Auvelity™
(dextromethorphan HBr and bupropion HCl)
extended-release tablets 45mg/105mg

Introducing Auvelity—with efficacy starting at 1 week, the first and only oral NMDA receptor antagonist approved for the treatment of major depressive disorder in adults.[1-3*]

Auvelity uses a new approach to treat major depressive disorder that is different from other oral antidepressants approved in more than 60 years[1-3†]

Please see Important Safety Information below and full Prescribing Information, including **Boxed Warning** for suicidal thoughts and behaviors.

Why Auvelity?

Rapid symptom improvement starting at Week 1 and sustained at Week 6*

People taking Auvelity had significant change from baseline in the MADRS total score compared to placebo at Week 1 (key secondary endpoint: LS mean difference of 2.2; *P*=0.007). This change was sustained and increased at Week 6 (primary endpoint: LS mean difference of 3.9; *P*=0.002).[1,4]

Rapid remission as early as Week 2*

Significantly more patients achieved remission with Auvelity at Week 2 vs placebo (key secondary endpoint: 17% vs 8%; *P*=0.013).[4]

Demonstrated safety profile*

The most common adverse reactions (≥5% and more than twice as frequently as placebo): dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, and hyperhidrosis.

Long-term safety and efficacy at 1 year‡

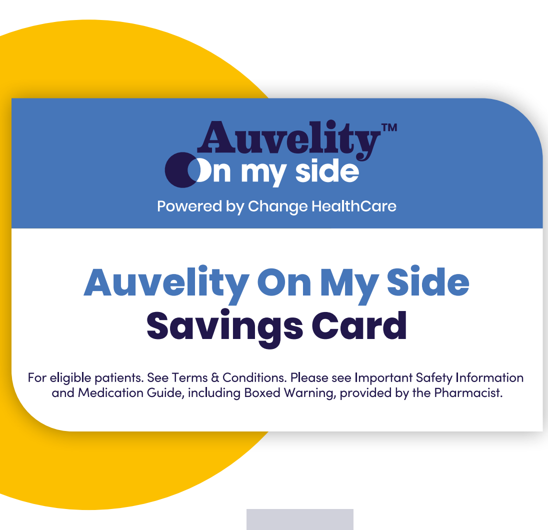
Open-label 1-year safety and efficacy data were consistent with the controlled clinical trials.[1,4-6]

*The GEMINI Phase 3 study evaluated Auvelity vs placebo in 327 patients (N=163 Auvelity and N=164 placebo) with MDD for 6 weeks. The mITT population was n=156 Auvelity and n=162 placebo. Key primary endpoint was change in MADRS total score from baseline at Week 6 (-15.2 Auvelity vs -12.1 placebo). Key secondary endpoints included change in MADRS total score from baseline at Week 1 (-7.2 Auvelity vs -5.0 placebo) and remission (MADRS total score ≤10) at Week 2. The safety population was n=162 Auvelity and n=164 placebo.
†The mechanism of action of Auvelity in the treatment of MDD is unclear.
‡The COMET Phase 3 open-label safety study assessed Auvelity up to 1 year in 876 patients (roll-over from prior Auvelity studies and newly enrolled) with MDD. Efficacy measures were secondary endpoints based on newly enrolled patients (n=609). At Week 6, patients previously untreated with Auvelity who did not achieve ≥25% improvement in MADRS total score were discontinued.

Auvelity patient support

Support and more

The **Auvelity On My Side Program** allows patients to sign up to receive helpful tips and resources, including real-life experiences from Auvelity patients, delivered directly to their inbox.



Saving can be simple

Auvelity On My Side Savings Copay Card helps eligible commercially-insured patients afford their medication.

INDICATION
Auvelity is indicated for the treatment of major depressive disorder (MDD) in adults.

IMPORTANT SAFETY INFORMATION

WARNING: SUICIDAL THOUGHTS AND BEHAVIORS
- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adult patients in short-term studies.**
- **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.**

CONTRAINDICATIONS
Seizure: Do not use Auvelity in patients with a seizure disorder.

Current or prior diagnosis of bulimia or anorexia nervosa: A higher incidence of seizure was observed in such patients treated with bupropion.

Undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs: Due to risk of seizure.

Monoamine Oxidase Inhibitors (MAOIs): Do not use Auvelity concomitantly with, or within 14 days of stopping, an MAOI due to the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome. Conversely, at least 14 days must be allowed after stopping Auvelity before starting an MAOI antidepressant. Do not use Auvelity with reversible MAOIs such as linezolid or intravenous methylene blue.

Hypersensitivity: Do not use in patients with known hypersensitivity to dextromethorphan, bupropion, or any component of Auvelity. Anaphylactoid/anaphylactic reactions and Stevens-Johnson syndrome have been reported with bupropion. Arthralgia, myalgia, fever with rash, and other serum sickness-like symptoms suggestive of delayed hypersensitivity have also been reported with bupropion.

WARNINGS AND PRECAUTIONS
Suicidal Thoughts and Behaviors in Pediatrics and Young Adults: Monitor all antidepressant-treated patients for any indication for clinical worsening and emergence of suicidal thoughts and behaviors, especially during the initial few months of drug therapy, and at times of dosage changes. Counsel family members or caregivers of patients to monitor for changes in behavior and to alert the healthcare provider. Consider changing the therapeutic regimen, including possibly discontinuing Auvelity, in patients whose depression is persistently worse, or who are experiencing emergent suicidal thoughts or behaviors.

Seizure: Bupropion, a component of Auvelity, can cause seizure and the risk is dose related. Because the risk of seizure with bupropion is dose-related, screen patients for use of other bupropion-containing products prior to initiating Auvelity. If concomitant use of Auvelity with other bupropion-containing products is clinically warranted, inform patients of the risk. Discontinue Auvelity and do not restart treatment if the patient experiences a seizure.

Increased Blood Pressure and Hypertension: Treatment with bupropion, a component of Auvelity, can cause elevated blood pressure and hypertension. The risk of hypertension is increased if Auvelity is used concomitantly with MAOIs or other drugs that increase dopaminergic or noradrenergic activity. Assess blood pressure before initiating treatment with Auvelity and monitor periodically during treatment. Monitor blood pressure, particularly in patients who receive the combination of bupropion and are receiving nicotine replacement.

Activation of Mania/Hypomania: Antidepressant treatment can precipitate a manic, mixed, or hypomanic episode. The risk appears to be increased in patients with bipolar disorder or who have risk factors for bipolar disorder. Prior to initiating Auvelity, screen patients for a history of bipolar disorder and the presence of risk factors for bipolar disorder (e.g., family history of bipolar disorder, suicide, or depression). Auvelity is not approved for use in treating bipolar depression.

Psychosis and Other Neuropsychiatric Reactions: Auvelity contains bupropion and dextromethorphan. Depressed patients treated with bupropion have had a variety of neuropsychiatric signs and symptoms, including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment. Dextromethorphan overdose can cause toxic psychosis, stupor, coma, and hyperexcitability.

Because the risks of neuropsychiatric reactions are dose-related, screen patients for use of other bupropion- or dextromethorphan-containing products prior to initiating Auvelity. If concomitant use of Auvelity with other bupropion- or dextromethorphan-containing products is clinically warranted, monitor patients for neuropsychiatric reactions and instruct patients to contact a healthcare provider if such reactions occur.

Angle-Closure Glaucoma: The pupillary dilation that occurs following use of many antidepressants, including Auvelity, may trigger an angle closure attack in a patient with anatomically narrow angles who does not have a patent iridectomy. Avoid use of antidepressants, including Auvelity, in patients with untreated anatomically narrow angles.

Dizziness: Auvelity may cause dizziness. Precautions to reduce the risk of falls should be taken, particularly for patients with motor impairment affecting gait or a history of falls. Caution patients about operating hazardous machinery, including motor vehicles, until they are reasonably certain that Auvelity therapy does not affect them adversely.

Serotonin Syndrome: Auvelity contains dextromethorphan. Concomitant use with selective serotonin reuptake inhibitors (SSRIs) or tricyclic antidepressants increases the risk of serotonin syndrome, a potentially life-threatening condition. Prior to initiating therapy with Auvelity, screen patients for use of other dextromethorphan-containing products. If concomitant use of Auvelity with other serotonergic drugs is clinically warranted, inform patients of the increased risk for serotonin syndrome, and monitor for symptoms. Discontinue Auvelity and/or concomitant serotonergic drug(s) immediately if symptoms of serotonin syndrome occur and initiate supportive symptomatic treatment.

Embryo-fetal Toxicity: Based on animal studies, Auvelity may cause fetal harm when administered during pregnancy. Discontinue treatment in pregnant females and advise the patient about the potential risk to a fetus. Use alternative treatment for females who are planning to become pregnant.

DRUG INTERACTIONS
Strong Inhibitors of CYP2D6: Concomitant use with Auvelity increases plasma concentrations of dextromethorphan. Dosage adjustment is necessary. Monitor patients for adverse reactions potentially attributable to dextromethorphan, such as somnolence and dizziness.

Strong CYP2B6 Inducers: Concomitant use with Auvelity decreases plasma concentrations of dextromethorphan and bupropion and may decrease efficacy of Auvelity. Avoid co-administration of Auvelity.

CYP2D6 Substrates: Concomitant use with Auvelity can increase the exposures of drugs that are substrates of CYP2D6. It may be necessary to decrease the dose of CYP2D6 substrates, particularly for drugs with a narrow therapeutic index.

Digoxin: Concomitant use with Auvelity may decrease plasma digoxin levels. Monitor plasma digoxin levels in patients treated concomitantly with Auvelity.

Drugs that Lower Seizure Threshold: Concomitant use with Auvelity may increase risk of seizure. Use Auvelity with caution. Discontinue Auvelity and do not restart treatment if the patient experiences a seizure.

Dopaminergic Drugs: Concomitant use with Auvelity can result in central nervous system toxicity. Use Auvelity with caution.

USE IN SPECIFIC POPULATIONS
Lactation: Because of the potential for neurotoxicity, advise patients that breast-feeding is not recommended during treatment with Auvelity and for 5 days following final dose.

Renal Impairment: Dosage adjustment is recommended in patient with moderate renal impairment (eGFR 30 to 59 mL/minute/1.73 m^2). Auvelity is not recommended in patients with severe renal impairment (eGFR 15 to 29 mL/minute/1.73 m^2).

Hepatic Impairment: Auvelity is not recommended in patients with severe hepatic impairment.

ADVERSE REACTIONS
Most common adverse reactions (≥5% and twice the rate of placebo): dizziness (16%), headache (8%), diarrhea (7%), somnolence (7%), dry mouth (6%), sexual dysfunction (6%), and hyperhidrosis (5%).

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Sign up for updates at Auvelity.com

LS=least square; MADRS=Montgomery-Åsberg Depression Rating Scale; MDD=major depressive disorder; mITT=modified intention-to-treat; NMDA=N-methyl-D-aspartate

References: **1.** Auvelity [Prescribing Information]. Axsome Therapeutics, Inc.: New York, NY. **2.** FDA Depression Medicines. https://www.fda.gov/media/132665/download. Accessed March 21, 2022. **3.** Thomas D, and Wessel C. The state of innovation in highly prevalent chronic diseases volume I: Depression therapeutics. December 2017. https://www.bio.org/sites/default/files/legacy/bioorg/docs/BIO_HPCD_Series-Depression_2018-01-03.pdf. Accessed March 21, 2022. **4.** Iosifescu 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. **5.** Data on File. AXS0060921. **6.** Data on File. AXS0070921.

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