INVESTIGATIVE PROCESS

AUVELITY received FDA approval for the treatment of MDD in adults on August 20, 2022. This program included studies like the GEMINI and ASCEND trials, which demonstrated the drug's efficacy and safety. In the GEMINI study, Auvelity was found to be significantly superior to placebo in reducing depressive symptoms, with improvements as early as one week into treatment. The ASCEND study showed that Auvelity was also more effective than bupropion alone, supporting the synergistic effect of the drug combination with dextromethorphan (McCarthy et al., 2023).

The drug was granted Breakthrough Therapy designation by the FDA in 2019, reflecting its potential to offer substantial benefits over existing treatments. This designation accelerated the review process, leading to its approval in 2022. Auvelity is now available for use in the U.S., with further studies likely to explore its potential for other psychiatric and neurological conditions (Axsome Therapeutics, 2022).

References!

Axsome Therapeutics, Inc. (2022). AUVELITY prescribing information. https://www.axsome.com/auvelity-prescribing-information.pdf

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McCarthy, B., Bunn, H., Santalucia, M., Wilmouth, C., Muzyk, A., & Smith, C. M. (2023). Dextromethorphan-bupropion (Auvelity) for the Treatment of Major Depressive Disorder. *Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology*, *21*(4), 609–616. https://doi.org/10.9758/cpn.23.1081

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Generative AI Statement: I declare that Generative Ai tools did not contribute to the making of this assignment

WHY?

Depression affects 1 in 8 people, with an even higher risk for those with chronic illnesses, like the patients we care for in hospital. More than that, we all likely know someone who is currently struggling or has struggled with depression, which is why I wanted to focus on a medication that targets this mental health condition. While therapy can be incredibly beneficial, many people with depression forget what it feels like to experience happiness. It saps a person's energy, which can make it difficult to take the first step to recovery. In these cases, relief from the depressive symptoms through medication can provide the necessary boost for someone to engage in therapy, exercise, or even reconnect with a friend. Moreover, some individuals cannot afford to wait the typical 6 weeks to see if their current medication is working, making faster-acting treatments crucial for their health and safety.

THANK YOU!

What you need to know about

AUVELITY

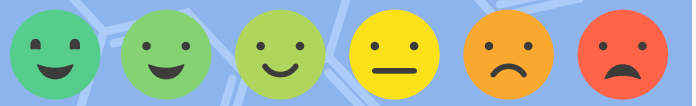
SARA GONZALEZ PEPE

INTEREST

AUVELITY (dextromethorphan and bupropion) is a novel, rapid-acting antidepressant approved for treating Major Depressive Disorder (MDD) in adults. It is the first oral NMDA receptor antagonist to be FDA-approved for depression, which is a new mechanism of action that works more quickly than traditional antidepressants.

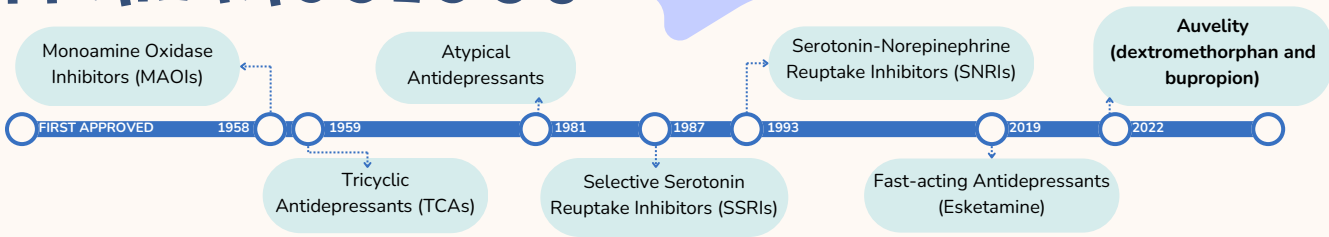
Traditional antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), often take several weeks to show efficacy and may not work for all patients. Considering that AUVELITY targets glutamate, there is a faster response time in which patients feel results. This is critical for patients with severe depression who need immediate relief from symptoms. The ability to modulate glutamate transmission, as well as bupropion's effects on dopamine and norepinephrine, positions AUVELITY as a treatment specifically for MDD rather than for other mental health conditions, like anorexia or general anxiety disorder (McCarthy et al., 2023).

The NMDA antagonism is what differentiates AUVELITY from other treatments, as excessive glutamatergic activity has been linked to the pathophysiology of depression. Studies have shown that ketamine, another NMDA antagonist, has rapid antidepressant effects, which is what Auvelity was based on (McCarthy et al., 2023).



PHARMACOLOGY

Brief Timeline of Antidepressant Drug Approval and Development



The AUVELITY drug is a combination of dextromethorphan and bupropion, with dextromethorphan acting as an NMDA (glutamate) receptor antagonist. Glutamate is an excitatory neurotransmitter that is important in terms of regulating mood, memory and learning. By antagonizing this receptor, dextromethorphan modulates glutamate, providing an antidepressant effect.

The bupropion component acts as a norepinephrine and dopamine reuptake inhibitor, which helps with the regulation of mood. However, in combination with dextromethorphan, it functions as a CYP2D6 inhibitor, prolonging the action of dextromethorphan by slowing its metabolism (McCarthy et al., 2023)

KINETIC INFORMATION

Auvelity, which contains dextromethorphan and bupropion, has a half-life of approximately 22 hours, meaning it takes this amount of time for the concentration of the drug in the blood to reduce by half. The drug is metabolized through two pathways: dextromethorphan is metabolized by the CYP2D6 enzyme through de-methylation, while bupropion is metabolized through the CYP2B6 enzyme through hydroxylation. In terms of excretion, dextromethorphan is eliminated through urine. Bupropion is also excreted through the urine and feces. Steady-state levels of Auvelity are achieved after about 8 days of consistent administration, ensuring stable drug concentrations in the bloodstream. (McCarthy et al., 2023).

TOXICITY

SIDE EFFECTS

3

Patients may also experience mood-related changes, such as agitation, anxiety, insomnia, or, in severe cases, hallucinations.

In addition, Auvelity has been associated with manic episodes*in individuals with bipolar disorder (Axsome Therapeutics, 2022)

2

More serious adverse effects are linked to **bupropion**, which increases the risk of seizures —especially at higher doses or in individuals with a history of eating disorders (ex., anorexia or bulimia). There is also a risk of increased blood pressure, so patients should monitor this regularly.

1

Common side effects include dizziness, headache, dry mouth, diarrhea, excessive sweating, and sexual dysfunction. These side effects tend to happen early in the treatment and subside as the body adjusts to the medication.