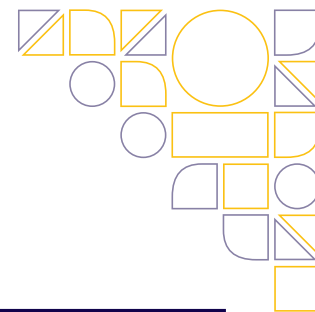




Auvelity™
(dextromethorphan HBr and bupropion HCl)
extended-release tablets 45mg/105mg



How-To Guide: Letter of Medical Necessity for Auvelity™

This resource will support you with the following when developing a letter of medical necessity to be submitted with a Prior Authorization (PA) request for Auvelity

- General guidance for developing a letter of medical necessity
- Instruction for completing the letter of medical necessity 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.**

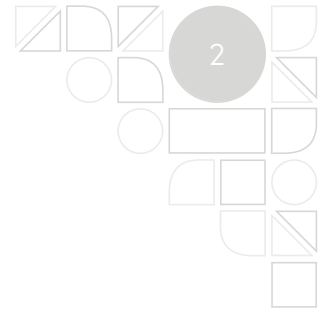
CONTRAINDICATIONS

- **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](#) for Auvelity, including the Boxed Warning for suicidal thoughts and behaviors.

General Guidance to Developing a Letter of Medical Necessity



An Effective Letter Is Tailored to Your Patient's Needs

Be clear about your patient's individual circumstances. The following are key considerations when writing a Letter of Medical Necessity



Background on your patient's condition

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



Why Auvelity is, in your opinion, the appropriate treatment choice for your patient

- Provide clinical justification supporting Auvelity treatment for your patient and cite any relevant literature
- State any patient-specific reasons for the treatment choice, such as expected effect of treatment
- Review the health plan's criteria and point out the specific criteria that your patient meets. Explain why your patient should be excluded from any criteria that they do not meet



Providing additional documentation that supports your decision may strengthen your request

Be sure to review the health plan's requirements to ensure that the requested information is incorporated. Additional documentation 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)

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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Instructions for Completing the Letter of Medical Necessity Template



Once you have identified the need for a letter of medical necessity, 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 medical necessity with the appropriate form for the PA request and any supplemental documents as appropriate

For independent consideration and review, please make all changes that you believe to be appropriate or disregard these suggestions in their entirety. 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 Medical Necessity Template* and the *Prior Authorization (PA) Guide: Key Steps in the PA Process and Handling Denied PAs 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

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.

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Fields required for customization are in blue text in brackets.

Please place template on official letter head, if applicable.

<Date>

ATTENTION: <Medical Director Name and/or Medical Review/Appeals>

<Payer/Health Plan Name>

<Payer Address>

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

REGARDING: Request for Medical Necessity 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>

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

Please provide claim rejection number, if applicable.

Dear <Health Plan Contact Name>:

I am writing this letter of medical necessity in support of my request to treat <Patient Name> with Auvelity for the treatment of major depressive disorder (MDD) in adults.

As a <board-certified> <Field of Certification> with <##> years caring for patients with MDD, I believe that treatment with Auvelity is warranted, appropriate, and medically necessary for this patient based on my clinical judgment and expertise.

The following is the medical history of <Patient Name> and the rationale for treatment with Auvelity. I have also attached to this letter the clinical findings that summarize my patient's current medical condition and the Auvelity package insert/prescribing information.

Date of Diagnosis	<MM/DD/YY>
Diagnosis	<ICD-10 code>
Summary of clinical symptoms	<ul style="list-style-type: none">• <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.

This paragraph should summarize the patient's clinical condition, as provided in the table above, and include specific reasoning for treatment with Auvelity.

I would like to prescribe Auvelity for <Patient Name> because I have concluded that it is a medically appropriate and necessary therapeutic option for the following reason(s):

<Rationale for treating the patient with Auvelity. In this rationale, include a description of the patient's disease state, treatment history, comorbid health issues, and any other factors that have influenced your treatment decision.>

<You may wish to include relevant background or clinical trial information about Auvelity in the letter. For additional information, please refer to the Auvelity Prescribing Information.>

Given the patient's history, <his/her/their> current condition, and the data of the effects of Auvelity in patients with MDD, I believe that treatment of <Patient Name> with this product is warranted, appropriate, and medically necessary. The totality of the data available to date supports the potential benefit of <treatment/continuing treatment> with Auvelity.

Please call my office at <telephone number> if I can provide you with any additional information. I look forward to receiving your timely response.

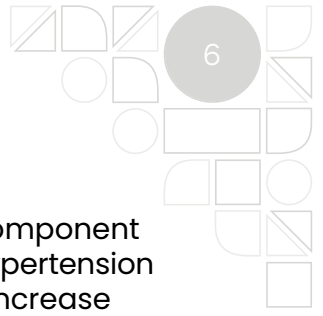
Best regards,
<Physician Signature>
<Physician Name>
<Physician Contact Information>

Including clinical trial information about Auvelity, specifically in patient populations similar to your patient, may strengthen your request.
Be sure to choose the correct language based on whether your patient is initiating or continuing treatment with Auvelity.
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 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.

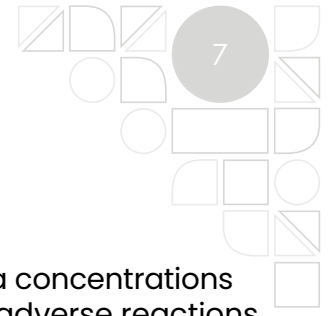
Dizziness: Auvelity may cause dizziness. Precautions to reduce the risk of falls should be taken, particularly for patients with motor impairment affecting gait or a history of falls. Caution patients about operating hazardous machinery, including motor vehicles, until they are reasonably certain that 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.

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IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (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 m²). Auvelity is not recommended in patients with severe renal impairment (eGFR 15 to 29 mL/minute/1.73 m²).

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

ADVERSE REACTIONS

Most common adverse reactions ($\geq 5\%$ 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

Please see the full [Prescribing Information](#) for Auvelity, including the **Boxed Warning** for suicidal thoughts and behaviors.

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