

Drug Policy

Policy:	Antidepressants – Bupropion Long-Acting Step Therapy Policy	Annual Review Date: 05/22/2025
Impacted Drugs:	<ul style="list-style-type: none"> 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) 	Last Revised Date: 05/22/2025

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

Brand / Generic name	Formulation	Strengths	Notes
Aplenzin® (bupropion HBr)	ER tablets	174, 348, 522 mg	Strengths are equivalent to 150, 300, and 450 mg of bupropion HCl, respectively.
Auvelity™ (dextromethorphan HBr and bupropion HCl)	ER tablets	45 mg/105 mg	Bupropion increases plasma levels of dextromethorphan by competitively inhibiting CYP2D6, which catalyzes a major biotransformation pathway for dextromethorphan.
Forfivo XL (bupropion HCl), authorized generics	ER tablets	450 mg	Use another bupropion formulation for initial dose titration. Patients being treated with other bupropion products at 450 mg/day can be switched to equivalent dose of Forfivo XL once daily.
Wellbutrin SR® (bupropion HCl), generic	SR tablets	100, 150, 200 mg	Available generically.
Wellbutrin XL® (bupropion HCl), generic	ER tablets	150, 300 mg	Available generically.

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

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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.

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.

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: Auvelity, Forfivo XL

Step 3: Aplenzin

CRITERIA

Step 2 Products

1. If the patient has tried two Step 1 Products (one being a bupropion product), approve a Step 2 Product.

Step 3 Products

1. If the patient has tried one step 2 product, approve Aplenzin.

Initial Approval/ Extended Approval.

A) Initial Approval: 2 years

B) Extended Approval: 2 years

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Step Therapy Exception Criteria

In certain situations, the patient is not required to trial preferred agents. Approve for 1 year if the patient meets the following (A, B, or C):

- A. The patient has an atypical diagnosis and/or unique patient characteristics which prevent use of all preferred agents. If so, please list diagnosis and/or patient characteristics*; **OR**
- B. The patient has a contraindication to all preferred agents. If so, please list the contraindications to each preferred agent*; **OR**
- C. The patient is continuing therapy with the requested non-preferred agent after being stable for at least 90 days. Verification in prescription claims history is required or, if not available, verification by prescribing physician is required **AND** meets **ONE** of the following:
 - 1. The patient has at least 130 days of prescription claims history on file and claims history supports that the patient has received the requested non-preferred agent for 90 days within a 130-day look-back period **AND** there is no generic equivalent available for the requested nonpreferred product (i.e. AA-rated or AB-rated to the requested nonpreferred product); **OR**
 - 2. When 130 days of the patient's prescription claims history file is unavailable for verification, the prescriber must verify that the patient has been receiving the requested non-preferred agent for 90 days **AND** that the patient has been receiving the requested non-preferred agent via paid claims (i.e. the patient has **NOT** been receiving samples or coupons or other types of waivers in order to obtain access to the requested non-preferred agent) **AND** there is no generic equivalent available for the requested nonpreferred product (i.e. AA-rated or AB-rated to the requested nonpreferred product).

Documentation Required: When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents, noted in the criteria as an asterisk (*). Documentation should include chart notes, prescription claims records, and/or prescription receipts.

Approval Duration: All approvals for continuation of therapy are provided for 1 year unless noted otherwise below. In cases where the initial approval is authorized in months, 1 month is equal to 30 days.

*Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Wellbutrin SR® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; December 2022.

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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. Zyban® sustained-release tablets [prescribing information]. Research Triangle Park, NC: GlaxoSmithKline; March 2021.