Auvelity™

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

Prior Authorization (PA) Guide: Key Steps in the PA Process and Handling Denied PAs for Auvelity™

- Introduction to PAs
- Key steps in the PA process
- How to handle a denied PA request

Indication and Important Safety Information for Auvelity

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.

DISCLAIMER: The completion and accuracy of this form is the sole responsibility of the healthcare provider.

Please see additional Important Safety Information throughout the guide and full Prescribing Information for Auvelity, including the Boxed Warning for suicidal thoughts and behaviors.

Introduction to PAs

What Is a PA[a]?

A health plan may require a prior approval before it will cover a prescribed medication such as Auvelity. This request for approval is referred to as a PA, precertification, or coverage determination.

How This Guide Can Help With PA Submissions

To help you understand the submission process for a PA for Auvelity, this guide will provide information on:

- **Key steps in the PA process**
- **Handling a denied PA request**

[a]Prior Authorization criteria are set by the applicable plan. Axsome makes no claim as to the safety or efficacy of the use of a product in any manner inconsistent with a product's label.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS (cont'd)

- **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.

Key Steps in the PA Process for Auvelity

Once you have identified the need for a PA, please follow the steps below:

Step 1 Complete the PA Request

- Make sure you have the proper PA form for that health plan. PAs can be denied simply because the wrong form has been submitted
- Remember to fill out the form completely. PAs are often denied because the form is missing information
  - Refer to the **Auvelity-Specific Considerations for Prior Authorizations**, available at www.auvelity.com/hcp/samples-support, for support
- Include a letter of medical necessity, if needed, to strengthen the request
  - Refer to the **Letter of Medical Necessity Template for Auvelity** and the **How-To Guide: Letter of Medical Necessity for Auvelity**, available at www.auvelityhcp.com/samples-support, for support
- Prepare supplemental documentation to help justify the use of Auvelity. Each health plan is unique so it is essential to identify the specific documents you will need. These documents may include
  - Patient clinical notes, including relevant medical records and treatment history
  - Clinical studies or peer-reviewed journal articles documenting the medical effectiveness of Auvelity
  - Auvelity full Prescribing Information available at www.axsome.com/auvelity-prescribing-information.pdf

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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Key Steps in the PA Process for Auvelity

Step 2 Submit the PA Request

- Determine whether the information should be phoned in, faxed, emailed, or submitted via the health plan's website. This information is often listed on the actual form. Include supplemental documents in your submission
- Keep a copy of everything your practice or facility submits with the request. You may need to reference these documents later

Step 3 Track the Status of the Request

- It is important to keep a thorough log of the PA submissions and denials for each patient

Step 4 Follow Up as Needed

- If additional documentation is requested at any point, make sure to provide it as soon as possible

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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 nicotine replacement.

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How to Handle a Denied PA Request for Auvelity

There could be several reasons that a PA may be denied

- One of the main reasons PA requests are denied is incomplete or inaccurate information on the PA form
- Check to ensure all information is complete and accurate and resubmit the form if necessary
- If the denial was for clinical reasons, determine what additional information may be required to demonstrate the medical necessity of Auvelity for the patient
- Refer to the **Auvelity-Specific Considerations for Prior Authorizations**, available at www.auvelity.com/hcp/samples-support, for Auvelity-specific PA guidance

A letter of medical necessity may be required when the PA is being resubmitted

- Review the **Letter of Medical Necessity Template for Auvelity** and the **How-To Guide: Letter of Medical Necessity for Auvelity,** available for download at www.auvelityhcp.com/samples-support

Next steps if the PA is denied

- The physician can appeal the decision by contacting the health plan directly to have a peer-to-peer discussion regarding the patient, the clinical issues, and the reasons for requesting Auvelity
- If a phone call is not possible, you may submit an appeal
  - Refer to the **Appeals Guide: Key Steps in Appealing a Denial and Process Checklist for Auvelity** and the **How-To Guide: Letter of Appeals for Auvelity** for additional guidance, available for download at www.auvelityhcp.com/samples-support

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

DRUG INTERACTIONS (cont'd)

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 patients 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%).

AUV HCP ISI 08/2022

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