a positive response to the alternative medication.

The AAP clinical practice guideline on the identification and management of eating disorders in children and adolescents (2021) notes that research on the treatment of binge eating disorder lags behind that for other eating disorders and has been focused primarily on adults.[26] Vyvanse was approved by the FDA in 2015 for the treatment of moderate to severe binge-eating disorder in adults. Vyvanse has demonstrated efficacy in reducing the frequency of binge-eating episodes. As with the use of other central nervous system stimulants, there is a potential for abuse and dependence as well as serious cardiovascular reactions. Topiramate has been shown to reduce binge eating and help with weight loss; however, the rates of adverse effects are relatively high. Selective serotonin reuptake inhibitors have rarely differed from placebo in their effect on binge-eating disorder and have not shown better outcome than behavioral therapy alone.

DOSING AND DOSAGE FORMS

The choice of formulation depends on factors such as the efficacy of each agent for a given child/adolescent, the preferred length of coverage time, whether a child can swallow tablets or capsules, and expense.[25] The extended-release (ER) formulations may be preferred over immediate-release (IR) formulations because they provide benefits of consistent and sustained coverage with fewer administrations per day. Long-acting formulations usually preclude the need for school-based administration of ADHD medications. Better coverage with fewer administrations leads to greater convenience for the family and, therefore, might also lead to better adherence to the medication management plan. Some patients, particularly adolescents, might require more than 12 hours of coverage to ensure adequate focus and concentration during evening study time and driving; in these cases, a short-acting (IR) preparation might be used in addition to a long-acting (ER) preparation.

Many of the generic ER stimulant medications for the treatment of ADHD are available as capsules: generic amphetamine/dextroamphetamine ER capsules (generic to Adderall XR; Mydayis, generic), generic dexmethylphenidate ER capsules (generic to Focalin XR), lisdexamfetamine capsules (Vyvanse, generic), and generic methylphenidate ER capsules (generic to Metadate CD, Ritalin LA, Adhansia XR, Aptensio

XR). According to the prescribing information, the capsules may be taken whole, or opened and the entire contents sprinkled on applesauce.[1,5,6,9,13,21] Patients should take the applesauce with sprinkled beads in its entirety without chewing.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic amphetamine/dextroamphetamine extended-release capsules (generic to Adderall XR), generic dexmethylphenidate extended-release capsules (generic to Focalin XR), generic dextroamphetamine extended-release capsules (generic to Dexedrine Spansules), generic lisdexamfetamine capsules, generic methylphenidate extended-release capsules (generic to Metadate CD and Ritalin LA), Metadate ER (generic according to First Data Bank [FDB]), generic methylphenidate sustained-release tablets (generic to Ritalin SR), generic methylphenidate extended-release tablets (generic to Concerta), generic mixed salts of a single-entity amphetamine product extended-release capsules (generic to Mydayis)

Step 2: Adderall XR, Adhansia XR, Adzenys ER, Adzenys XR-ODT, Aptensio XR (brand and generic), Azstarys, Concerta, Cotempla XR-ODT, Daytrana (brand and generic methylphenidate transdermal system), Dexedrine Spansules, Dyanavel XR (tablets and oral solution), Focalin XR, Jornay PM, Metadate CD, Mydayis, QuilliChew ER, Quillivant XR, Relexxii (brand and authorized generic), Ritalin LA, Vyvanse capsules, Vyvanse chewable tablets (brand and generic), Xelstrym

CRITERIA

4. If the patient has tried one Step 1 Product, approve a Step 2 Product.

5. No other exceptions are recommended.

REFERENCES

1. Adderall XR® extended-release capsules [prescribing information]. Lexington, MA: Takeda; February 2022.
2. Concerta® extended-release tablets [prescribing information]. Titusville, NJ: Janssen; June 2021.
3. Daytrana® transdermal system [prescribing information]. Miami, FL: Noven; June 2021.
4. Dexedrine® Spansule® sustained-release capsule [prescribing information]. Bridgewater, NJ: Amneal; January 2022.
5. Focalin XR® extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; June 2021.
6. Metadate CD® extended-release capsules [prescribing information]. Philadelphia, PA: Lannett; April 2022.
7. Metadate® ER extended-release tablet [prescribing information]. Philadelphia, PA: Lannett; June 2021.
8. Methylin™ tablets and Methylin™ ER extended-release tablets [prescribing information]. Hazelwood, MO: Mallinckrodt; June 2021.
9. Ritalin LA® extended-release capsules [prescribing information]. East Hanover, NJ: Novartis; June 2021.
10. Ritalin® tablets and Ritalin SR® sustained-release tablets [prescribing information]. East Hanover, NJ: Novartis; November 2019.
11. Vyvanse® capsules [prescribing information]. Lexington, MA: Takeda; January 2022.
12. Quillivant® XR extended-release oral suspension [prescribing information]. Monmouth Junction, NJ: NextWave; June 2021.
13. Aptensio XR® extended-release capsules [prescribing information]. Coventry, RI: Rhodes; June 2021.
14. QuilliChew ER® extended-release chewable tablets [prescribing information]. Monmouth Junction, NJ: NextWave; June 2021.
15. Dyanavel® XR extended-release tablets and oral suspension [prescribing information]. Monmouth Junction, NJ: Tris; June 2022.
16. Adzenys XR-ODT™ extended-release orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos; January 2022.
17. Mydayis® extended-release capsules [prescribing information]. Lexington, MA: Takeda; January 2022.
18. Cotempla XR-ODT™ orally disintegrating tablets [prescribing information]. Grand Prairie, TX: Neos; June 2021.
19. Adzenys ER™ extended-release oral solution [prescribing information]. Grand Prairie, TX: Neos; January 2022.
20. Jornay PM® extended-release capsules [prescribing information]. Cherry Hill, NJ: Ironshore; June 2021.
21. Adhansia XR® extended-release capsules [prescribing information]. Stamford, CT: Adlon; June 2021.
22. Relexxii® extended-release tablets [prescribing information]. Alpharetta, GA: Vertical; June 2022.
23. Azstarys™ capsules [prescribing information]. Grand Rapids, MI: Corium; March 2021.
24. Xelstrym® transdermal system [prescribing information. Miami, FL: Noven; March 2022.
25. Wolraich ML, Hagan JF Jr, Allan C, et al. Clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics*. 2019;144(4):e20192528.

26. Hornberger LL, Lane MA; AAP the Committee on Adolescence. Identification and management of eating disorders in children and adolescents. *Pediatrics.* 2021;147(1):e2020040279.

STEP THERAPY POLICY

POLICY: Benign Prostatic Hyperplasia – 5-Alpha-Reductase Inhibitors Step Therapy Policy
- Avodart® (dutasteride capsules – GlaxoSmithKline, generic)
- Jalyn® (dutasteride/tamsulosin – GlaxoSmithKline, generic)
- Proscar® (finasteride tablets - Organon, generic)

REVIEW DATE: 12/11/2024

OVERVIEW

The 5-alpha-reductase inhibitors and alpha$_1$-blockers are therapies in the treatment of symptomatic benign prostatic hyperplasia (BPH).[1] Finasteride and dutasteride are both 5-alpha reductase inhibitors indicated to **improve symptoms, reduce the risk of acute urinary retention, and to reduce the need for BPH-related surgery in men with enlarged prostates**.[2-4] Finasteride is also indicated to **decrease the risk of symptomatic progression of BPH in combination with the alpha$_1$-blocker doxazosin**.[2] Dutasteride is also indicated for the treatment of **symptomatic BPH in men with an enlarged prostate in combination with the alpha$_1$-blocker, tamsulosin**.[3,5] Jalyn is the commercially available product which combines dutasteride and tamsulosin in one capsule for patients who require dual therapy.[5] The same dosage of dutasteride and tamsulosin can be obtained by taking the respective products individually.

Guidelines

The American Urological Association (AUA) guidelines on the management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (2023) recommends that 5-alpha-reductase inhibitors can be used by men with demonstrable prostatic enlargement.[1] This class of medication does have a slow onset of action and alpha-blocker would provide more immediate relief for men with voiding symptoms. The 5-alpha-reductase inhibitors can be used with alpha-blocker therapy. AUA does not recommend one 5-alpha-reductase inhibitor over another.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic finasteride 5 mg

Step 2: Avodart, dutasteride, Jalyn, dutasteride/tamsulosin, Proscar

CRITERIA

1. If the patient has tried the Step 1 Product, approve a Step 2 Product.

2. If the patient has tried generic finasteride or brand Proscar, approve Avodart, dutasteride, Jalyn, or dutasteride/tamsulosin.

3. A Step 2 Product is not covered when it is being used for the treatment of hair loss. Hair loss is considered a cosmetic use.

4. No other exceptions are recommended.

REFERENCES

1. Sandhu JS, Bixler BR, Dahm P, et al. Management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (BPH): AUA Guideline amendment 2023. J Urol. 2023;211:1-8.
2. Proscar® tablets [prescribing information]. Jersey City, NJ: Organon; November 2023.
3. Avodart® capsules [prescribing information]. Wixom, MI: Woodward; October 2023.
4. Dutasteride capsules [prescribing information]. Bridgewater, NJ: Amneal; August 2023.
5. Jalyn® [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2024.

STEP THERAPY POLICY

POLICY: Benign Prostatic Hyperplasia – Alpha Blockers Step Therapy Policy
- Cardura® (doxazosin mesylate tablets – Pfizer, generic)
- Cardura® XL (doxazosin mesylate extended-release tablets – Pfizer)
- Flomax® (tamsulosin capsules – Sanofi-Aventis, generic)
- Terazosin capsules – Avet Pharmaceuticals, generic
- Rapaflo® (silodosin capsules – Allergan, generic)
- Uroxatral® (alfuzosin extended-release tablets – Concardia, generic)

REVIEW DATE: 12/11/2024

OVERVIEW

Alpha blockers in the treatment of benign prostatic hyperplasia (BPH) are selective for $alpha_{1A}$ receptors. $Alpha_{1A}$ blocker receptors are more predominant in the prostate and $alpha_{1B}$ receptors are more predominant in the vascular smooth muscle.[1] Doxazosin (immediate-release) and terazosin are indicated for the symptomatic treatment of BPH and for hypertension.[2,3] Cardura XL is only indicated for the treatment of signs and symptoms of BPH.[4] Tamsulosin has 10 times greater selectivity for the $alpha_{1A}$ receptor versus the $alpha_{1B}$ receptor[1] and is only indicated for BPH[5]. Silodosin has 162 times greater selectivity for the $alpha_{1A}$ receptor versus the alpha-$_{1B}$ receptor[1] and is only indicated for BPH[6]. Alfuzosin is not selective for a specific $alpha_1$ receptor subtype, but instead exhibits selectivity for $alpha_1$-adrenergic receptors in the lower urinary tract; it is only indicated for BPH.[7] Theoretically, agents with high selectivity for the $alpha_{1A}$-receptor should have less effect on blood pressure compared with other non-selective $alpha_1$-blockers.

Guidelines

The American Urological Association (AUA) guidelines on the management of lower urinary tract symptoms attributed to benign prostatic hyperplasia (2023) recommends that clinicians should offer one of the following alpha blockers as a treatment for patients with moderate to severe lower urinary tract symptoms/BPH: alfuzosin, doxazosin, silodosin, tamsulosin, or terazosin.[8] AUA also recommends the choice of alpha blocker should be based on patient age and comorbidities.

POLICY STATEMENT

This program has been developed to encourage use of Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic alfuzosin extended-release tablets, generic doxazosin tablets, generic silodosin capsules, generic tamsulosin capsules, generic terazosin capsules

Step 2: Cardura tablets, Cardura XL extended-release tablets, Flomax capsules, Rapaflo capsules, Uroxatral extended-release tablets

STEP THERAPY POLICY

POLICY: Beta Blocker Step Therapy Policy

Products available generically

- acebutolol capsules (generic only)
- Tenormin® (atenolol tablets – AstraZeneca, generic)
- betaxolol tablets (generic only)
- bisoprolol tablets (generic only)
- Coreg® (carvedilol tablets – Woodword, generic)
- Coreg CR™ (carvedilol extended-release capsules – Woodword, generic)
- labetalol tablets (generic only)
- Lopressor® (metoprolol tartrate tablets – Novartis, Mylan, generic)
- Toprol XL® (metoprolol succinate extended-release tablets – Aralez, generic)
- Corgard® (nadolol tablets – King, generic)
- pindolol tablets (generic only)
- propranolol tablets (generic only)
- Inderal® LA (propranolol extended-release capsules – Wyeth Ayerst, generic)
- Betapace® (sotalol tablets – Covis, generic)
- Betapace® AF (sotalol tablets – Covis, generic)
- timolol tablets (generic only)
- Tenoretic® (atenolol/chlorthalidone tablets – AstraZeneca, generic)
- Ziac® (bisoprolol/hydrochlorothiazide tablets – Barr, generic)
- Lopressor® HCT (metoprolol/hydrochlorothiazide tablets – Novartis, generic)
- nadolol/bendroflumethiazide tablets (generic only)
- propranolol/hydrochlorothiazide tablets (generic only)

Products not available generically

- Dutoprol™ (metoprolol succinate extended-release tablets/hydrochlorothiazide – AstraZeneca)
- Bystolic™ (nebivolol tablets – Allergan)
- Inderal XL® (propranolol extended-release capsules – Mist)
- InnoPran XL® (propranolol extended-release capsules – Reliant)
- Kapspargo™ Sprinkle (metoprolol succinate capsules extended-release – Ohm/Sun)
- Metoprolol succinate/hydrochlorothiazide extended release tablets – Solubiomix (brand product)

REVIEW DATE: 06/26/2024

OVERVIEW

Beta-blockers can be classified into four pharmacologic subgroups based on their effect on beta and alpha receptors: cardioselective beta-blockers, nonselective beta-blockers, combined alpha-beta blockers, and beta-blockers with intrinsic sympathomimetic activity (ISA). Cardioselective beta-blockers are those agents that preferentially block beta-1 receptors over beta-2 receptors. Nonselective beta-blockers block both the beta-1 and beta-2 receptors. Based on mechanism of action, cardioselective beta-blockers may be safer than nonselective beta-blockers in patients with asthma, chronic obstructive pulmonary disease, peripheral arterial disease, and diabetes mellitus who require beta-blocker therapy. However, cardioselectivity appears to be dose-dependent and at higher doses, cardioselective agents may lose their selectivity. The dose at which cardioselectivity is lost varies from patient to patient. Combined alpha-beta blockers nonselectively block beta receptors as well as alpha receptors. Beta-blockers with ISA act as

partial beta-receptor agonists and therefore, resting heart rate, cardiac output, and peripheral blood flow are not as reduced.[1-3] Table 1 classifies the beta-blockers by subgroup.

Table 1. Beta-Blockers by Pharmacologic Subgroup.[1-4]
ISA – Intrinsic sympathomimetic activity; [+] May have vasodilatory properties; [*] In extensive metabolizers and at doses less than or equal to 10 mg nebivolol is preferentially beta$_1$ selective. In poor metabolizers and at higher doses, it is nonselective; [†] Available as Bystolic; [‡] Available as a generic and as InnoPran XL; [°] Available as Coreg CR; [^] Available as Levatol.

All of the beta-blockers included in this policy are approved for the **treatment of hypertension**. Various reviews and guidelines address the role of beta-blockers in hypertension.[1-8] Betaxolol, bisoprolol, labetalol, Bystolic™ (nebivolol tablets), Levatol® (penbutalol tablets), and pindolol are only indicated for the treatment of hypertension.[1-9] The remaining beta-blockers (non-combination products) have at least one other indication. Such indications include angina pectoris, select arrhythmias, to treat and reduce cardiovascular (CV) mortality following a myocardial infarction (MI), to treat and reduce CV mortality in heart failure (HF), migraine prophylaxis, essential tremor, pheochromocytoma, and hypertrophic subaortic stenosis. All of the beta-blocker/diuretic combination products are indicated for the treatment of hypertension, although often not as initial therapy. It is notable that sotalol (Betapace, Betapace AF) is not indicated for use in hypertension but instead is used for the management of arrhythmias.[3,4,10] Specifically, Betapace/Betapace AF are indicated for the treatment of life-threatening ventricular arrhythmias as well as for the maintenance of normal sinus rhythm in patients with atrial fibrillation or flutter.[10] Sotylize™ (sotalol hydrochloride oral solution) is not included in this program as a generic is not available.[3,4,11] Also, Hemangeol™ (propranolol hydrochloride oral solution) is not included as this is indicated for the treatment of proliferating infantile hemangioma requiring systemic therapy.[12]

Carvedilol, metoprolol succinate extended-release (XL) and Coreg CR™ (carvedilol extended-release capsules) are the only beta-blockers indicated in patients with HF[14-16] with published data to support their use.[17-20] Metoprolol succinate XL is indicated to reduce the risk of cardiovascular mortality and HF hospitalization in patients with HF.[14] Carvedilol and Coreg CR are indicated for the treatment of mild to severe HF of ischemic or cardiomyopathic origin.[15,16] In combination with angiotensin converting enzyme inhibitors, diuretics, and digitalis, both metoprolol succinate and carvedilol have been shown to decrease the rate of mortality and hospitalization. In addition, carvedilol and Coreg CR are indicated to reduce CV mortality in clinically stable patients who have survived the acute phase of an MI and have a left ventricular ejection fraction ≤ 40% with or without symptomatic HF. Data are available with bisoprolol in patients with HF.[21]

Guidelines

Beta blockers are mentioned in a variety of guidelines. Main guidelines are briefly summarized.

- **Heart Failure:** In 2022, the American Heart Association (AHA), American College of Cardiology (ACC), and the Heart Failure Society of America published guidelines for the management of HF.[22] The three beta-blockers proven to reduce mortality in patients with HF with reduced ejection fraction are bisoprolol, carvedilol, and sustained-release metoprolol succinate. Hospitalizations can also be reduced with these agents.
- **Hypertension:** The 2017 guidelines regarding the management of high blood pressure in adults by the ACC and the AHA prominently mention the benefits with beta blockers in selected patients.[7]
- **Chronic Coronary Disease:** Guidelines for the management of patients with chronic coronary disease (CCD) from the AHA and the ACC (2023) state that in adults with CCD and hypertension (systolic blood pressure ≥ 130 and/or diastolic blood pressure ≥ 80 mm Hg), in addition to nonpharmacological strategies, guideline-directed medication therapy with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), or beta blockers are recommended as first-line therapy for compelling indications (e.g., recent MI or angina), with additional antihypertensive medications (e.g., dihydropyridine calcium channel blockers [CCB], long-acting

thiazide diuretics, and/or mineralocorticoid receptor antagonists) added as needed to optimize blood pressure control.[13] In patients with CCD and left ventricular ejection fraction (LVEF) ≤ 40% with or without previous MI, the use of beta-blocker therapy is recommended to reduce the risk of future major adverse CV events, including CV death. Also, in patients with CCD and LVEF < 50%, the use of sustained release metoprolol succinate, carvediolol, or bisprolol with titration to target doses is recommended in preference to other beta blockers.

POLICY STATEMENT

The program is comprised of two rules: 1) Beta-Blocker Step Therapy rule (Step A) and 2) Sotalol Step Therapy rule (Step B). This program has been developed to encourage the use of a Step 1A product prior to a Step 2A Product and a Step 1B Product prior to the use of a Step 2B Product. If the Step Therapy rule is not met for the Step 2A or Step 2B Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: For the Beta-Blocker Step Therapy Rule (Step A), a patient with a history of one Step 1A Product within the 130-day look-back period is excluded from Step Therapy. For the Sotalol Step Therapy Rule (Step B), a patient with a of one Step 1B Product within the 130-day look-back period is excluded from Step Therapy.

Beta-Blocker Step Therapy Rule

Step 1A: generic beta-blockers (i.e., acebutolol, atenolol, betaxolol, bisoprolol, carvedilol, carvedilol extended-release, labetalol, metoprolol tartrate, nadolol, pindolol, propranolol, timolol, metoprolol succinate extended-release, propranolol extended-release), and generic beta-blocker combination products (i.e., atenolol/chlorthalidone, bisoprolol/hydrochlorthiazide, metoprolol/hydrochlorothiazide, propranolol/hydrochlorothiazide, nadolol/bendroflumethiazide)

Step 2A: brand name beta-blockers (i.e., Bystolic, Tenormin, Coreg, Coreg CR, Lopressor, Toprol XL, Corgard, Inderal LA, InnoPran XL, Inderal XL) and brand name beta-blocker combination products (i.e., Tenoretic, Ziac, Lopressor HCT, Dutoprol, Metoprolol succinate/hydrochlorothiazide extended-release), Kapspargo Sprinkle

Sotalol Step Therapy Rule

Step 1B: generic sotalol

Step 2B: brand name Betapace, Betapace AF

CRITERIA

Beta Blocker Step Therapy Rule

1. If the patient has tried one Step 1A Product, approve a Step 2A Product.
Note: Sotalol products do not count toward this requirement.

2. No other exceptions are recommended.

Sotalol Step Therapy Rule

1. If the patient has tried one Step 1B Product, approve a Step 2B Product.

2. If the strength of the requested Step 2B Product is not available generically, approve the Step 2B Product.

3. No other exceptions are recommended.

REFERENCES

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2. Warmack TS, Estes MA, Heldenbrand S, Franks AM. Beta-adrenergic antagonists in hypertension: a review of the evidence. *Ann Pharmacother*. 2009;43(12):2031-2043.
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10. Betapace®/Betapace® AF tablets [prescribing information]. Zug, Switzerland: made for Covis Pharma; June 2023.
11. Sotylize® oral solution [prescribing information]. Woburn, MA: Patheon/Azurity; January 2024.
12. Hemangeol™ oral solution [prescribing information]. Parsippany, NJ: Pierre Fabre; June 2021.
13. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2023;82(9):833-955.
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15. Coreg® tablets [prescribing information]. Wixom, MI: Woodward; July 2023.
16. Coreg phosphate extended-release capsules [prescribing information]. Wixom, MI: Woodward; February 2022.
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19. Packer M, Coats AJS, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med*. 2001;344(22):1651-1658.
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STEP THERAPY POLICY

POLICY: Bile Acid Sequestrants Step Therapy Policy

- Questran®, Questran® Light, Prevalite® (cholestyramine oral suspension – Par, Upsher Smith, generic)
- Colestid® (colestipol oral suspension and micronized tablets – Pfizer, generic)
- Welchol® (colesevelam tablets and oral suspension – Cosette, generic)

REVIEW DATE: 06/26/2024

OVERVIEW

Cholestyramine is indicated for use as adjunctive therapy for the **lowering of serum cholesterol** in patients with primary hypercholesterolemia who have not responded to diet or other measures alone.[1] Colestipol is indicated as adjunctive therapy to diet for the **reduction of elevated serum total and low-density lipoprotein cholesterol (LDL-C)** in patients with primary hypercholesterolemia (elevated LDL-C) who do not respond adequately to diet.[2,3] Colesevelam is indicated as an adjunct to diet and exercise to **reduce elevated LDL-C** in adults with primary hyperlipidemia.[4] Colesevelam is also approved to reduce LDL-C levels in boys and postmenarchal girls, aged 10 to 17 years, with heterozygous familial hypercholesterolemia who are unable to reach LDL-C target levels despite an adequate trial of dietary therapy and lifestyle modification. Colesevelam is also indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes mellitus**.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: cholestyramine oral suspension, colestipol oral suspension, colestipol micronized tablets, colesevelam tablets, colesevelam for oral suspension, and Prevalite oral suspension

Step 2: Welchol tablets, Welchol for oral suspension, Questran oral suspension, Questran light oral suspension, Colestid oral suspension, and Colestid micronized tablets

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. WelChol® tablets and oral suspension [prescribing information]. South Plainfield, NJ: Cosette; February 2022.
2. Colestid®, Flavored Colestid® oral suspension [prescribing information]. New York, NY: Pfizer; April 2018.
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STEP THERAPY POLICY

POLICY: Bisphosphonates (Oral) Enhanced Step Therapy Policy

- Actonel® (risedronate tablets – Abbvie [5, 30, 35 mg and 150 mg, generic])
- Atelvia® (risedronate delayed-release tablets – Abbvie, generic)
- Binosto® (alendronate effervescent tablets for oral solution – Radius)
- Boniva® (ibandronate tablets – Genentech/Roche, generic)
- Fosamax® (alendronate tablets – Organon, generic)
- Fosamax® Plus D (alendronate/cholecalciferol tablets – Organon)

REVIEW DATE: 10/02/2024

OVERVIEW

Alendronate tablets are indicated for the following uses:[1]

- Treatment and prevention of **postmenopausal osteoporosis**.
- Treatment of **glucocorticoid-induced osteoporosis** in men and women.
- Treatment of **Paget's disease** in men and women.
- Increase **bone mass** in men with osteoporosis.

Binosto and **Fosamax Plus D** tablets are indicated for the following uses:[5,6]

- Treatment of **postmenopausal osteoporosis**.
- Treatment to increase **bone mass** in men with osteoporosis.

Ibandronate tablets are indicated for the treatment and prevention of **postmenopausal osteoporosis**.[4]

Risedronate tablets are indicated for the following uses:[2]

- Treatment and prevention of **postmenopausal osteoporosis**.
- Treatment and prevention of **glucocorticoid-induced osteoporosis** in men and women.
- Treatment of **Paget's disease** in men and women.
- Increase **bone mass** in men with osteoporosis.

Risedronate delayed-release tablets are indicated for the treatment of **postmenopausal osteoporosis**.[3]

Alendronate, risedronate, risedronate delayed-release tablets, and ibandronate tablets are orally administered bisphosphonates.[1-4] Fosamax Plus D contains alendronate plus vitamin D_3 in one tablet; both are available as single-entity products.[5] Binosto provides alendronate in a 70 mg effervescent tablet for oral solution.[6] The prescribing information for Fosamax notes that although an oral solution of alendronate may be available in the marketplace, Fosamax oral solution is no longer marketed.[1]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product, and the use of a Step 2 Product prior to the use of a Step 3 Product. If the Step Therapy rule is not met for the Step 2 Product or the Step 3 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: Generic alendronate oral solution (70 mg/75 mL) is not included in this policy.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period can receive the Step 2 Product. A patient with a of one Step 1 Product and a Step 2 Product within the 130-day look-back period can receive a Step 3 Product.

Step 1: alendronate 5, 10, 35, 40 and 70 mg tablets, ibandronate 150 mg tablets, risedronate 5, 30, 35, and 150 mg tablets, risedronate 35 mg delayed-release tablets

Step 2: Atelvia delayed-release tablets

Step 3: Actonel tablets, Binosto effervescent tablets, Boniva tablets, Fosamax tablets, Fosamax Plus D tablets

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient has tried one Step 1 Product and one Step 2 Product, approve a Step 3 Product.

3. Approve Binosto if the patient meets one the following (A or B):
A) Patient has a gastrostomy tube (G-tube); OR
B) Patient cannot swallow or has difficulty swallowing tablets or capsules.

4. No other exceptions are recommended.

REFERENCES

1. Fosamax® tablets and oral solution [prescribing information]. Jersey City, NJ: Organon; June 2021.
2. Actonel® tablets [prescribing information]. North Chicago, IL: Abbvie; October 2023.
3. Atelvia® delayed-release tablets [prescribing information]. North Chicago, IL: Abbvie; October 2023.
4. Boniva® tablets [prescribing information]. South San Francisco, CA: Genentech/Roche; April 2020.
5. Fosamax® Plus D tablets [prescribing information]. Jersey City, NJ: Organon; August 2021.
6. Binosto® effervescent tablets for oral solution [prescribing information]. Boston, MA: Radius; October 2023.

STEP THERAPY POLICY

POLICY: Bisphosphonates (Oral) Step Therapy Policy

- Actonel® (risedronate tablets – Abbvie [5, 30, 35 and 150 mg, generic])
- Atelvia® (risedronate delayed-release tablets – Abbvie, generic)
- Binosto® (alendronate effervescent tablets for oral solution – Radius)
- Boniva® (ibandronate tablets – Genentech/Roche, generic)
- Fosamax® (alendronate tablets – Merck, generic)
- Fosamax® Plus D (alendronate/cholecalciferol tablets – Merck)

REVIEW DATE: 10/02/2024

OVERVIEW

Alendronate tablets are indicated for the following uses:[1]

- Treatment and prevention of **postmenopausal osteoporosis**.
- Treatment of **glucocorticoid-induced osteoporosis** in men and women.
- Treatment of **Paget's disease** in men and women.
- Increase **bone mass** in men with osteoporosis.

Binosto and Fosamax Plus D tablets are indicated for the following uses:[5,6]

- Treatment of **postmenopausal osteoporosis**.
- Treatment to increase **bone mass** in men with osteoporosis.

Ibandronate tablets are indicated for the treatment and prevention of **postmenopausal osteoporosis**.[4]

Risedronate tablets are indicated for the following uses:[2]

- Treatment and prevention of **postmenopausal osteoporosis**.
- Treatment and prevention of **glucocorticoid-induced osteoporosis** in men and women.
- Treatment of **Paget's disease** in men and women.
- Increase **bone mass** in men with osteoporosis.

Risedronate delayed-release tablets are indicated for the treatment of **postmenopausal osteoporosis**.[3]

Alendronate, Actonel, Atelvia and ibandronate tablets are orally administered bisphosphonates.[1-4] Fosamax Plus D contains alendronate plus vitamin D_3 in one tablet; both are available as single-entity products.[5] Binosto provides alendronate in a 70 mg effervescent tablet for oral solution.[6] The prescribing information for Fosamax notes that although an oral solution of alendronate may be available in the marketplace, Fosamax oral solution is no longer marketed.[1]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Generic alendronate oral solution (70 mg/75 mL) is not included in this policy.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: alendronate 5, 10, 35, 40 and 70 mg tablets, ibandronate 150 mg tablets, risedronate 5, 30, 35 and 150 mg tablets, risedronate 35 mg delayed-release tablets

Step 2: Actonel tablets, Atelvia delayed-release tablets, Binosto effervescent tablets, Boniva tablets, Fosamax tablets, Fosamax Plus D tablets

CRITERIA

5. If the patient has tried one Step 1 Product, approve a Step 2 Product.

6. Approve Binosto if the patient meets one of the following (A or B):
A) Patient has a gastrostomy tube (G-tube); OR
B) Patient cannot swallow or has difficulty swallowing tablets or capsules.

3. No other exceptions are recommended.

REFERENCES

7. Fosamax® tablets and oral solution [prescribing information]. Jersey City, NJ: Organon; June 2021.
8. Actonel® tablets [prescribing information]. North Chicago, IL: Abbvie; October 2023.
9. Atelvia® delayed-release tablets [prescribing information]. North Chicago, IL: Abbvie; October 2023.
10. Boniva® tablets [prescribing information]. South San Francisco, CA: Genentech/Roche; April 2020.
11. Fosamax® Plus D tablets [prescribing information]. Jersey City, NJ: Organon; August 2021.
12. Binosto® effervescent tablets for oral solution [prescribing information]. Boston, MA: Radius; October 2023.

STEP THERAPY POLICY

POLICY: Calcium Channel Blockers – Dihydropyridine Products Step Therapy Policy

- Cardene® (nicardipine immediate-release capsules – generic only)
- Conjupri® (levamlodipine tablets – CSPC Ouyi)
- DynaCirc® (isradipine immediate-release capsules – generic only)
- Katerzia™ (amlodipine oral suspension – Azurity)
- Norvasc® (amlodipine tablets – Pfizer, generic)
- Levamlodipine tablets – Xspire/CSPC Ouyi (authorized generic)
- Norliqva® (amlodipine oral solution – CMP)
- Plendil® (felodipine extended-release tablets – generic only)
- Prestalia® (perindopril arginine and amlodipine tablets – Adhera)
- Procardia XL® (nifedipine extended-release tablets – Pfizer, generic)
- Procardia® (nifedipine immediate-release capsules – Pfizer, generic)
- Sular® (nisoldipine extended-release tablets – Shionogi, generic)

REVIEW DATE: 06/26/2024

OVERVIEW

All of the dihydropyridine (DHP) calcium channel blockers (CCBs), with the exception of immediate-release (IR) nifedipine and nimodipine, are indicated for the **treatment of hypertension in adults**.[1-14,9] Some of the DHB CCBs have unique indications:

- Agents that are indicated for the **management of chronic stable angina** include amlodipine, nicardipine IR, nifedipine IR, and nifedipine extended-release (ER) [Procardia XL formulation].
- Agents that are indicated for the **treatment of vasospastic angina** include amlodipine, nifedipine IR, and nifedipine ER (Procardia XL formulation).
- **Amlodipine** possess a unique indication in **patients with recently documented coronary artery disease by angiography and without heart failure (HF) or an ejection fraction < 40% to reduce the risk of hospitalization due to angina** and to **reduce the risk of a coronary revascularization procedure**. Amlodipine is indicated for use in adults and pediatric patients ≥ 6 years of age.
- **Conjupri** is indicated for the **treatment of hypertension** in adults and pediatric patients ≥ 6 years of age to lower blood pressure.[24] An authorized generic is available.[27]
- **Katerzia** may be used alone or in combination with other antihypertensive or antianginal medications for the **treatment of hypertension** in adults and children ≥ 6 years of age and **coronary artery disease (CAD)** [chronic stable angina, vasospastic angina, and angiographically documented CAD in patients without heart failure or an ejection fraction < 40%].[25]
- **Norliqva** may be used alone or in combination with other antihypertensive or antianginal medications for the **treatment of hypertension** in adults and children ≥ 6 years of age and **CAD** [chronic stable angina, vasospastic angina, and angiographically documented CAD in patients without heart failure or an ejection fraction < 40%].[26]

Prestalia contains amlodipine and perindopril, an angiotensin converting enzyme (ACE) inhibitor.[6] The DHP CCB nimodipine is not discussed in this document since it is only indicated to improve neurological deficits associated with subarachnoid hemorrhage and is given every 4 hours for a 21-day period.[13,14]

Many of the available DHP CCBs can be dosed once daily (QD), which may be important in the treatment of hypertension to ensure adequate blood pressure control over a 24-hour period and in the treatment of angina to avoid fluctuations in blood pressure and heart rate. The only DHP CCBs that are not dosed QD

are isradipine IR, dosed twice daily (BID), and nicardipine IR and nifedipine IR, both of which are dosed three to four times daily (TID to QID).

Hypertension

The DHP CCBs indicated in the treatment of hypertension have been found to be effective. These agents are useful for many reasons, such that the blood pressure response is less contingent on patient factors such as race and age, the agents are metabolically neutral and do not disturb glucose homeostasis, and some agents have conferred cardiovascular benefit.[15] In 2017, the **American College of Cardiology (ACC)**, along with other nationally-recognized groups, published extensive guidelines regarding the management of high blood pressure in adults. CCBs are recommended among the choice of first-line agents as antihypertensive medications. Refer to the full guidelines for additional details.[23] The Eighth Report of the **Joint National Committee** (JNC 8) 2014 evidence-based guideline for the management of high blood pressure in adults recommends CCBs as one of the initial choices of therapy in various scenarios.[16] Currently, the only DHP CCB indicated for the treatment of hypertension in children is amlodipine (patients aged 6 to 17 years).[1] In 2017, the **American Academy of Pediatrics** published a clinical practice guideline regarding the management of high blood pressure in children and adolescents.[17] Long-acting CCBs are among the first-line choices for patients initiating antihypertensive therapy.

Angina

In 2023, the **American Heart Association** and the **American College of Cardiology**, along with other national organizations, published guidelines regarding the management of patients with chronic coronary disease.[18] Either a calcium channel blocker or beta blocker is recommended as first-line antianginal therapy. In adults with chronic coronary disease and hypertension (systolic blood pressure ≥ 130 and/or diastolic blood pressure BP ≥ 80 mm Hg), in addition to nonpharmacological strategies, guideline-directed medication therapy with angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), or beta blockers are recommended as first-line therapy for compelling indications (e.g., recent MI or angina), with additional antihypertensive medications (e.g., dihydropyridine calcium channel blockers [CCB], long-acting thiazide diuretics, and/or mineralocorticoid receptor antagonists) added as needed to optimize blood pressure control. In patients with chronic coronary disease and angina, antianginal therapy with either a beta blocker, CCB, or long-acting nitrate is recommended for relief of angina or equivalent symptoms. In such patients who remain symptomatic after initial treatment, addition of a second antianginal agent from a different therapeutic class (beta blockers, CCBs, long-acting nitrates) is recommended for relief of angina or equivalent symptoms.

Heart Failure (HF)

Most of the clinical data available on the use of DHP CCBs in patients with HF are with amlodipine, followed by felodipine, although neither product is indicated for HF.[19-21] The amlodipine prescribing information notes that amlodipine has been compared with placebo in several studies of 8 to 12 weeks duration in patients with New York Heart Association (NYHA) Class II/III HF (n = 697) and no evidence of worsening HF was noted.[1] The Prospective Randomized Amlodipine Evaluation (PRAISE) study (n = 1,153) is also detailed which involved use of amlodipine (5 to 10 mg) in patients with Class III/IV HF who were receiving other medications for HF (diuretics, digoxin, ACE inhibitors).[1,19] Amlodipine had no effect on the primary endpoint, which was the combined endpoint of all-cause mortality and cardiac morbidity. The primary endpoint occurred in 42% of patients given placebo vs. 39% in the amlodipine group after a median follow-up of 13.8 months.[1,19] The PRAISE-2 trial is also mentioned in the amlodipine prescribing information which randomized patients with NYHA Class III (80%) or IV (20%) HF who had no clinical symptoms or objective evidence of underlying ischemic disease to receive placebo or amlodipine, in addition to other HF therapies. After a mean follow-up of 33 months, there was no difference between amlodipine and placebo in the primary endpoint of all-cause mortality.[1] The 2022 **American College of Cardiology Foundation (ACCF)/American Heart Association (AHA)/Heart Failure Society of**

America guideline for the management of HF states that DHP CCBs are not recommended for patients with heart failure and a reduced ejection fraction; no distinct benefits are noted.[22] DHP CCBs may be used for the treatment of hypertension in patients who have elevated blood pressure despite optimization of guideline-directed medication therapy. Among the DHP CCBs, amlodipine and felodipine are thought to have less myocardial depressant activity and may be more favorable agents.[22]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product, for all agents except Prestalia. For Prestalia, this program requires the patient to try one Step 1 Product (a generic dihydropyridine-calcium channel blocker [DHP CCB] or a generic DHP CCB-combination product) and one angiotensin converting enzyme (ACE) inhibitor. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy, except for Prestalia. For Prestalia, a patient with a of one Step 1 Product and one brand or generic ACE inhibitor within the 130-day look-back period is excluded from Step Therapy.

Step 1: Afeditab CR, amlodipine, amlodipine/atorvastatin, amlodipine/benazepril, felodipine ER, isradipine IR, nicardipine IR, nifedipine ER, nifedipine IR, nifedipine XL, Nifediac CC, Nifedical XL, nisoldipine ER

Step 2: Conjupri, Katerzia, Levamlodipine (authorized generic), Norliqva, Norvasc, Prestalia, Procardia, Procardia XL, Sular

CRITERIA

5. For all agents except Prestalia, if the patient has tried one Step 1 Product, approve a Step 2 Product.

6. For Prestalia, if the patient has tried one Step 1 Product AND one angiotensin converting enzyme inhibitor, approve Prestalia.
Note: Examples of angiotensin converting enzyme inhibitors include perindopril, enalapril, lisinopril, benazepril.

7. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve Katerzia or Norliqva.

4. No other exceptions are recommended.

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23. Felodipine extended-release tablets [prescribing information]. Morgantown, WV: Mylan; February 2013.
24. Isradipine capsules [prescribing information]. Parsippany, NJ: Actavis; November 2023.
25. DynaCirc CR® controlled-release tablets [prescribing information]. Research Triangle Park, NC; GlaxoSmithKline; November 2009.
26. Nicardipine capsules [prescribing information]. Morgantown, WV: Mylan; September 2016.
27. Prestalia® tablets [prescribing information]. Durham, NC: Adhera; August 2019.
28. Adalat® capsules [prescribing information]. West Haven, CT: Bayer; June 2000.
29. Procardia® capsules [prescribing information]. New York, NY: Pfizer; December 2014.

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46. Katerzia™ oral suspension [prescribing information]. Woborn, Azurity; April 2023.
47. Norliqva® oral solution [prescribing information]. Farmville, NC: CMP; February 2022.
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STEP THERAPY POLICY

POLICY: Calcium Channel Blockers – Verapamil Products Step Therapy Policy

- Calan® SR (verapamil sustained-release caplets – Pfizer, generic)
- Verelan® PM (verapamil extended-release capsules, controlled onset – Lannett/Recro/Alkermes, generic)
- verapamil extended-release tablets, controlled onset (brand Covera-HS® is no longer available)
- verapamil sustained-release tablets – generic only (brand Isoptin SR® is no longer available)

REVIEW DATE: 06/26/2024

OVERVIEW

All of the available verapamil formulations are indicated for the treatment of **hypertension**. Covera-HS is also indicated for the treatment of angina. Verapamil immediate-release is also indicated for the treatment of angina and specific cardiac arrhythmias.[1-3] Verapamil has also been used for off label conditions, such as adjunctive treatment of hypertrophic cardiomyopathy and prophylaxis of migraine and cluster headaches. Both immediate-release and once-daily verapamil formulations are available generically.

Covera-HS and Verelan PM are extended-release controlled onset (COER) formulations designed to release verapamil 4 to 5 hours after ingestion and should be administered once daily at bedtime. Both COER formulations result in a maximum plasma concentration of verapamil in the morning hours, approximately 11 hours after ingestion.[1,2] It has been hypothesized that the COER verapamil formulations may be more safe and effective in patients with hypertension than other verapamil formulations because their concentrations during a 24-hour period are synchronized with biological rhythm (chronotherapy).[5-7] In theory, these formulations may have an advantage over other sustained-/extended-release verapamil formulations as they would attenuate the increase in blood pressure, heart rate, cardiac ischemia, and catecholamines that naturally occur upon awakening and they would not cause hypotension during sleep. However, the role of verapamil as it relates to chronotherapy in the primary prevention of cardiovascular (CV) morbidity and mortality (e.g., myocardial infarction [MI], stroke) has not been demonstrated in controlled, comparative clinical trials.[7,8] The Controlled ONset Verapamil InvestigatioN of Cardiovascular Endpoints (CONVINCE) trial, which was terminated two years early for commercial reasons, was conducted in part to determine if there is a difference in the incidence of fatal or nonfatal MI, fatal or nonfatal stroke, or CV-related death between extended-release controlled onset verapamil ± hydrochlorothiazide (HCTZ), HCTZ alone, atenolol alone, or HCTZ in combination with atenolol.[9] The trial results did not provide evidence to support the concept of chronotherapeutics. Also, one small study comparing the effects of COER verapamil on the diurnal pattern of forearm vascular resistance in hypertensive and normotensive patients noted that COER verapamil minimized the diurnal pattern in forearm vascular resistance but it did not hinder the early morning rate of blood pressure rise, despite being at peak concentration.[10]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: verapamil extended-release capsules, verapamil extended-release PM capsules, verapamil immediate-release tablets, verapamil sustained-release tablets

Step 2: Calan SR, Verelan, Verelan PM

CRITERIA

~~**8.**~~ If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Covera-HS® extended-release tablets controlled-onset [prescribing information]. New York, NY: Pfizer; November 2023.
2. Verelan® PM extended-release capsules controlled-onset [prescribing information]. Philidelphia, PA, and Gainesville, GA: Lannett/Recro/Alkermes; October 2019.
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STEP THERAPY POLICY

POLICY: Carbinoxamine Step Therapy Policy

- Carbinoxamine maleate 6 mg tablets (generics)
- RyVent™ (carbinoxamine maleate 6 mg tablets – Carwin)
- Karbinal™ ER (carbinoxamine maleate 4 mg/5 ml oral suspension, extended-release – Aytu)

REVIEW DATE: 04/24/2024

OVERVIEW

Carbinoxamine maleate, a histamine H_1 receptor blocker with anticholinergic and sedative properties, is effective (indicated) for the symptomatic treatment of seasonal and perennial **allergic rhinitis**, **vasomotor rhinitis**, **allergic conjunctivitis**, mild and uncomplicated allergic manifestations of urticarial and angioedema, and **dermatographism**.[1-4] It is also effective (indicated) as a therapy for anaphylactic reactions as an adjunct to epinephrine and other standard measures after acute manifestations are controlled and amelioration of the severity of allergic reactions to blood or plasma. All carbinoxamine maleate products are contraindicated in children < 2 years of age.[1-4]

Table 1. Comparison of Carbinoxamine Dose[1-5]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: carbinoxamine 4 mg tablets, carbinoxamine 4 mg/5 ml liquid

Step 2: carbinoxamine maleate 6 mg tablets, RyVent 6 mg tablets, Karbinal ER 4 mg/5 ml suspension

CRITERIA

7. If the patient has tried one Step 1 Product, approve a Step 2 Product.

8. No other exceptions are recommended.

REFERENCES

10. Carbinoxamine maleate tablets and oral solution [prescribing information]. Berlin, CT: Breckenridge; May 2019.
11. Carbinoxamine maleate 6 mg tablets [prescribing information]. Trussville, AL: Foxland; November 2017.
12. RyVent™ tablets [prescribing information]. Hazlet, NJ: Carwin; September 2016.
13. Karbinal™ ER oral suspension [prescribing information]. Englewood, CO: Aytu; August 2021.
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STEP THERAPY POLICY

POLICY: Cardiology – Ranolazine Products Step Therapy Policy
- Aspruzyo Sprinkle™ (ranolazine extended-release granules – Sun)
- Ranexa® (ranolazine extended-release tablets – Gilead, generic)

REVIEW DATE: 12/13/2023

OVERVIEW

Aspruzyo Sprinkle and ranolazine extended-release tablets are both indicated for the treatment of chronic angina.[1,2] The precise mechanism of action of ranolazine, a piperazine derivative, has not been determined, although the agent selectively inhibits the late sodium cardiac current. Ranolazine extended-release tablets are available generically. Aspruzyo Sprinkle was approved through the 505(b)(2) pathway and as such relied upon existing safety and efficacy information for ranolazine extended-release tablets to support approval. Ranolazine extended-release tablets (supplied in strengths of 500 mg and 1,000 mg) must be swallowed whole; do not crush, break or chew. Aspruzyo Sprinkle (supplied in unit-dose sachets in strengths of 500 mg and 1,000 mg) can be sprinkled on one tablespoonful of soft food (applesauce and yogurt) and immediately consumed. Also, this formulation can be administered via nasogastric and gastrostomy/gastric tube.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic ranolazine extended-release tablets

Step 2: Aspruzyo Sprinkle, Ranexa

CRITERIA

9. If the patient has tried one Step 1 Product, approve a Step 2 Product.

10. Approve Aspruzyo Sprinkle if the patient meets one of the following criteria (A or B):
- **C)** Patient requires administration by nasogastric or gastrostomy/gastric tube; OR
- **D)** Patient is unable to swallow or has difficulty swallowing tablets or capsules.

11. No other exceptions are recommended.

REFERENCES

15. Aspruzyo Sprinkle™ extended-release granules [prescribing information]. Cranbury, NJ: Sun; February 2022.
16. Ranexa® extended-release tablets [prescribing information]. Foster City, CA: Gilead; October 2019.

STEP THERAPY POLICY

POLICY: Contraceptives – Oral, Patch, and Vaginal Ring Products Step Therapy Policy

Note: This is not an all-inclusive list.

BRAND COMBINATION HORMONAL CONTRACEPTIVES – BIPHASIC

BRAND COMBINATION HORMONAL CONTRACEPTIVES - TRIPHASIC

BRAND COMBINATION HORMONAL CONTRACEPTIVES - FOUR-PHASIC

GENERIC COMBINATION HORMONAL CONTRACEPTIVES – MONOPHASIC (CONTINUED)

GENERIC COMBINATION HORMONAL CONTRACEPTIVES – TRIPHASIC (CONTINUED)

PROGESTIN-ONLY CONTRACEPTIVES

REVIEW DATE: 08/21/2024; selected revision 12/04/2024

OVERVIEW

Combined oral contraceptives are sometimes called "the pill" and are one of the most commonly used forms of contraception.[1] Along with the oral tablets, hormonal contraceptives are also available as transdermal patches and vaginal rings. Hormonal contraceptives contain a combination of estrogen and progestin or progestin alone.[2] The hormones prevent ovulation and can also prevent fertilized eggs from implanting in the womb. Estrogens suppress follicle-stimulating hormone (FSH) release from the pituitary, which may block the luteinizing hormone (LH) surge and prevent ovulation. Progestins provide most of the other contraceptive effects such as cervical mucus changes, which inhibit sperm penetration and motility. Progestins also induce endometrial atrophy, which helps to prevent pregnancy. Oral contraceptives are an effective method of reversible birth control.[3]

Combined Oral contraceptives (COCs)

COCs are available in monophasic, biphasic, triphasic, or four-phasic combinations.[2] The monophasic COCs maintain the same dose of estrogen and progestin throughout the cycle (21 days of active pills, 7 days of placebo). An extended cycle 84-day monophasic regimen is also available (e.g., Seasonale, generic). The estrogen and/or progestin doses are varied throughout the cycle for different time intervals in the bi-, tri-, and four-phasic COCs. All COCs have similar efficacy irrespective of monophasic or multiphasic regimens. The multiphasic regimens are generally used to minimize patient specific symptoms (e.g., nausea, breakthrough bleeding).

Progestin-Only Oral Contraceptives

Progesterone-only products provide an alternative for patients with contraindications to estrogen-containing hormonal contraceptives. Progestin-only contraceptives may be more favorable in women with certain medical conditions (e.g., venous thromboembolism) or women who are breastfeeding.[4] Most progesterone-only oral contraceptives contain norethindrone 0.35 mg. Slynd™ is a progesterone-only oral contraceptive containing drospirenone.[6] Drospirenone is also available as the progesterone component of numerous oral contraceptives containing ethinyl estradiol. Because drospirenone has antimineralocorticoid activity, drospirenone-containing products are contraindicated in patients with conditions which predispose them to hyperkalemia, including renal disease, hepatic dysfunction, and adrenal insufficiency.

Transdermal Patches

Ortho Evra® and its generics, Xulane® and Zafemy™, are transdermal patches composed of ethinyl estradiol and norelgestromin (35 mcg ethinyl estradiol and 150 mcg norelgestromin released every 24 hours).[5,8] The brand, Ortho Evra, was discontinued in 2015 by the manufacturer, but the generics are still available. The only other transdermal contraceptive patch is Twirla®, composed of ethinyl estradiol and levonorgestrel (30 mcg ethinyl estradiol and 120 mcg levonorgestrel released every 24 hours).[7] Both transdermal patches are contraindicated (Boxed Warning) for use in women with a body mass index (BMI) $\geq$ 30 kg/m^2.[5,7] Generics for Ortho Evra have a limitation of use that it may be less effective in preventing pregnancy in women who weigh more than 198 pounds (90 kg).[5,8] Twirla has a limitation of use to consider the reduced effectiveness in women with a BMI $\geq$ 25 to < 30 kg/m^2.[7] Generic Ortho Evra products also have additional warnings in

the labeling regarding higher estrogen exposure compared with oral contraceptives containing ethinyl estradiol 35 mcg.[5,8]

Vaginal Rings
NuvaRing® and its generics, etonogestrel-ethinyl estradiol, EluRyng™, EnilloRing®, and Haloette®, are vaginal rings indicated to prevent pregnancy.[9,11,12] These products are disposable rings; one ring used continuously for 3 weeks, followed by a 1-week ring-free interval. Annovera® is a reusable ring with one ring providing contraception for 13 cycles.[10] The cycles are 3 weeks with vaginal ring inserted and 1 week with the vaginal ring removed. Annovera contains ethinyl estradiol and segesterone acetate.

POLICY STATEMENT
This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: When compliance with the Affordable Care Act, Health Resources and Services Administration Guidelines, and Public Health Services Act section 2713 is required and the conditions for coverage listed under the Criteria are not met, approval is granted when the requested drug is used primarily for the prevention of pregnancy and, according to the prescriber, the alternative Step 1 Products would not be as medically appropriate for the patient as the requested drug.
Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic oral contraceptives, transdermal Xulane, transdermal Zafemy, etonogestrel-ethinyl estradiol vaginal ring, Eluryng vaginal ring, EnilloRing vaginal ring, Haloette vaginal ring

Step 2: Brand oral contraceptives, transdermal Twirla, NuvaRing, Annovera, Femlyv

CRITERIA

12. If the patient has tried one Step 1 Product, approve a Step 2 Product.

13. No other exceptions are recommended.

REFERENCES

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22. Slynd™ [prescribing information]. Florham Park, NJ: Exeltis: July 2024.
23. Twirla® (levonorgestrel and ethinyl estradiol) transdermal patch [prescribing information]. Princeton, NJ: Agile Therapeutics; April 2022.
24. Zafemy™ transdermal patch [prescribing information]. Bridgewater, NJ: Amneal; April 2022.
25. NuvaRing® [prescribing information]. Jersey City, NJ: Organon; June 2024.

26. Annovera® [prescribing information]. Raleigh, NC: Mayne; January 2023.
27. EluRyng™ vaginal ring [prescribing information]. Bridgewater, NJ: Amneal; May 2022.
28. Haloette® vaginal ring [prescribing information]. Greenville, NC: Mayne; May 2022.
29. EnilloRing® vaginal ring [prescribing information]. Florham Park, NJ: Xiromed; June 2024.

STEP THERAPY POLICY

POLICY: Diabetes – Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy

- Janumet® (sitagliptin/metformin tablets – Merck)
- Janumet® XR (sitagliptin/metformin extended-release tablets – Merck)
- Januvia® (sitagliptin tablets – Merck)
- Jentadueto® (linagliptin/metformin tablets – Boehringer Ingelheim)
- Jentadueto® XR (linagliptin/metformin extended-release tablets – Boehringer Ingelheim)
- Kazano™ (alogliptin/metformin tablets – Takeda, authorized generic)
- Kombiglyze® XR (saxagliptin/metformin extended-release tablets – AstraZeneca, generic)
- Nesina® (alogliptin tablets – Takeda, authorized generic)
- Onglyza® (saxagliptin tablets – AstraZeneca, generic)
- Oseni™ (alogliptin/pioglitazone tablets – Takeda, authorized generic)
- Tradjenta® (linagliptin tablets – Boehringer Ingelheim)
- Zituvimet™ (sitagliptin/metformin tablets – Zydus, authorized generic)
- Zituvimet™ XR (sitagliptin/metformin extended-release tablets – Zydus)
- Zituvio™ (sitagliptin tablets – Zydus, authorized generic)

REVIEW DATE: 05/22/2024; selected revision 08/07/2024 and 11/20/2024

OVERVIEW

The dipeptidyl peptidase-4 (DPP-4) inhibitors and combination products are indicated to improve glycemic control in adults with **type 2 diabetes mellitus** (as monotherapy and as combination therapy) when used as adjuncts to diet and exercise.[1-11,15,17,18]

Various combination products are available which combine DPP-4 inhibitors with metformin, sodium glucose co-transporter-2 (SGLT-2) inhibitors, and/or thiazolidinediones (TZDs). Of note, the SGLT-2/DPP-4 combination products are not addressed in this policy; refer to the *Diabetes – Sodium Glucose Co-Transporter-2 and Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy*.

GUIDELINES

The American Diabetes Association Standards of Care (2024) note that therapy for patients with type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification.[12] Very high circulating levels of metformin have been associated with lactic acidosis. However, the occurrence of this complication is now known to be very rare. In patients with contraindications or intolerance to metformin, initial therapy should be based on patient factors. Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.[14] DPP-4 inhibitors are among the classes of medications recommended as add-on therapy after metformin (or as initial therapy if metformin cannot be used). Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets. Other guidelines have similar recommendations.[13,16]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one of the following within the 130-day look-back period is excluded from Step Therapy:

- One Step 1 Product; OR
- One of the following metformin-containing products: Glumetza ER, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Invokamet, Invokamet XR, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release (authorized generic to Xigduo XR), Segluromet; OR
- One Step 2 Product.

Step 1: generic metformin, generic metformin extended-release (generic to Glucophage XR only)

Step 2: Januvia, Janumet, Janumet XR, saxagliptin (Onglyza, generic), saxagliptin/metformin extended-release (Kombiglyze XR, generic), Tradjenta, Jentadueto, Jentadueto XR, alogliptin (Nesina, authorized generic), alogliptin/metformin (Kazano, authorized generic), alogliptin/pioglitazone (Oseni, authorized generic), sitagliptin (Zituvio, authorized generic), sitagliptin/metformin (Zituvimet, authorized generic), Zituvimet XR

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: A trial of one of the following metformin-containing products also satisfies the requirement: Fortamet ER (obsolete), Glucophage (obsolete), Glucophage XR (obsolete), Glumetza ER, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR (obsolete), repaglinide/metformin (obsolete), Invokamet, Invokamet XR, Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release (authorized generic to Xigduo XR), Segluromet.

2. If the patient has tried one Step 2 Product, approve the requested Step 2 Product.

3. If the patient is initiating dual (combination) therapy with a single-entity DPP-4 inhibitor (Januvia, saxagliptin [Onglyza, generic], Tradjenta, alogliptin [Nesina, authorized generic], or sitagliptin [Zituvio, authorized generic]) AND metformin, approve a single-entity DPP-4 inhibitor.

4. If the patient has a contraindication to metformin, according to the prescriber, approve a single-entity DPP-4 inhibitor.
Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

5. No other exceptions are recommended.

REFERENCES

1. Janumet® tablets [prescribing information]. Whitehouse Station, NJ: Merck; June 2022.

2. Janumet® XR tablets [prescribing information]. Whitehouse Station, NJ: Merck; June 2022.
3. Januvia® tablets [prescribing information]. Rahway, NJ: Merck; December 2023.
4. Jentadueto® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
5. Jentadueto® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
6. Kazano™ tablets [prescribing information]. Lexington, MA: Takeda; July 2023.
7. Kombiglyze® XR tablets [prescribing information]. Wilmington, DE. AstraZeneca; July 2019.
8. Nesina® tablets [prescribing information]. Lexington, MA: Takeda; July 2023.
9. Onglyza® tablets [prescribing information]. Wilmington, DE: AstraZeneca; June 2019.
10. Oseni™ tablets [prescribing information]. Lexington, MA: Takeda; March 2022.
11. Tradjenta® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; June 2023.
12. American Diabetes Association – standards of care in diabetes – 2024. *Diabetes Care.* 2024;47(Suppl 1):S1-S321.
13. Blonde L, Umpierrez GE, Reddy SS, et al. American Association of Clinical Endocrinology clinical practice guideline: developing a diabetes mellitus comprehensive care plan – 2022 update. *Endocr Pract.* 2022;18:923-1049.
14. Metformin tablets [prescribing information]. Raleigh, NC: Indicus Pharma; June 2020.
15. Zituvio™ tablets [prescribing information]. Pennington, NJ: Zydus; October 2023.
16. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.
17. Zituvimet ™ tablets [prescribing information]. Pennington, NJ: Zydus; November 2023.
18. Zituvimet™ XR tablets [prescribing information]. Pennington, NJ: Zydus; July 2024.

STEP THERAPY POLICY

POLICY: Diabetes – Metformin Step Therapy Policy

Immediate-release products

- metformin tablets (generic only)
- Riomet® (metformin oral solution – Sun Pharmaceuticals, generic)

Extended-release products

- metformin extended-release tablets (generic to obsolete brand Fortamet – generic only)
- Glumetza® (metformin extended-release tablets – Salix, generic)
- metformin extended-release tablets (generic to obsolete brand Glucophage XR – generic only)

REVIEW DATE: 10/09/2024

OVERVIEW

The extended-release metformin products, generic metformin extended-release tablets (generic to the obsolete brand Glucophage XR and generic to the obsolete brand Fortamet XR), and Glumetza (generic) are indicated as adjuncts to diet and exercise to **improve glycemic control** in adults with type 2 diabetes mellitus.[1-4]

The immediate-release metformin products, metformin tablets and Riomet oral solution (generic), are indicated for the **treatment of type 2 diabetes mellitus** in conjunction with diet and exercise in patients ≥ 10 years of age.[1] Generic metformin immediate-release tablets are available in strengths of 500 mg, 625 mg, 850 mg, and 1,000 mg. In the prescribing information for immediate-release metformin, it is noted that the recommended starting dose is 500 mg twice daily or 850 mg once daily. Increase the dose in increments of 500 mg weekly or 850 mg once every 2 weeks on the basis of glycemic control and tolerability, up to a maximum dose of 2,550 mg per day, given in divided doses.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product (or the use of a Step 1 and a Step 2 Product prior to the use of a Step 3 Product, where applicable). If the Step Therapy rule is not met for the Step 2 or Step 3 Product at the point of service, coverage will be determined by Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: For immediate-release products, a patient with a of one Step 1 immediate-release product within the 130-day look-back period is excluded from Step Therapy. For extended-release products, there is no automation.

Immediate-Release Products:

Step 1: generic metformin immediate-release tablets (500 mg, 850 mg, and 1,000 mg strengths)

Step 2: Riomet (brand and generic), metformin 625 mg tablets

Extended-Release Products:

Step 1: metformin extended-release tablets (generic to obsolete brand Glucophage XR only)

Step 2: metformin extended-release tablets (generic to obsolete brand Fortamet only)

Step 3: Glumetza (brand and generic)

CRITERIA

Immediate-Release Products

1. If the patient has tried one Step 1 immediate-release product, approve a Step 2 immediate-release product.

2. If the patient is unable to swallow or has difficulty swallowing tablets containing metformin, approve metformin oral solution (Riomet, generic).

3. No other exceptions are recommended.

Extended-Release Products

1. If the patient has tried one Step 1 extended-release product, approve a Step 2 extended-release product.

2. If the patient has tried one Step 1 extended-release product AND one Step 2 extended-release product, approve a Step 3 extended-release product.

3. No other exceptions are recommended.

REFERENCES

1. Metformin ER 500 and 750 mg tablet [prescribing information]. Hyderabad, India: Granules India Limited; November 2022.
2. Glumetza® extended-release tablets [prescribing information]. Bridgewater, NJ: Salix/Valeant; March 2024.
3. Fortamet® extended-release tablets [prescribing information]. Florham Park, NJ: Shionogi; November 2018.
4. Riomet® oral solution [prescribing information]. Jacksonville, FL: Sun Pharmaceuticals; November 2018.

STEP THERAPY POLICY

POLICY: Diabetes – Sodium Glucose Co-Transporter-2 Inhibitors Step Therapy Policy

- Brenzavvy™ (bexagliflozin tablets – TheracosBio)
- Farxiga® (dapagliflozin tablets – Bristol-Myers Squibb, authorized generic)
- Invokana® (canagliflozin tablets – Janssen)
- Invokamet® (canagliflozin and metformin hydrochloride tablets – Janssen)
- Invokamet® XR (canagliflozin and metformin hydrochloride extended-release tablets – Janssen)
- Jardiance® (empagliflozin tablets – Boehringer Ingelheim/Lilly)
- Segluromet® (ertugliflozin and metformin tablets – Merck)
- Steglatro® (ertugliflozin tablets – Merck)
- Synjardy® (empagliflozin/metformin hydrochloride tablets – Boehringer Ingleheim/ Lilly)
- Synjardy® XR (empagliflozin/metformin extended-release tablets – Boehringer Ingleheim/Lilly)
- Xigduo® XR (dapagliflozin/metformin extended-release tablets – Bristol-Meyers Squibb, authorized generic)

REVIEW DATE: 05/01/2024; selected revision 08/07/2024, 09/18/2024 (effective 01/01/2025), and 11/20/2024

OVERVIEW

Brenzavvy, dapagliflozin, Invokana, Jardiance, and Steglatro are sodium glucose co-transporter-2 (SGLT-2) inhibitors indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes**.[1-4] Dapagliflozin, Invokana, and Jardiance are also indicated in pediatric patients ≥ 10 years of age with type 2 diabetes as an adjunct to diet and exercise to improve glycemic control.[1-3]

The SGLT-2 inhibitors also possess the following additional indications in patients with diabetes:

- Jardiance: To reduce the risk of cardiovascular (CV) death in adults with type 2 diabetes mellitus and established CV disease.
- Invokana: 1) To reduce the risk of major adverse CV events in adults with type 2 diabetes mellitus and established CV disease; AND 2) To reduce the risk of end-stage kidney disease, doubling of serum creatinine, CV death, and hospitalization for heart failure in adults with type 2 diabetes mellitus and diabetic nephropathy with albuminuria.
- Dapagliflozin: To reduce the risk of hospitalization for heart failure (HHF) in adults with type 2 diabetes mellitus and established CV disease or multiple CV risk factors.

In addition to indications in diabetes, dapagliflozin and Jardiance are indicated for the following indications in patients with and without diabetes:[1,3]

- **Heart failure,** to reduce the risk of CV death, HHF, and urgent heart failure visits in adults with heart failure (included both reduced and preserved ejection fraction).
- **Chronic kidney disease,** to reduce the risk of sustained estimated glomerular filtration rate (eGFR) decline, end-stage kidney disease, CV death, and hospitalization for heart failure in adults with chronic kidney disease at risk of progression.

Guidelines

Diabetes

The American Diabetes Association Standards of Care (2024) note that first-line therapy for type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs; it generally includes metformin and comprehensive lifestyle modification.[5] Other medications (glucagon-like peptide-1 receptor agonists, SGLT-2 inhibitors), with or without metformin based on glycemic needs, are appropriate initial therapy for individuals with type 2 diabetes with or at high risk of atherosclerotic CV disease, heart failure, and/or chronic kidney disease. American Association of Clinical Endocrinology (AACE) Consensus Statement: Comprehensive Type 2 Diabetes Management Algorithm (2023) makes similar recommendations.[12] It is noted that an agent with proven benefit should be utilized; with "proven benefit" referring to a label indication.

Heart Failure

The American College of Cardiology (ACC) Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment was updated in 2022.[6] In patients with symptomatic chronic heart failure with reduced ejection fraction, SGLT-2 inhibitors (dapagliflozin or Jardiance) are recommended to reduce HHF and CV mortality, irrespective of the presence of type 2 diabetes (class 1 recommendation, level of evidence A). In patients with heart failure with preserved ejection fraction, SGLT-2 inhibitors (Jardiance) can be beneficial in decreasing heart failure hospitalizations and CV mortality, irrespective of the presence of type 2 diabetes (class 2a recommendation, level of evidence B-R). Note: This does not reflect the updated indication for dapagliflozin in patients with preserved ejection fraction.

The ACC Expert Consensus Decision Pathway on Management of Heart Failure with Preserved Ejection Fraction (2023) recommends that all individuals with heart failure with preserved ejection fraction be started on an SGLT-2 inhibitor unless contraindicated.[10] SGLT-2 inhibitors are noted to have demonstrated significant CV benefits in individuals without type 2 diabetes, particularly in individuals with heart failure. In such patients, SGLT-2 inhibitors have significantly reduced the risk of HHF and CV death across all ejection fraction subgroups. Clinical trials with Jardiance and dapagliflozin are mentioned. For both agents, a significant decrease in HHF was observed.

Kidney Disease

Kidney Diseases Improving Global Outcomes (KDIGO) 2024 guidelines for the clinical evaluation and management of chronic kidney disease recommend treating patients with type 2 diabetes, chronic kidney disease, and an eGFR $\geq$ 20 mL/min/1.73 m^2 with an SGLT-2 inhibitor.[13] Once an SGLT-2 inhibitor is initiated, it is reasonable to continue the agent, even if the eGFR falls to < 20 mL/min/1.73 m^2, unless it is not tolerated or kidney replacement therapy is initiated. In adults with chronic kidney disease, an SGLT-2 inhibitor is recommended for patients with eGFR $\geq$ 20 mL/min/1.73 m^2 with urine albumin:creatinine ratio $\geq$ 200 mg/g or with heart failure, irrespective of the level of albuminuria. SGLT-2 inhibitors are also recommended in adults with eGFR $\geq$ 20 to $\leq$ 45 mL/min/1.73 m^2 with urine albumin:creatinine ratio < 200 mg/g.

In patients with diabetes and chronic kidney disease, the KDIGO guidelines for diabetes management in chronic kidney disease (2022) recommend first-line pharmacotherapy with metformin and an SGLT-2 inhibitor with documented kidney or CV benefit (Invokana, dapagliflozin, and Jardiance).[7]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product, and the use of a Step 2 Product prior to the use of a Step 3 Product. If the Step Therapy rule is not met for a Step 2 or Step 3 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: The following automation is applied in this policy:

- **Requests for a Step 2 Product:** A patient with a history of one of the following within the 130-day look-back period is excluded from Step Therapy:
  - One Step 1 Product; OR
  - One of the following metformin-containing products: Glumetza ER, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, saxagliptin/metformin extended-release, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR; OR
  - One Step 2 Product; OR
  - One Step 3 Product.
- **Requests for a Step 3 Product:** A patient with a of one Step 2 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic metformin, generic metformin-extended release (generic to Glucophage XR only)

Step 2: Farxiga, Jardiance, Synjardy, Synjardy XR, Xigduo XR

Step 3: Brenzavvy, Invokana, Invokamet, Invokamet XR, dapagliflozin (authorized generic to Farxiga), dapagliflozin/metformin extended-release (authorized generic to Xigduo XR), Segluromet, Steglatro

CRITERIA

Step 2 Products

- If the patient has tried one Step 1 Product, approve a Step 2 Product.

Note: A trial of one of the following metformin-containing products also satisfies the requirement: Fortamet ER (obsolete), Glucophage (obsolete), Glucophage XR (obsolete), Glumetza ER, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), glyburide/metformin, glipizide/metformin, Actoplus Met, pioglitazone/metformin, Actoplus Met XR (obsolete), repaglinide/metformin (obsolete), Kazano, alogliptin/metformin, Jentadueto, Jentadueto XR, Kombiglyze XR, saxagliptin/metformin extended-release, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR.

- If the patient has tried one Step 2 Product, approve the requested Step 2 Product.
- If the patient has tried one Step 3 Product, approve the requested Step 2 Product.
- If the patient will be initiating dual therapy with metformin AND Farxiga or Jardiance, approve Farxiga or Jardiance.
- If the patient has a contraindication to metformin, according to the prescriber, approve Farxiga, or Jardiance.

Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

- If the patient has heart failure, approve Farxiga or Jardiance.

- If the patient has chronic kidney disease, approve Farxiga or Jardiance.

- If the patient has atherosclerotic cardiovascular disease or, according to the prescriber, the patient has at least two risk factors for cardiovascular disease, approve Farxiga or Jardiance.

- No other exceptions are recommended.

Step 3 Products

1. If the patient has tried one Step 2 Product, approve a Step 3 Product.
Note: A trial of a Step 1 Product is required prior to a Step 2 Product, unless exception criteria are met.

2. No other exceptions are recommended.

REFERENCES

1. Farxiga® tablets [prescribing information]. Wilmington, DE: AstraZeneca; September 2023.
2. Invokana® tablets [prescribing information]. Titusville, NJ: Janssen; December 2024.
3. Jardiance® tablets [prescribing information]. Ridgefield, CT and Indianapolis, IN: Boehringer Ingelheim/Lilly; September 2023.
4. Steglatro® tablets [prescribing information]. Whitehouse Station, NJ: Merck; September 2023.
5. American Diabetes Association. Standards of medical care in diabetes – 2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S321.
6. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2022;145(8):e153-e639.
7. Boer IH, Khunti K, Sadusky T, et al. Diabetes management in chronic kidney disease: a consensus report by the American Diabetes Association (ADA) and Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney International.* 2022;102:974-989.
8. The EMPA-KIDNEY Collaborative group. Empagliflozin in patients with Chronic Kidney Disease. *N Engl J Med.* 2023; 388:117-127.
9. Solomon SD, McMurray JJV, Claggett B, et al.; DELIVER Trial Committees and Investigators. Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction. *N Engl J Med*. 2022;387(12):1089-109.
10. Kittleson MM, Panjrath GS, Amancherla K, et al. 2023 ACC expert consensus decision pathway on management of heart failure with preserved ejection fraction. *JACC*. 2023;81(18):1835-1878.
11. Brenzavvy™ tablets [prescribing information]. Marlborough, MA: TheracosBio; September 2023.
12. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.
13. Kidney Diseases Improving Global Outcomes (KDIGO). KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int.* 2024;105(4S):S117-S314.

STEP THERAPY POLICY

POLICY: Diabetes – Sodium Glucose Co-Transporter-2 and Dipeptidyl Peptidase-4 Inhibitors Step Therapy Policy

- Glyxambi® (empagliflozin and linagliptin tablets – Boehringer Ingelheim)
- Qtern® (dapagliflozin and saxagliptin tablets – AstraZeneca)
- Steglujan® (ertugliflozin and sitagliptin tablets – Merck)
- Trijardy® XR (empagliflozin, linagliptin, and metformin extended-release tablets – Boehringer Ingelheim)

REVIEW DATE: 05/22/2024; selected revision 08/07/2024 and 11/20/2024

OVERVIEW

Glyxambi, Qtern, Steglujan, and Trijardy XR are sodium glucose co-transporter-2 inhibitor (SGLT-2) and dipeptidyl peptidase-4 (DPP-4) inhibitor combination products indicated as an adjunct to diet and exercise to improve glycemic control in adults with **type 2 diabetes mellitus**; Trijardy XR also contains metformin.[1-4] Various single-entity SGLT-2 inhibitors and DPP-4 inhibitors are available. In addition to their indications for type 2 diabetes, Jardiance® (empagliflozin tablets), Invokana® (canagliflozin tablets), and dapagliflozin (Farxiga®, authorized generic) possess indications related to cardiovascular, renal, and/or heart failure benefits. Efficacy of the SGLT-2/DPP-4 inhibitor combination products has not been established in these settings. Refer to Table 1 for a summary of the available products containing SGLT-2 and/or DPP-4 inhibitors.

Table 1. SGLT-2 and DPP-4 inhibitor-containing combination products.

Table 1 (continued). SGLT-2 and DPP-4 inhibitor-containing combination products.
SGLT-2 – Sodium glucose co-transporter-2; DPP-4 – Dipeptidyl peptidase-4; CANA – canagliflozin; DAPA – dapagliflozin; EMPA – empagliflozin; ERTU – ertugliflozin; ALO – alogliptin; LINA – linagliptin; SAXA – saxagliptin; SITA – sitagliptin; XR – extended-release.

GUIDELINES

The American Diabetes Association Standards of Care (2024) note that therapy for patients with type 2 diabetes depends on comorbidities, patient-centered treatment factors, and management needs and generally includes metformin and comprehensive lifestyle modification.[5] Pharmacologic approaches, specified as metformin or agent(s), including combination therapy, that provide adequate efficacy to achieve and maintain treatment goals should be considered. For patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD) or indicators of high ASCVD risk, heart failure, or chronic kidney disease, an SGLT-2 inhibitor and/or glucagon-like peptide-1 receptor agonist with demonstrated cardiovascular disease benefit is recommended independent of hemoglobin A_{1c} or metformin use, and in consideration of patient-specific factors.

Very high circulating levels of metformin have been associated with lactic acidosis. However, the occurrence of this complication is now known to be very rare.[5] In patients with contraindications or intolerance to metformin, initial therapy should be based on patient factors. Metformin is contraindicated in patients with severe renal impairment (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m^2) and in patients with acute or chronic metabolic acidosis, including diabetic ketoacidosis, with or without coma.[7] DPP-4 inhibitors and SGLT-2 inhibitors are among the classes of medications recommended as add-on therapy after metformin (or as initial therapy if metformin cannot be used).[5] Because type 2 diabetes is often a progressive disease, combination therapy may be needed for many patients over time to achieve glycemic targets. Other guidelines have similar recommendations.[6,8]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one of the following within the 130-day look-back period is excluded from Step Therapy:

- One Step 1 Product; OR
- One of the following metformin-containing products: Glumetza ER, Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), metformin/glyburide, metformin/glipizide, Actoplus Met, pioglitazone/metformin, Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR, Kombiglyze XR, saxagliptin/metformin extended-release, Jentadueto, Jentadueto XR, Kazano, aloglitpin/metformin (authorized generic to Kazano), Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release (authorized generic to Xigduo XR), Invokamet, Invokamet XR, Segluromet; OR
- One of the following DPP-4 inhibitor products: Januvia, Nesina, alogliptin (authorized generic to Nesina), Onglyza, saxagliptin, Tradjenta, Oseni, alogliptin/pioglitazone (authorized generic to Oseni), Zituvio, sitagliptin (authorized generic to Zituvio); OR
- One SGLT-2 inhibitor (Brenzavvy, Farxiga, dapagliflozin [authorized generic to Farxiga], Invokana, Jardiance, Steglatro).

Step 1: generic metformin, generic metformin extended-release (generic to Glucophage XR only)

Step 2: Glyxambi, Qtern, Steglujan, Trijardy XR

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: A trial of one of the following metformin-containing products also satisfies the requirement: Glucophage (obsolete), Glucophage XR (obsolete), Glumetza ER, Fortamet ER (obsolete), Riomet, metformin oral solution, Riomet ER, metformin extended-release (generics to Fortamet ER and Glumetza ER), metformin/glyburide, metformin/glipizide, Actoplus Met, pioglitazone/metformin, Actoplus Met XR (obsolete), Janumet, Janumet XR, sitagliptin/metformin (authorized generic to Zituvimet), Zituvimet, Zituvimet XR, repaglinide/metformin (obsolete), Kombiglyze XR, saxagliptin/metformin extended-release, Jentadueto, Jentadueto XR, Kazano, aloglitpin/metformin (authorized generic to Kazano), Synjardy, Synjardy XR, Xigduo XR, dapagliflozin/metformin extended-release (authorized generic to Xigduo XR), Invokamet, Invokamet XR, Segluromet.

2. If the patient has tried a DPP-4 inhibitor, a DPP-4 inhibitor-containing product, or an SGLT-2 inhibitor, other than Glyxambi, Qtern, Steglujan, or Trijardy XR, approve a Step 2 Product.
Note: Examples of DPP-4 inhibitors include but are not limited to Januvia, Nesina, alogliptin (authorized generic to Nesina), Onglyza, saxagliptin, Tradjenta, Zituvio, and sitagliptin (authorized generic to Zituvio). Examples of DPP-4 inhibitor-containing products include but are not limited to Oseni and alogliptin/pioglitazone (authorized generic to Oseni). Examples of SGLT-2 inhibitors include but are not limited to Brenzavvy, Farxiga, dapagliflozin (authorized generic to Farxiga), Invokana, Jardiance, Steglatro.

3. If the patient has a contraindication to metformin, according to the prescriber, approve Glyxambi, Qtern, or Steglujan.
Note: Examples of contraindications to metformin include acute or chronic metabolic acidosis, including diabetic ketoacidosis.

4. No other exceptions are recommended.

REFERENCES

1. Glyxambi® tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2023.
2. Qtern® tablets [prescribing information]. Wilmington, DE: AstraZeneca; September 2023.
3. Steglujan® tablets [prescribing information]. Whitehouse Station, NJ: Merck; September 2023.
4. Trijardy® XR tablets [prescribing information]. Ridgefield, CT: Boehringer Ingelheim; October 2023.
5. American Diabetes Association. Standards of medical care in diabetes – 2024. *Diabetes Care*. 2024;47(Suppl 1):S1-S321.
6. Davies MJ, Aroda VR, Collins BS, et al. Management of hyperglycemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care.* 2022;45(11):2753-2786.
7. Metformin tablets [prescribing information]. Raleigh, NC: Indicus; June 2020.
8. Samson SL, Vellanki P, Blonde L, et al. American Association of Clinical Endocrinology consensus statement: comprehensive type 2 diabetes management algorithm – 2023 update. *Endocr Pract.* 2023;29:305-340.

STEP THERAPY POLICY

POLICY: Diuretics – Loop Products Step Therapy Policy

- bumetanide tablets (generic only)
- Edecrin® (ethacrynic acid tablets – Bausch/Patheon, generic)
- Furoscix® (furosemide subcutaneous injection by on-body infusor – scPharmaceuticals)
- Lasix® (furosemide tablets – Validus, generic)
- Soaanz® (torsemide tablets – Sarfez)
- torsemide tablets (generic only)

REVIEW DATE: 06/26/2024

OVERVIEW

The medications included in this policy are loop diuretics. For most products, the indications for use are very similar and are noted below.

Bumetanide tablets (generic) are indicated for:[1]

- Treatment of **edema** associated with congestive heart failure, hepatic and renal disease, including the nephrotic syndrome.

Ethacrynic acid tablets are indicated for:[2]

- Treatment of **edema** associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome.

Furosemide tablets are indicated for:[3]

- Treatment of **edema** associated with congestive heart failure, cirrhosis of the liver, and renal disease, including the nephrotic syndrome, in adults and pediatric patients.
- Treatment of **hypertension**, alone or in combination with other antihypertensive agents, in adults.

Furoscix is indicated for:[4]

- Treatment of **congestion due to fluid overload in adults with New York Heart Association Class II and III chronic heart failure**. Limitations of Use: Furoscix is not indicated for use in emergency situations or in patients with acute pulmonary edema. Of note, the single-use, on-body infusor with prefilled cartridge is pre-programmed to deliver 30 mg of Furoscix subcutaneously (SC) over the first hour, followed by 12.5 mg per hour for the subsequent 4 hours (80 mg SC over a total of 5 hours). Furoscix is not for chronic use and should be replaced with oral diuretics as soon as practical.

Soaanz is indicated for:[5]

- Treatment of **edema** associated with heart failure or renal disease in adults.

Torsemide tablets (generic) are indicated for:[6]

- Treatment of **edema** associated with heart failure, renal disease or hepatic disease.
- Treatment of **hypertension**, to lower blood pressure.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: bumetanide tablets, ethacrynic acid tablets, furosemide tablets, torsemide tablets

Step 2: Edecrin tablets, Lasix tablets, Soaanz tablets, Furoscix

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Bumex® tablets [prescribing information]. Parsippany, NJ: Validus; January 2024.
2. Edecrin® tablets and Sodium Edecrin® intravenous solution [prescribing information]. Bridgewater, NJ and Greenville, NC; Bausch and Patheon; August 2020.
3. Lasix® tablets [prescribing information]. Parsippany, NJ: Validus; August 2018.
4. Furoscix® subcutaneous injection by on-body infusor [prescribing information]. Burlington, MA: scPharmaceuticals; October 2023.
5. Soaanz® tablets [prescribing information]. Vienna, VA: Sarfex; November 2021.
6. Demadex® tablets [prescribing information]. Somerset, NJ: Meda; February 2017.

STEP THERAPY POLICY

POLICY: Epinephrine Auto-Injectors Step Therapy Policy

- EpiPen® (**epinephrine injection, USP auto-injector – Mylan Specialty, generic**)
- EpiPen Jr® (**epinephrine injection, USP auto-injector – Mylan Specialty, generic**)

REVIEW DATE: 01/24/2024

OVERVIEW

EpiPen and EpiPen Jr. (generics) are indicated for the emergency treatment of **severe allergic reactions** (Type I) including anaphylaxis to stinging and biting insects, allergen immunotherapy, foods, drugs, diagnostic testing substances, and other allergens, as well as anaphylaxis to unknown substances and exercise-induced anaphylaxis.[1] Auvi-Q® (epinephrine injection, USP auto-injector), an authorized generic to Adrenaclick® (epinephrine injection, USP auto-injector) and Symjepi™ (epinephrine injection, USP prefilled syringe), a self-administered epinephrine prefilled syringe, are also available and have the same indication as the EpiPen/EpiPen auto-injectors.[2-5] However, these agents are not targeted in this policy.

All of the epinephrine auto-injectors are administered and dosed similarly.[1] Patients who weigh ≥ 30 kg should be administered a dose of 0.3 mg (given via EpiPen [generic]), while patients weighing 15 kg to 30 kg should be administered 0.15 mg (EpiPen Jr. [generic]).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Auvi-Q, Symjepi, Adrenaclick (no longer available) and the authorized generic to Adrenaclick are not targeted in this policy.

Automation: None.

Step 1: epinephrine auto-injector 0.15 mg and 0.3 mg (generic to EpiPen/EpiPen Jr.)

Step 2: EpiPen 0.15 mg, EpiPen Jr. 0.3 mg

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. EpiPen® and EpiPen Jr® injection [prescribing information]. Morgantown, WV: Mylan Specialty; February 2023.
2. Auvi-Q® auto-injector [prescribing information]. Richmond, VA: Kaleo; September 2019.
3. Epinephrine auto-injector [prescribing information]. Bridgewater, NJ: Amneal; March 2021.
4. FDA listing of authorized generics. U.S. Food and Drug Administration Web site. Available at: https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm126391.htm. Updated January 4, 2024. Accessed on January 16, 2024.
5. Symjepi® injection [prescribing information]. San Diego, CA: Adamis; June 2021.

STEP THERAPY POLICY

POLICY: Estrogen – Transdermal Step Therapy Policy

- Climara® (estradiol patches – Bayer, generics)
- Divigel® (estradiol gel 0.1% – Vertical, generics)
- Elestrin™ (estradiol gel 0.06% – Meda)
- EstroGel® (estradiol gel 0.06% – Ascend, generic)
- Evamist™ (estradiol transdermal spray – Padagis)
- Minivelle® (estradiol patches – Noven, generics)
- Vivelle-Dot® (estradiol patches – Novartis, generics)

REVIEW DATE: 06/12/2024

OVERVIEW

All of the transdermal estrogen products are indicated for the treatment of **moderate to severe vasomotor symptoms associated with menopause**.[1-7,12] EstroGel (estradiol gel 0.06%, generic) and the estradiol patches, Climara and Vivelle-Dot (and generics), are also indicated for the treatment of moderate to **severe symptoms of vulvar and vaginal atrophy associated with menopause**.[1,5,7] Climara, Minivelle, and Vivelle-Dot (and generics) are all additionally indicated for the **prevention of postmenopausal osteoporosis**.[5-7] Climara and Vivelle-Dot (and generics) have an additional indication for the treatment of **hypoestrogenism due to hypogonadism, castration, or primary ovarian failure**.[5,7]

Guidelines

Hormone therapy is the most effective treatment for vasomotor symptoms associated with menopause and genitourinary symptoms of menopause.[8] Systemic estrogen therapy can be used when vasomotor symptoms are present.[9] Hormone therapy should be individualized, taking into account the indication(s) or evidence-based treatment goals and considering the woman's age and/or time since menopause in relation to initiation or continuation, the woman's personal health risks and preferences, and the balance of potential benefits and risk of hormonal versus non-hormonal therapies. Multiple guidelines, including from the American Academy of Clinical Endocrinologists (2017) and the American College of Obstetricians and Gynecologists (reaffirmed 2019), note that transdermal use of estrogen as compared with oral estrogen products may be less likely to produce thrombotic risk; although neither guidelines recommend a specific transdermal agent.[10,11]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy

Step 1: estradiol patches (generic)

Step 2: Elestrin, EstroGel, Evamist, Divigel, estradiol 0.1% gel, estradiol 0.06% gel

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient has tried brand Climara patches, brand Minivelle patches, or brand Vivelle-Dot patches, approve a Step 2 Product.

3. No other exceptions are recommended.

REFERENCES

1. EstroGel® gel [prescribing information]. Morristown, NJ: Ascend; March 2024.
2. Elestrin™ gel [prescribing information]. Canonsburg, PA: Meda; December 2023.
3. Divigel® gel [prescribing information]. Alpharetta, GA: Vertical; May 2023.
4. Evamist™ transdermal spray [prescribing information]. Allegan, MI: Padagis; December 2023.
5. Climara® patches [prescribing information]. Whippany, NJ: Bayer; December 2023.
6. Minivelle® patches [prescribing information]. Miami, FL: Noven; February 2024.
7. Vivelle-Dot® patches [prescribing information]. East Hanover, NJ: Novartis; October 2021.
8. North American Menopause Society. The 2022 hormone therapy position statement of the North American Menopause Society. *Menopause.* 2022;29:767-794.
9. North American Menopause Society (NAMS). NAMS Position Statement. The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Available at: http://www.menopause.org/publications/professional-publications/position-statements-other-reports. Accessed on May 31, 2024.
10. AACE Reproductive Endocrinology Scientific Committee. American Association of Clinical Endocrinologists and American College of Endocrinology position statement on menopause 2017 update. *Endocr Pract.* 2017:23(7):869-880.
11. The American College of Obstetricians and Gynecologists. Postmenopausal estrogen therapy: route of administration and risk of venous thromboembolism. Committee on Gynecologic Practice. Committee Opinion Number 556. April 2013 (reaffirmed 2019).
12. Estradiol gel 0.1% [prescribing information]. Florham Park, NJ: Xiromed; February 2024.
13. Estradiol gel 0.06% [prescribing information]. Bridgewater, NJ: Solaris; April 2024.

STEP THERAPY POLICY

POLICY: Fenofibrate Step Therapy Policy

- Antara® (fenofibrate capsules – Lupin)
- Fenofibrate (fenofibrate capsule – H2 Pharma)
- fenofibrate capsules and tablets (generic only)
- fenofibric acid tablets and capsules (generic only)
- Fenoglide® (fenofibrate tablets – Salix/Bausch, generic)
- Fibricor® (fenofibric acid tablets – Athena Bioscience, generic)
- Lipofen® (fenofibrate capsules – Kowa)
- TriCor® (fenofibrate tablets – AbbVie, generic)
- Trilipix® (fenofibric capsules, delayed-release – AbbVie, generic)

REVIEW DATE: 10/02/2024

OVERVIEW

Fenofibrate/fenofibric acid is a lipid regulating agent available in various oral formulations.[1-5,8-12] Several products are indicated as an adjunct to diet as follows:

- To reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (total-C), triglycerides (TG) and apolipoprotein B (Apo B), and to increase high-density lipoprotein cholesterol (HDL-C) in adults with **primary hypercholesterolemia or mixed dyslipidemia**.
- For the treatment of adults with **hypertriglyceridemia**.

Triglide and Antara differ slightly in their cited FDA-approved indications.[6,7] These agents are indicated as an adjunct to diet as follows:

- **Primary hyperlipidemia**, to reduce low-density lipoprotein cholesterol (LDL-C), in adults when use of recommended LDL-C lowering therapy is not possible.
- **Severe hypertriglyceridemia**, to reduce TG levels, in adults (with TG levels greater than or equal to 500 mg/dL).

A limitation of use is that the products have not been shown to reduce coronary heart disease morbidity and mortality in patients with type 2 diabetes mellitus.[1-12] Also, the labeling for Triglide and Antara note that markedly elevated levels of serum triglycerides (e.g., 2,000 mg/dL) may increase the risk of developing pancreatitis.[6,7] The products have been studied for use in combination with other agents.[13,14] Also, many fenofibrate products are available, both brand and generic, and some have undergone reformulations.[15]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic fenofibrate capsules (43 mg, 67 mg, 134 mg, and 200 mg), generic fenofibrate tablets (48 mg, 54 mg, 145 mg, and 160 mg), generic fenofibric acid capsules (45 mg and 135 mg), generic fenofibric acid tablets (35 mg and 105 mg)

Step 2: Antara, Fenofibrate, fenofibrate 40 mg tablets, fenofibrate 50 mg capsules, fenofibrate 120 mg tablets, fenofibrate 130 mg capsules, fenofibrate 150 mg capsules, Fenoglide, Fibricor, Lipofen, Tricor, Trilipix

CRITERIA

14. If the patient has tried one Step 1 Product, approve a Step 2 Product.

15. No other exceptions are recommended.

REFERENCES

1. TriCor® tablets [prescribing information]. North Chicago, IL: AbbVie; June 2021.
2. Lipofen® capsules [prescribing information]. Montgomery, AL: Kowa; June 2021.
3. Fenoglide® tablets [prescribing information]. Bridgewater, NJ: Salix/Bausch; June 2021.
4. Trilipix® capsules, delayed-release [prescribing information]. North Chicago, IL: AbbVie; March 2021.
5. Fibricor® tablets [prescribing information]. Athens, GA: Athena Bioscience; June 2021.
6. Antara® capsules [prescribing information]. Naples, FL: Lupin; July 2024.
7. Triglide® tablets [prescribing information]. East Brunswick, NJ: Casper; May 2024.
8. Fenofibrate capsules [prescribing information]. Baudette, MN: ANI/Cipher; June 2021.
9. Fenofibrate tablets [prescribing information]. Warren, NJ: Cipla; July 2021.
10. Fenofibric acid delayed-release pellets [prescribing information]. Morgantown, WV: Mylan; June 2021.
11. Fenofibric acid delayed release capsules [prescribing information]. Wilmington, DE: Graviti; September 2019.
12. Fenofibrate capsules [prescribing information]. Montgomery, AL: H2-Pharma; May 2014.
13. ACCORD Study Group, Ginsberg NH, Elam MB, Lovato LC, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. *N Engl J Med*. 2010;362(17):1563-1574.
14. McKeage K, Keating GM. Fenofibrate. A review of its use in dyslipidemia. *Drugs*. 2011;71(14):1917-1946.
15. Downing NS, Ross JS, Jackevicius CA, Krumholz HM. Avoidance of generic competition by Abbott Laboratories' fenofibrate franchise. *Arch Intern Med*. 2012;172(9):724-730.

STEP THERAPY POLICY

POLICY: Gabapentin Step Therapy Policy

- Gralise® (gabapentin extended release tablets – Almatica, generic)
- Horizant® (gabapentin enacarbil extended-release tablets – Arbor)
- Neurontin® (gabapentin capsules, tablets, and solution – Pfizer, generic)

REVIEW DATE: 02/07/2024

OVERVIEW

Gabapentin, gabapentin ER (Gralise, generic), and Horizant are indicated for the following uses:[1-3]

- Management of **postherpetic neuralgia** in adults.
- Gabapentin is also approved as adjunctive therapy in the treatment of **partial onset seizures**, with and without secondary generalization, in adults and children ≥ 3 years of age with epilepsy.
- Horizant is also indicated for moderate-to-severe **restless leg syndrome** (RLS) in adults.

Gabapentin ER (Gralise, generic) and gabapentin (Neurontin, generic) are analogs of the neurotransmitter gamma-aminobutyric acid (GABA).[1,2] Horizant is a prodrug of gabapentin.[3] These drugs exert their pharmacologic action by binding to the alpha-2-delta subunit of voltage-gated calcium channels.[1-3] The binding of this subunit reduces the release of several neurotransmitters including glutamate, noradrenaline, and substance P. Gabapentin is available as capsules, tablets, and oral solution; gabapentin ER and Horizant are available as extended-release (ER) tablets. Product labeling for gabapentin ER and Horizant note that they are not to be used interchangeably with other gabapentin products due to different pharmacokinetic profiles that affect frequency of administration or different plasma concentrations relative to other gabapentin products. Gabapentin ER and Horizant are dosed once daily and should be taken with evening meals, whereas gabapentin is dosed three times a day and can be taken without regard to food.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic gabapentin capsules, tablets, and oral solution

Step 2: Gralise (brand and generic), Horizant, Neurontin

CRITERIA

3. If the patient has tried one Step 1 Product (brand [Neurontin] or generic), approve a Step 2 Product.

4. No other exceptions are recommended.

REFERENCES

7. Neurontin® capsules, tablets, oral solution [prescribing information]. New York, NY: Pfizer; July 2022.
8. Gralise® tablets [prescribing information]. Morristown, NJ: Almatica; April 2023.
9. Horizant® extended-release tablets [prescribing information]. Atlanta, GA: Arbor; August 2022.

STEP THERAPY POLICY

POLICY: Gout Medications Step Therapy Policy
- Uloric® (febuxostat tablets – Takeda, generic)
- Zyloprim® (allopurinol tablets – Casper, generic)

REVIEW DATE: 01/17/2024

OVERVIEW

Allopurinol (Zyloprim, generic), a xanthine oxidase inhibitor, is indicated for the following uses:[1]
- **Signs and symptoms of primary or secondary gout** (e.g., acute attacks, tophi, joint destruction, uric acid lithiasis, and/or nephropathy) in adults.
- **Cancer therapy which causes elevations of serum and urinary uric acid levels**, in adult and pediatric patients with leukemia, lymphoma, and malignancies.
- **Recurrent calcium oxalate calculi**, in adults whose daily uric acid excretion exceeds 800 mg/day for male patients and 750 mg/day for female patients.

Febuxostat (Uloric, generic), a xanthine oxidase inhibitor, is indicated for the **chronic management of hyperuricemia in adults with gout** who have had an inadequate response to a maximally titrated dose of allopurinol, who are intolerant to allopurinol, or for whom treatment with allopurinol is not advisable.[2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: allopurinol tablets (Zyloprim, generic)

Step 2: febuxostat tablets (Uloric, generic)

CRITERIA

16. If the patient has tried one Step 1 Product, approve a Step 2 Product.

17. If the patient is receiving concomitant medications that have significant drug-drug interactions with the Step 1 Product, which are not noted with Uloric/febuxostat tablets (e.g., cyclosporine, chlorpropamide), approve the Step 2 Product.

18. No other exceptions are recommended.

REFERENCES

30. Zyloprim® tablets [prescribing information]. East Brunswick, NJ: Casper; October 2023.
31. Uloric® tablets [prescribing information]. Lexington, MA: Takeda; April 2023.

STEP THERAPY POLICY

POLICY: Hydrocortisone Acetate Suppository Step Therapy Policy

- Anucort- HC™ (hydrocortisone acetate 25 mg suppository – Cosette, [branded generic])
- Anusol-HC® (hydrocortisone acetate 25 mg suppository – Salix, generic)
- Hemmorex-HC™ (hydrocortisone acetate 25 mg or 30 mg suppository – Laser [branded generic])
- Hydrocortisone acetate suppository (25 or 30 mg – multiple manufacturers)
- Proctocort® (hydrocortisone acetate 30 mg suppository – Salix, generic)

REVIEW DATE: 01/17/2024

OVERVIEW

Anucort-HC, Anusol-HC, Hemmorex-HC, Proctocort, and generic hydrocortisone acetate suppositories are indicated for the **management of inflamed hemorrhoids, postirradiation (factitial) proctitis**; as an adjunct in the treatment of chronic ulcerative colitis; cryptitis; and other inflammatory conditions of anorectum and pruritus ani.[1-5]

Rectal corticosteroids are used to help relieve swelling, itching, and discomfort associated with rectal problems, including hemorrhoids and inflammation of the rectum caused by radiation therapy and mild or moderate ulcerative colitis. They can also be used in conjunction with systemic (oral or injectable) corticosteroids and/or other medications to treat severe disease or mild to moderate disease that has spread too far to be treated effectively by medicine inserted into the rectum alone.[4]

Anusol-HC contains 25 mg of hydrocortisone acetate and Proctocort contains 30 mg of hydrocortisone acetate.[1,2] Branded generic hydrocortisone acetate suppositories (25 mg and 30 mg) [e.g., Anucort-HC] and generic hydrocortisone acetate suppositories (25 mg and 30 mg) are available.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic hydrocortisone acetate suppository (25 mg or 30 mg), Anucort-HC (25 mg), Hemmorex-HC (25 mg or 30 mg)

Step 2: Anusol HC (25 mg), Proctocort (30 mg)

CRITERIA

3. If the patient has tried one Step 1 Product, approve a Step 2 Product.

4. No other exceptions are recommended.

REFERENCES

1. Anusol-HC® suppository [prescribing information]. Bridgewater, NJ: Salix; October 2017.
2. Proctocort® suppository [prescribing information]. Bridgewater, NJ: Salix; April 2016.
3. Hydrocortisone acetate suppository [prescribing information]. Pulaski, TN: AvKARE; January 2022.
4. Hemmorex HC™ suppository [prescribing information]. Alpharetta, GA: Laser; April 2020.
5. Anucort HC™ suppository [prescribing information]. South Plainfield, NJ: Cosette; December 2019.
6. Corticosteroids (rectal route). Updated November 2023. Available at: http://www.mayoclinic.org/drugs-supplements/corticosteroid-rectal-route/description/drg-20070430. Accessed on January 12, 2024.

STEP THERAPY POLICY

POLICY: Hydroxy-Methylglutaryl-Coenzyme A Reductase Inhibitors Step Therapy Policy

- Altoprev® (lovastatin extended-release tablets – Covis)
- Atorvaliq® (atorvastatin oral suspension – CMP)
- Caduet® (atorvastatin/amlodipine tablets – Pfizer, generic)
- Crestor® (rosuvastatin tablets – AstraZeneca, generic)
- Ezallor Sprinkle™ (rosuvastatin capsules – Sun)
- Flolipid® (simvastatin oral suspension – Salerno/Rosemont)
- Fluvastatin capsules (generic only)
- Lescol® XL (fluvastatin extended-release tablets – Novartis, generic)
- Lipitor® (atorvastatin tablets – Pfizer, generic)
- Livalo® (pitavastatin tablets – Lily/Kowa, generic)
- Mevacor® (lovastatin tablets – generic only)
- Pravachol® (pravastatin tablets – Bristol-Myers Squibb, generic)
- Roszet® (rosuvastatin and ezetimibe tablets – Althera)
- Rosuvastatin and ezetimibe tablets – SCOV3 LLC
- Vytorin® (ezetimibe/simvastatin tablets – Organon, generic)
- Zocor® (simvastatin tablets – Organon, generic)
- Zypitamag® (pitavastatin magnesium tablets – Medicure)

REVIEW DATE: 06/26/2024

OVERVIEW

Available hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (HMGs), excluding combination products, include lovastatin, simvastatin, atorvastatin, pravastatin, fluvastatin, fluvastatin extended-release, pitavastatin, rosuvastatin, Altoprev, Ezallor Sprinkle, and Zypitamag; combination products are available as well.[1-14] All of the HMGs are indicated as an **adjunct to diet for patients with primary hypercholesterolemia and/or mixed dyslipidemia** (to impact lipid parameters such as to reduce elevated total cholesterol [total-C] and low-density lipoproprotein cholesterol [LDL-C]). Several agents have additional indications, including those related to improvement in cardiovascular (CV) outcomes. Flolipid (simvastatin oral suspension) is available and it has the same indications as simvastatin tablets.[15] Atorvaliq is an oral suspension that has the same indications as atorvastatin tablets.[16] Ezallor Sprinkle has administration options for patients who cannot swallow an intact capsule whole.[3] The contents can be opened and sprinkled over soft food (e.g., applesauce, pudding). Also, Ezallor Sprinkle capsules can be opened and administered by a nasogastric tube.

Guidelines

In November 2013, the **American College of Cardiology** and the **American Heart Association** published guidelines on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk in adults[17] with an update published in 2019.[18] The guideline emphasizes the appropriate intensity of statin therapy to reduce cardiovascular risk. No statin is preferred, but instead, statins with related doses are categorized as "high-intensity" (lowers low-density lipoprotein cholesterol [LDL-C] by approximately ≥ 50%), moderate-intensity (lowers LDL-C by approximately 30% to < 50%), and low-intensity (lowers LDL-C by < 30%). Only atorvastatin and rosuvastatin are categorized as acceptable "high-intensity" statin therapies. According to the guidelines, clinical trial evidence clearly shows that ASCVD events are reduced by using the maximum-tolerated statin intensity in groups shown to benefit (e.g., those at risk). There is

relatively less evidence for non-statin medications in reducing ASCVD risk. Table 1 categorizes the different statin regimens as high-, moderate-, and low-intensity. Refer to the guideline for the most appropriate intensity for the individual patient.

Table 1. High-, Moderate-, and Low-Intensity Statin Therapy.[17,18*]

[*] Used in the randomized controlled trials reviewed by the expert panel. Of note, individual responses to statin therapy varied in the randomized controlled trials and should be expected to vary in clinical practice. There might be a biologic basis for a less-than-average response; LDL-C – Low-density lipoprotein cholesterol; [†] Evidence from one randomized controlled trial only and down titration is recommended if the patient is unable to tolerate atorvastatin 80 mg; [‡] Although simvastatin 80 mg was assessed in randomized controlled trials, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis; BID – Twice daily.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Note: When compliance with the Affordable Care Act, Health Resources and Services Administration Guidelines, and Public Health Services Act section 2713 is required and the conditions for coverage listed under the Criteria are not met, approval is granted when the requested single-entity drug is used for the primary prevention of cardiovascular disease (CVD) in an adult aged 40 to 75 years who has one or more CVD risk factors (i.e., dyslipidemia, diabetes, hypertension, or smoking) and an estimated 10-year CVD event risk of 10% or greater and who does NOT have a history of (or signs or symptoms of) CVD and, according to the prescriber, the alternative Step 1 Products would not be as medically appropriate for the patient as the requested single-entity drug.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: atorvastatin, atorvastatin/amlodipine, ezetimibe/simvastatin, fluvastatin, fluvastatin extended-release, lovastatin, pravastatin, pitavastatin, rosuvastatin, simvastatin

Step 2: Altoprev, Atorvaliq, Caduet, Crestor, Ezallor Sprinkle, Flolipid, Lescol XL, Lipitor, Livalo, Pravachol, ezetimibe and rosuvastatin (brand product), Roszet, Vytorin, Zocor, Zypitamag

CRITERIA

19. If the patient has tried one Step 1 Product, approve a Step 2 Product.

20. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve Atorvaliq, Flolipid, or Ezallor Sprinkle.

21. No other exceptions are recommended.

REFERENCES

1. Lovastatin tablets [prescribing information]. Baltimore, MD/Goa, India: Lupin/BluePoint; September 2021.
2. Crestor® tablets [prescribing information]. Wilmington, DE: AstraZeneca; July 2023.
3. Zypitamag® tablets [prescribing information]. Princeton, NJ: Medicure; January 2024.
4. Ezallor™ Sprinkle capsules [prescribing information]. Cranbury, NJ: Sun; March 2024.
5. Zocor® tablets [prescribing information]. Jersey City, NJ: Organon; August 2023.
6. Lipitor® tablets [prescribing information]. New York, NY: Pfizer, April 2024.
7. Lescol® XL extended-release tablets [prescribing information]. East Hanover, NJ: Novartis; November 2023.
8. Altoprev® extended-release tablets [prescribing information]. Zug, Switzerland: Covis; April 2024.
9. Pravachol® tablets [prescribing information]. Princeton, NJ: Bristol-Myers Squibb; May 2022.
10. Livalo® tablets [prescribing information]. Montgomery, AL: Kowa; March 2024.
11. Vytorin® tablets [prescribing information]. Jersey City, NJ: Organon; March 2024.
12. Caduet® tablets [prescribing information]. New York, NY: Pfizer; May 2024.
13. Roszet® tablets [prescribing information]. Morristown, NJ: Althera; March 2021.
14. Rosuvastatin and ezetimibe tablets [prescribing information]. Wilmington, DE: SCOV3 LLC; August 2021.
15. Flolipid® oral suspension [prescribing information]. Brooksville, FL: Salerno/Rosemont; September 2020.
16. Atorvaliq® oral suspension [prescribing information]. Farmville, NC: CMP; February 2023.
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18. Grundy SM, Stone NJ, Bailey AL, et al. ACC/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139:e1082-e1143.

STEP THERAPY POLICY

POLICY: Isotretinoin Step Therapy Policy

- Absorica® (isotretinoin capsules – Sun, generic)
- Absorica LD™ (isotretinoin capsules – Sun)
- Accutane® (isotretinoin capsules – JG Pharma, generic)
- Amnesteem® (isotretinoin capsules – Mylan, generic)
- Claravis™ (isotretinoin capsules – Teva, generic)
- Myorisan™ (isotretinoin capsules – Akorn, generic; [brand obsolete 2023])
- Zenatane™ (isotretinoin capsules – Dr Reddy's, generic)

REVIEW DATE: 01/17/2024

OVERVIEW

Isotretinoin is indicated for the treatment of **severe recalcitrant nodular acne**.[1-6]

Table 1. Available Strengths for the Isotretinoin Products.[1-6]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Accutane, Amnesteem, Claravis, isotretinoin capsules (all true generic isotreinoin products), Myorisan, Zenatane, authorized generic to Absorica (from Sun Pharmaceuticals)

Step 2: Absorica, Absorica LD

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: Absorica with DAW 9 (indicating that substitution is allowed by the prescriber but the Plan requests brand) will also count as a Step 1 Product.

2. No other exceptions are recommended.

REFERENCES

1. Amnesteem® [prescribing information]. Morgantown, WV: Mylan; August 2022.
2. Claravis™ [prescribing information]. North Wales, PA: Teva; August 2022.
3. Myorisan® [prescribing information]. Lake Forest, IL: Akorn; February 2022.
4. Zenatane™ [prescribing information]. Bachupally India: Dr. Reddy's; September 2022.
5. Absorica® and Absorica LD™ [prescribing information]. Cranbury, NJ: Sun; June 2023.
6. Accutane® [prescribing information]. Scottsdale, AZ: JG Pharma; April 2022.

LEVOTHYROXINE PRODUCTS STEP THERAPY POLICY

POLICY: Levothyroxine Products Step Therapy Policy

- Ermeza™ (levothyroxine sodium 30 mcg/mL solution – Mylan)
- Levothyroxine sodium tablets (generics)
- Tirosint®-SOL (levothyroxine sodium solution [various strengths] – IBSA Pharma)
- Thyquidity™ (levothyroxine sodium 20 mcg/mL solution – Azurity)

REVIEW DATE: 03/20/2024

OVERVIEW

All of the products contain levothyroxine sodium and are indicated for the following uses[1-4]:

- **Hypothyroidism**: As replacement therapy in primary (thyroidal), secondary (pituitary), and tertiary (hypothalamic) congenital or acquired hypothyroidism.
- **Pituitary Thyrotropin (Thyroid-Stimulating Hormone, TSH) Suppression:** As an adjunct to surgery and radioiodine therapy in the management of thyrotropin-dependent well-differentiated thyroid cancer.

Labeling for all of the products additionally contains the following Limitations of Use:

- Not indicated for suppression of benign thyroid nodules and nontoxic diffuse goiter in iodine-sufficient patients.
- Not indicated for treatment of transient hypothyroidism during the recovery phase of subacute thyroiditis.

All of the products can be used in pediatric patients, including newborns (0 to 3 months of age).[1-4] Ermeza, Thyquidity, and Tirosint-SOL were approved under the 505(b)(2) pathway and relied on efficacy data from previously approved levothyroxine products.[5-7] No new clinical efficacy studies were undertaken with any of the products.[2-4] The labeling for Ermeza states that the product may have a different concentration from other levothyroxine oral solution products and to consider the total dosage in terms of mcg and not volume when converting between products.[2] All levothyroxine products are dosed based on the patient's weight (e.g., 1.6 mcg/kg/day for adults with hypothyroidism).[1-4] Table 1 shows the availability of each levothyroxine solution.

Table 1. Availability of Levothyroxine Solutions.[2-4]

Guidelines

The American Thyroid Association guidelines for the treatment of hypothyroidism (2014) state that levothyroxine has been considered the standard of care for this condition for many years.[8] These guidelines do not address levothyroxine solutions.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. Approval for a Step 3 Product may be authorized if the patient has tried a Step 1 Product and a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product or a Step 3 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy for a Step 2 Product. Additionally, a patient with a of one Step 1 Product and one Step 2 Product within the 130-day look-back period is excluded from Step Therapy for a Step 3 Product.

Step 1: generic levothyroxine tablets

Step 2: Ermeza solution

Step 3: Thyquidity solution, Tirosint-SOL

CRITERIA

22. If the patient has tried one Step 1 Product, approve the Step 2 Product (Ermeza solution).
Note: If the patient has tried brand Synthroid (levothyroxine sodium tablet) or another brand of levothyroxine tablets, such as Levoxyl (levothyroxine sodium tablet), this would satisfy the criterion.

23. Approve the Step 2 Product (Ermeza solution) if the patient is unable to swallow or has difficulty swallowing tablets.

24. Approve either Step 3 Products (Thyquidity Solution or Tirosint-SOL) if the patient meets BOTH of the following criteria (A and B):
- **a.** Patient meets one of the following criteria (i or ii):
  - i. Patient has tried one Step 1 Product; OR
    Note: If the patient has tried brand Synthroid (levothyroxine sodium tablet) or another brand of levothyroxine tablets, such as Levoxyl (levothyroxine sodium tablet), this would satisfy the criteria for the Step 1 product.
  - ii. Patient is unable to swallow or has difficulty swallowing tablets; AND
- **b.** Patient has tried the Step 2 Product (Ermeza solution).

25. No other exceptions are recommended.

REFERENCES

32. Levothyroxine sodium tablets [prescribing information]. Bridgewater, NJ: Amneal; September 2023.
33. Ermeza™ (levothyroxine sodium solution) [prescribing information]. Morgantown, WV: Mylan Specialty; April 2022.
34. Thyquidity™ (levothyroxine sodium solution) [prescribing information]. Woburn, MA: Azurity; February 2023.
35. Tirosint®-SOL (levothyroxine sodium solution) [prescribing information]. Parsippany, NJ: IBSA Pharma; November 2023.
36. FDA. Drugs@FDA. Ermeza approval letter. May 2022. Available at: Ermeza (levothyroxine sodium) oral solution. (fda.gov). Accessed on March 11, 2024.
37. FDA. Drugs@FDA. Thyquidity approval letter. November 2020. Available at: Thyquidity (levothyroxine sodium) oral solution (fda.gov). Accessed on March 11, 2024.
38. FDA. Drugs@FDA. Tirosint-SOL approval letter. December 2016. Available at: Tirosint-SOL (levothyroxine sodium oral solution) (fda.gov). Accessed on March 11, 2024.
39. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association task force on thyroid hormone replacement. *Thyroid.* 2014;24(12):1670-751.

STEP THERAPY POLICY

POLICY: Methotrexate Injection Step Therapy Policy

- Methotrexate sodium (solution for injection - various manufacturers)
- Otrexup® (methotrexate subcutaneous injection autoinjector– Antares)
- Rasuvo® (methotrexate subcutaneous injection autoinjector – Medac)
- RediTrex® (methotrexate subcutaneous injection prefilled syringe – Cumberland [*obsolete 11/01/2023*])

REVIEW DATE: 12/04/2024

OVERVIEW

Methotrexate has been widely studied and is commonly used for treatment of **inflammatory conditions**, including rheumatoid arthritis, juvenile idiopathic arthritis, and plaque psoriasis.[1]

All of the injectable methotrexate products require proper patient training in sterile injection technique and require a patient to have the manual dexterity to self-inject.[5] For inflammatory conditions, the dose of methotrexate is initiated low and adjusted gradually to achieve optimal response and/or tolerability, generally to a maximum of 25 to 30 mg/week.[1,6-8] Flexibility to decrease or increase methotrexate dosing, including in 2.5-mg increments, may be needed in clinical practice. Generic injectable methotrexate is available as a 25 mg/mL injection solution (single-dose and multi-dose vials) and provides flexibility in dose adjustments.[5] Otrexup, Rasuvo, and RediTrex are available as preservative-free, single-dose injections for subcutaneous use.[6-8] A formulation other than Otrexup, Rasuvo, or RediTrex should be used for patients who require a route of administration other than subcutaneous, for doses that are not available in the respective product, and for dose adjustments in < 2.5 mg increments.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Unless administered by a healthcare provider, all of the injectable methotrexate products, including Rasuvo, Otrexup, and RediTrex, require proper patient training in sterile injection technique and require a patient or caregiver to have the manual dexterity to inject.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic methotrexate injection (single- or multi-dose vials)

Step 2: Otrexup, Rasuvo, RediTrex

CRITERIA

26. If the patient has tried ONE Step 1 Product, approve a Step 2 Product.

27. If, according to the prescriber, the patient and/or caregiver is/are unable to administer generic methotrexate injection (single-dose or multi-dose vial NOT including Otrexup, Rasuvo, or RediTrex), approve a Step 2 Product.

28. No other exceptions are recommended.

REFERENCES

40. Methotrexate injection [prescribing information]. Durham, NC: Accord; June 2021.
41. Braun J, Kästner P, Flaxenberg P, et al. Comparison of the clinical efficacy and safety of subcutaneous versus oral methotrexate in patients with active rheumatoid arthritis: results of a six-month, multicenter, randomized, double-blind, controlled, phase IV trial. *Arthritis Rheum.* 2008;58(1):73-81.
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45. Otrexup® subcutaneous injection [prescribing information]. Ewing, NJ: Antares; November 2022.
46. Rasuvo® subcutaneous injection [prescribing information]. Chicago, IL: Medac; September 2023.
47. RediTrex® subcutaneous injection [prescribing information]. Nashville, TN: Cumberland; November 2019.

STEP THERAPY POLICY

POLICY: Migraine Medication Step Therapy Policy

Injectable Triptans

- Imitrex® (sumatriptan injection – GlaxoSmithKline, generic)
- Zembrace® SymTouch® (sumatriptan injection – Dr. Reddy's Labs)

Oral Triptans

- Almotriptan tablets (generic to discontinued Axert®)
- Amerge® (naratriptan tablets – GlaxoSmithKline [brand discontinued 7/2022], generic)
- Frova® (frovatriptan tablets – Endo, generic)
- Imitrex® (sumatriptan tablets – GlaxoSmithKline, generic)
- Maxalt® (rizatriptan tablets – Merck, generic)
- Maxalt MLT® (rizatriptan orally disintegrating tablets – Merck, generic)
- Relpax® (eletriptan tablets – Pfizer, generic)
- Treximet® (sumatriptan and naproxen sodium tablets – Pernix, generic)
- Zomig® (zolmitriptan tablets – AstraZeneca [brand discontinued 1/2023], generic)
- Zomig-ZMT® (zolmitriptan orally disintegrating tablets – AstraZeneca [brand discontinued 8/2021], generic)

Nasal Medications

- Imitrex® (sumatriptan nasal spray – GlaxoSmithKline, generic)
- Migranal® (dihydroergotamine mesylate nasal spray – Valeant, generic)
- Onzetra® Xsail® (sumatriptan nasal powder – Currax)
- Tosymra® (sumatriptan nasal spray – Promius)
- Trudhesa™ (dihydroergotamine mesylate nasal spray – Impel)
- Zomig® (zolmitriptan nasal spray – AstraZeneca, generic)

REVIEW DATE: 04/03/2024

OVERVIEW

All of the triptan medications, including Treximet (the combination sumatriptan-naproxen sodium agent), are indicated for the **treatment of migraine headache** with or without aura in adults and are not intended to be used as prophylactic migraine therapy or to manage hemiplegic or basilar migraine.[1-14] Only sumatriptan injection is approved for the treatment of cluster headache.[10] Safety and efficacy have not been established for treatment of cluster headache for the oral dosage forms of all triptans.[1-8] Some of the triptan medications are also indicated for use in children and/or adolescents. Almotriptan is approved for the treatment of migraine headache pain in adolescent patients 12 to 17 years of age with a history of migraine attacks with or without aura usually lasting 4 hours or more (when untreated).[6] Rizatriptan is approved for the acute treatment of migraine with or without aura in patients ≥ 6 years of age.[3] Treximet and zolmitriptan nasal spray are approved for the acute treatment of migraine with or without aura in patients ≥ 12 years of age.[8,11]

Rizatriptan orally disintegrating tablets and zolmitriptan orally disintegrating tablets offer the convenience of not requiring liquids for oral administration.[4,5] Treximet offers the convenience of two agents (triptan

and non-steroidal anti-inflammatory drug [NSAID]) with pharmacologically different mechanisms of action in one tablet.[9]

Migranal and Trudhesa, ergot alkaloids, are nasal sprays indicated for the **acute treatment of migraine headaches** in adults with or without aura.[15,16] Migranal and Trudhesa are not intended for the prophylactic therapy of migraine or for the management of hemiplegic or basilar migraine.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic almotriptan tablets, generic eletriptan tablets, generic frovatriptan tablets, generic naratriptan tablets, generic rizatriptan tablets, generic rizatriptan orally disintegrating tablets, generic sumatriptan tablets, generic sumatriptan nasal spray, generic sumatriptan injection, generic zolmitriptan orally disintegrating tablets, generic zolmitriptan tablets

Step 2: Amerge tablets, Frova tablets, Imitrex tablets, Imitrex Nasal Spray, Imitrex Injection, Maxalt tablets, Maxalt MLT, Migranal (brand and generic), Onzetra Xsail, Relpax, Tosymra, Treximet tablets (brand and generic), Trudhesa, Zembrace Symtouch, Zomig tablets, Zomig-ZMT, Zomig nasal spray, zolmitriptan nasal spray

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: Zomig Nasal Spray with DAW 9 (indicating that substitution is allowed by the prescriber but the Plan requests brand) will also count as a Step 1 Product.

2. No other exceptions are recommended.

REFERENCES

1. Frova® tablets [prescribing information]. Malvern, PA; Endo; August 2018.
2. Amerge® tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; November 2016.
3. Maxalt® tablets and Maxalt-MLT® orally disintegrating tablets [prescribing information]. Whitehouse Station, NJ: Merck; October 2019.
4. Zomig® tablets and Zomig-ZMT® orally disintegrating tablets [prescribing information]. Wilmington, DE: AstraZeneca; December 2018.
5. Imitrex® tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2020.
6. Almotriptan tablets [prescribing information]. Morgantown, WV: Mylan; May 2017.
7. Relpax® tablets [prescribing information]. New York, NY: Pfizer; March 2020.
8. Treximet® tablets [prescribing information]. Morristown, NJ: Pernix; April 2021.
9. Imitrex® nasal spray [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2017.
10. Imitrex® injection [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2021.
11. Zomig® nasal spray [prescribing information]. Wilmington, DE: AstraZeneca; December 2018.
12. Onzetra® Xsail® nasal powder [prescribing information]. Morristown, NJ: Currax; December 2019.
13. Zembrace® SymTouch® injection [prescribing information]. Princeton, NJ: Promius; June 2019.
14. Tosymra® nasal spray [prescribing information]. Princeton, NJ: Promius; January 2019.

15. Migranal® nasal spray [prescribing information]. Bridgewater, NJ: Valeant; April 2022.
16. Trudhesa™ nasal spray [prescribing information]. Seattle, WA: Impel; September 2021.

STEP THERAPY POLICY

POLICY: Nasal Steroids Step Therapy Policy

- Beconase AQ® (beclomethasone nasal spray – GlaxoSmithKline)
- Dymista® (azelastine hydrochloride/fluticasone propionate nasal spray – MEDA, generic)
- flunisolide nasal spray (generic only)
- fluticasone propionate nasal spray (generic only)
- mometasone furoate nasal spray (generic only)
- Omnaris® (ciclesonide nasal spray – Covis)
- Qnasl®/Qnasl® Children's (beclomethasone dipropionate nasal aerosol – Teva)
- Ryaltris® (olopatadine hydrochloride/mometasone furoate nasal spray – Hikma)
- Xhance® (fluticasone propionate nasal spray – OptiNose)
- Zetonna® (ciclesonide nasal aerosol – Covis)

REVIEW DATE: 05/22/2024

OVERVIEW

Prescription nasal corticosteroids, with the exception of Xhance, are indicated for the treatment of symptoms of seasonal allergic rhinitis (SAR) and/or perennial allergic rhinitis (PAR).[1-8,19] Some of the agents in the class are also approved for additional indications (refer to Table 1 for a complete list of FDA-approved indications). Xhance is indicated for the treatment of chronic rhinosinusitis (CRS) with or without nasal polyps in adults.[9] Xhance utilizes an OptiNose® Exhalation Delivery System (EDS) for bi-directional drug delivery, which differs from traditional nasal sprays.[9,10] Xhance and mometasone nasal spray provided comparable benefits in terms of polyp grade and congestion scores.[4,9] In addition to mometasone and Beconase AQ, which are also indicated for use in patients with nasal polyps, several of the other nasal steroids have been proven effective in reducing nasal polyp size and associated symptoms in clinical trials.[11-18] The FDA-approvals of several other nasal steroids have been changed from prescription to over-the-counter (OTC) status. OTC nasal steroid products are not addressed in this policy. Prescription brand Nasonex® (mometasone nasal spray) was indicated in patients ≥ 2 years of age prior to its approval being switched from a prescription product to an OTC product. Generic prescription mometasone nasal spray remains on the market and now is indicated in patients ≥ 12 years of age. However, the same data that supported Nasonex's use in younger patients supports the use of mometasone nasal spray.

Table 1. Prescription Nasal Steroid Indications.[1-9,19]
Table 1 (continued). Prescription Nasal Steroid Indications.[1-9,19]

SAR – Seasonal allergic rhinitis; PAR – Perennial allergic rhinitis; VMR – Vasomotor rhinitis; * Prevention of nasal polyp recurrence following surgery; CRSwNP – Chronic rhinosinusitis with nasal polyps; ^ Prescription mometasone furoate is indicated for prophylaxis of seasonal allergic rhinitis (in patients ≥ 12 years), and treatment of nasal polyps (in patients ≥ 18 years).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration. Note: Over-the-counter nasal steroids are not addressed in this policy.

Automation: A patient with a of one Step 1 drug within the 130-day look-back period is excluded from step therapy.

Step 1: fluticasone propionate nasal spray

Step 2: azelastine hydrochloride/fluticasone propionate nasal spray, Beconase AQ, Dymista, flunisolide nasal spray, mometasone furoate nasal spray, Omnaris, Qnasl, Qnasl Children's, Ryaltris, Xhance, Zetonna

CRITERIA

29. If the patient has tried one Step 1 Product, approve a Step 2 Product.

30. If the patient is < 4 years of age, approve mometasone furoate nasal spray.

31. No other exceptions are recommended.

REFERENCES

6. Beconase AQ® nasal spray [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; February 2021.
7. Flonase® nasal spray [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; January 2019.
8. Flunisolide solution [prescribing information]. Bridgewater, NJ: Bausch & Lomb; February 2024.
9. Nasonex® [prescribing information]. Whitehouse Station, NJ: Merck; June 2022.
10. Omnaris® nasal spray [prescribing information]. Zug, Switzerland: Covis; November 2022.
11. Qnasl®/Qnasl® Children's [prescribing information]. Frazer, PA: Teva; September 2022.
12. Zetonna® [prescribing information]. Zug, Switzerland: Covis; February 2023.
13. Dymista® nasal spray [prescribing information]. Somerset, New Jersey: MEDA; August 2022.
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21. Bachert C. Evidence-based management of nasal polyposis by intranasal corticosteroids: from the cause to the clinic. *Int Arch Allergy Immunol*. 2011;155:309-321.
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23. Vento SI, Blomgren K, Hytoren M, et al. Prevention of relapses of nasal polyposis with intranasal triamcinolone acetonide after polyp surgery: a prospective double-blind, placebo-controlled, randomized study with a 9-month follow-up. *Clin. Otolaryngol*. 2012;37:117-123.
24. Ryaltris® nasal spray [prescribing information]. Columbus, OH: Hikma Specialty; August 2023.

STEP THERAPY POLICY

POLICY: Nonsteroidal Anti-Inflammatory Drugs Step Therapy Policy

REVIEW DATE: 01/17/2024; selected revision 02/14/2024

Note: This list is not all-inclusive.
NSAID – Nonsterioidal anti-inflammatory drug; OTC – Over-the-counter.

OVERVIEW

Nonsteroidal anti-inflammatory drugs (NSAIDs) are indicated primarily for the **treatment of acute and chronic conditions that require an agent with analgesic and anti-inflammatory activity**, although other uses exist.[1] For example, Cambia® (diclofenac potassium oral solution) is the only NSAID indicated for the acute treatment of migraine attacks with or without aura in adults ≥ 18 years of age[2]; however, other NSAIDs are also supported in clinical practice guidelines.[3]

Overall, it appears that NSAID products have similar clinical efficacy when given at equipotent doses for the management of acute pain and other pain-related conditions; however, individual responses to NSAIDs may vary among patients for reasons that are not well understood. No one product can be distinguished from another on a consistent basis. All of the products have Boxed Warnings outlining cardiovascular (CV) and gastrointestinal (GI) risks.[1]

Guidelines and Recommendations

The American College of Rheumatology (ACR)/Arthritis Foundation hand, hip, and knee osteoarthritis (OA) guidelines (2019) strongly recommend topical NSAIDs for knee OA and conditionally recommend topical NSAIDs for hand OA.[4] Topical NSAIDs are not expected to be efficacious in hip OA due to the depth of the affected joint. Oral NSAIDs are strongly recommended for patients with hand, hip, and/or knee OA and are recommended over all other oral therapies. These agents are the mainstay of pharmacological management of OA. Safe use of NSAIDs is recommended, including utilization of the lowest possible doses for the shortest period of time. The relative merits of different oral NSAIDs were considered outside the scope of the guideline review.

The European League Against Rheumatism (EULAR) hand OA guidelines (2018) state that optimal management of hand OA generally requires a multidisciplinary approach, including non-pharmacological therapies and pharmacological therapies.[5] The guidelines specifically recommend topical treatments as preferred over oral therapies because of safety reasons. Topical NSAIDs are the first pharmacological topical treatment of choice for hand OA. The guidelines cite pooled safety data comparing topical diclofenac gel with placebo, which showed similar low rates of adverse events (AEs) in subgroups of low-risk versus high-risk patients (≥ 65 years of age with comorbid hypertension, type 2 diabetes or cerebrovascular and/or CV disease). The guidelines additionally note that when a large number of joints are affected, oral pharmacological treatment may be preferred.

OA Research Society International guidelines for non-surgical management of knee, hip, and polyarticular OA (2019) comment on oral and topical NSAID use in a variety of settings.[6] For knee OA, topical NSAIDs are strongly recommended (Level 1A) for patients without comorbidities, as well as for patients with GI or CV comorbidities. For patients with GI comorbidities, selective cyclooxygenase-2 (COX-2) inhibitors and nonselective oral NSAIDs, in combination with a proton pump inhibitor (PPI), were conditionally recommended due to their benefits on pain and functional outcomes. Topical and oral NSAIDs are both conditionally recommended in the setting of widespread pain; it is noted that for topical NSAIDs, the number of joints being treated should be monitored due to potential risk of exceeding recommended doses. Oral NSAIDs, but not topical NSAIDs, are conditionally recommended in the setting of hip OA.

Beers Criteria

In 2023, the American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults.[7] The Beers Criteria acknowledge that many nonselective NSAIDs increase the risk of GI bleeding or peptic ulcer disease in high-risk groups, which include patients > 75 years of age or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. It is noted that use of a PPI or misoprostol reduces but does not eliminate the risks. Indomethacin and ketorolac (including the parenteral

formulation) should be avoided due to the increased risk of GI bleeding/peptic ulcer disease and acute kidney injury in older adults. Indomethacin is more likely to cause central nervous system AEs and appears to have the most AEs among the NSAIDs. NSAIDs and COX-2 inhibitors should be avoided in patients with symptomatic heart failure due to the potential to promote fluid retention and/or exacerbate heart failure. In patients with kidney or urinary tract disease (creatinine clearance < 30 mL/min) it is noted that NSAIDs (non-COX and COX selective, oral and parenteral, nonacetylate salicylates) may increase the risk of acute kidney injury and further decline in renal function. It is recommended to avoid these agents.

POLICY STATEMENT

This program has been developed to encourage the use of two Step 1a Products prior to the use of a Step 2a Product. Of note, naproxen/esomeprazole delayed-release tablets (Vimovo, generic) and ibuprofen/famotidine tablets (Duexis, generic) are not included in Step 2a. A trial of one prescription naproxen product (Step 1b) and one prescription proton pump inhibitor (PPI) [Step 1b] is required prior to the use of naproxen/esomeprazole delayed-release tablets (Vimovo, generic) [Step 2b]. A trial of one prescription oral ibuprofen product (Step 1c) and one prescription oral histamine$_2$-receptor antagonist (H_2RA) [Step 1c] is required prior to the use of ibuprofen/famotidine tablets (Duexis, generic) [Step 2c]. If the Step Therapy rule is not met for a Step 2 Product (a, b, or c) at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: For single-entity NSAIDs (Step 2a), a patient with a history of two Step 1a Products within the 130-day look-back period is excluded from Step Therapy. (Note: Naproxen/esomeprazole delayed-release tablets [Vimovo, generic] and ibuprofen/famotidine tablets [Duexis, generic] are not included in Step 2a.) For naproxen/esomeprazole delayed-release tablets (Vimovo, generic) [Step 2b], a patient with a history of one prescription PPI and one naproxen product within the 130-day look-back period is excluded from Step Therapy. For ibuprofen/famotidine tablets (Duexis, generic) [Step 2c], a patient with a history of one prescription H_2RA and one prescription oral ibuprofen product within the 130-day look-back period is excluded from Step Therapy.

Step 1a/2a

Step 1a NSAIDs:

- Cataflam
- diclofenac potassium 50 mg
- diclofenac potassium 25 mg capsules
- diclofenac sodium (IR and ER)
- diclofenac sodium and misoprostol
- diclofenac sodium topical solution 1.5%*
- etodolac (IR and ER)
- flurbiprofen
- ibuprofen
- indomethacin (IR and ER)
- ketoprofen IR 50 mg and 75 mg
- ketorolac (tablets)
- meclofenamate
- mefenamic acid
- meloxicam tablets
- nabumetone
- naproxen**
- oxaprozin

- piroxicam
- sulindac
- tolmetin 200 mg

Step 2a NSAIDs:

- Anaprox DS
- Arthrotec
- Cambia, diclofenac potassium powder packet
- Coxanto
- Daypro
- diclofenac potassium 25 mg tablets
- diclofenac sodium 1% topical gel*
- diclofenac sodium 2% topical solution*
- Feldene
- Fenoprofen (brand), fenoprofen 600 mg
- Fenortho
- Flector patch, diclofenac epolamine 1.3% patch*
- Indocin
- indomethacin oral suspension
- ketoprofen ER 200 mg
- ketoprofen IR 25 mg
- Licart*
- Lodine
- Lofena
- meloxicam capsules
- meloxicam suspension
- Mobic
- Nalfon
- Naprelan and generics
- Naprosyn, EC-Naprosyn, and generic suspension
- Pennsaid 2%*
- Qmiiz
- Relafen
- Relafen DS
- Sprix, ketorolac nasal spray
- Tivorbex, indomethacin 20 mg capsule
- tolmetin 400 mg, 600 mg
- Vivlodex
- Voltaren Gel 1%*
- Voltaren XR
- Zipsor
- Zorvolex, diclofenac 35 mg capsule

IR – Immediate-release; ER – Extended-release
* Denotes topical product
** Some generic naproxen products are Step 2a

Step 1b/2b

Step 1b (brand or generic):

- Prescription naproxen sodium
- Prescription naproxen

AND

- Prescription dexlansoprazole
- Prescription esomeprazole magnesium
- Prescription esomeprazole strontium
- Prescription lansoprazole
- Prescription omeprazole
- Prescription omeprazole magnesium
- Prescription omeprazole/sodium bicarbonate
- Prescription pantoprazole (oral)
- Prescription rabeprazole

Step 2b NSAID:

- Vimovo
- naproxen/esomeprazole delayed-release tablets

Step 1c/2c

Step 1c (brand or generic):

- Prescription ibuprofen (oral)

AND

- Prescription cimetidine (oral)
- Prescription famotidine (oral)
- Prescription nizatidine (oral)
- Prescription ranitidine (oral)

Step 2c NSAID:

- Duexis
- ibuprofen/famotidine tablets

CRITERIA

Step 2a NSAIDs

1. If the patient has tried two different Step 1a prescription-strength NSAIDs for the current condition, approve a Step 2a NSAID.
Note: Celecoxib is accepted as a generic NSAID. Also, over-the-counter (OTC) NSAIDs count as alternatives if the patient used prescription-strength doses.

2. If the patient has tried ibuprofen suspension, approve naproxen suspension, meloxicam suspension, or Indocin suspension.
Note: OTC ibuprofen suspension would count as an alternative.

3. If the patient has tried generic diclofenac sodium topical solution 1.5% and the patient has difficulty swallowing or cannot swallow tablets or liquid dosage forms (solution/suspension), approve ketorolac nasal spray (Sprix, authorized generic), Pennsaid 2%, diclofenac sodium 2% topical solution, Flector Patch, diclofenac epolamine 1.3% patch, Licart topical system, diclofenac sodium 1% topical gel, or Voltaren Gel.

4. If the patient has tried generic diclofenac sodium topical solution 1.5% and the patient has a chronic musculoskeletal pain condition (e.g., osteoarthritis) and is at risk of NSAID-associated toxicity, approve Pennsaid 2%, diclofenac sodium 2% topical solution, diclofenac sodium 1% topical gel, or Voltaren Gel.
Note: Examples of risk factors of NSAID-associated toxicity include patients with a previous gastrointestinal bleed, of peptic ulcer disease, impaired renal function, cardiovascular disease, hypertension, heart failure, elderly patients with impaired hepatic function, or taking concomitant anticoagulants.

5. If the patient has tried generic diclofenac sodium topical solution 1.5% and the patient has hand or knee osteoarthritis, approve Pennsaid 2%, diclofenac sodium 2% topical solution, diclofenac sodium 1% topical gel, or Voltaren Gel.

6. No other exceptions are recommended.

Step 2b NSAID (Vimovo, generic)

1. If the patient has tried one prescription proton pump inhibitor (PPI) [e.g., omeprazole, lansoprazole, pantoprazole] and one prescription naproxen product (brand or generic), approve naproxen/esomeprazole delayed-release tablets (Vimovo, generic).
Note: Do not approve naproxen/esomeprazole delayed-release tablets (Vimovo, generic) if the patient has only tried over-the-counter (OTC) naproxen, NSAIDs other than naproxen, a COX-2 inhibitor (celecoxib), or OTC PPIs.
Note: Separate trials of a prescription PPI and a prescription naproxen product are required; a previous trial of Vimovo or generic naproxen/esomeprazole does not count.

2. No other exceptions are recommended.

Step 2c NSAID (Duexis, generic)

1. If the patient has tried one prescription histamine$_2$-receptor antagonist (H_2RA) [e.g., famotidine, ranitidine, nizatidine] and one prescription ibuprofen product (brand or generic), approve ibuprofen/famotidine tablets (Duexis, generic).

Note: Do not approve ibuprofen/famotidine tablets (Duexis, generic) if the patient has only tried over-the-counter (OTC) ibuprofen, NSAIDs other than ibuprofen, a COX-2 inhibitor (celecoxib), or OTC H_2RAs.
Note: Separate trials of a prescription H_2RA and a prescription ibuprofen product are required; a previous trial of Duexis or generic ibuprofen/famotidine does not count.

2. No other exceptions are recommended.

REFERENCES

1. Facts and Comparisons Online®. Wolters Kluwer Health, Inc.; Last updated September 1, 2023. Available at: http://fco.factsandcomparisons.com/action/home. Accessed on January 9, 2024. Search term: Nonsteroidal anti-inflammatory agents.
2. Cambia® oral solution [prescribing information]. Lake Forest, IL: Assertio; April 2021.
3. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019; 59:1-18.
4. Kolasinki SL, Neogi T, Hochberg MC, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the management of osteoarthritis of the hand, hip, and knee. *Arthritis Rheumatol*. 2020; 72(2):220–233.
5. Kloppenburg M, Kroon F, Blanco FJ, et al. 2018 update of the EULAR recommendations for the management of hand osteoarthritis. *Ann Rheum Dis.* 2019; 78:16-24.
6. Bannuru RR, Osani MC, Vaysbrot EE, et al. OARSI guidelines for the non-surgical management of knee, hip, and polyarticular osteoarthritis. *Osteoarthritis Cartilage*. 2019; 27(11):1578-1589.
7. The American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*. 2023;71(7):2052-2081.

STEP THERAPY POLICY

POLICY: Ophthalmic – Glaucoma – Alpha-Adrenergic Agonists Step Therapy Policy

- Alphagan® P (brimonidine tartrate 0.1% ophthalmic solution; 0.15% ophthalmic solution – Allergan, generic)
- Apraclonidine 0.5% ophthalmic solution (generic only)
- Brimonidine tartrate 0.2% ophthalmic solution (generic only)
- Iopidine® (apraclonidine 1% ophthalmic solution – Alcon)

REVIEW DATE: 10/23/2024

OVERVIEW

The brimonidine tartrate ophthalmic products (0.1%, 0.15%, and 0.2% strengths) are indicated for the **reduction of elevated intraocular pressure** (IOP) in patients with open-angle glaucoma or ocular hypertension.[1,2] Apraclonidine 0.5% ophthalmic solution is indicated as short-term adjunctive therapy in patients on maximally tolerated medical therapy who require additional **IOP reduction**.[3] Patients on maximally tolerated medical therapy who are treated with apraclonidine 0.5% ophthalmic solution to delay surgery should have frequent follow-up examinations and treatment should be discontinued if the IOP rises significantly. Iopidine 1% is indicated to **control or prevent post-surgical elevations in IOP that occur in patients after argon laser trabeculoplasty, argon laser iridotomy or Nd:YAG posterior capsulotomy**.[4]

Brimonidine 0.1% ophthalmic solution and brimonidine 0.15% ophthalmic solution (generics for Alphagan P) contain the preservative Purite® 0.005%.[1] Brimonidine 0.2% ophthalmic solution contains the preservative benzalkonium chloride 0.005%.[2] Iopidine 1% and apraclonidine 0.5% ophthalmic solution contain the preservative benzalkonium chloride 0.01%.[3,4]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic apraclonidine 0.5% ophthalmic solution, generic brimonidine tartrate 0.1% ophthalmic solution, generic brimonidine tartrate 0.15% ophthalmic solution, generic brimonidine tartrate 0.2% ophthalmic solution

Step 2: Alphagan P 0.1%, Alphagan P 0.15%, Iopidine 1%

CRITERIA

32. If the patient has tried one Step 1 Product, approve a Step 2 Product.

33. If the patient is undergoing argon laser trabeculoplasty, argon laser iridotomy or Nd:YAG posterior capsulotomy, approve Iopidine 1%.

34. No other exceptions are recommended.

REFERENCES

1. Alphagan P 0.1% and 0.15% [prescribing information]. North Chicago, IL: Abbvie; June 2024.
2. Brimonidine 0.2% ophthalmic solution [prescribing information]. Gurnee, IL: Akorn; May 2022.
3. Apraclonidine 0.5% ophthalmic solution [prescribing information]. Gurnee, IL: Akorn; January 2022.
4. Iopidine® 1% ophthalmic solution [prescribing information]. Nashville, TN: Harrow Eye; February 2023.

STEP THERAPY POLICY

POLICY: Ophthalmic – Glaucoma – Beta-Adrenergic Blockers Step Therapy Policy

- Betaxolol 0.5% ophthalmic solution (generic only)
- Betimol® (timolol 0.25% and 0.5% ophthalmic solution – Akorn)
- Carteolol 1% ophthalmic solution (generic only)
- Istalol® (timolol maleate 0.5% ophthalmic solution – Bausch + Lomb, generic)
- Levobunolol 0.5% ophthalmic solution (generic only)
- Timoptic® (timolol maleate 0.25% and 0.5% ophthalmic solution – Bausch + Lomb, generic)
- Timoptic® in Ocudose® (timolol maleate 0.25% and 0.5% ophthalmic solution – Bausch + Lomb, generic)
- Timoptic XE® (timolol maleate 0.25% and 0.5% ophthalmic gel forming solution – Bausch + Lomb, generic)

REVIEW DATE: 10/23/2024

OVERVIEW

The beta-adrenergic blocker ophthalmic products are indicated for the treatment of **elevated intraocular pressure (IOP)** in patients with ocular hypertension or open-angle glaucoma.[1-7]

Ophthalmic beta-adrenergic blockers have demonstrated good efficacy and tolerability and are commonly prescribed to treat glaucoma. In general, ophthalmic beta-adrenergic blockers lower IOP by 20% to 25%.[8]

Timoptic in Ocudose is a preservative-free product.[6] All of the other listed ophthalmic beta-blockers are preserved with benzalkonium chloride (BAK), except timolol gel forming solution, which is preserved with benzododecinium bromide.[1-5,7]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic betaxolol 0.5% ophthalmic solution, generic carteolol 1% ophthalmic solution, generic levobunolol 0.5% ophthalmic solution, generic timolol maleate 0.25% ophthalmic gel forming solution, generic timolol maleate 0.5% ophthalmic gel forming solution, generic timolol maleate 0.25% ophthalmic solution, generic timolol maleate 0.5% ophthalmic solution, generic timolol maleate 0.25% ophthalmic solution (generic to Timoptic in Ocudose), generic timolol maleate 0.5% ophthalmic solution (generic to Timoptic in Ocudose)

Step 2: Betimol, Istalol, Timoptic, Timoptic in Ocudose, Timoptic XE

CRITERIA

35. If the patient has tried one Step 1 Product, approve a Step 2 Product.

36. No other exceptions are recommended.

REFERENCES

48. Istalol® ophthalmic solution [prescribing information]. Tampa, FL: Bausch + Lomb; March 2022.
49. Timoptic® ophthalmic solution [prescribing information]. Bridgewater, NJ: Bausch + Lomb; April 2022.
50. Timoptic XE® ophthalmic gel forming solution [prescribing information]. Bridgewater, NJ: Bausch + Lomb; March 2022.
51. Betaxolol 0.5% ophthalmic solution [prescribing information]. Lake Forest, IL: Akorn; June 2016.
52. Carteolol 1% ophthalmic solution [prescribing information]. Fort Worth, TX: Alcon; August 2021.
53. Timoptic® in Ocudose® ophthalmic solution [prescribing information]. Bridgewater, NJ: Bausch + Lomb; April 2022.
54. Betimol® ophthalmic solution [prescribing information]. Waltham, MA: Thea; May 2023.
55. Prum BE, Rosenberg LF, Gedde SJ, et al. The American Academy of Ophthalmology. Primary Open-Angle Glaucoma Preferred Practice Pattern®. 2021. Available at: https://www.aaojournal.org/article/S0161-6420(20)31024-1/fulltext. Accessed on October 17, 2024.

STEP THERAPY POLICY

POLICY: Ophthalmic – Glaucoma – Carbonic Anhydrase Inhibitors Step Therapy Policy
- Trusopt® (dorzolamide 2% ophthalmic solution – Merck, generic)

REVIEW DATE: 10/23/2024

OVERVIEW

Dorzolamide 2% ophthalmic solution is indicated in the treatment of **elevated intraocular pressure (IOP)** in patients with ocular hypertension or open-angle glaucoma.[1]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic dorzolamide 2% ophthalmic solution

Step 2: Trusopt

CRITERIA

1. If the patient has tried one Step 1 drug, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

56. Dorzolamide 2% ophthalmic solution [prescribing information]. Bridgewater, NJ: Bausch & Lomb; December 2022.

STEP THERAPY POLICY

POLICY: Ophthalmic – Glaucoma – Combination Products Step Therapy Policy

- Combigan® (brimonidine tartrate 0.2%/timolol maleate 0.5% ophthalmic solution – Allergan, generic)
- Cosopt® (dorzolamide hydrochloride 2%/timolol maleate 0.5% ophthalmic solution – Thea, generic)
- Cosopt® PF (dorzolamide hydrochloride 2%/timolol maleate 0.5% ophthalmic solution – Thea, generic)

REVIEW DATE: 10/23/2024

OVERVIEW

Combigan, a combination product containing brimonidine and timolol, is indicated for the reduction of **elevated intraocular pressure (IOP)** in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP.[1] Combigan is preserved with benzalkonium chloride. Both Cosopt and Cosopt PF contain dorzolamide and timolol and are indicated for the reduction of **elevated IOP** in patients with open-angle glaucoma or ocular hypertension who are insufficiently responsive to beta-blockers (failed to achieve target IOP determined after multiple measurements over time).[2,3] These two products contain the same ingredients in the same concentrations; the only difference is that Cosopt is preserved with benzalkonium chloride and Cosopt PF does not contain a preservative.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic brimonidine 0.2%/ timolol maleate 0.5% ophthalmic solution (generic Combigan), generic dorzolamide 2%/timolol maleate 0.5% ophthalmic solution (generic Cosopt), generic dorzolamide 2%/ timolol maleate 0.5% ophthalmic solution (generic Cosopt PF)

Step 2: Combigan, Cosopt, Cosopt PF

CRITERIA

37. If the patient has tried one Step 1 Product, approve a Step 2 Product.

38. No other exceptions are recommended.

REFERENCES

57. Combigan® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; July 2024.
58. Cosopt® ophthalmic solution [prescribing information]. Waltham, MA: Thea; May 2023.
59. Cosopt® PF ophthalmic solution [prescribing information]. Lexington, MA: Thea; May 2022.

STEP THERAPY POLICY

POLICY: Ophthalmic – Glaucoma – Prostaglandins and Rho Kinase Inhibitors Step Therapy Policy

- Bimatoprost 0.03% ophthalmic solution (generic to discontinued Lumigan® 0.03% ophthalmic solution)
- Iyuzeh™ (latanoprost 0.005% ophthalmic solution – Thea)
- Lumigan® (bimatoprost 0.01%ophthalmic solution – Allergan)
- Rhopressa® (netarsudil 0.02% ophthalmic solution – Aerie)
- Rocklatan™ (netarsudil 0.02%/latanoprost 0.005% ophthalmic solution – Aerie)
- Travatan® Z (travoprost 0.004% ophthalmic solution – Novartis, generic)
- Vyzulta™ (latanoprostene bunod 0.024% ophthalmic solution – Bausch Health)
- Xalatan® (latanoprost 0.005% ophthalmic solution –Pfizer, generic)
- Xelpros™ (latanoprost 0.005% ophthalmic emulsion – Sun)
- Zioptan® (tafluprost 0.0015% ophthalmic solution – Thea, generic)

REVIEW DATE: 10/30/2024

OVERVIEW

The ophthalmic prostaglandins, rho kinase inhibitor, and rho kinase inhibitor-prostaglandin combination product are indicated for the **reduction of elevated intraocular pressure (IOP)** in patients with open-angle glaucoma or ocular hypertension.[1-10]

Guidelines

The American Academy of Ophthalmology (AAO) Preferred Practice Pattern® guidelines (2020) for the treatment of primary open-angle glaucoma note that the initial therapy choice may be influenced by potential cost, side effects, and dosing schedules as well as the patient's comorbid conditions (e.g., asthma, chronic obstructive lung disease, cardiac arrhythmia).[11] Lowering the pretreatment IOP by 25% or more has been shown to slow progression of primary open-angle glaucoma. The prostaglandins are often selected as the initial medical therapy unless there are considerations that would preclude its use (e.g., contraindications, cost, side effects). Moreover, the prostaglandins are the most frequently prescribed eye drops for lowering IOP due to efficacy and tolerability and they are dosed once daily. Other ophthalmic drugs for the treatment of glaucoma include beta-adrenergic blockers, alpha$_2$-adrenergic agonists, rho kinase inhibitors, and carbonic anhydrase inhibitors. If a drug fails to reduce IOP sufficiently, then either switching to an alternative medication as monotherapy or adding medication is appropriate, until the desired IOP level is attained.

Preservatives

All of the products listed in this policy are preserved with benzalkonium chloride (BAK) except tafluprost 0.0015% ophthalmic solution (Zioptan, generic), travoprost 0.004% ophthalmic solution (Travatan Z, generic), Iyuzeh, and Xelpros.[1-9] Travoprost 0.004% ophthalmic solution is preserved with an ionic buffered system, sofZia (boric acid, propylene glycol, sorbitol, zinc chloride).[5] Xelpros is preserved with potassium sorbate 0.47%.[8] Tafluprost 0.0015% ophthalmic solution and Iyuzeh are preservative-free products.[9]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic bimatoprost 0.03% ophthalmic solution, generic latanoprost 0.005% ophthalmic solution, generic travoprost 0.004% ophthalmic solution (generic to Travatan Z)

Step 2: Iyuzeh, Lumigan, Rhopressa, Rocklatan, Travatan Z, Xalatan, Xelpros, Vyzulta, Zioptan (brand and generic)

CRITERIA

3. If the patient has tried one Step 1 Product, approve a Step 2 Product.

4. If the patient has a known benzalkonium chloride (BAK) sensitivity AND a known sensitivity to other ophthalmic preservatives, approve Iyuzeh, Xelpros or Zioptan (brand and generic).

5. No other exceptions are recommended.

REFERENCES

7. Bimatoprost 0.03% ophthalmic solution [prescribing information]. Somerset, NJ: Micro Labs; January 2023.
8. Lumigan® 0.01% ophthalmic solution [prescribing information]. North Chicago, IL: AbbVie; June 2024.
9. Rhopressa® [prescribing information]. Irvine, CA: Aerie; March 2019.
10. Rocklatan™ [prescribing information]. Irvine, CA: Aerie; June 2020.
11. Travatan® Z 0.004% ophthalmic solution [prescribing information]. East Hanover, NJ: Novartis; October 2021.
12. Vyzulta® [prescribing information]. Bridgewater, NJ: Bausch + Lomb; January 2024.
13. Xalatan® 0.005% ophthalmic solution [prescribing information]. New York, NY: Pfizer; December 2022.
14. Xelpros™ [prescribing information]. Cranbury, NJ: Sun; June 2022.
15. Zioptan® 0.0015% ophthalmic solution [prescribing information]. Waltham, MA: Thea; May 2023.
16. Iyuzeh™ 0.005% ophthalmic solution [prescribing information]. Waltham, MA: Thea; April 2024.
17. Gedde SJ, Vinod K, Wright MW, et al. The American Academy of Ophthalmology Primary Open-Angle Glaucoma Preferred Practice Pattern®. Available at https://www.aaojournal.org/article/S0161-6420(20)31024-1/fulltext. Accessed on October 24, 2024.

STEP THERAPY POLICY

POLICY: Ophthalmic Anti-Allergics – Mast Cell Stabilizers Step Therapy Policy

- Alocril® (nedocromil sodium 2% ophthalmic solution – Allergan)
- Alomide® (lodoxamide tromethamine 0.1% ophthalmic solution – Alcon/Novartis)
- Cromolyn sodium 4% ophthalmic solution (generic only)

REVIEW DATE: 02/14/2024

OVERVIEW

The ophthalmic mast cell stabilizers are indicated for the treatment of **allergic conjunctivitis**.[1-3] Cromolyn sodium 4% ophthalmic solution and Alomide are specifically indicated for the treatment of vernal keratoconjunctivitis, vernal conjunctivitis, and vernal keratitis. Alomide is dosed four times daily; Alocril is dosed twice daily; and cromolyn sodium 4% ophthalmic solution is dosed four to six times daily at regular intervals.

Guidelines

The Conjunctivitis Preferred Practice Pattern® (2018) and Cornea/External Disease Summary Benchmarks (2022) from the American Academy of Ophthalmology state that mast cell stabilizers can be used if the patient's conjunctivitis is frequently recurrent or persistent despite treatment with a topical antihistamine/vasoconstrictor or topical histamine (H1)-receptor antagonist.[4,5] The Panel does not note a preference for one mast cell stabilizer over another.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic cromolyn sodium ophthalmic solution

Step 2: Alocril, Alomide

CRITERIA

39. If the patient has tried one Step 1 Product, approve a Step 2 Product.

40. No other exceptions are recommended.

REFERENCES

60. Alomide® ophthalmic solution [prescribing information]. Fort Worth, TX: Alcon; July 2022.
61. Alocril® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; July 2018.
62. Cromolyn sodium ophthalmic solution [prescribing information]. Princeton, NJ: Sandoz; August 2021.
63. Varu DM, Rhee MK, Akpek EK, et al. for the American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern. *Ophthalmology*. 2019;26(1):94-169.
64. American Academy of Ophthalmology Preferred Practice Pattern Cornea/External Disease Panel, Hoskins Center for Quality Eye Care. Summary benchmarks for preferred practice patter guidelines. Available at: https://www.aao.org/summary-benchmark-detail/cornea-external-disease-summary-benchmarks-2020. Updated December 2022. Accessed on January 29, 2024.

STEP THERAPY POLICY

POLICY: Ophthalmic Anti-Allergics – Miscellaneous Step Therapy Policy

- Alrex® (loteprednol etabonate 0.2% ophthalmic suspension – Bausch & Lomb, generic)
- azelastine hydrochloride 0.05% ophthalmic solution (generic only)
- Bepreve® (bepotastine besilate 1.5% ophthalmic solution – Bausch & Lomb, generic)
- epinastine hydrochloride 0.05% ophthalmic solution (generic only)
- Lastacaft® (alcaftadine 0.25% ophthalmic solution – Allergan)
- olopatadine hydrochloride 0.2% ophthalmic solution (generic only)
- olopatadine hydrochloride 0.1% ophthalmic solution (generic only)
- Zerviate™ (cetirizine 0.24% ophthalmic solution – Eyevance)

REVIEW DATE: 02/14/2024; selected revision 02/21/2024

OVERVIEW

All of the ophthalmic anti-allergic agents are generally indicated for the treatment of allergic conjunctivitis.[2-9] Table 1 provides mechanism of action, indication, and dosing information for the ophthalmic anti-allergic products. Of note, in 2020, all of the prescription olopatadine products had their FDA-approval switched from prescription to over-the-counter (OTC) status.[10] Therefore, prescription brand olopatadine products are no longer available, but prescription generic olopatadine products are still currently on the market. The OTC olopatadine products are not targeted in this policy. In December of 2021, Lastacaft's FDA-approval was also switched from prescription to OTC status. However, OTC Lastacaft is also not targeted in this policy.

Table 1. Ophthalmic Anti-Allergics (by Mechanism of Action).[2-9]

Table 1 (continued). Ophthalmic Anti-Allergics (by Mechanism of Action).[2-9]
H_1 – Histamine-1; BID – Twice daily; QID – Four times daily; QD – Once daily; † Over-the-counter product available, but not targeted in this policy.

Guidelines

The Conjunctivitis Preferred Practice Pattern (2018) and Cornea/External Disease Summary Benchmarks (2022) recommend treating mild allergic conjunctivitis with an OTC antihistamine/vasoconstrictor combination product or with an ophthalmic H_1-receptor antagonist.[1,13] In frequently recurrent or persistent cases, mast cell stabilizers may be utilized; combination antihistamine/mast cell stabilizers may also be used to treat either acute or chronic disease. A short course of ophthalmic corticosteroids can be added to the regimen if the symptoms are not adequately controlled.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: OTC Pataday and OTC Lastacaft products are not targeted in this policy.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic azelastine ophthalmic solution, generic bepotastine besilate 1.5% ophthalmic solution, generic epinastine ophthalmic solution, prescription generic olopatadine 0.1% ophthalmic solution, prescription generic olopatadine 0.2% ophthalmic solution

Step 2: generic loteprednol etabonate 0.2% ophthalmic suspension, Alrex, Bepreve, Lastacaft, Zerviate

CRITERIA

41. If the patient has tried one Step 1 Product, approve a Step 2 Product.

42. If the patient requires the concurrent use of Alrex or generic loteprednol etabonate 0.2% ophthalmic suspension and an H_1 antagonist or an H_1 antagonist/mast cell stabilizer, approve Alrex or generic loteprednol etabonate 0.2% ophthalmic suspension.
Note: An example of an H_1 antagonist is Zerviate. Examples of H_1 antagonist/mast cell stabilizers are azelastine ophthalmic solution, epinastine ophthalmic solution, bepotastine ophthalmic solution [Bepreve, generic], Lastacaft, olopatadine 0.1% ophthalmic solution, and olopatadine 0.2% ophthalmic solution.

43. If the patient has tried a different ophthalmic steroid for the current condition, approve Alrex or generic loteprednol etabonate 0.2% ophthalmic suspension.

44. No other exceptions are recommended.

REFERENCES

65. Varu DM, Rhee MK, Akpek EK, et al. for the American Academy of Ophthalmology Preferred Practice Pattern Cornea and External Disease Panel. Conjunctivitis Preferred Practice Pattern. *Ophthalmology*. 2019;26(1):94-169.
66. Olopatadine 0.1% ophthalmic solution [prescribing information]. Bridgewater, NJ: Alembic; December 2018.

67. Azelastine hydrochloride ophthalmic solution [prescribing information]. Weston, FL: Apotex; December 2022.
68. Epinastine 0.05% ophthalmic solution [prescribing information]. Hollywood, FL: Somerset; July 2021.
69. Olopatadine 0.2% ophthalmic solution [prescribing information]. Weston, FL: Apotex; December 2022.
70. Bepreve® ophthalmic solution [prescribing information]. Tampa, FL: Bausch & Lomb; August 2022.
71. Lastacaft® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; June 2020.
72. Alrex® ophthalmic suspension [prescribing information]. Tampa, FL: Bausch & Lomb; March 2022.
73. Zerviate™ ophthalmic solution [prescribing information]. Fort Worth, TX: Eyevance; November 2022.
~~74.~~ FDA Prescription to Over-the-counter (OTC) Switch List. U.S. Food and Drug Administration Web site. Available at: https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/prescription-over-counter-otc-switch-list. Updated March 17, 2022. Accessed on February 9, 2024.
75. American Academy of Ophthalmology Preferred Practice Pattern Cornea/External Disease Panel, Hoskins Center for Quality Eye Care. Summary benchmarks for preferred practice patter guidelines. Available at: https://www.aao.org/summary-benchmark-detail/cornea-external-disease-summary-benchmarks-2020. Updated December 2022. Accessed on February 9, 2024.

STEP THERAPY POLICY

POLICY: Ophthalmic Corticosteroids Step Therapy Policy

- Clobetasol propionate 0.05% ophthalmic suspension – Formosa (branded product)
- Dexamethasone sodium phosphate ophthalmic solution 0.1% (generic only)
- Durezol® (difluprednate ophthalmic emulsion 0.05% – Novartis, generic)
- Flarex® (fluorometholone acetate ophthalmic suspension 0.1% – Eyevance)
- Fluorometholone ophthalmic suspension 0.1% (generic only)
- FML® Forte (fluorometholone ophthalmic suspension 0.25% – Allergan)
- FML® Liquifilm (fluorometholone ophthalmic suspension 0.1% – Allergan, generic)
- Inveltys™ (loteprednol etabonate ophthalmic suspension 1% – Kala)
- Lotemax® (loteprednol etabonate ophthalmic gel 0.5% [generic], ophthalmic suspension 0.5% [generic], ophthalmic ointment 0.5% – Bausch + Lomb)
- Lotemax® SM (loteprednol etabonate ophthalmic gel 0.38% – Bausch + Lomb)
- Maxidex® (dexamethasone ophthalmic suspension 0.1% – Novartis)
- Pred Mild® (prednisolone acetate ophthalmic suspension 0.12% – Allergan)
- Prednisolone acetate ophthalmic suspension 1% (generic only)

REVIEW DATE: 10/09/2024

OVERVIEW

The ophthalmic corticosteroid products are (generally) indicated for treatment of a variety of **conditions, including anterior uveitis; corneal injury; inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe; postoperative inflammation and/or pain following ocular injury; and seasonal allergic conjunctivitis**.[1] Some of the products are also indicated for the treatment of **post-operative inflammation and/or pain following ocular surgery**. Durezol is also indicated for the treatment of **endogenous anterior uveitis**.[2] Two clinical studies demonstrated Durezol to be equally effective as prednisolone acetate ophthalmic suspension 1% in treating patients with endogenous anterior uveitis.

Clinical studies that directly compare all of the currently available ophthalmic corticosteroid products have not been performed. It is generally recognized that all ophthalmic corticosteroids are effective agents for treating a variety of ocular inflammatory conditions.[3]

Many of the ophthalmic corticosteroid products are preserved with benzalkonium chloride.[1] The following products included in this policy are <u>not</u> preserved with benzalkonium chloride: Durezol (sorbic acid) and Lotemax ophthalmic ointment (prescribing information does not note a preservative).[2,4]

POLICY STATEMENT

This program has been developed to encourage the use of two Step 1 Products prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

<u>Automation</u>: A patient with a of two Step 1 Products within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic dexamethasone sodium phosphate ophthalmic solution 0.1%, generic difluprednate ophthalmic emulsion 0.05%, generic fluorometholone ophthalmic suspension 0.1%, generic

loteprednol etabonate ophthalmic suspension 0.5%, generic prednisolone acetate ophthalmic suspension 1%

Step 2: Clobetasol propionate 0.05% ophthalmic suspension, Durezol, Flarex, FML Forte, FML Liquifilm, Inveltys, Lotemax ophthalmic ointment 0.5%, Lotemax ophthalmic gel 0.5%, Lotemax SM, Maxidex, Pred Mild

CRITERIA

1. If the patient has tried two Step 1 Products, approve a Step 2 Product.

2. If the patient has an allergy to benzalkonium chloride, approve Durezol or Lotemax ophthalmic ointment.

3. No other exceptions are recommended.

REFERENCES

18. Facts and Comparisons Online. Wolters Kluwer Health, Inc.; 2024. Available at https://fco.factsandcomparisons.com/lco/action/home. Accessed on October 04, 2024. Search terms: ophthalmic corticosteroids.
19. Durezol® [prescribing information]. East Hanover, NJ: Novartis; November 2020.
20. Fung AT, Tran T, Lim LL, et al. Local delivery of corticosteroids in clinical ophthalmology: A review. *Clin Exp Ophthalmol*. 2020;48(3):366-401.
21. Lotemax® ophthalmic ointment [prescribing information]. Bridgewater, NJ: Bausch Health; November 2022.

STEP THERAPY POLICY

POLICY: Ophthalmic Nonsteroidal Anti-Inflammatory Drugs Step Therapy Policy

- Acular® (ketorolac tromethamine 0.5% ophthalmic solution – Allergan, generic)
- Acular LS® (ketorolac tromethamine 0.4% ophthalmic solution – Allergan, generic)
- Acuvail® (ketorolac tromethamine 0.45% ophthalmic solution – Allergan)
- Bromfenac 0.09% ophthalmic solution (generic only)
- BromSite® (bromfenac 0.075% ophthalmic solution – Sun, generic)
- Diclofenac 0.1% ophthalmic solution (generic only)
- Flurbiprofen 0.03% ophthalmic solution (generic only)
- Nevanac® (nepafenac 0.1% ophthalmic suspension – Novartis)
- Prolensa® (bromfenac 0.07% ophthalmic solution – Bausch & Lomb, generic)

REVIEW DATE: 09/18/2024

OVERVIEW

In general, the ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDS) are indicated for the management of **ocular pain and inflammation in the postoperative setting**.[1-7] Note that the specific labeled indications may differ among the products. Ketorolac 0.5% ophthalmic solution is also indicated for the treatment of seasonal allergic conjunctivitis.[1] Flurbiprofen 0.03% ophthalmic solution is not indicated for use in the postoperative setting; flurbiprofen is indicated for the inhibition of intraoperative miosis.[8] All of the ophthalmic products included in this Step Therapy are preserved with benzalkonium chloride, except Acuvail, diclofenac 0.1% ophthalmic solution, and flurbiprofen 0.03% ophthalmic solution.[1-8]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Ilevro is not included in this policy.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic bromfenac 0.07% ophthalmic solution, generic bromfenac 0.075% ophthalmic solution, generic bromfenac 0.09% ophthalmic solution, generic diclofenac 0.1% ophthalmic solution, generic flurbiprofen 0.03% ophthalmic solution, generic ketorolac 0.4% ophthalmic solution generic ketorolac 0.5% ophthalmic solution

Step 2: Acular, Acular LS, Acuvail, BromSite, Nevanac, Prolensa

CRITERIA

45. If the patient has tried one Step 1 Product, approve a Step 2 Product.

46. No other exceptions are recommended.

REFERENCES

76. Acular® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; May 2012.
77. Acular LS® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; June 2016.
78. Acuvail® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; February 2019.
79. Nevanac® ophthalmic suspension [prescribing information]. East Hanover, NJ: Novartis; November 2020.
80. Bromfenac 0.09% ophthalmic solution [prescribing information]. Bedminister, NJ: Alembic; November 2022.
81. Diclofenac 0.1% ophthalmic solution [prescribing information]. Tampa, FL: Bausch & Lomb; June 2022.
82. BromSite® ophthalmic solution [prescribing information]. Cranbury, NJ: Sun; March 2023.
83. Flurbiprofen 0.03% ophthalmic solution [prescribing information]. Tampa, FL: Bausch & Lomb; September 2022.
84. Prolensa® 0.07% ophthalmic solution [prescribing information]. Bridgewater, NJ: Bausch & Lomb; January 2023.

STEP THERAPY POLICY

POLICY: Ophthalmic Quinolone Antibiotics Step Therapy Policy

- Besivance (besifloxacin 0.6% ophthalmic suspension – Bausch + Lomb)
- Ciloxan® (ciprofloxacin 0.3% ophthalmic ointment – Novartis)
- Ciloxan® (ciprofloxacin 0.3% ophthalmic solution – Alcon, generic)
- Levofloxacin 0.5% ophthalmic solution (generic only)
- Moxeza® (moxifloxacin 0.5% ophthalmic solution – Alcon, generic)
- Ocuflox® (ofloxacin 0.3% ophthalmic solution – Allergan, generic)
- Vigamox® (moxifloxacin 0.5% ophthalmic solution – Novartis, generic)
- Zymaxid® (gatifloxacin 0.5% ophthalmic solution – Allergan, generic)

REVIEW DATE: 10/30/2024

OVERVIEW

The ophthalmic fluoroquinolone products (besifloxacin, ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, and ofloxacin) are indicated for the treatment of **bacterial conjunctivitis** caused by susceptible strains of certain microorganisms.[1-8] Ciprofloxacin ophthalmic solution and levofloxacin ophthalmic solution are also indicated for the treatment of corneal ulcers caused by susceptible strains of certain microorganisms.[2,7] The prescribing information for these products lists the specific strains.

Moxifloxacin ophthalmic solution 0.5% and Ciloxan ointment are preservative free.[1-8] The other ophthalmic products are preserved with benzalkonium chloride.[1-8]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 drug within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic ciprofloxacin 0.3% ophthalmic solution, generic gatifloxacin 0.5% ophthalmic solution, generic levofloxacin 0.5% ophthalmic solution, generic moxifloxacin hydrochloride 0.5% ophthalmic solution, generic ofloxacin 0.3% ophthalmic solution

Step 2: Besivance, Ciloxan ointment

CRITERIA

47. If the patient has tried one Step 1 Product, approve a Step 2 Product.

48. If the patient has already started treatment with Besivance or Ciloxan ointment, approve Besivance or Ciloxan ointment to complete the course of therapy.

49. No other exceptions are recommended.

REFERENCES

85. Ciloxan® ointment [prescribing information]. East Hanover, NJ: Novartis; November 2019.
86. Ciloxan® ophthalmic solution [prescribing information]. Fort Worth, TX: Alcon; April 2018.
87. Zymaxid® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; September 2016.
88. Moxeza® ophthalmic solution [prescribing information]. Fort Worth, TX: Alcon; August 2023.
89. Vigamox® ophthalmic solution [prescribing information]. East Hanover, NJ: Novartis; June 2020.
90. Ocuflox® ophthalmic solution [prescribing information]. Irvine, CA: Allergan; April 2017.
91. Levofloxacin ophthalmic solution [prescribing information]. Lake Forest, IL: Akorn; February 2017.
92. Besivance ophthalmic suspension [prescribing information]. Tampa, FL: Bausch + Lomb; February 2022.

STEP THERAPY POLICY

POLICY: Otic Quinolone – Ciprofloxacin Step Therapy Policy

- Cetraxal® (ciprofloxacin 0.2% otic solution – WraSer)
- Ciprodex® (ciprofloxacin 0.3%/dexamethasone 0.1% otic suspension – Novartis, generic)
- Cipro® HC OTIC (ciprofloxacin 0.2%/hydrocortisone 1% otic suspension – Alcon)
- Ciprofloxacin 0.2% otic solution (generic only)
- Ciprofloxacin 0.3%/fluocinolone acetonide 0.25% otic solution – Xspire (branded product)
- Otovel® (ciprofloxacin 0.3%/fluocinolone acetonide 0.025% otic solution – Arbor)

REVIEW DATE: 10/09/2024

OVERVIEW

All of these products are indicated for the treatment of patients with ear infection.

- Acute otitis externa due to susceptible isolates of Pseudomonas aeruginosa and Staphylococcus aureus: Cetraxal, Ciprodex, generic ciprofloxacin 0.2% otic solution, Cipro HC OTIC.1-4 Cipro HC OTIC is also active against acute otitis externa due to Proteus mirabilis.4
- Acute otitis media with tympanostomy tubes due to S. aureus, Haemophilus influenzae, Moraxella catarrhalis, and P. aeruginosa: Ciprodex, Otovel, ciprofloxacin 0.3%/fluocinolone acetonide 0.025% otic solution.2,5,8

Cetraxal is a brand-only single-entity product containing ciprofloxacin 0.2%; ciprofloxacin 0.2% otic solution is also available as a generic product.1,3 Ciprodex, Cipro HC OTIC, ciprofloxacin 0.3%/fluocinolone acetonide 0.025% otic solution, and Otovel are combination products containing a corticosteroid.2,4,5,8

Ciprofloxacin otic solution, Cetraxal, ciprofloxacin 0.3%/fluocinolone acetonide 0.025% otic solution, and Otovel are preservative-free products.1,3,5,8 Ciprodex is preserved with benzalkonium chloride and Cipro HC OTIC is preserved with benzyl alcohol.2,4

Guidelines

The American Academy of Otolaryngology-Head and Neck Surgery Foundation (AAO-HNSF) published their clinical practice guidelines for acute otitis externa in patients ≥ 2 years of age (2014; reaffirmed 2019).6 The guidelines recommend the use of an ototopical antibiotic for initial therapy of diffuse acute otitis externa because of excellent clinical and bacteriologic outcomes, low incidence of adverse events (AE), likelihood of adherence to therapy, and cost. The guidelines do not prefer one agent over another.

The AAO-HNSF guidelines for the management of children with tympanostomy tubes (2022) recommend the use of ototopical antibiotics, without oral antibiotics, in children with uncomplicated acute tympanostomy tube otorrhea.7 The guidelines do not prefer one ototopical product over another. The advantages of ototopical products in acute otitis media with tympanostomy tubes include increased drug concentration at the site of infection, improved coverage of likely pathogens, and no systemic AEs.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic ciprofloxacin otic solution, generic ciprofloxacin-dexamethasone otic solution

Step 2: Cetraxal, Ciprodex, Cipro HC OTIC, ciprofloxacin 0.3%/fluocinolone acetonide 0.025% otic solution (branded product), Otovel

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Cetraxal® otic solution [prescribing information]. Ridgeland, MS: WraSer; December 2017.

2. Ciprodex® otic suspension [prescribing information]. East Hanover, NJ: Novartis; November 2020.

3. Ciprofloxacin otic solution [prescribing information]. Ridgeland, MS: Xspire; August 2012.

4. Cipro® HC OTIC suspension [prescribing information]. East Hanover, New Jersey: Arbor; August 2020.

5. Otovel® otic solution [prescribing information]. Atlanta, GA: Arbor; April 2016.

6. Rosenfeld RM, Schwartz SR, Cannon CR, et al. Clinical practice guideline: Acute otitis externa. Otolaryngol Head Neck Surg. 2014;150:S1-S24.

7. Rosenfeld RM, Tunkel DE, Schwartz SR, et al. Clinical Practice Guideline: Tympanostomy tubes in children (Update). Otolaryngol Head Neck Surg. 2022;166(1 Suppl):S1-55.

8. Ciprofloxacin/fluocinolone acetonide otic solution [prescribing information]. Ridgeland, MS: Xspire; June 2021.

STEP THERAPY POLICY

POLICY: Overactive Bladder Medications Step Therapy Policy

- Darifenacin extended-release tablets (generic only)
- Detrol® (tolterodine tartrate tablets – Pfizer, generic)
- Detrol LA® (tolterodine tartrate extended-release capsules – Pfizer, generic)
- Ditropan XL® (oxybutynin chloride extended-release tablets – Janssen, generic)
- Gelnique® (oxybutynin 10% gel – Allergan)
- Gemtesa® (virabegron tablets – Urovant Sciences)
- Myrbetriq® (mirabegron extended-release tablets – Astellas, generic)
- Myrbetriq® Granules (mirabegron for extended-release oral suspension – Astellas)
- Oxybutynin chloride tablets, syrup (generic only)
- Oxytrol® (oxybutynin transdermal system – Allergan)
- Oxytrol® for Women (oxybutynin transdermal system – Actavis) [over-the-counter]
- Toviaz® (fesoterodine fumarate extended-release tablets – Pfizer, generic)
- Trospium chloride tablets (generic only)
- Trospium chloride extended-release capsules (generic only)
- Vesicare® (solifenacin succinate tablets – Astellas, generic)
- Vesicare LS™ (solifenacin succinate oral suspension – Astellas)

REVIEW DATE: 5/8/2024

OVERVIEW

These products, except oxybutynin tablets and syrup and Vesicare LS, are indicated for the **treatment of overactive bladder** (OAB) with symptoms of urge urinary incontinence, urgency, and frequency.[1-15] Gemtesa and Myrbetriq are beta3-adrenergic agonists; the other products are antimuscarinics. Myrbetriq is indicated for use as monotherapy or in combination with solifenacin.[14]

The Oxytrol transdermal patch is available as a prescription and an over-the-counter (OTC) product. Prescription Oxytrol is indicated for the treatment of OAB in men with symptoms of urge urinary incontinence, urgency, and frequency.[4] The OTC formulation is marketed as Oxytrol for Women and is indicated for use in women ≥ 18 years of age.[16] The prescription and OTC Oxytrol contain the same dose of oxybutynin (3.9 mg/day).[4,16]

Pediatric Indications

Oxybutynin tablets and syrup are indicated for the **relief of symptoms of bladder instability** associated with voiding in patients (≥ 5 years of age) with uninhibited neurogenic or reflex neurogenic bladder (i.e., urgency, frequency, urinary leakage, urge incontinence, dysuria).[1,2] Oxybutynin extended-release (ER) tablets are indicated for the treatment of pediatric patients ≥ 6 years of age with symptoms of **detrusor overactivity associated with a neurological condition** (e.g., spina bifida).[3] Myrbetriq, Toviaz, Vesicare LS are indicated for the treatment of **neurogenic detrusor overactivity** in pediatric patients ≥ 3 years of age, ≥ 6 years, and ≥ 2 years of age, respectively.[11,13,14]

Guidelines

The American Urological Association (AUA) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) guidelines for the diagnosis and treatment of idiopathic overactive bladder (2024).[17] The guidelines recommend behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as the first-line treatment in patients with OAB. Oral antimuscarinics and oral beta-3 adrenergic agonists are second-line therapies. Myrbetriq appears to be similar in efficacy to the antimuscarinic agents. Combination therapy (an antimuscarinic with a beta-3 adrenergic agonist) as a potential second-line treatment for patients refractory to monotherapy with either antimuscarinics or beta-3 adrenergic agonists. The guidelines note that oral antimuscarinics are similar in efficacy and the choice of agent for a particular patient is dependent on many factors, including the patient's history of antimuscarinic use; information regarding adverse events (AEs) experienced in the past; impact of the AEs on the patient; patient preference, comorbidities, use of other medications; and cost. Patients who experienced inadequate symptom control and/or unacceptable AEs with one antimuscarinic may experience better symptom control and/or a more acceptable AE profile if the dose were modified or if they were treated with another antimuscarinic or with a beta-3 adrenergic agonist. Even though the guidelines do not prefer one antimuscarinic over another, when given a choice between an immediate-release (IR) and an ER formulation, the ER formulation is preferred over the IR formulation due to lower rates of dry mouth. Transdermal and topical formulations of oxybutynin can be offered in lieu of oral antimuscarinics to patients who are at risk of or who have experienced dry mouth with the oral agents.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic darifenacin extended-release tablets, generic fesoterodine fumarate extended-release tablets, generic mirabegron extended-release tablets, generic oxybutynin immediate-release tablets, generic oxybutynin immediate-release syrup, generic oxybutynin extended-release tablets, generic solifenacin succinate tablets, generic tolterodine tartrate tablets, generic tolterodine tartrate extended-release capsules, generic trospium chloride tablets, generic trospium chloride extended-release capsules

Step 2: Detrol, Detrol LA, Ditropan XL, Enablex, Gelnique, Gemtesa, Myrbetriq, Myrbetriq Granules, Oxytrol (prescription), Oxytrol for Women (over-the-counter), Toviaz, Vesicare, Vesicare LS

CRITERIA

4. If the patient has tried one Step 1 Product, approve a Step 2 Product.

5. If the patient cannot swallow or has difficulty swallowing tablets or capsules, approve Gelnique, Myrbetriq Granules, or Oxytrol (prescription or over-the-counter).

6. If the patient is < 3 years of age, approve Vesicare LS.

7. No other exceptions are recommended.

REFERENCES

1. Oxybutynin tablets [prescribing information]. Princeton, NJ: Eywa; May 2019.
2. Oxybutynin syrup [prescribing information]. Philadelphia, PA: Lannett; February 2020.
3. Ditropan XL® extended release tablets [prescribing information]. Titusville, NJ: Janssen; December 2022.
4. Oxytrol® transdermal system [prescribing information]. Irvine, CA: Allergan; November 2023.
5. Detrol® tablets [prescribing information]. New York, NY: Pfizer; October 2016.
6. Detrol® LA extended release capsules [prescribing information]. New York, NY: Pfizer; July 2018.
7. Trospium tablets [prescribing information]. Mahway, NJ: Glenmark; December 2023.
8. Trospium extended-release capsules [prescribing information]. Chantilly, VA: Granules; September 2020.
9. Vesicare® tablets [prescribing information]. Northbrook, IL: Astellas; October 2022.
10. Darifenacin extended-release tablets [prescribing information]. Warren, NJ: Cipla; August 2021.
11. Toviaz®extended-release tablets [prescribing information]. New York, NY: Pfizer; February 2024.
12. Gelnique® 10% gel [prescribing information]. Madison, NJ: Allergan; March 2019.
13. Vesicare LS™ [prescribing information]. Northbrook, IL: Astellas; October 2022.
14. Myrbetriq® extended-release tablets, Myrbetriq® Granules [prescribing information]. Northbrook, IL: Astellas; April 2021.
15. Gemtesa® [prescribing information]. Irvine, CA: Urovant Sciences; July 2023.
16. Oxytrol® for Women transdermal system. [prescribing information]. Madison, NJ: Allergan; August 2016.
17. Cameron AP, Chung DE, Dielubanza EJ, et al. The AUA/SUFU guideline on the diagnosis and treatment of idiopathic overactive bladder. *J Urol.* Published online April 23, 2024.

STEP THERAPY POLICY

POLICY: Parkinson's Disease – Carbidopa-Levodopa (Oral) Step Therapy Policy

- Carbidopa-Levodopa immediate-release tablets (generic)
- Carbidopa-Levodopa extended-release tablets (generic only)
- Crexont® (carbidopa-levodopa extended-release capsule – Amneal)
- Rytary® (carbidopa-levodopa extended-release capsule – Amneal)

REVIEW DATE: 11/20/2024

OVERVIEW

Carbidopa-levodopa, an aromatic amino acid decarboxylation inhibitor and an aromatic amino acid, is indicated for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication or manganese intoxication.[1-4] Carbidopa-levodopa extended-release tablets, may be split in half but not crushed and Crexont and Rytary must be swallowed whole.

Table 1. Carbidopa-Levodopa Summary Table.[1-4]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: The brand carbidopa-levodopa product Sinemet is not included in either Step 1 or Step 2 of this program. However, if a patient has tried brand Sinemet, they can receive a Step 2 product.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic carbidopa-levodopa tablets, generic carbidopa-levodopa extended-release tablets

Step 2: Crexont capsules, Rytary capsules

CRITERIA

50. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: A trial of Sinemet also satisfies the requirement.

51. If the patient is currently taking Crexont capsules or Rytary capsules, approve continuation of therapy.

52. No other exceptions are recommended.

REFERENCES

93. Carbidopa-Levodopa tablets [prescribing information]. Parsippany, NJ: Teva; September 2020.
94. Carbidopa-Levodopa ER tablets [prescribing information]. Bridgwater, NJ: Amneal; December 2022.
95. Crexont® ER capsules [prescribing information]. Bridgwater, NJ: Amneal; August 2024.
96. Rytary® ER capsules [prescribing information]. Bridgwater, NJ: Amneal; December 2019.

STEP THERAPY POLICY

POLICY: Parkinson's Disease – Monoamine Oxidase Type B Inhibitors Step Therapy Policy
- Azilect® (rasagiline tablets – Teva, generic)
- Selegiline capsules and tablets (generic only)
- Xadago® (safinamide mesylate tablets – US WorldMeds)

REVIEW DATE: 01/17/2024

OVERVIEW

Azilect, oral selegiline products, and Xadago are monoamine oxidase type B (MAO-B) inhibitors and have similar indications for the **treatment of Parkinson's disease**.[1-3] Azilect is indicated for the treatment of Parkinson's disease. Selegiline tablets and capsules are indicated as adjuncts in the management of Parkinsonian patients being treated with levodopa/carbidopa who exhibit deterioration in the quality of their response to this therapy. Xadago is indicated as adjunctive treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes.

The International Parkinson and Movement Disorder Society published an evidence-based review for treatment for motor symptoms of Parkinson's disease (2018).[4] The review categorically divides treatment recommendations by Parkinson's disease characteristics. Azilect and selegiline are treatments considered to be efficacious and clinically useful for symptomatic monotherapy. For the treatment of motor fluctuations, Azilect and Xadago are noted to be efficacious and clinically useful while selegiline is considered efficacious and possibly useful.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. Of note, Zelapar® (selegiline orally disintegrating tablets) does not require Step Therapy for coverage. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic selegiline tablets and capsules, generic rasagiline tablets

Step 2: Azilect, Xadago

CRITERIA

53. If the patient has tried one Step 1 Product, approve a Step 2 Product.

54. No other exceptions are recommended.

REFERENCES

1. Azilect® tablets [prescribing information]. North Wales, PA: Teva; June 2020.
2. Selegiline capsules and tablets [prescribing information]. Weston, FL: Apotex; November 2018.
3. Xadago® tablets [prescribing information]. Louisville, KY: US WorldMeds; October 2022.
4. Fox SH, Katzenschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: Update on treatments for the motor symptoms of Parkinson's disease. *Mov Disord*. 2018;33(8):1248-1266.

STEP THERAPY POLICY

POLICY: Proton Pump Inhibitors Step Therapy Policy

OTC – Over-the-counter.

REVIEW DATE: 12/04/2024

OVERVIEW

Although proton pump inhibitors (PPIs) vary in their specific FDA-approved indications, all PPIs are used for the treatment and/or management of acid-related diseases, including duodenal and gastric ulcerations, gastroesophageal reflux disease, Zollinger-Ellison syndrome, and *Helicobacter pylori* infections.[1-14,19,20] Several PPIs are available over-the-counter (OTC).[1-4] Patients should not take the OTC products for more than a 14 day period or more often than every 4 months unless under the supervision of a physician.

Several treatment guidelines support the overall safety and efficacy of these agents for acid-related diseases.[15-18] PPIs are the treatment of choice for many gastrointestinal disorders in adults and pediatrics. Though the available clinical data are not entirely complete for the comparison of these agents, many clinical trials have shown the PPIs to be similar in efficacy and safety.

Pediatrics

Esomeprazole magnesium capsules, Nexium oral suspension, omeprazole capsules, and Prilosec oral suspension are indicated for use in children ≥ 1 month old.[5-7] Aciphex Sprinkle, lansoprazole capsules, and lansoprazole orally disintegrating tablets (ODT) are indicated for use in children ≥ 1 year of age.[8,9] Pantoprazole products are only indicated for patients ≥ 5 years of age.[10] Rabeprazole tablets are not recommended for use in pediatric patients < 12 years of age because the lowest available tablet strength (20 mg) exceeds the recommended dose for these patients.[11] Dexilant is indicated in patients ≥ 12 years of age.[13] Omeprazole/sodium bicarbonate capsules and oral suspension, Konvomep, Voquezna, and the OTC PPI products lack pediatric indications.[12,13,19,20]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product or Nexium 24HR (OTC) within the 130-day look-back period is excluded from Step Therapy.
Note: Automation is NOT in place for Step 2 Konvomep, Zegerid, Zegerid OTC, and generic omeprazole/sodium bicarbonate products (Rx/OTC).

Step 1: Generic esomeprazole delayed-release capsules (Rx and OTC), generic lansoprazole delayed-release capsules (Rx and OTC), generic omeprazole delayed-release capsules and tablets (Rx and OTC), generic pantoprazole delayed-release tablets, generic rabeprazole delayed-release tablets

Step 2: Aciphex, Aciphex Sprinkle, Dexilant, generic dexlansoprazole capsules, generic esomeprazole delayed-release granules for oral suspension, esomeprazole strontium delayed-release capsules, generic lansoprazole orally disintegrating tablets, Konvomep, Nexium, Prevacid, Prevacid 24HR, Prevacid SoluTab, Prilosec (Rx and OTC), Protonix, generic pantoprazole

granules, Voquezna, Zegerid, Zegerid OTC, generic omeprazole/sodium bicarbonate capsules (Rx and OTC)

CRITERIA

55. If the patient is < 1 year of age, approve generic esomeprazole delayed-release granules for oral suspension (packets), Nexium delayed-release granules for oral suspension (packets), or Prilosec delayed-release granules for oral suspension (packets).

56. If the patient requires administration via a feeding tube and has tried a Step 1 Product under the supervision of a physician, approve a Step 2 Product (except Konvomep, Zegerid, Zegerid OTC, and generic omeprazole/sodium bicarbonate capsules [Rx and OTC]).
Note: A trial of a generic OTC PPI would qualify.

57. If the patient has tried a Step 1 Product under the supervision of a physician, approve a Step 2 Product (except Konvomep, Zegerid, Zegerid OTC, and generic omeprazole/sodium bicarbonate capsules [Rx and OTC]).
Note: A trial of a generic OTC PPI would qualify, if OTC PPIs are a covered benefit and the patient was using it for at least 14 days.

58. If the requested product is Konvomep, Zegerid, Zegerid OTC, or generic omeprazole/sodium bicarbonate capsules (Rx or OTC), approve if the patient has tried five generic PPIs (i.e., esomeprazole [Rx and OTC], lansoprazole [Rx or OTC], omeprazole [Rx or OTC], pantoprazole, AND rabeprazole).
Note: A trial of a generic OTC PPI would qualify, if OTC PPIs are a covered benefit and the patient was using it for at least 14 days.

59. No other exceptions are recommended.

REFERENCES

1. Prilosec OTC® delayed-release tablets [prescribing information]. Cincinnati, OH: Procter and Gamble; October 2024.
2. Prevacid® 24HR delayed-release capsules [prescribing information]. Allegan, MI: Perrigo; August 2023.
3. Zegerid OTC® capsules [prescribing information]. Whippany, NJ: Bayer; November 2023.
4. Nexium® 24HR delayed-release capsules and tablets [prescribing information]. Warren, NJ: GlaxoSmithKline; June 2022.
5. Omeprazole delayed-release capsules [prescribing information]. North Wales, PA: Teva; November 2020.
6. Prilosec® delayed-release suspension [prescribing information]. Zug, Switzerland: Covis; November 2020.
7. Nexium® delayed-release capsules [prescribing information]. Wilmington, DE: AstraZeneca; August 2021.
8. Prevacid® delayed-release capsules and orally disintegrating tablets [prescribing information]. Deerfield, IL: Takeda; March 2022.
9. Aciphex® Sprinkle™ delayed-release capsules [prescribing information]. Woodcliff Lake, NJ: Eisai; December 2020.
10. Protonix® delayed-release tablets and oral suspension [prescribing information]. Philadelphia, PA: Wyeth; March 2022.
11. Aciphex® delayed-release tablets [prescribing information]. Woodcliff Lake, NJ: Eisai; November 2020.
12. Zegerid® capsules [prescribing information]. Bridgewater, NJ: Salix; March 2022.
13. Dexilant™ delayed-release capsules [prescribing information]. Deerfield, IL: Takeda; March 2022.
14. Esomeprazole strontium delayed-release capsules [prescribing information]. Glasgow, KY: Amneal; January 2021.
15. Moayyedi P, Lacy BE, Andrews CN, et al. ACG and CAG Clinical Guideline: Management of Dyspepsia. *Am J Gastroenterol.* 2017; 112(7):988-1013.
16. Katz PO, Dunbar KB, Schnoll-Sussman FH, et al. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. *Am J Gastroenterol*. 2022;117(1):27-56.
17. Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. *J Pediatr Gastroenterol Nutr.* 2018; 66(3):516-554.
18. Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. *Am J Gastroenterol*. 2022; 117(4):559-587.

19. Konvomep oral suspension [prescribing information]. Woburn, MA. Azurity; August 2023.
20. Voquezna® tablets [prescribing information]. Buffalo Grove, IL: Phathom; July 2024.

STEP THERAPY POLICY

POLICY: Pulmonary – Airsupra Step Therapy Policy

- Airsupra® (albuterol and budesonide inhalation aerosol – AstraZeneca)

REVIEW DATE: 12/18/2024

OVERVIEW

Airsupra is a combination of albuterol, a short-acting beta$_2$-agonist (SABA), and budesonide, an inhaled corticosteroid (ICS).[1] It is indicated for the as-needed treatment or prevention of bronchoconstriction and to reduce the risk of exacerbations in patients ≥ 18 years of age with **asthma**. Airsupra is a metered-dose inhaler that utilizes a hydrofluoroalkane propellant.

Generic albuterol sulfate inhalation aerosol, albuterol sulfate inhalation aerosol (branded generics), levalbuterol tartrate inhalation aerosol (branded generics), ProAir Digihaler, ProAir HFA, ProAir RespiClick, Proventil HFA, Ventolin HFA, and Xopenex HFA are all SABA inhalers.[2-7] They are indicated for relief of acute **asthma** symptoms and prevention of **exercise induced bronchospasm**. All of the short-acting beta$_2$-agonist inhalers are indicated in patients ≥ 4 years of age. The SABA inhalers are all metered-dose inhalers that utilize a hydrofluoroalkane propellant, with the exception of ProAir Digihaler and ProAir RespiClick, which are dry-powder inhalers.

Guidelines

The Global Initiative for Asthma (GINA) [2024] provides a step-wise approach for asthma management utilizing controller and reliever therapies.[9] In adult and adolescent patients, an as-needed low-dose ICS-formoterol combination is the preferred initial reliever agent. If the preferred regimen is not possible, an as-needed ICS/SABA (e.g., Airsupra) or as-needed SABA are recommended similarly as alternative reliever therapy options. However, if a SABA is chosen as the reliever therapy, the guidelines make additional recommendations regarding administering an ICS separately at the same time as the SABA. Guidelines note that if an ICS is being administered at the same time as a SABA, this may be accomplished using a combination inhaler or separate inhalers.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic albuterol sulfate inhalation aerosol, albuterol sulfate inhalation aerosol (branded generics), levalbuterol tartrate inhalation aerosol (branded generics), ProAir Digihaler, ProAir HFA, ProAir RespiClick, Proventil HFA, Ventolin HFA, Xopenex HFA

Step 2: Airsupra

CRITERIA

60. If the patient has tried one Step 1 Product, approve a Step 2 Product.

61. No other exceptions are recommended.

REFERENCES

97. Airsupra® [prescribing information]. Wilmington, DE: AstraZeneca; March 2024.
98. Ventolin® HFA inhalation aerosol [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2024.
99. Proventil® HFA inhalation aerosol [prescribing information]. Whitehouse Station, NJ: Merck; October 2019.
100. ProAir® RespiClick inhalation powder [prescribing information]. Horsham, PA: Teva; September 2022.
101. ProAir® HFA inhalation aerosol [prescribing information]. Horsham, PA: Teva; February 2019.
102. Xopenex HFA® inhalation aerosol [prescribing information]. Baltimore, MD: Lupin; January 2024.
103. ProAir® Digihaler® inhalation powder [prescribing information]. Horsham, PA: Teva; June 2022.
104. Global Initiative for Asthma. Global strategy for asthma management and prevention: updated 2024. Available at: http://www.ginasthma.org. Accessed on December 10, 2024.

STEP THERAPY POLICY

POLICY: Pulmonary – Short-Acting Beta$_2$-Agonist Inhalers Step Therapy Policy

- albuterol sulfate inhalation aerosol (branded generic to Ventolin® HFA)
- ProAir® Digihaler® (albuterol sulfate inhalation powder – Teva) [discontinued]
- ProAir® HFA (albuterol sulfate inhalation aerosol – Teva, generic)
- ProAir® RespiClick (albuterol sulfate inhalation powder – Teva)
- Proventil® HFA (albuterol sulfate inhalation aerosol – Merck, generic [brand discontinued])
- Xopenex HFA® (levalbuterol tartrate inhalation aerosol – Sunovion, branded generic)

REVIEW DATE: 12/18/2024

OVERVIEW

Inhaled short-acting beta$_2$-agonists are indicated for relief of acute **asthma** symptoms and prevention of **exercise induced bronchospasm**.[1-6] All of the short-acting beta$_2$-agonist inhalers are indicated in patients ≥ 4 years of age. The short-acting beta$_2$-agonist inhalers are all metered-dose inhalers that utilize a hydrofluoroalkane propellant, with the exception of ProAir Digihaler and ProAir RespiClick, which are dry-powder inhalers. All of the devices contain dose-counters. ProAir Digihaler is unique in that it contains a built-in electronic module which detects, records, and stores data on inhaler events, including peak inspiratory flow rate, for transmission to a mobile application where inhaler events are categorized.[6] Use of the application is not required for administration and there are no data to show that the use of the application results in enhanced safety or effectiveness, or improved clinical outcomes.

All synthetic beta$_2$-agonists exist chemically as racemic mixtures; however, the therapeutic activity primarily resides in the R-enantiomers and not the S-enantiomers.[7] *In vitro* data have suggested a possible deleterious effect of the S-enantiomer of albuterol on airway smooth muscle responsiveness and other airway cells. Therefore, levalbuterol, which contains only the R-enantiomer of albuterol, was developed and approved for clinical use. Some studies suggested an improved efficacy of levalbuterol over racemic albuterol when administered in equal R-albuterol doses; however, other trials have failed to detect any advantage of levalbuterol.[7-9]

Guidelines

The Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention (2024)[10] and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of chronic obstructive pulmonary disease (2025)[11] do not prefer any one product in this category, but rather refer to them as a class of medications.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: Brand Ventolin HFA is not targeted in this policy.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic albuterol sulfate inhalation aerosol

Step 2: albuterol sulfate inhalation aerosol (branded generics), levalbuterol tartrate inhalation aerosol (branded generics), ProAir Digihaler, ProAir HFA, ProAir RespiClick, Proventil HFA, Xopenex HFA

CRITERIA

62. If the patient has tried one Step 1 Product, approve a Step 2 Product.

63. If the patient is unable to coordinate breath and actuation with a metered-dose inhaler, approve ProAir Digihaler or ProAir RespiClick.

64. No other exceptions are recommended.

REFERENCES

1. Ventolin® HFA inhalation aerosol [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; April 2024.
2. Proventil® HFA inhalation aerosol [prescribing information]. Whitehouse Station, NJ: Merck; October 2019.
3. ProAir® RespiClick inhalation powder [prescribing information]. Horsham, PA: Teva; September 2022.
4. ProAir® HFA inhalation aerosol [prescribing information]. Horsham, PA: Teva; February 2019.
5. Xopenex HFA® inhalation aerosol [prescribing information]. Baltimore, MD: Lupin; January 2024.
6. ProAir® Digihaler® inhalation powder [prescribing information]. Horsham, PA: Teva; June 2022.
7. National Asthma Education and Prevention Program Expert Panel Report 3: Guidelines for the diagnosis and management of asthma. Updated 2007. Available at: https://www.jacionline.org/action/showPdf?pii=S0091-6749%2807%2901823-4. Accessed on December 9, 2024.
8. Kelly A, Kennedy A, John BM, et al. A comparison of heart rate changes associated with levalbuterol and racemic albuterol in pediatric cardiology patients. *Ann Pharmacother*. 2013;47(5):644-650.
9. Jat KR, Khairwa A. Levalbuterol versus albuterol for acute asthma: a systematic review and meta-analysis. *Pulm Pharmacol Ther*. 2013;26(2):239-248.
10. Global Initiative for Asthma. Global strategy for asthma management and prevention: updated 2024. Available at: http://www.ginasthma.org. Accessed on December, 9, 2024.
11. National Institutes of Health, National Heart, Lung, and Blood Institute. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated 2025. Available at: http://www.goldcopd.org/. Accessed on December 9, 2024.

STEP THERAPY POLICY

POLICY: Sedative Hypnotics Step Therapy Policy

- Ambien® (zolpidem tablets – Sanofi-Aventis, generic)
- Ambien CR® (zolpidem extended-release tablets – Sanofi-Aventis, generic)
- Belsomra® (suvorexant tablets – Merck)
- Dayvigo® (lemborexant tablets – Eisai)
- Edluar® (zolpidem 5 and 10 mg sublingual tablets – Meda)
- Intermezzo® (zolpidem 1.75 and 3.5 mg sublingual tablets –Purdue, generic)
- Lunesta® (eszopiclone tablets – Sepracor, generic)
- Quviviq™ (daridorexant tablets – Idorsia)
- Rozerem® (ramelteon tablets – Takeda, generic)
- Silenor® (doxepin 3 mg and 6 mg tablets – Currax, generic)
- Sonata® (zaleplon capsules – King, generic)
- Zolpimist® (zolpidem oral spray – Aytu BioScience)
- Zolpidem Capsule (Almatica Pharma)

REVIEW DATE: 09/04/2024

OVERVIEW

The products included in this policy are indicated for the treatment of insomnia.

- Zolpidem immediate-release (IR), Edluar, Zolpimist, and zaleplon, non-benzodiazepine sedative hypnotics, are indicated for the **short-term treatment of insomnia**.[1,3,5,6]
- Eszopiclone, a non-benzodiazepine; Silenor, a tricyclic compound; and Rozerem, a melatonin receptor agonist, are also indicated for the treatment of **insomnia**, but their product labeling does not specifically limit their use to short-term.[2,4,8,9]
- Zaleplon and Rozerem are specifically indicated for the treatment of insomnia characterized by difficulty with sleep onset.[3,8]
- Zolpidem IR, zolpidem extended-release (ER), Silenor, and eszopiclone have also been shown to improve sleep maintenance or increase the duration of sleep.[1,2,4,9]
- Belsomra, Dayvigo, and Quviviq, orexin receptor antagonists, are indicated for the **treatment of insomnia, characterized by difficulties with sleep onset and/or sleep maintenance**.[10-12]
- Zolpidem sublingual tablets are indicated for use as needed for the treatment of insomnia when a **middle-of-the-night awakening is followed by difficulty returning to sleep**.[7] However, zolpidem sublingual tablets are not indicated for treatment of middle-of-the-night insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking.
- Zolpidem Capsules is a branded product indicated for **short-term treatment of transient insomnia** in adults < 65 years of age.[17]

Eszopiclone, zaleplon, zolpidem, Belsomra, Dayvigo, and Quviviq are schedule IV controlled substances.[1-7,10-12,17] Neither Rozerem nor Silenor are controlled substances.[8,9]

Doxepin is also available generically as oral capsules (10, 25, 50, 75, 100, and 150 mg) and oral solution (10 mg/mL). These higher dose formulations are recommended for use in patients with depression and/or anxiety of varying etiologies.

Use in the Elderly

Although no specific adverse events (AEs) have been noted in elderly patients, changes in pharmacokinetics and/or use of high doses could put this population at increased risk of AEs. The general sensitivity of the elderly population to sedative hypnotics applies to all drugs with hypnotic effects.[15,16] However, because the potential for memory/cognitive/psychomotor impairment exists (primarily at peak concentrations) with certain non-benzodiazepine sedative hypnotics (the long-acting agents in particular), Rozerem's unique mechanism of action may be beneficial in older patients with or at risk for memory/cognitive/psychomotor impairment. Downward dosage adjustments of zolpidem IR, zolpidem ER, Edluar, zolpidem sublingual tablets, Zolpimist, zaleplon, Silenor, and eszopiclone are recommended when used in elderly or debilitated patients.[1-7,9] Zolpidem capsules are not indicated for use in geriatric patients.[17] The product labeling for Rozerem does not recommend a dosage adjustment in the elderly.[8] Belsomra, Dayvigo, and Quviviq have been studied in patients ≥ 65 years of age, and no clinically meaningful differences in safety or effectiveness were observed between these patients and younger patients at the recommended doses.[10-12] However, in addition to daytime somnolence, Belsomra and Dayvigo have the potential to cause sleep paralysis, hypnagogic/hypnopompic hallucinations, and cataplexy-like symptoms, which are not seen with the other agents.

GUIDELINES

In 2017, an updated American Academy of Sleep Medicine (AASM) clinical guideline for the pharmacologic treatment of chronic insomnia in adults was published.[13] The guideline indicates that hypnotic medications, along with management of comorbidities and non-pharmacological interventions such as cognitive behavioral therapy for insomnia (CBT-I), are an important therapeutic option for chronic insomnia. The recommendations are intended as a guide for choosing a specific pharmacological agent (vs. no treatment) for treatment of chronic insomnia in adults, when such treatment is indicated. Each of the recommendations listed is weak, meaning it reflects a lower degree of certainty in the outcome and appropriateness of the patient-care strategy for all patients but should not be construed as an indication of ineffectiveness. The guideline suggests that clinicians can use Belsomra as a treatment for sleep maintenance insomnia; eszopiclone can be used as a treatment for sleep onset and sleep maintenance insomnia; zaleplon can be used as a treatment for sleep onset insomnia; zolpidem can be used as a treatment for sleep onset and sleep maintenance insomnia; triazolam can be used as a treatment for sleep onset insomnia; temazepam can be used as a treatment for sleep onset and sleep maintenance insomnia; Rozerem can be used as a treatment for sleep onset insomnia; and Silenor can be used as a treatment for sleep maintenance insomnia. The authors note that CBT-I is a standard of care for this condition; however, the AASM guideline does not address the relative benefits of CBT-I vs. pharmacotherapy. In addition, several agents used for insomnia are on the 2023 Beers list of medications that are categorized as potentially inappropriate agents for elderly persons aged ≥ 65 years (e.g., amitriptyline, benzodiazepines, doxepin [> 6 mg/day]); zolpidem, zaleplon, and eszopiclone should also be avoided.[14]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy. For Silenor and generic doxepin 3 mg and 6 mg tablets, a patient who is ≥ 65 years of age will not be targeted by this Step Therapy program.

Step 1: generic eszopiclone tablets, generic ramelteon tablets, generic zaleplon capsules, generic zolpidem immediate-release tablets, generic zolpidem extended-release tablets, generic zolpidem sublingual tablets

Step 2: Ambien, Ambien CR, Belsomra, Dayvigo, Edluar, Intermezzo, Lunesta, Quviviq, Rozerem, Silenor, generic doxepin 3 mg and 6 mg tablets, Sonata, Zolpidem Capsule, Zolpimist

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient has a documented of substance use disorder, approve Silenor or generic doxepin 3 mg or 6 mg tablets.

3. If the patient is ≥ 65 years of age, approve Silenor or generic doxepin 3 mg or 6 mg tablets.

4. If the patient has difficulty swallowing or cannot swallow tablets/capsules, approve Edluar or Zolpimist.

5. No other exceptions are recommended.

REFERENCES

1. Ambien® tablets [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; February 2022.
2. Ambien CR® tablets [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; February 2022.
3. Sonata® capsules [prescribing information]. New York, NY: Pfizer; August 2019.
4. Lunesta® tablets [prescribing information]. Marlborough, MA: Sunovion; August 2019.
5. Edluar® sublingual tablets [prescribing information]. Somerset, NJ: Meda; August 2019.
6. Zolpimist® oral spray [prescribing information]. Englewood, CO: Aytu BioScience; August 2019.
7. Intermezzo® sublingual tablets [prescribing information]. Stamford, CT: Purdue; August 2019.
8. Rozerem® tablets [prescribing information]. Lexington, MA: Takeda; November 2021.
9. Silenor® tablets for oral administration [prescribing information]. Morristown, NJ: Currax; December 2022.
10. Belsomra® tablets [prescribing information]. Whitehouse Station, NJ: Merck; February 2023.
11. Dayvigo® tablets [prescribing information]. Woodcliff Lake, NJ: Eisai; December 2023.
12. Quviviq™ tablets [prescribing information]. Radnor, PA: Idorsia; October 2023.
13. Sateia MJ, Buysse DJ, Krystal AD, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(2):307–349.
14. The American Geriatrics Society 2023 Beers Criteria Update Expert Panel. American Geriatrics Society 2023 updated AGS Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2023;71(7):2052-2081.
15. Drover DR. Comparative pharmacokinetics and pharmacodynamics of short-acting hypnosedatives. Zaleplon, zolpidem and zopiclone. *Clin Pharmacokinet*. 2004;43(4):227-238.
16. Patel D, Steinberg J, Patel P. Insomnia in the elderly: a review. *J Clin Sleep Med.* 2018;14(6):1017-1024.
17. Zolpidem tartrate capsules [prescribing information]. Morristown, NJ. Almatica Pharma. May 2023.

STEP THERAPY POLICY

POLICY: Tetracyclines (Oral) Step Therapy Policy

- Acticlate™ (doxycycline hyclate tablets – Almirall, generic)
- Avidoxy™ DK Kit (doxycycline monohydrate tablets – Avidas)
- Doryx® DR (doxycycline hyclate delayed-release tablets – Mayne, generic)
- Doryx® MPC (doxycycline hyclate delayed-release tablets – Mayne)
- Doxycycline IR-DR 40 mg capsules (Mayne [authorized generic])
- Minolira™ (minocycline extended-release tablets – EPI Health)
- Monodox® (doxycycline monohydrate capsules – Almirall, generic)
- Morgidox® Kit (doxycycline hyclate capsules – Medimetriks)
- Oracea™ (doxycycline delayed-release capsules – Galderma, generic)
- Seysara™ (sarecycline tablets – Almirall)
- Solodyn® (minocycline hydrochloride extended-release tablets – Bausch Health, generic)
- Tetracycline tablets and capsules – generic only
- Targadox™ (doxycycline hyclate tablets – Journey Medical)
- Vibramycin® (doxycycline hyclate capsules – Pfizer, generic)
- Ximino™ (minocycline hydrochloride extended-release capsules – Ohm)

REVIEW DATE: 2/28/2024; selected revision 4/24/2024

OVERVIEW

Demeclocycline, doxycycline, minocycline, sarecycline and tetracycline are broad-spectrum oral antibiotic agents.[1-10,20] In general, these medications are FDA-approved to treat a wide **variety of infections caused by gram-negative and gram-positive microorganisms**. Common infections include respiratory tract infections, sexually transmitted infections, skin/skin structure infections, and urinary tract infections; and they can be used in conjunction with other therapies for the management of acne. The tetracycline products are also used in situations where penicillin is contraindicated due to allergy.

There are some doxycycline and minocycline products with unique indications: **Oracea** (brand only) and **doxycycline immediate-release – delayed-release 40 mg capsules** (an authorized generic) are indicated for the treatment of only inflammatory lesions (papules and pustules) of rosacea in adults.[11,12] **Minolira**, **Seysara**, **Solodyn**, and **Ximino** are indicated for the treatment of inflammatory lesions of non-nodular moderate to severe acne vulgaris; Seysara is indicated for use in patients ≥ 9 years of age and Minolira, Solodyn and Ximino are indicated for use in patients ≥ 12 years of age.[13-16] **Doxycycline 20 mg** tablets are indicated only for use as an adjunct to scaling and root planning to promote attachment level gain and reduce pocket depth in patients with adult periodontitis.[10]

In addition, some of the doxycycline and minocycline products are packaged with other items and sold as kits for specific uses. Table 1 summarizes these kits.[17,18] The doxycycline products in these kits can be purchased separately.

Table 1. Kits that include doxycycline or minocycline antibiotics.[17,18]

Guidelines

The American Academy of Dermatology guidelines for the management of acne vulgaris (2024) note that the tetracyclines are typically the antibiotics used for this condition.[19] These products have antibacterial as well as anti-inflammatory actions. Doxycycline, minocycline, and sarecycline are similar in efficacy and are more effective than tetracyclines. Systemic antibiotics should be used for the shortest possible duration to minimize the development of bacterial resistance. In addition, systemic antibiotics should not be used as monotherapy; they should be used in conjunction with a topical product.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1:

IR – Immediate release.

Step 2:

DR – Delayed-release; IR – Immediate-release; ER – Extended-release.

CRITERIA

3. If the patient has tried one Step 1 Product, approve a Step 2 Product.

4. No other exceptions are recommended.

REFERENCES

1. Demeclocycline tablets [prescribing information]. Bridgewater, NJ: Amneal; May 2018.
2. Acticlate™ tablets [prescribing information]. Exton, PA: Almirall; December 2019.
3. Doryx® tablets [prescribing information]. Greenville, NC: Mayne; July 2022.
4. Vibramycin® calcium syrup, Vibramycin® hyclate capsules, Vibramycin® monohydrate powder for oral suspension, Vibra-tabs® [prescribing information]. New York, NY: Pfizer; January 2024.
5. Dynacin® tablets [prescribing information]. Spring Valley, NY: Par; November 2011.
6. Minocin® pellet-filled capsules [prescribing information]. Bridgewater, NJ: Valeant; January 2019.
7. Monodox® capsules [prescribing information]. Fort Lauderdale, FL: Watson; March 2017.
8. Tetracycline capsules [prescribing information]. Parsippany, NJ: Actavis; November 2018.
9. Targadox™ tablets [prescribing information]. Scottsdale, AZ: Journey Medical; January 2019.
10. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: https://fco.factsandcomparisons.com/lco/action/home. Accessed on February 20, 2024. Search terms: tetracycline.
11. Oracea™ delayed-release capsules [prescribing information]. Fort Worth, TX: Galderma; January 2023.
12. Doxycycline IR-DR 40 mg capsules [prescribing information]. Raleigh, NC. Mayne; October 2022.
13. Minolira™ extended release [prescribing information]. Charleston, SC: EPI Health; June 2018.
14. Seysara™ [prescribing information]. Exton, PA: Almirall; March 2023.
15. Solodyn® extended release tablet [prescribing information]. Bridgewater, NJ: Valeant; September 2017.
16. Ximino™ [prescribing information]. New Brunswick, NJ: Ohm; December 2023.
17. Avidoxy™ DK defence Kit. Available at: http://www.avidaspharma.com/pressrelease004.html. Accessed on February 20, 2024.
18. Morgidox® Kit [prescribing information]. Fairfield, NJ: Medimetriks; October 2021.
19. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol. 2024 [published online ahead of print]*.
20. Tetracycline tablets [prescribing information]. Fairmont, WV. Pharmaka Generics. January 2024.

STEP THERAPY POLICY

POLICY: Topical Acne – Cleansers Step Therapy Policy

Note: This is not an inclusive list.

- Avar™ (sodium sulfacetamide/sulfur 9.5%/5% cleansing pads – Mission)
- Avar™ LS (sodium sulfacetamide/sulfur 10%/2% cleansing pads – Mission)
- BP 10-1 Wash (sodium sulfacetamide 10%/sulfur 1% wash – Acella, generic)
- BP Cleansing Wash (sulfacetamide 10%/sulfur 4%/urea 10% – Acella, generic)
- Pacnex® 7% Topical Wash (benzoyl peroxide 7% topical wash – Medimetriks, generic)
- Pacnex® HP (benzoyl peroxide 7% cleansing pads – Medimetriks)
- Pacnex® LP (benzoyl peroxide 4.25% cleansing pads – Medimetriks)
- Plexion® (sulfacetamide/sulfur 9.8/4.8% cleanser; sulfacetamide/sulfur 9.8/4.8% cleansing pads – Brava)
- Rosula® (sodium sulfacetamide/sulfur 10%/4.5% wash, 10%-5% cleansing cloths – Avion)
- Sulfacleanse® 8-4 Suspension (sodium sulfacetamide 8%/sulfur 4% – Prugen, generic)
- Sumadan® (sodium sulfacetamide/sulfur 9%/4.5% wash – Medimetriks)
- Sumadan® XLT (sodium sulfacetamide/sulfur 9%/4.5% wash – Medimetriks)
- Sumaxin® (sodium sulfacetamide/sulfur 9%/4% cleansing pads – Medimetriks, generic)
- Sumaxin® (sodium sulfacetamide/sulfur 9%/4% wash – Medimetriks)
- Sumaxin® CP (sodium sulfacetamide/sulfur 10%/4% Kit – Medimetriks)
- Sumaxin® TS (sodium sulfacetamide/sulfur 8%/4% topical suspension – Medimetriks)

REVIEW DATE: 12/18/2024

OVERVIEW

Many topical products are available for the **treatment of acne vulgaris**.[1,2] Benzoyl peroxide-containing products are generally indicated for the treatment and prevention of mild to moderate acne vulgaris. Sulfacetamide sodium have antimicrobial properties and sulfur have antiseptic properties which aid in the removal of keratin and drying of the skin and are available in a variety of strengths and vehicles. These products (sulfacetamide/sulfur) are additionally used for acne rosacea and seborrheic dermatitis. Acne treatment guidelines do not prefer any of the brand name products over similar generic products.[3]

The topical products for treatment of acne are available in multiple formulations.[1,2] Creams and lotions may be best for dry or sensitive skin and gels or foams may be best for more oily skin (although newer aqueous gels may also be suitable for sensitive skin).[3]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: For the purpose of this policy, a topical cleanser is defined as a cleanser, solution, liquid, wash, foaming cloth, cleansing cloth, or soap.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic prescription topical acne cleansers containing benzoyl peroxide or sulfacetamide/sulfur

Note: This is not an inclusive list.

- Benzoyl Peroxide 10% Topical Wash
- Sodium Sulfacetamide/Sulfur 10%-4% Cleansing Pads
- Sodium Sulfacetamide 10% and Sulfur 2% Topical Cleanser
- Sulfacetamide Sodium/Sulfur 10%-5% Topical Cleanser
- Sodium Sulfacetamide-Sulfur 9.8%-4.8% Topical Cleanser

Step 2: Branded prescription topical acne cleansers containing benzoyl peroxide or sulfacetamide/sulfur

Note: This is not an inclusive list.

- Avar™
- Avar™ LS
- BP 10-1 Wash
- BP Cleansing Wash
- Pacnex® 7% Topical Wash
- Pacnex® HP Cleansing Pads
- Pacnex® LP Cleansing Pads
- Plexion® Cleanser
- Plexion® Cleansing Pads
- Rosula®
- Sulfacleanse® 8-4 Suspension
- Sumadan®
- Sumadan® XLT
- Sumaxin®
- Sumaxin® CP Kit
- Sumaxin® TS Topical Suspension

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: https://fco.factsandcomparisons.com/lco/action/home. Accessed on December 12,2024. Search terms: benzoyl peroxide, clindamycin, sulfacetamide/sulfur.
2. Clinical Pharmacology © 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed on December 12, 2024. Search Terms: benzoyl peroxide and sulfur/sulfacetamide.
3. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2024;90(5):1006.e1-1006.e30.

STEP THERAPY POLICY

POLICY: Topical Acne – Kits Step Therapy Policy
- Clindacin® ETZ 1% Kit (clindamycin phosphate 1% pledget and Acuwash® cleanser – Medimetriks)
- Clindacin® PAC Kit (clindamycin phosphate 1% pledget and Acuwash® cleanser – Medimetriks)
- Clindavix Kit (clindamycin phosphate topical solution 1% and Dynashield [dimethicone 1.8%, zinc oxide 2%] – Perrigo [obsolete 08/01/2022])

REVIEW DATE: 12/18/2024

OVERVIEW

Many topical products are available for the **treatment of acne vulgaris**.[1,2] Benzoyl peroxide-containing products are generally indicated for the treatment and prevention of mild to moderate acne vulgaris. Sulfacetamide sodium and sulfur are antimicrobial and antiseptic agents, respectively, and are available in a variety of strengths and formulations. They help to remove keratin and to dry the skin. These products (sulfacetamide/sulfur) are additionally used for acne rosacea and seborrheic dermatitis. Topical clindamycin products are indicated for the treatment of acne vulgaris.[3-5] Both Clindacin ETZ kit and Clindacin PAC kit include topical clindamycin pledgets and a bottle of Acuwash® moisturizing daily cleanser.[3,4] Clindavix kit includes clindamycin topical solution and a tube of Dynashield (dimethicone, zinc oxide), which is a general skin protectant.[5] Acne treatment guidelines do not prefer any of the brand name products over similar generic products.[6]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product (one prescription topical acne product and one prescription acne cleanser) prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one prescription topical acne product (Step 1) and one prescription acne cleanser (Step 1) within the 130-day look-back period is excluded from Step Therapy.

Step 1: Prescription topical acne products: brand or generic topical adapalene, azelaic acid, benzoyl peroxide, clindamycin, dapsone, sulfacetamide or sulfacetamide/sulfur-containing products (see Appendix A for examples); AND
Prescription topical acne cleansers: brand or generic topical benzoyl peroxide- or sulfacetamide/sulfur-containing products (see Appendix A for examples)

Step 2: Acne kits (Clindacin ETZ, Clindacin PAC, Clindavix Kit)

CRITERIA

1. If the patient has tried one prescription topical acne product (Step 1) AND one prescription acne cleanser (Step 1), approve a Step 2 Product.
2. No other exceptions are recommended.

REFERENCES

1. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: https://fco.factsandcomparisons.com/lco/action/home. Accessed on December 12, 2024. Search terms: benzoyl peroxide, clindamycin, sulfacetamide/sulfur.
2. Clinical Pharmacology © 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed on December 12, 2024. Search Terms: sulfur and sulfacetamide, clindamycin, benzoyl peroxide.
3. Clindacin® ETZ [prescribing information]. Fairfield, NJ: Medimetriks; September 2022.
4. Clindacin® PAC [prescribing information]. Fairfield, NJ: Medimetriks; November 2022.
5. Clindavix [prescribing information]. Allegan, MI: Perrigo; May 2018.
6. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2024;90(5):1006.e1-1006.e30.

Appendix A

Examples (not a complete list)

Prescription Topical Acne Products (not cleansers).
Refer to *Topical Acne – Topical Product Step Therapy Policy* for more examples.

Prescription Acne Cleansers.
Refer to *Topical Acne – Cleansers Step Therapy Policy* for more examples.

STEP THERAPY POLICY

POLICY: Topical Acne – Topical Products Step Therapy Policy

Note: This is not an all-inclusive list.

REVIEW DATE: 09/04/2024

OVERVIEW

All of these products are indicated for use in the management of **acne vulgaris**.[1,2] Some of the benzoyl peroxide-containing products are available over-the-counter (OTC) and these products are generally indicated for the treatment or prevention of mild to moderate acne vulgaris. Sulfacetamide sodium and sulfur are used together to treat acne vulgaris; sulfacetamide is an antimicrobial and sulfur is an antimicrobial and a keratolytic agent that causes a peeling and drying effect. In addition to being indicated for the treatment of acne, sulfacetamide/sulfur products are used for acne rosacea and seborrheic dermatitis. Please refer to the product labeling for specific details.

The topical products for treatment of acne are available in multiple formulations.[1,2] Creams and lotions may be best for dry or sensitive skin and gels or foams may be best for more oily skin (although newer aqueous gels may also be suitable for sensitive skin).[3]

Acne treatment guidelines do not prefer any of the specific brand name agents over similar products available as generics for the treatment of acne.[3] Acne management should focus on preventing formation of microcomedones and minimizing the potential for visible acne lesions.[1,2] A multimodal approach is recommended and therapy should include therapies combining multiple mechanisms of actions.[3] Topical antibiotics are not recommended as monotherapy and should be used in combination with benzoyl peroxide or topical retinoids. Unlike topical antibiotics, benzoyl peroxide, a topical antimicrobial, has not been associated with the development of antibiotic resistance.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.
Note: For the purpose of this policy, a topical acne product is defined as a gel, cream, lotion, solution/pledget, pad, foam, or ointment.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic prescription topical adapalene-, benzoyl peroxide-, clindamycin products other than generic Clindagel, dapsone-, erythromycin-, sodium sulfacetamide-, or sodium sulfacetamide/sulfur-containing products

Step 2: Brand name prescription topical acne products: Aklief, Amzeeq, Azelex, or brand name topical acne products containing adapalene (e.g., Differin), benzoyl peroxide (e.g., Inova Easy Pad), clindamycin (e.g., Cleocin T, Evoclin), dapsone (e.g., Aczone), erythromycin (e.g., Erygel), sulfacetamide (e.g., Klaron), sulfacetamide/sulfur (e.g., Avar-e, Avar-e LS), or combinations containing these active ingredients (e.g., Acanya, Benzamycin, Cabtreo, Epiduo [brand], Twyneo, Ziana, Veltin), generic adapalene swabs, generic Clindagel

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. No other exceptions are recommended.

REFERENCES

1. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: http://fco.factsandcomparisons.com/lco/action/home. Accessed on September 3, 2024. Search terms: benzoyl peroxide, clindamycin, minocycline, sulfacetamide/sulfur, Twyneo.
2. Clinical Pharmacology © 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed on September 3, 2024. Search terms: benzoyl peroxide and sulfur/sulfacetamide.
3. Reynolds RV, Yeung H, Cheng CE, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2024;90(5):1006.e1-1006.e30.

STEP THERAPY POLICY

POLICY: Topical Agents for Atopic Dermatitis Step Therapy Policy

- Elidel® (pimecrolimus 1% cream – Bausch Health/Valeant, generic)
- Eucrisa® (crisaborole 2% ointment – Pfizer)
- Protopic® (tacrolimus 0.03% and 0.1% ointment – LEO, generic)
- Zoryve® (roflumilast 0.15% cream – Arcutis)

REVIEW DATE: 10/23/2024

OVERVIEW

Tacrolimus ointment and pimecrolimus cream are topical calcineurin inhibitors that are indicated as *second-line therapy* for the short-term and non-continuous chronic treatment of **atopic dermatitis** in non-immunocompromised patients who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.[1,2] Tacrolimus ointment is indicated for moderate to severe atopic dermatitis while pimecrolimus cream is indicated for mild to moderate atopic dermatitis. Eucrisa and Zoryve 0.15% cream, topical phosphodiesterase 4 inhibitors, are indicated for the topical treatment of mild to moderate **atopic dermatitis.**[3,7]

Tacrolimus 0.03% ointment and pimecrolimus cream are indicated for use in adults and children ≥ 2 years of age.[1,2] Although there are data documenting the tacrolimus 0.1% strength's safety and efficacy in children, this product is not approved for use in pediatric patients. Neither tacrolimus 0.03% ointment nor pimecrolimus cream are indicated for use in children < 2 years of age; however, both agents have been studied in this patient population. Eucrisa is indicated for use in patients ≥ 3 months of age.[3] Zoryve 0.15% cream is indicated for use in patients ≥ 6 years of age.[7]

Topical corticosteroids are generally indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.[4]

Guidelines

The American Academy of Dermatology (AAD) Guidelines of Care for the Management of Atopic Dermatitis in Adults with Topical Therapies (2023) recommend the use of topical corticosteroids and note that these products are commonly used as first-line topical treatment as they suppress the release of proinflammatory cytokines and target a variety of immune cells.[5] Topical calcineurin inhibitors (i.e., tacrolimus ointment and pimecrolimus cream) are noted to be a safe topical anti-inflammatory option, particularly if topical corticosteroid adverse events are of concern. Tacrolimus ointment is recommended for use in all adults with atopic dermatitis, while pimecrolimus cream is a recommended treatment option for patients with mild-to-moderate disease. Similarly, Eucrisa is a recommended treatment option for adults with mild-to-moderate atopic dermatitis. Zoyrve 0.15% cream is not addressed.

Recommendations for the management of pediatric patients have not been updated. However, AAD guidelines from 2014 make similar recommendations regarding the use of topical corticosteroids and topical calcineurin inhibitors in pediatric patients.[6] Eucrisa and Zoryve 0.15% cream are not addressed.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: prescription topical corticosteroids (brand or generic)

Step 2: generic pimecrolimus 1% cream, Elidel, Eucrisa, generic tacrolimus ointment (0.03% and 0.1% strengths), Protopic, Zoryve 0.15% cream

CRITERIA

1. If the patient has tried a Step 1 Product, approve a Step 2 Product.
2. If the patient has a dermatologic condition on or around the face, eyes/eyelids, axilla, or genitalia, approve a Step 2 Product.
3. If the patient is < 2 years of age, approve Eucrisa.
4. No other exceptions are recommended.

REFERENCES

1. Elidel® cream [prescribing information]. Bridgewater, NJ: Bausch/Valeant; September 2020.
2. Protopic® ointment [prescribing information]. Madison, NJ: LEO; June 2022.
3. Eucrisa® ointment [prescribing information]. New York, NY: Pfizer; January 2024.
4. Triamcinolone acetonide cream [prescribing information]. Hawthorne, NY: Taro; February 2023.
5. Sidbury R, Alikhan A, Bercovitch L, et al. Guidelines of care for the management of atopic dermatitis in adults with topical therapies. *J Am Acad Dermatol*. 2023;89(1):e1-e20.
6. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis. Section 2: management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-132.
7. Zoryve® cream [prescribing information]. Westlake Village, CA: Arcutis; July 2024.

STEP THERAPY POLICY

POLICY: Topical Antibacterials Step Therapy Policy

- Altabax® (repatamulin ointment – Almirall)
- Centany® (mupirocin ointment – Medimetriks)
- Centany® AT (mupirocin ointment – Medimetriks)
- Mupirocin cream (generic only)
- Mupirocin ointment (generic only)
- Xepi™ (ozenoxacin cream – Biofrontera)

REVIEW DATE: 11/20/2024

OVERVIEW

These topical antibacterials are generally indicated for the treatment of **dermatologic infections** caused by *Staphylococcus aureus* or *Streptococcus pyogenes*.[1-6]

The approved indications for these products are as follows:

- Altabax is indicated for use in adults and **pediatric patients ≥ 9 months of age** for the topical **treatment of impetigo** (up to 100 cm^2 in total area in adults or 2% total body surface area in pediatric patients ≥ 9 months of age) due to *S. aureus* (methicillin-susceptible isolates only) or *S. pyogenes.*
- Centany/Centany AT/mupirocin ointment are indicated for the topical **treatment of impetigo** due to *S. aureus* and *S. pyogenes*. The safety and effectiveness of Centany/mupirocin ointment have been established in **pediatric patients 2 months to 16 years of age**. Centany AT differs from Centany in that it is packaged with gauze pads and cloth tape strips.
- Mupirocin cream is indicated for the treatment of **secondarily infected traumatic skin lesions** (up to 10 cm in length or 100 cm^2 in area) due to susceptible isolates of *S. aureus* and *S. pyogenes*. The safety and effectiveness of mupirocin cream have been established in **pediatric patients 3 months to 16 years of age**.
- Xepi, a topical quinolone antimicrobial, is indicated for the topical **treatment of impetigo** due to *S. aureus* or *S. pyogenes* in adults and **pediatric patients ≥ 2 months of age**.

Guidelines

The Infectious Diseases Society of America (IDSA) updated their practice guidelines for the diagnosis and management of skin and soft tissue infections in 2014.[7] (Note: The guidelines were released prior to the approval of Xepi). The IDSA notes that either topical mupirocin or Altabax should be used for 5 days for the treatment of bullous and nonbullous impetigo. Topical treatment with mupirocin or Altabax is as effective as oral antimicrobials for impetigo. However, systemic therapy is preferred in patients with numerous lesions or in outbreaks affecting several people, to decrease transmission of infection. A 7-day regimen of an oral agent active against *S. aureus* is recommended unless cultures show streptococci alone (and oral penicillin is the recommended agent).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic mupirocin ointment

Step 2: Altabax, Centany, Centany AT, generic mupirocin cream, Xepi

CRITERIA

5. If the patient has tried one Step 1 Product, approve a Step 2 Product.

6. No other exceptions are recommended.

REFERENCES

10. Altabax® ointment [prescribing information]. Exton PA: Almirall; June 2023
11. Centany® ointment [prescribing information]. Fairfield, NJ: Medimetriks; May 2017.
12. Centany® AT ointment [prescribing information]. Fairfield NJ: Medimetriks; May 2017.
13. Mupirocin cream [prescribing information]. Mahwah, NJ: Glenmark; March 2020.
14. Xepi™ cream [prescribing information]. Woburn, MA: Biofrontera; January 2020.
15. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: http://online.factsandcomparisons.com/login.aspx?url=/index.aspx&qs=. Accessed on November 7, 2024. Search terms: mupirocin.
16. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections, 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59(2):e10-e52.

STEP THERAPY POLICY

POLICY: Topical Antifungals for Onychomycosis Step Therapy Policy

- Ciclodan® 8% Kit (ciclopirox topical solution 8% – Medimetriks)
- Ciclodan 8% (ciclopirox topical solution 8% – Medimetriks, generic)
- Ciclopirox 8% treatment kit (generic only)
- Ciclopirox topical solution 8% (generic only)
- Jublia® (efinaconazole topical solution 10% – Valeant)
- Kerydin™ (tavaborole topical solution 5% – PharmaDerm/Sandoz, generic)

REVIEW DATE: 12/11/2024

OVERVIEW

Ciclopirox topical solution 8%, Ciclodan, Jublia, and Kerydin are topical antifungals indicated for the **treatment of onychomycosis**.[1-4]

Treatment options include oral and topical antifungals.[5] Oral antifungals are the gold standard as they are significantly more effective than topical antifungals. However, they may be associated with significant adverse effects (e.g., hepatotoxicity, ventricular dysfunction) and risk of drug-drug interactions. Commonly used topical antifungals include ciclopirox topical solution (Ciclodan, generics), Jublia, and tavaborole topical solution (Kerydin, generic). Some patients require both an oral and a topical antifungal for treatment.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Ciclodan 8% topical solution (branded generic), generic ciclopirox 8% topical solution, generic ciclopirox 8% treatment kit

Step 2: Ciclodan 8% Kit, Jublia, Kerydin, generic tavaborole topical solution 5%

CRITERIA

6. If a patient has tried one Step 1 Product, approve a Step 2 Product.

7. No other exceptions are recommended.

REFERENCES

1. Ciclopirox topical solution [prescribing information]. Gurnee, IL: Akorn; July 2022.
2. Ciclodan® topical solution [prescribing information]. Fairfield, NJ: Medimetriks; October 2019.
3. Jublia® topical solution [prescribing information]. Bridgewater NJ: Valeant; March 2022.
4. Kerydin™ topical solution [prescribing information]. New York, NY: Pfizer; August 2018.
5. Leung AKC, Lam JM, Leong KF, et al. Onychomycosis: an updated review. *Inflamm Allergy Drug Targets*. 2020;14(1):32-45.

STEP THERAPY POLICY

POLICY: Topical Antifungals for Seborrheic Dermatitis Step Therapy Policy

- Ciclopirox shampoo (generic)
- Ciclopirox gel (generic)
- Extina® (ketoconazole foam – Mylan, generic)
- Ketodan® (ketoconazole foam – Medimetriks)
- Ketodan Kit® (ketoconazole foam and salicyclic acid cleanser – Medimetriks)
- Ketoconazole foam (generic)
- Ketoconazole shampoo (generic)

REVIEW DATE: 07/03/2024

OVERVIEW

These topical antifungal agents are indicated for the treatment of **seborrheic dermatitis** caused by *Malassezia* yeast.[1,2,3]

- Ciclopirox shampoo/gel and ketoconazole shampoo/foam are indicated for the treatment of scalp and non-scalp seborrheic dermatitis. All ciclopirox products are indicated in **patients ≥ 16 years of age** while all ketoconazole products are indicated in **patients ≥ 12 years of age**.

GUIDELINES

The American Academy of Family Physicians (AAFP) 2015 and Clinical, Cosmetic, and Investigational Dermatology (CCID) 2022 provide recommendations on management of seborrheic dermatitis (SD). AAFP note ciclopirox shampoo or ketoconazole shampoo may be used for scalp SD and ciclopirox gel or ketoconazole foam may be used for non-scalp SD.[4] CCID non-preferentially recommend ciclopirox or ketoconazole for scalp and non-scalp SD; formulation is guided by patient preference.[5]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic ketoconazole 2% shampoo, generic ciclopirox 1% shampoo, generic ciclopirox 0.77% gel

Step 2: Ketodan, Ketodan Kit, generic ketoconazole 2% foam, Extina Foam

CRITERIA

65. If the patient has tried one Step 1 Product, approve a Step 2 Product.

66. If the patient has tried a combination product containing topical ciclopirox, approve a Step 2 product.

67. No other exceptions are recommended.

REFERENCES

105. Ciclopirox shampoo [prescribing information]. Parsippany, NJ: Actavis; October 2023.
106. Ciclopirox gel [prescribing information]. Mahwah, NJ: Glenmark; January 2017.
107. Ketodan® foam [prescribing information]. Fairfield, NJ: Medimetriks; September 2021.
108. Clark GW, Pope SM, Jaboori KA. Diagnosis and Treatment of Seborrheic Dermatitis. *Am Fam Physician.* 2015;91(3):185-190.
109. Dall'Oglio F, Nasca MR, Gerbino G, et al. An overview of the diagnosis and management of seborrheic dermatitis. *Clinical, Cosmetic and Investigational Dermatology.* 2022:15 1537–1548.

STEP THERAPY POLICY

POLICY: Topical Corticosteroids Step Therapy Policy

* This list is not all-inclusive and may not include all available topical corticosteroids (strength or formulation).

REVIEW DATE: 11/06/2024

OVERVIEW

Topical corticosteroids are, in general, indicated for **symptomatic relief of inflammation and/or pruritus associated with acute and chronic corticosteroid-responsive skin disorders (dermatoses)**.[1]

Topical corticosteroids are adrenocorticosteroid derivatives that possess anti-inflammatory, antipruritic, and vasoconstrictive properties.[1] These products are thought to depress the formation, release, and activity of endogenous chemical mediators of inflammation (kinins, histamine, liposomal enzymes, prostaglandins) through the induction of phospholipase A2 inhibitory proteins (lipocortins), thereby inhibiting the release of arachidonic acid. Skin diseases that are responsive to topical corticosteroids usually have an inflammatory, hyperproliferative, and/or immunologic component (Table 1).

Table 1. Conditions Treated with Topical Corticosteroids.[2]

Topical corticosteroids are incorporated into a vehicle appropriate for application to the skin and external mucous membranes. Ointments are more occlusive and are generally preferred for dry scaly lesions.[1] Creams are generally preferred on oozing lesions or in intertriginous areas where a less occlusive preparation may be beneficial. Additionally, patients may prefer creams for aesthetic reasons although their water content makes them more drying than ointments. Gels, aerosols, lotions, and solutions are easier to apply on hairy areas.

POLICY STATEMENT

This program has been developed to encourage the use of two prescription Step 1a Products prior to the use of a Step 2a Product (Duobrii is not included); or the use of a prescription Step 1b Product prior to the use of Duobrii (Step 2b). If the Step Therapy rule is not met for a Step 2 Product (a or b) at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a history of two prescription Step 1a Products within the 130-day look-back period is excluded from Step Therapy (Note: Duobrii is not included in this Step). For Duobrii (Step 2b), a patient with a of one prescription Step 1b Product within the 130-day look-back period is excluded from Step Therapy.

Step 1a/2a

Step 1a Generic Topical Corticosteroid Products:

Note: This is not an inclusive list.

Step 2a Topical Corticosteroid Products:

Note: This is not an inclusive list.

Step 1b/2b (Duobrii)

Step 1b Generic Topical Corticosteroid Products:

Note: This is not an inclusive list.

Step 2b Topical Corticosteroid Product:

- Duobrii

CRITERIA

Step 2a Topical Corticosteroid Products

1. If the patient has tried two prescription Step 1a Products for the *current* condition, approve a Step 2a Product.

Note: Products with the same chemical entity and same strength should not be considered as separate products.

2. No other exceptions are recommended.

Step 2b Topical Corticosteroid Product (Duobrii)

1. If the patient has tried one prescription Step 1b Product for the *current* condition, approve Duobrii.

2. No other exceptions are recommended.

REFERENCES

1. Facts and Comparisons® eAnswers. Wolters Kluver; 2024. Available at: http://fco.factsandcomparisons.com/lco/action/home Accessed on October 31, 2024. Search terms: topical corticosteroids.
2. Ference JD. Choosing topical corticosteroids. *Am Fam Physician*. 2009;79(2):135-140.

STEP THERAPY POLICY

POLICY: Topical Doxepin Step Therapy Policy

- Generic doxepin cream 5% (Mylan, generic)
- Prudoxin™ (doxepin hydrochloride cream 5% – Mylan, generic)
- Zonalon® (doxepin hydrochloride cream 5% – Mylan, generic)

REVIEW DATE: 05/22/2024

OVERVIEW

Topical doxepin cream 5% (Prudoxin™, Zonalon®, generics) is indicated for the short-term (up to 8 days) **management of moderate pruritus** in adults with atopic dermatitis or lichen simplex chronicus.[1-3]

Doxepin has H_1 and H_2 histamine receptor blocking actions, but the exact mechanism by which it exerts its antipruritic effect is unknown.[1-3] There are no data to establish the safety and effectiveness of doxepin cream when used for > 8 days. Furthermore, chronic use (beyond 8 days) may result in higher systemic levels and increased likelihood of contact sensitization.

Guidelines/Recommendations

The American Academy and American College of Allery, Asthma and Immunology Joint Task Force guidelines for atopic dermatitis (eczema) [2023] recommend moisturizers as first line therapy for mild disease.[4] For refractory atopic dermatitis, guidelines recommend the addition of topical corticosteroids. Topical doxepin is not addressed in the guidelines.

Topical corticosteroids are the current treatment of choice for lichen simplex chronicus because they decrease inflammation and itch while concurrently softening the hyperkeratosis.[5] Alternatives to topical corticosteroids include topical doxepin.

Table 1. Topical Corticosteroids, Classified According to Potency* (Adapted from Facts/Comparisons).[6]

Table 1 (continued). Topical Corticosteroids, Classified According to Potency* (Adapted from Facts/Comparisons).[6]
* This table may not include all available topical corticosteroids (strength or formulation).

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are for 2 months in duration.

Automation: A patient with a of two Step 1 Products within the 130-day look-back period are excluded from Step Therapy.

Step 1: generic prescription topical corticosteroids (see Table 1)

Step 2: Doxepin cream, Prudoxin cream, Zonalon cream

CRITERIA

8. If the patient has tried two Step 1 Products, approve a Step 2 Product.

9. No other exceptions are recommended.

REFERENCES

22. Doxepin hydrochloride cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; May 2017.
23. Prudoxin™ (doxepin hydrochloride) cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; June 2017.
24. Zonalon® (doxepin hydrochloride cream, 5% [prescribing information]. San Antonio, TX: DPT Laboratories; June 2017.
25. AAAAI/ACAAI JTF Atopic Dermatitis Guideline Panel, Chu DK, Schneider L, et al. Atopic dermatitis (eczema) guidelines: 2023 American Academy of Allergy, Asthma and Immunology/American College of Allergy, Asthma and Immunology Joint Task Force on Practice Parameters GRADE- and Institute of Medicine-based recommendations. *Ann Allergy Asthma Immunol.* 2024;132(3):274-312.
26. Lichen simplex chronicus: https://emedicine.medscape.com/article/1123423-treatment?src=refgatesrc1. Updated August 20, 2020 . Accessed on May 16, 2024.
27. Facts and Comparisons® Online. Wolters Kluwer; © 2024 UpToDate, Inc. Available at: http://online.factsandcomparisons.com/login.aspx?url=/index.aspx&qs=. Accessed on May 16, 2024. Search terms: doxepin, corticosteroid.

STEP THERAPY POLICY

POLICY: Topical Medications for Inflammatory Rosacea Step Therapy Policy

- Epsolay® (benzoyl peroxide 5% cream – Galderma)
- Finacea® foam (azelaic acid aerosol 15% – LEO Pharma)
- Finacea® gel (azelaic acid 15% – Bayer Healthcare, generic)
- MetroCream® (metronidazole cream 0.75% – Galderma, generic)
- MetroGel® (metronidazole gel 1% – Galderma, generic)
- MetroLotion® (metronidazole lotion 0.75% – Galderma, generic)
- Noritate® (metronidazole cream 1% – Bausch Health)
- Rosadan® Kits (metronidazole 0.75% gel or 0.75% cream and Rehyla™ Wash – MediMetriks)
- Soolantra® (ivermectin cream 1% – Galderma, generic)
- Zilxi™ (minocycline foam 1.5% – Foamix)

REVIEW DATE: 03/06/2024

OVERVIEW

Topical metronidazole, topical azelaic acid, topical ivermectin, Epsolay, and Zilxi are all indicated for the treatment of **inflammatory lesions of rosacea**.[1-12] The topical metronidazole products are available generically as 0.75% cream, gel, and lotion and 1% gel; as brand Noritate® cream; and as kits (Rosadan® cream or gel with a Rehyla™ wash [moisturizing wash]).[1-5,7,8] Noritate is also indicated for the treatment of erythema of rosacea.[4] Topical azelaic acid 15% is available as a gel (Finacea gel, generic) and a foam (Finacea foam).[9,10] Topical ivermectin (Soolantra, generic) and Epsolay are only available as a cream and Zilxi is only available as a foam.[6,11,12]

Guidelines/Recommendations

The American Acne & Rosacea Society (AARS) updated guidelines on the management of rosacea in 2019 (neither Epsolay nor Zilxi is addressed in the guidelines).[13] A gentle skin care and photoprotection regimen is recommended for all patients with rosacea. In patients with diffuse centrofacial erythema with papulopustular lesions, treatment options are topical metronidazole, topical azelaic acid, topical ivermectin, oral tetracyclines, topical alpha-agonists, and oral isotretinoin.

The ROSacea COnsensus (ROSCO) international expert panel, consisting of 17 dermatologists and three ophthalmologists, released their consensus recommendations in 2017 (updated in 2019).[14,15] The panel notes first-line therapies for patients with mild or moderate inflammatory papules/pustules are topical azelaic acid, topical ivermectin, topical metronidazole, and oral doxycycline. Recommended therapies for patients with severe inflammatory papules/pustules are topical ivermectin, oral doxycycline, and oral isotretinoin.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic azelaic acid gel 15%, generic ivermectin cream 1%, generic metronidazole cream 0.75%, generic metronidazole gel 0.75%, generic metronidazole gel 1%, generic metronidazole lotion 0.75%, Rosadan cream, Rosadan gel

Step 2: Epsolay, Finacea foam, Finacea gel, MetroCream, MetroGel, MetroLotion, Noritate cream, Rosadan Cream Kit, Rosadan Gel Kit, Soolantra, Zilxi

CRITERIA

10. If the patient has tried one Step 1 Product, approve a Step 2 Product.
Note: Soolantra with DAW 9 (indicating that substitution is allowed by the prescriber but the Plan requests brand) will also count as a Step 1 Product.

11. No other exceptions are recommended.

REFERENCES

1. MetroCream® [prescribing information]. Fort Worth, TX: Galderma; January 2017.
2. MetroGel® [prescribing information]. Fort Worth, TX: Galderma; November 2023.
3. MetroLotion® [prescribing information]. Fort Worth, TX: Galderma; February 2017.
4. Noritate® [prescribing information]. Bridgewater, NJ: Bausch Health; June 2020.
5. Facts and Comparisons® Online. Wolters Kluwer Health, Inc.; 2024. Available at: https://fco.factsandcomparisons.com/lco/action/home. Accessed on February 29, 2024. Search terms: azelaic acid, ivermectin, metronidazole, minocycline.
6. Epsolay® cream [prescribing information]. Fort Worth, TX; Galderma; April 2023
7. Rosadan® gel kit. Available at: https://pharmacy.services.conduent.com/mohealthnet/September%202012%20Drug/Rosadan%20gel-kit.pdf. Accessed on February 29, 2024.
8. Rosadan® cream kit [prescribing information]. Available at: https://www.drugs.com/pro/rosadan-cream.html#s-34069-5. February 29, 2024.
9. Finacea® gel [prescribing information]. Whippany, NJ: Bayer Healthcare; August 2016.
10. Finacea® foam [prescribing information]. Madison, NJ: LEO Pharma; December 2020.
11. Soolantra® cream [prescribing information]. Fort Worth, TX: Galderma; October 2022.
12. Zilxi™ topical foam {1.5%} [prescribing information]. Bridgewater, NJ: Foamix; September 2022.
13. Del Rosso JQ, Tanghetti E, Webster G, et al. Update on the management of rosacea from the American Acne & Rosacea Society (AARS). *J Clin Aesthet Dermatol*. 2019;12:17-24.
14. Schaller M, Almeida LMC, Bewley A, et al. Rosacea treatment update: recommendations from the global ROSacea COnsensus (ROSCO) panel. *Br J Derm*. 2017;176:465-471.
15. Scaller M, Almeida LMC, Beley A, et al. Recommendations for rosacea diagnosis, classification and management: update from the global ROSacea COnsensus 2019 panel. *Br J Dermatol*. 2020;182(5):1269-1276.

STEP THERAPY POLICY

POLICY: Topical Podofilox Products Step Therapy Policy

- Condylox® Gel (podofilox 0.5% gel – Allergan, generic)
- Podofilox 0.5% solution – generic only

REVIEW DATE: 01/17/2024

OVERVIEW

Podofilox gel (Condylox, generic) and podofilox solution are topical medications indicated for the topical treatment of **external genital warts**.[1,2] Podofilox gel is also indicated for **perianal warts**.[1]

Podofilox gel and podofilox solution are not indicated in the treatment of mucous membrane warts.[1,2] Although genital and perianal warts have a characteristic appearance, histopathologic confirmation should be obtained if there is any doubt of the diagnosis. Differentiating warts from squamous cell carcinoma (Bowenoid papulosis) is of particular concern. Squamous cell carcinoma may also be associated with human papillomavirus but should not be treated with these products.

For both products, the safety and effectiveness in pediatric patients have not been established.[1,2]

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: podofilox 0.5% topical solution

Step 2: podofilox 0.5% topical gel (Condylox, generic)

CRITERIA

68. If the patient has tried one Step 1 Product, approve a Step 2 Product.

69. If the patient has perianal warts, approve podofilox 0.5% gel (Condylox, generic).

70. No other exceptions are recommended.

REFERENCES

110. Condylox® Gel [prescribing information]. Madison, NJ: Allergan; May 2018.
111. Podofilox topical solution [prescribing information]. Parsippany, NJ: Actavis; October 2022.

STEP THERAPY POLICY

POLICY: Topical Products – Vtama and Zoryve 0.3% Cream Step Therapy Policy
- Vtama® (tapinarof 1% cream – Dermavant)
- Zoryve™ (roflumilast 0.3% cream – Arcutis Biotherapeutics)

REVIEW DATE: 10/16/2024

OVERVIEW

Vtama, an aryl hydrocarbon receptor agonist, is indicated for the topical treatment of **plaque psoriasis** in adults.[1] Zoryve 0.3% cream, a phosphodiesterase 4 (PDE4) inhibitor, is indicated for the topical treatment of **plaque psoriasis**, including intertriginous areas, in patients ≥ 6 years of age.[2] Of note, two other Zoryve products are available. Zoryve 0.15% cream is indicated for the topical treatment of mild to moderate atopic dermatitis in patients ≥ 6 years of age and Zoryve 0.3% foam is indicated for the topical treatment of seborrheic dermatitis in patients ≥ 9 years of age.[6,7] These products are not included in this policy.

Guidelines

The mainstay of treatment of plaque psoriasis is topical therapy, including corticosteroids, vitamin D analogs, calcineurin inhibitors, keratolytics (e.g., tazarotene), and combination therapies (e.g., a corticosteroid with a vitamin D analog).[3] Joint guidelines from the American Academy of Dermatology (AAD) and the Medical Board of the National Psoriasis Foundation (NPF) [2021] have been published for the management of psoriasis with topical therapies.[4] Neither Vtama nor Zoryve 0.3% cream are addressed in the guidelines. Use of a topical corticosteroid for up to 4 weeks is recommended for plaque psoriasis not involving intertriginous areas (strength of recommendation, A). A topical vitamin D analog can be used long-term (up to 52 weeks) for the treatment of psoriasis [strength of recommendation, A]. Guidelines also address use of topical calcineurin inhibitors, topical tazarotene, topical salicyclic acid, and phototherapy.

POLICY STATEMENT

This program has been developed to encourage the use of one or two Step 1 Product(s) prior to the use of a Step 2 Product. A trial of one Step 1a Product (Topical Corticosteroid) and one Step 1b Product (Topical Vitamin D Analog) is required prior to the use of a Step 2 Product; OR a trial of one Step 1c Product (Topical Corticosteroid/Topical Vitamin D Analog combination product) is required prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1a and one Step 1b Product within the 130-day look-back period is excluded from Step Therapy. A patient with one Step 1c Product within the 130-day look-back period is also excluded from Step Therapy. This policy includes age edits: a patient < 6 years of age will be denied coverage for Zoryve 0.3% cream and a patient < 18 years of age will be denied coverage for Vtama.

Step 1a: Topical Corticosteroids (medium-, medium-high, high-, and/or super-high potency prescription topical corticosteroid) [Brand and Generic Products] {See Table 1}

Table 1. Topical Corticosteroids (Groups 1, 2, 3, and 4).[5]

Step 1b: Topical Vitamin D Analogs: calcipotriene 0.005% cream (Dovonex, generic), calcipotriene 0.005% foam, calcipotriene 0.005% ointment, calcipotriene 0.005% solution, calcitriol 3 mcg/g ointment (Vectical, generic), Sorilux

Step 1c: calcipotriene 0.005% and betamethasone dipropionate 0.064% ointment (Taclonex, generic), calcipotriene 0.005% and betamethasone dipropionate 0.064% suspension (Taclonex, generic), Enstilar, Wynzora

Step 2: Vtama, Zoryve 0.3% cream

CRITERIA

1. **Vtama.** Approve if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** Patient has tried one Step 1a Product and one Step 1b product; OR
     - **ii.** Patient has tried one Step 1c Product.
     - **iii.** Patient is treating plaque psoriasis affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia and has tried one Step 1b Product.

2. **Zoryve 0.3% Cream.** Approve if the patient meets BOTH of the following (A and B):
   - **A)** Patient is ≥ 6 years of age; AND
   - **B)** Patient meets ONE of the following (i, ii, or iii):
     - **i.** Patient has tried one Step 1a Product and one Step 1b product; OR
     - **ii.** Patient has tried one Step 1c Product; OR
     - **iii.** Patient is treating plaque psoriasis affecting one of the following areas: face, eyes/eyelids, skin folds, and/or genitalia and has tried one Step 1b Product.

3. No other exceptions are recommended.

REFERENCES

6. Vtama® topical cream [prescribing information]. Long Beach, CA: Dermavant; May 2022.
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8. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. *Lancet*. 2021;397:1301-1315.
9. Elmets C, Korman NJ, Farley Prater E, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021;84:432-470.
10. Facts and Comparisons® Online. Wolters Kluwer Health; 2021. Available at: https://fco.factsandcomparisons.com/lco/action/home. Accessed on October 09, 2023. Search terms: topical corticosteroids.
11. Zoryve® 0.15% topical cream [prescribing information]. Westlake Village, CA: Arcutis; July 2024.
12. Zoryve® 0.3% topical foam [prescribing information]. Westlake Village, CA: Arcutis; December 2023.

STEP THERAPY POLICY

POLICY: Topical Products – Zoryve Foam Step Therapy Policy
- Zoryve™ Foam (roflumilast 0.3% topical foam – Arcutis)

REVIEW DATE: 02/14/2024

OVERVIEW

Seborrheic dermatitis is a chronic inflammatory skin disorder affecting primarily the skin of the scalp, face, chest, and intertriginous areas, causing scaling and redness of the skin.[1,2] Primary treatment options include topical antifungals and topical anti-inflammatory agents.

- Topical antifungals indicated for the treatment of **seborrheic dermatitis** caused by *Malassezia* yeast include:[3-6]
  - Ciclopirox shampoo/gel. The gel formulation is indicated for the treatment of scalp and non-scalp seborrheic dermatitis. All ciclopirox products are indicated in **patients ≥ 16 years of age**.
  - Ketoconazole shampoo/foam. The foam formulation is indicated for the treatment of scalp and non-scalp seborrheic dermatitis. All ketoconazole products are indicated in **patients ≥ 12 years of age**.
- Topical corticosteroids are, in general, indicated for the **symptomatic relief of inflammation and/or pruritus associated with various skin disorders (dermatoses).**[7] Low potency steroids are generally reserved for facial application while higher potency steroids are utilized for the body or scalp.[1,2]

Zoryve foam is indicated for the treatment of **seborrheic dermatitis in patients ≥ 9 years of age**.[8] It is a selective, highly potent phosphodiesterase-4 (PDE4) inhibitor with 25- to 300-fold greater potency than other topical PDE4 inhibitors *in vitro*.[9] The exact mechanism by which Zoryve foam exerts its therapeutic action in SD is not well defined; however, it is a non-steroidal therapy that provides anti-inflammatory benefits.

GUIDELINES

There are no formal treatment guidelines for the management of seborrheic dermatitis. The current standard of care for seborrheic dermatitis is to use multiple agents (usually an antifungal and/or anti-inflammatory). The American Academy of Dermatology cite topical antifungal agents as typical first-line therapy.[1] Low potency topical corticosteroids may be considered as first-line or second-line therapy; however, use is limited to short durations due to the potential for adverse effects. Additionally, recommendations provided by the Clinical, Cosmetic, and Investigational Dermatology (CCID) [2022] non-preferentially recommend topical ciclopirox or topical ketoconazole for scalp and non-scalp seborrheic dermatitis; formulation is guided by patient preference.[2]

POLICY STATEMENT

This program has been developed to encourage the use of one Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: Generic topical corticosteroid, Generic topical antifungal

* This list is not all-inclusive and may not include all available topical corticosteroids (strength or formulation).

Step 2: Zoryve 0.3% foam

CRITERIA

71. If the patient has tried one Step 1 Product, approve a Step 2 Product.

72. If the patient has tried a combination product containing a topical antifungal, approve a Step 2 product.

73. If the patient has tried a combination product containing a topical corticosteroid, approve a Step 2 product.

74. No other exceptions are recommended.

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STEP THERAPY POLICY

POLICY: Topical Vitamin D Analogs Step Therapy Policy

- Calcipotriene 0.005% foam– Trifluent Pharma (authorized generic)
- Calcipotriene 0.005% solution (generic only)
- Dovonex® (calcipotriene cream 0.005% – LEO Pharma, generic)
- Enstilar® (calcipotriene 0.005% and betamethasone dipropionate 0.064% foam – LEO Pharma)
- Sorilux® (calcipotriene foam 0.005% – Mayne Pharma, generic)
- Taclonex® (calcipotriene 0.005% and betamethasone dipropionate 0.064% ointment – LEO Pharma, generic)
- Wynzora® (calcipotriene 0.005% and betamethasone dipropionate 0.064% cream – MC2 Therapeutics)

REVIEW DATE: 11/06/2024

OVERVIEW

The topical vitamin D analog products are indicated for the treatment of **plaque psoriasis**. The specific indications are as follows:[1-10]

- Calcipotriene cream and ointment are indicated for the treatment of **plaque psoriasis of the body in adults**.
- Calcipotriene solution is indicated for the treatment of **plaque psoriasis of the scalp in adults**.
- Dovonex cream is indicated for the treatment of **plaque psoriasis in adults**.
- Enstilar is indicated for the topical treatment of **plaque psoriasis in patients ≥ 12 years** of age.
- Calcipotriene foam 0.005% (authorized generic) and Sorilux are indicated for the topical treatment of **plaque psoriasis of the scalp and body in adults and pediatric patients ≥ 4 years** of age.
- Taclonex ointment is indicated for the topical treatment of **plaque psoriasis in patients ≥ 12 years** of age.
- Wynzora cream is indicated for the topical treatment of **plaque psoriasis in patients ≥ 18 years** of age.

Several of the topical vitamin D analogs are indicated for use in patients < 18 years of age: calcipotriene foam (authorized generic), generic calcipotriene-betamethasone dipropionate ointment, Enstilar foam, Sorilux foam, and Taclonex ointment.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic calcipotriene cream, generic calcipotriene ointment, generic calcipotriene solution

Step 2: generic calcipotriene-betamethasone dipropionate ointment, calcipotriene foam (authorized generic), Dovonex cream, Enstilar foam, Sorilux foam, Taclonex ointment, Wynzora cream

CRITERIA

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.

2. If the patient is < 18 years of age, approve calcipotriene foam (authorized generic), generic calcipotriene-betamethasone dipropionate ointment, Enstilar foam, Sorilux foam, or Taclonex ointment.

3. No other exceptions are recommended.

REFERENCES

1. Calcipotriene cream [prescribing information]. Mahwah, NJ: Glenmark; April 2023.
2. Calcipotriene and betamethasone propionate ointment [prescribing information]. Allegan, MI: Perrigo; January 2020.
3. Dovonex® cream [prescribing information]. Madison, NJ: LEO Pharma.; June 2021.
4. Calcipotriene foam [prescribing information]. Greenville, NC: Mayne Pharma; December 2020.
5. Sorilux® foam [prescribing information]. Greenville, NC: Mayne Pharma; April 2024.
6. Taclonex® ointment [prescribing information]. Madison, NJ: LEO Pharma; January 2023.
7. Taclonex® suspension [prescribing information]. Madison, NJ: LEO Pharma; August 2020.
8. Wynzora® cream [prescribing information]. Dover, DE: MC2 Therapeutics; November 2023.
9. Enstilar® foam [prescribing information]. Madison, NJ: LEO Pharma; April 2022.
10. Calcipotreine solution [prescribing information]. Gurnee, IL: Akorn; June 2022.

STEP THERAPY POLICY

POLICY: Vitamin B12 (Cyanocobalamin) Products Step Therapy Policy
- Cyanocobalamin injection (generic only – various)
- Nascobal® (cyanocobalamin 500 mcg/0.1 mL nasal spray – Par, generic)

REVIEW DATE: 01/17/2024

OVERVIEW

Cyanocobalamin nasal spray (Nascobal, generic) is a vitamin B12 indicated for the following:[1]
- **Pernicious anemia**, vitamin B12 maintenance therapy in adults who are in remission following intramuscular vitamin B12 therapy and who have no nervous system involvement.
- **Vitamin B12 deficiency, treatment**, in adults with dietary, drug-induced, or malabsorption-related vitamin B12 deficiency not due to pernicious anemia.
- **Vitamin B12 deficiency, prevention**, in adults with vitamin B12 requirements in excess of normal.

Cyanocobalamin is also available as an intramuscular injection (1,000 mcg per mL), which is indicated for **vitamin B12 deficiencies** due to malabsorption, which may be associated with the following conditions: pernicious anemia; gastrointestinal pathology, dysfunction, or surgery (including gluten enteropathy or sprue, small bowel bacteria overgrowth, or total or partial gastrectomy); fish tapeworm infestation; malignancy of the pancreas or bowel, or folic acid deficiency.[2]

Over-the-counter vitamin B12 oral supplements are also available, although these are poorly absorbed when intrinsic factor is absent (i.e., pernicious anemia).[3]

Disease Overview

Vitamin B12 (cobalamin), a water-soluble vitamin, is necessary for proper red blood cell formation, neurological function, and DNA synthesis.[3] Vitamin B12, bound to protein in food, is released by hydrochloric acid and gastric protease in the stomach. Vitamin B12 then complexes with intrinsic factor and is absorbed in the distal ileum. Thus, patients with deficiencies in stomach acid, intrinsic factor, or gastrointestinal absorption are at risk for development of vitamin B12 deficiency. Oral vitamin B12 supplements are provided in the free (not protein bound) form, therefore individuals with hydrochloric acid deficiency are typically able to meet their vitamin B12 needs with oral vitamin supplementation or fortified foods. Likewise, oral vitamin B12 supplementation has demonstrated efficacy in correcting deficiency related to gastrointestinal malabsorption, including gastric bypass and Crohn's disease.[4-6] Conversely, in pernicious anemia (characterized by the absence of intrinsic factor), only 1% of oral vitamin B12 is absorbed.[3] Thus, patients with pernicious anemia are typically treated with injectable vitamin B12.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: cyanocobalamin injection

Step 2: cyanocobalamin nasal spray (Nascobal, generic)

CRITERIA

75. If the patient has tried one Step 1 Product, approve a Step 2 Product.

76. No other exceptions are recommended.

REFERENCES

121. Nascobal® nasal spray [prescribing information]. Chestnut Ridge, NY: Par; November 2018.
122. Cyanocobalamin injection [prescribing information]. Shirley, NY: American Regent; October 2018.
123. Vitamin B12 Fact Sheet for Health Professionals. National Institutes of Health Office of Dietary Supplements. Updated December 15, 2023. Available at: https://ods.od.nih.gov/factsheets/VitaminB12-HealthProfessional/. Accessed on January 8, 2024.
124. Andrès E, Zulfiqar AA, Serraj K, et al. Systematic review and pragmatic clinical approach to oral and nasal vitamin B12 (cobalamin) treatment in patients with vitamin B12 deficiency related to gastrointestinal disorders. *J Clin Med*. 2018; 7(10):304.
125. Gomollón F, Gargallo CJ, Muñoz JF, et al. Oral Cyanocobalamin is Effective in the Treatment of Vitamin B12 Deficiency in Crohn's Disease. *Nutrients*. 2017; 9(3):308.
126. Schijns W, Homan J, van der Meer L, et al. Efficacy of oral compared with intramuscular vitamin B-12 supplementation after Roux-en-Y gastric bypass: a randomized controlled trial. *Am J Clin Nutr*. 2018; 108(1):6-12.

STEP THERAPY POLICY

POLICY: Vitamin D Analog (Oral) Step Therapy Policy

- Doxercalciferol capsules (generic only)
- Rayaldee® (calcifediol extended-release capsule – OPKO)
- Rocaltrol® (calcitriol capsules and oral solution – Validus, generic)
- Zemplar® (paricalcitol capsules – Abbvie, generic)

REVIEW DATE: 09/18/2024

OVERVIEW

The **oral vitamin D analogs** are all **indicated for the management of secondary hyperparathyroidism associated with chronic kidney disease (CKD) in patients not on dialysis.**[1-4] All of the oral agents, with the exception of Rayaldee, are also indicated for secondary hyperparathyroidism in patients receiving dialysis. Additionally, calcitriol capsules and oral solution are indicated for the management of hypocalcemia in patients with certain hypoparathyroidism diagnoses.

Guidelines

The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of chronic kidney disease-metabolic bone disease (2017) no longer recommend routine use of calcitriol and the vitamin D analogs in patients with CKD Stages 3a through 5 (not receiving dialysis).[5] Calcitriol and vitamin D analogs may be used in patients with CKD G4 to G5 with severe and progressive hyperparathyroidism. In patients with CKD G5D requiring parathyroid hormone-lowering therapy, treatment with calcimimetics, calcitriol, or vitamin D analogs, or a combination of calcimimetics with calcitriol or vitamin D analogs are suggested. The guidelines do not note a preference for one product over another; all would be appropriate initial therapy choices.

POLICY STATEMENT

This program has been developed to encourage the use of a Step 1 Product prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

Automation: A patient with a of one Step 1 Product within the 130-day look-back period is excluded from Step Therapy.

Step 1: generic calcitriol capsules, generic calcitriol oral solution

Step 2: generic doxercalciferol capsules, generic paricalcitol capsules, Rayaldee capsules, Rocaltrol capsules (brand), Rocaltrol oral solution (brand), Zemplar capsules

CRITERIA

4. If the patient has tried one Step 1 Product, approve a Step 2 Product.

5. If the patient has tried intravenous (IV) calcitriol injection, approve a Step 2 Product.

6. No other exceptions are recommended.

REFERENCES

11. Doxercalciferol capsules [prescribing information]. Congers, NY: Chartwell Rx; January 2023.
12. Rayaldee® extended-release capsules [prescribing information]. Miami, FL: OPKO; January 2024
13. Zemplar® capsules [prescribing information]. North Chicago, IL: Abbvie; August 2024.
14. Rocaltrol® capsules and oral solution [prescribing information]. Parsippany, NJ: Validus; January 2021
15. Kidney Disease Improving Global Outcomes (KDIGO). KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease – mineral and bone disorder (CKD-MBD). *Kid Int Supp*. 2017;7:1-59.