Clinical Update:

NEW ADDITIONS TO THE AEGIS BEHAVIORAL HEALTH TESTING MENU

Benztropine & Trihexyphenidyl

Pharmacology:
Benztropine and trihexyphenidyl are anticholinergic drugs that block muscarinic acetylcholine receptors in the nervous system. They are mainly used to treat movement disorders caused by antipsychotic medications, which work by blocking dopamine receptors. This dopamine blockade can lead to an imbalance between dopamine and acetylcholine in the brain. By reducing acetylcholine activity, these medications help restore balance and improve symptoms like tremors, stiffness, and involuntary movements, collectively known as extrapyramidal symptoms (EPS).

There is also some evidence that these drugs may indirectly increase dopamine activity in the brain's limbic system, which could explain their potential for misuse. They are not selective for specific muscarinic receptor subtypes (M1, M2, M3, etc.), which contributes to both their therapeutic effects and side effects.

Indications:
These medications are commonly used to treat drug-induced parkinsonism (DIP), a condition that resembles Parkinson's disease and is caused by antipsychotic drugs. DIP usually appears shortly after starting treatment and involves symptoms like tremors, slow movement, and muscle stiffness. In contrast, tardive dyskinesia (TD) typically develops after long-term use and is characterized by repetitive, involuntary facial and body movements.

Anticholinergics like benztropine and trihexyphenidyl are helpful in managing DIP, but they are not recommended for TD and may worsen it. They are sometimes used cautiously in TD if other treatments fail.

Place in Therapy:
Benztropine and trihexyphenidyl are frequently prescribed when initiating antipsychotic therapy to prevent or treat DIP. However, they should be used for short periods (typically no more than 3 months) and reassessed regularly to determine if they are still needed.

They are not suitable for long-term use in most cases due to risks such as worsening TD, memory problems, and confusion, particularly in older adults. Common side effects include dry mouth, constipation, blurry vision, and difficulty urinating.

In patients with both DIP and TD, these medications should generally be avoided or used very cautiously, as they may worsen TD.

Misuse Potential:
Both drugs have potential for misuse, especially at high doses. They are usually taken by mouth, but some individuals inject them illicitly. Misuse has been associated with psychiatric effects like hallucinations, confusion, and aggression, as well as physical symptoms like a fast heart rate and high blood pressure. Chronic use may lead to tolerance and withdrawal symptoms.

Benztropine may produce euphoric effects and cause hallucinations, while trihexyphenidyl appears to have even higher potential for misuse, possibly due to its greater central nervous system effects.

Lemborexant

Pharmacology:
Lemborexant is a dual orexin receptor antagonist. It blocks orexin-1 and orexin-2 receptors, which are part of the brain's wakefulness system. Orexins are neuropeptides that help regulate sleep and arousal. By blocking these receptors, lemborexant helps promote sleep. Its selective targeting allows it to promote sleep without the wide range of effects seen in older sleep medications that affect multiple neurotransmitter systems.

Indications:
Lemborexant is approved to treat insomnia, specifically for patients who have trouble falling asleep or staying asleep.

Place in Therapy:
Lemborexant may be especially useful for older adults with insomnia. Compared to traditional sleep medications like benzodiazepines or "Z-drugs" (e.g., zolpidem), lemborexant carries a lower risk of cognitive impairment, motor problems, and falls. However, like all sleep aids, it should only be used if sleep issues cannot be resolved with non-drug therapies like cognitive behavioral therapy for insomnia (CBT-I).

Although lemborexant is classified as a Schedule IV controlled substance, it has a lower potential for abuse and dependence than many older sleep drugs.

Misuse Potential:
Studies show lemborexant has limited potential for misuse. People who have misused sedatives in the past are less likely to report euphoria or other rewarding effects from lemborexant compared to drugs like zolpidem or suvorexant. It has also been associated with fewer withdrawal symptoms after long-term use. Nevertheless, some cases of misuse have been reported, usually involving excessive drowsiness or disorientation after taking high doses.

Lumateperone

Pharmacology:
Lumateperone is an antipsychotic with a unique mechanism. It blocks serotonin 5-HT_2A receptors and dopamine D_2 receptors, while also enhancing dopamine release through serotonin 5-HT_1A receptor activity. It also inhibits serotonin transporters (like SSRIs do) and affects glutamate pathways. This combination may improve symptoms of schizophrenia and bipolar depression while causing fewer side effects than traditional antipsychotics.

Indications:
Lumateperone is approved to treat schizophrenia and depressive episodes in bipolar I and II disorder, either alone or in combination with lithium or valproate.

Place in Therapy:
Because of its unique receptor profile, lumateperone may cause fewer movement disorders (like EPS or TD), less weight gain, and less sedation than older antipsychotics. It's particularly helpful for patients who are sensitive to side effects or have had poor responses to other medications.

Misuse Potential:
There is little evidence that lumateperone is misused. It does not produce significant rewarding effects or euphoria and has not been linked to drug-seeking behavior.

Viloxazine

Pharmacology:
Viloxazine is a norepinephrine reuptake inhibitor (NRI), meaning it increases levels of norepinephrine in the brain by blocking its reabsorption. It also modulates serotonin levels and interacts with several serotonin receptor subtypes. These effects may improve attention and mood, especially in people with attention-deficit/hyperactivity disorder (ADHD).

Indications:
Viloxazine is approved for treating ADHD in children aged 6–17 and in adults.

Place in Therapy:
Viloxazine provides a non-stimulant treatment option for ADHD. This can be beneficial for patients who do not tolerate stimulants or who have a history of substance misuse. Unlike stimulant medications, viloxazine does not increase dopamine in reward pathways, which lowers its risk for misuse and addiction.

Misuse Potential:
Studies show viloxazine does not produce euphoria or other pleasurable effects, even in people who have misused drugs in the past. It is not classified as a controlled substance and has a low potential for abuse. So far, there are no significant reports of misuse or diversion.

NOTICE: The information above is intended as a resource for health care providers. Providers should use their independent medical judgment based on the clinical needs of the patient when making determinations of who to test, what medications to test, testing frequency, and the type of testing to conduct. (Calibri 10pt)

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