Clinical Policy: Dextromethorphan/Bupropion (Auvelity)

Reference Number: ERX.NPA.166
Effective Date: 12.01.22
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Dextromethorphan/bupropion (Auvelity™) is an extended-release, fixed-dose combination of dextromethorphan hydrobromide, an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist and sigma-1 receptor agonist, and bupropion hydrochloride, an aminoketone and CYP450 2D6 inhibitor.

FDA Approved Indication(s)
Auvelity is indicated for the treatment of major depressive disorder (MDD) in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Auvelity is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Major Depressive Disorder (must meet all)**:**

1. Diagnosis of MDD;
2. Age ≥ 18 years;
3. Failure of TWO of the following, each tried for ≥ 4 weeks at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: SSRI, SNRI, bupropion, mirtazapine;
4. Dose does not exceed both of the following (a and b):
   a. 90 mg dextromethorphan and 210 mg bupropion per day;
   b. 2 tablets per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Major Depressive Disorder (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed both of the following (a and b):
   a. 90 mg dextromethorphan and 210 mg bupropion per day;
   b. 2 tablets per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor
MDD: major depressive disorder
SNRI: serotonin norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bupropion (Wellbutrin® XL)	150-450 mg PO QAM	450 mg/day
mirtazapine (Remeron®)	15-45 mg PO QHS	45 mg/day
SSRIs		
citalopram (Celexa®)	20 mg PO QD	40 mg/day (≤ 60 years) 20 mg/day (> 60 years)
escitalopram (Lexapro®)	10-20 mg PO QD	20 mg/day
Fluvoxamine® (Luvox CR®)	50-300 mg PO QD	300 mg/day
fluoxetine (Prozac®)	20 mg PO QD	80 mg/day
paroxetine (Paxil®)	20 mg PO QD	50 mg/day
paroxetine controlled release (Paxil CR®)	25 mg PO QD	62.5 mg/day
sertraline (Zoloft®)	50 mg PO QD	200 mg/day
SNRIs		
desvenlafaxine (Pristiq®)	50 mg PO QD	400 mg/day
duloxetine (Cymbalta®)	20 mg PO BID, 30 mg BID, or 60 mg PO QD	120 mg/day
venlafaxine (Effexor®)	75 mg PO BID to TID	225 mg/day
Fetzima® (levomilnacipran)	40-120 mg PO QD	120 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): seizure disorder; current or prior diagnosis of bulimia or anorexia nervosa; abrupt discontinuation of alcohol, benzodiazepine, barbiturates, and antiepileptic drugs; use with an MAOI or within 14 days of stopping treatment with Auvelity - do not use Auvelity within 14 days of discontinuing an MAOI; hypersensitivity to bupropion, dextromethorphan, or other components of Auvelity
- Boxed warning(s): increased risk of suicidal thoughts and behavior in pediatric and young adult patients taking antidepressants. Closely monitor all antidepressant-treated patients for clinical worsening and emergence of suicidal thoughts and behaviors. Auvelity is not approved for use in pediatric patients

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MDD	1 tablet PO QD for the first 3 days, then 1 tablet PO BID given at least 8 hours apart	2 tablets/day (dextromethorphan 90 mg/ bupropion 210 mg)

VI. Product Availability

Extended-release tablet: dextromethorphan 45 mg/bupropion 105 mg

VII. References

1. Auvelity Prescribing Information. New York, NY: Axsome Therapeutics, Inc. August 2022. Available at www.auvelity.com. Accessed September 6, 2022.
2. Auvelity Drug Monograph. Clinical Pharmacology. Accessed September 6, 2022. www.clinicalkey.com/pharmacolgy.
3. Losifescu DV, Jones A, O'Gorman C, et al. Efficacy and safety of AXS-05 (dextromethorphan-bupropion in patients with major depressive disorder: a phase 3 randomized clinical trial (GEMINI). J Clin Psychiatry 2022;83(4):21m14345. https://doi.org/10.4088/JCP.21m14345.
4. Tabuteau H, Jones A, Anderson A, Jacobson M, Losifescu DV. Effect of AXS-05 (dextromethorphan-bupropion) in major depressive disorder: a randomized double-blind controlled trial. Am J Psychiatry 2022; 179:490. https://doi.org/10.1176/appi.ajp.21080800.
5. Gelenberg AJ, Freeman MP, Markowitz JC, et al. Practice guideline for the treatment of patients with major depressive disorder, third edition. Arlington, VA: American Psychiatric Association; May 2010. Available online at: http://www.psychiatryonline.org/guidelines. Accessed September 6, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.27.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.