



**BlueCross
BlueShield**

Federal Employee Program.

Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.60.058

Section:	Prescription Drugs	Effective Date:	April 1, 2026
Subsection:	Central Nervous System Drugs	Original Policy Date:	April 14, 2023
Subject:	Auvelity	Page:	1 of 4

Last Review Date: March 6, 2026

Auvelity

Description

Auvelity (dextromethorphan and bupropion)

Background

Auvelity is a combination of dextromethorphan, an uncompetitive N-methyl D-aspartate (NMDA) receptor antagonist and a sigma-1 receptor agonist, and bupropion, an aminoketone and cytochrome P450 2D6 inhibitor. Bupropion increases plasma levels of dextromethorphan by competitively inhibiting cytochrome P450 2D6, which catalyzes a major biotransformation pathway for dextromethorphan. Bupropion is a relatively weak inhibitor of neuronal reuptake of norepinephrine and dopamine and does not inhibit monoamine oxidase or the reuptake of serotonin. The mechanism of Auvelity in the treatment of major depressive disorder (MDD) is unclear (1).

Regulatory Status

FDA-approved indications: Auvelity is indicated for the treatment of major depressive disorder (MDD) in adults (1).

Auvelity has a boxed warning regarding increased risk of suicidal thoughts and behaviors in pediatric and young adult patients taking antidepressants. Antidepressant-treated patients should be closely monitored for clinical worsening and emergence of suicidal thoughts and behaviors (1).

Contraindications to Auvelity include the following: seizure disorder; current or prior diagnosis of bulimia or anorexia nervosa; abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs; and use with a monoamine oxidase inhibitor (MAOI) or within 14 days of stopping treatment (1).

Section:	Prescription Drugs	Effective Date:	April 1, 2026
Subsection:	Central Nervous System Drugs	Original Policy Date:	April 14, 2023
Subject:	Auvelity	Page:	2 of 4

The use of Auvelity has been associated with seizures, increased blood pressure, activation of mania or hypomania, psychosis and other neuropsychiatric reactions, and angle-closure glaucoma. Patients should be screened and monitored for these outcomes and the medication discontinued as medically indicated. The use of this medication in combination with selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants increase the risk of serotonin syndrome. If this occurs, the medication should be discontinued (1).

The components of Auvelity, dextromethorphan and bupropion, have abuse potential. Prescribers should proceed with caution in patients with a history of substance abuse and consider the risks and benefits of using Auvelity in this patient population (1).

Auvelity may cause fetal harm when administered to pregnant women. Pregnant women should be advised of the potential risk to a fetus. Discontinue treatment in pregnant females and use alternative treatment for females who are planning to become pregnant (1).

The safety and effectiveness of Auvelity in pediatric patients less than 18 years of age have not been established (1).

Related policies

Spravato

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Auvelity may be considered **medically necessary** if the conditions indicated below are met.

Auvelity may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Major depressive disorder (MDD)

Section:	Prescription Drugs	Effective Date:	April 1, 2026
Subsection:	Central Nervous System Drugs	Original Policy Date:	April 14, 2023
Subject:	Auvelity	Page:	3 of 4

AND the following:

- a. Patient has had an inadequate response, intolerance, or contraindication to at least **TWO** different antidepressants

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Major depressive disorder (MDD)

AND the following:

- a. Condition has improved or stabilized on therapy

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 180 tablets per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Auvelity is a combination of dextromethorphan and bupropion. Increased risk of suicidal thoughts and behavior in pediatric and young adult patients may occur. Auvelity should be discontinued in pregnant females due to risk of embryo-fetal toxicity. The safety and

Section:	Prescription Drugs	Effective Date:	April 1, 2026
Subsection:	Central Nervous System Drugs	Original Policy Date:	April 14, 2023
Subject:	Auvelity	Page:	4 of 4

effectiveness of Auvelity in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Auvelity while maintaining optimal therapeutic outcomes.

References

1. Auvelity [package insert]. New York, NY: Axsome Therapeutics, Inc.; November 2025.

Policy History

Date	Action
April 2023	Addition to PA
June 2023	Annual review
December 2023	Annual review
March 2024	Annual review
December 2024	Annual review and reference update
March 2025	Annual review
March 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 6, 2026 and is effective on April 1, 2026.