Mirtazapine - (Remeron)

Mechanism of Action

Mirtazapine is an antidepressant belonging to the class of noradrenergic and specific serotonergic antidepressants (NaSSA). This drug works through multiple receptor systems. The primary action is α2-adrenergic receptor blockade, which leads to the release of serotonin and norepinephrine and overall elevated neurotransmitter activity of these systems.

Mirtazapine also works by blocking serotonin and histamine activity. Blockage at serotonin (5-HT2A, 5-HT2C, and 5-HT3) receptors increases serotonin activation at 5-HT1A receptors, which results in antidepressant and anxiolytic effects. Histamine (H1) receptor blockage results in increased appetite and weight gain.

Indications

Mirtazapine is FDA-approved for treating major depressive disorder in adults, yet it lacks approval for use in patients under 18 years old. Mirtazapine is commonly used off-label for the treatment of major depression, generalized anxiety disorder, panic disorder, and post-traumatic stress disorder in children and adolescents, especially for patients who have sleep issues, poor appetite, or gastrointestinal symptoms that cannot tolerate other antidepressants.

Dosing and Formulation

Mirtazapine's sedative effects require patients to take their medication only at night.

The recommended daily dose is between 15 mg to 45 mg nightly. It is available in four tablet strengths (7.5 mg, 15 mg, 30 mg, and 45 mg) and three orally disintegrating tablet strengths (15 mg, 30 mg, and 45 mg).

Food does not affect mirtazapine absorption into the body.

It has a 20 to 40 hour half-life, which allows patients to take it once per day.

Metabolism and Elimination

The liver breaks down mirtazapine through the actions of CYP2D6 and CYP3A4 enzymes and possibly CYP1A2 enzymes. The body eliminates most of this medication through urine excretion. The drug has a lower potential for drug interactions because of its metabolic pathway, but healthcare providers need to monitor patients who take strong CYP inhibitors or inducers.

Side Effects and Black Box Warning

The most common adverse reactions from this medication include sedation, increased appetite, weight gain, dry mouth, constipation, and dizziness. Weight gain and sedation are two particularly common side effects that can affect patients. The pediatric trials showed that half of the patients exceeded their baseline body weight by more than 7%. The medication may cause additional side effects, which include unusual dreams, confusion, and urinary system changes. The occurrence of flu-like symptoms remains rare, but they can indicate blood cell alterations that result in leukopenia or granulocytopenia. The medication carries three rare yet dangerous side effects, which include seizures, mania development in bipolar patients, and a black box warning for suicidal thoughts and behaviors that may affect young patients.

Monitoring

The monitoring of BMI and growth curves in children and adolescents taking mirtazapine should be performed by clinicians because of weight and metabolic issues. Baseline liver function tests may be helpful in patients with hepatic risk factors, and blood counts may be considered if there is a history of blood dyscrasias.

Clinical Pearls

Mirtazapine can be especially helpful in young patients who present with depression plus insomnia, poor appetite, or low body weight, because of its dual sedating and appetite-stimulating effects. The use of caution is necessary for clinicians when treating young patients who have developmental disorders or brain injuries because paradoxical activation has been observed in these cases.

References

Elbe, D., Black, T. R., McGrane, I. R., & Choi, S. (Eds.). (2023). *Clinical handbook of psychotropic drugs for children and adolescents*. Hogrefe Publishing GmbH.

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