

Auvelity® (dextromethorphan/bupropion)

Policy # 00830

Original Effective Date: 03/13/2023

Current Effective Date: 03/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Auvelity®‡ (dextromethorphan/bupropion) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for Auvelity (dextromethorphan/bupropion) will be considered when the following criteria are met:

- Patient has a diagnosis of major depressive disorder; AND
- Patient is 18 years of age or older; AND
- Patient has tried and failed (for example, intolerance or inadequate response) at least THREE other formulary drugs to treat major depressive disorder, which includes citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, desvenlafaxine, duloxetine, venlafaxine, bupropion, vilazodone, and Trintellix, unless there is clinical evidence or patient history that suggests the use of the alternative agents will be ineffective or cause an adverse reaction to the patient.

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Auvelity (dextromethorphan/bupropion) when the patient has not tried and failed at least THREE formulary alternatives to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Auvelity (dextromethorphan/bupropion) when patient selection criteria are not met (except those denoted to be **not medically necessary****) to be **investigational**.*

Background/Overview

Auvelity is a combination of dextromethorphan and bupropion and is indicated for the treatment of major depressive disorder in adults. The dextromethorphan component of the product exerts its antidepressant effect by antagonizing the N-methyl-D-aspartate (NMDA) receptor, making this product the first oral agent with this mechanism to be approved for major depressive disorder. The bupropion component increases the plasma levels of dextromethorphan by inhibiting the primary metabolic enzyme for dextromethorphan in addition to exerting its own antidepressant effects. The maintenance dose of Auvelity is one tablet taken by mouth twice daily. Each tablet contains 45 mg of dextromethorphan hydrobromide and 105 mg bupropion hydrochloride. Auvelity is contraindicated in patients with a seizure disorder; patients undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, or antiepileptic drugs; and patients who are pregnant. Although it is not a controlled substance, there is a potential for this agent to be misused, diverted, and/or abused due to its ability to cause dissociative effects. Therefore, patients with a history of substance use disorder should be observed closely for signs of misuse or abuse. Auvelity is a therapeutic alternative to the multiple other antidepressant therapies available, including bupropion products, of which many have well established efficacy and safety profiles and broader utility in clinical practice.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Auvelity was approved in August 2022 for the treatment of major depressive disorder in adults.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Auvelity for the treatment of major depressive disorder in adults was demonstrated in a placebo-controlled clinical study (Study 1) and confirmatory evidence which included a second study comparing Auvelity to bupropion sustained-release tablets (Study 2).

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In Study 1, adult patients who met the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for MDD were randomized to receive Auvelity twice daily (n=156) or placebo twice daily (n=162) for 6 weeks. The primary outcome measure was the change from baseline to Week 6 in the total score of the Montgomery-Asberg Depression Rating Scale (MADRS). The MADRS is a clinician-rated scale used to assess the severity of depressive symptoms. Patients are rated on 10 items to assess feelings of sadness, inner tension, reduced sleep or appetite, difficulty concentrating, lassitude, lack of interest, pessimism, and suicidality. Scores on the MADRS range from 0 to 60, with higher scores indicating more severe depression. Auvelity was statistically significantly superior to placebo in improvement of depressive symptoms as measured by decrease in MADRS total score at Week 6. The Auvelity group experienced a LS mean change from baseline (SE) of -15.9 (0.9) compared to -12.1 (0.9) in the placebo group.

In Study 2, patients with MDD were randomized to receive Auvelity or bupropion hydrochloride sustained-release tablets 105 mg twice daily for 6 weeks. The primary outcome measure was calculated by assessing the change from baseline in total MADRS score at each on-site visit from Week 1 to Week 6 and then taking the average of those scores. The results of the study demonstrated that dextromethorphan contributes to the antidepressant properties of Auvelity.

References

1. Auvelity [package insert]. Axsome Therapeutics, Inc. New York, NY. Updated December 2022.
2. Auvelity Drug Evaluation. Express Scripts. Updated August 2022.

Policy History

Original Effective Date: 03/13/2023

Current Effective Date: 03/01/2026

02/02/2023 Medical Policy Committee review

02/08/2023 Medical Policy Implementation Committee approval. New policy.

02/01/2024 Medical Policy Committee review

02/14/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/06/2025 Medical Policy Committee review

02/12/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

02/05/2026 Medical Policy Committee review

02/11/2026 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 02/2027

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***Investigational** – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

****Medically Necessary (or “Medical Necessity”)** - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.