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; 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.

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

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 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.

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 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

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 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.

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 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

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.
7. Prozac® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
8. Paxil® tablets and oral suspension [prescribing information]. Weston, FL: Apotex; August 2023.
9. Zoloft® tablets, oral concentrate [prescribing information]. New York, NY: Pfizer; August 2023.
10. Celexa® tablets and oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
11. Paxil CR® controlled-release tablets [prescribing information]. Weston, FL: Apotex; February 2024.
12. Lexapro® tablets/oral solution [prescribing information]. Irvine, CA: Allergan; August 2023.
13. Pexeva® paroxetine mesylate tablets [prescribing information]. Roswell, GA: Sebela; August 2023.
14. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI: August 2023.
15. Fluvoxamine extended-release capsules [prescribing information]. Chestnut Ridge, NY: Par; October 2023.
16. Sarafem® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
17. Viibryd® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.
18. Trintellix™ tablets [prescribing information]. Lexington, MA and Deerfield, IL: Takeda and Lundbeck; August 2023.
19. Brisdelle® capsules [prescribing information]. Roswell, GA: Sebela; August 2023.
20. Sertraline capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
21. Citalopram capsules [prescribing information]. Morristown, NJ: Almatica; August 2023.
22. Cymbalta® capsules [prescribing information]. Indianapolis, IN: Lilly; August 2023.
23. Effexor XR® extended-release capsules [prescribing information]. Morgantown, WV: Viatris; August 2023.
24. Venlafaxine hydrochloride tablets [prescribing information]. Parsippany, NJ: Teva; August 2023.
25. Pristiq® extended-release tablets [prescribing information]. Philadelphia, PA: Wyeth; August 2023.
26. Venlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; September 2023.
27. Venlafaxine besylate extended-release tablets [prescribing information]. Morristown, NJ: Almatica; August 2023.
28. Fetzima® extended-release capsules [prescribing information]. North Chicago, IL: AbbVie; August 2023.
29. Desvenlafaxine extended-release tablets [prescribing information]. Cranbury, NJ: Sun; August 2023.
30. Drizalma Sprinkle™ delayed-release capsules [prescribing information]. Cranbury, NJ: Sun; August 2023.
31. Savella® tablets [prescribing information]. Madison, NJ: Allergan; August 2023.