Auvelity®

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

How-To Guide: Letter of Appeal for Auvelity®

This resource will support you with the following when developing a letter of appeal to be submitted when appealing a denial for Auvelity
- General guidance for developing a letter of appeal
- Instruction for completing the letter of appeal template
- Sample letter

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, including Boxed Warning for suicidal thoughts and behaviors.

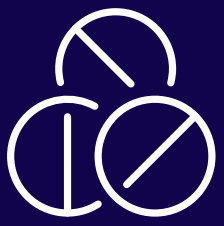
General Guidance to Developing a Letter of Appeal

An Effective Letter Provides Appeal Specific Rationale

The following are key considerations when writing a Letter of Appeal

Background on your patient's condition

- Summarize their clinical status by citing diagnostic evidence of MDD, including baseline functional exam results
- If appropriate, list their current and prior treatment(s) and provide reasons why it is not sufficient, including any side effects, lack of response, or disease progression



Address health plan's denial and justify why Auvelity is, in your opinion, the appropriate treatment choice for your patient

- Be sure to review the health plan's denial and provide clinical justification that supports overturning the denial. Cite any relevant literature and documentation as appropriate
- If denial was due to incomplete information, review the health plan's criteria and ensure all the required criteria is provided
- If denial was due to the plan's preferred formulary agents not being used, including suggested completion of step therapy or formulary exclusions, provide clinical rationale for why these agents are not appropriate for the patient
  - Address each specific preferred agent mentioned in denial reason
  - Include documentation of any prior trial/failures with specific required formulary alternatives
  - Provide relevant medical notes that support clinical rational for not prescribing preferred alternatives

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.

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General Guidance to Developing a Letter of Appeal (cont'd)

- If denial was due to providing the incorrect indication, please confirm the diagnosis of the patient
  - Auvelity is indicated for the treatment of MDD in adults[1]
- If denial was due to the plan's requirement to use individual components, then state that alterations in the dose or recommendations that the patient attempt to take the components separately have not been proven to be safe or effective
  - Dextromethorphan, when given in combination with bupropion as Auvelity, has demonstrated antidepressant effects in clinical trials. There is no other formulation or combination of dextromethorphan approved for the treatment of MDD by the FDA[1,2]
  - Dextromethorphan alone, or any combination of dextromethorphan with another agent, is not approved by the FDA for MDD, has not been shown to be safe and effective for MDD, and any prescription for it to treat MDD would be considered off-label use[2]
  - The doses of the individual components of Auvelity were based on extensive Phase 1 pharmacokinetic studies, with a variety of doses for both dextromethorphan and bupropion. Because bupropion impacts the metabolism of dextromethorphan in a non-linear fashion, small dose variations may have a potentially large and unpredictable impact on the amount of dextromethorphan available in the blood. As there is no 45 mg tablet available of dextromethorphan, nor is there a commercially available 105 mg dosage of bupropion, it is not possible for a patient to create a combination of dextromethorphan and bupropion to mimic Auvelity[1,3]

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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Instructions for Completing the Letter of Appeal Template

Once you have identified the need for a letter of appeal, please follow the steps below

01 Populate the template as medically appropriate

02 Delete any specific instructions for completion, disclaimers, trademarks, and document numbers

03 Submit the letter of appeal with the appropriate appeal form and any supplemental documents as appropriate

The content in this document is not an attempt to provide specific guidance. It is merely for your consideration and review. Please make all changes that you believe to be appropriate or disregard as needed. The medical professional is ultimately responsible for the accuracy and completeness of all claims submitted to third-party payers. Please see the FDA-approved label for information relevant to any prescribing decisions.

This sample letter, along with the *Letter of Appeal Template* and the *Appeals Guide: Key Steps in Appealing a Denial and Process Checklist for Auvelity* available at www.auvelityhcp.com/samples-support, can help you craft a letter to your patient's health plan to support patient access to Auvelity.

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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Fields required for customization are in blue text in brackets.

Please place template on official letter head, if applicable.

Ensure Health Plan information is correct. This can be found on the appeal form or the health plan's website.

Fill out patient information completely and accurately. Ensure the policy ID number matches what is on the patient's insurance card.

<Date>
ATTENTION: <Medical Director Name and/or Medical Review/Appeals>
<Payer/Health Plan Name>
<Payer Address>

REGARDING: Denied Claim for Auvelity (dextromethorphan-bupropion) extended-release tablets
PATIENT NAME: <Patient Name>
DATE OF BIRTH: <Patient Date of Birth>
POLICY ID NUMBER: <Patient Policy ID Number>
PROVIDER ID NUMBER: <Provider ID Number>
<Optional: Claim rejection number>

Please provide claim rejection number, if applicable.

It is important to understand the reason for denial and state the reason specifically. If it is unclear, you may call and speak with the health plan directly.

Dear <Health Plan Contact Name>:

I am writing to appeal the denied claim for Auvelity for my patient, <Patient Name>, for which the reason for denial was <quote the specific reason for denial in denial letter>. I have prescribed Auvelity because this patient has been diagnosed with major depressive disorder (MDD). Attached to this request are clinical notes regarding this patient's disease state and the Auvelity package insert.

Auvelity is indicated for the treatment of MDD in adults. The following is the medical history of <Patient Name> and the rationale for treatment with Auvelity.

Date of Diagnosis	<MM/DD/YY>
Diagnosis	<ICD-10 code>
Summary of clinical symptoms	• <Patient's current condition, including an overview of symptoms and quality of life or functional impairment as applicable> • <Evaluation test score(s)> • <Prognosis without treatment>
Previous and current treatment regimens	<If applicable, include previous and current pharmacologic treatments for MDD, including drug name, dates of use, and reasons for stopping>

Fill out the table with objective, patient-specific information.

<Restate the denial reason and your clinical rationale for why the denial should be overturned and why Auvelity is medically necessary for this patient.>

Thank you for taking the time to read this letter. I believe treatment with Auvelity is appropriate for this patient. I look forward to your prompt review of this request.

This paragraph should provide specific rationale to overturn the denial. Excess information beyond denial reason may influence payer to deny coverage again.

Best regards,

<Physician Signature>
<Physician Name>
<Physician Contact Information>

Include your office or clinic's contact information, including a phone number, fax number, and email.

ATTACHMENTS:
- Auvelity package insert/prescribing information
- Patient clinical notes and other relevant supporting documentation

Please update the list of attachments to only include documents being sent with the request.

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.

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.

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IMPORTANT SAFETY INFORMATION (cont'd)

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 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 10/2022

Please see the full Prescribing Information, including Boxed Warning for suicidal thoughts and behaviors.

References: 1. AUVELITY [prescribing information]. Axsome Therapeutics, Inc. New York, NY. **2.** Axsome Therapeutics. August 19, 2022. Accessed June 21, 2023. https://axsometherapeuticsinc.gcs-web.com/node/10466/pdf **3.** O' Gorman C. Poster presented at: American Society for Clinical Pathology Annual Meeting; May 29-June 1, 2018; Miami Beach, FL.

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