

AUVELITY **(dextromethorphan and bupropion)**

RATIONALE FOR INCLUSION IN PA PROGRAM

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).

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

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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).

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 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.; June 2024.