Nonbenzodiazepine Hypnotics

Nonbenzodiazepines hypnotics include Zolpidem (Ambien), zaleplon and eszopiclone, and are indicated for short term treatment of insomnia. This class of hypnotics is more selective than benzodiazepines, as they are not indicated for chronic anxiety, muscle relaxation, or seizure disorders. Nonbenzodiazepines hypnotics act on BZ1 GABA subtype receptors to increase chloride conductance. They are rapidly metabolized by the liver and have a short half-life of roughly 2.5 hours. Patients taking these medications may display ataxia and confusion shortly after administration. Those who overdose on this class of medication can be treated with flumazenil as an antidote.



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Indications

Insomnia
Taped-awake-insomniac
Insomnia is a sleep disorder characterized by difficulty initiating or maintaining sleep, or waking up too early and not being able to return to sleep, despite having the opportunity to sleep. This condition leads to daytime impairment or distress, such as fatigue, mood disturbances, or cognitive dysfunction. Insomnia diagnostically occurs despite adequate opportunity for sleep, is present for at least three months, and is not attributable to another sleep-wake disorder (e.g., narcolepsy, a breathing-related sleep disorder, a circadian rhythm sleep-wake disorder, a parasomnia).

Mechanism of Action

Short Half-Life
Shorts Half-Life-clock
Nonbenzodiazepine hypnotics—commonly known as "Z-drugs" (e.g., zolpidem, zaleplon, eszopiclone)—are characterized by their rapid onset of action and short elimination half-lives due to swift hepatic metabolism. This pharmacokinetic profile makes them particularly effective for initiating sleep, with a reduced risk of next-day residual sedation. In cases of overdose, flumazenil, a benzodiazepine receptor antagonist, can be used to reverse the sedative effects of Z-drugs.

Acts on BZ1 GABA receptor
Bee-Z-(1) Wand GABA-goose receptor
These drugs work by acting in an inhibitory neurotransmission role via the ?1 subtype of the GABA receptor (?1GABA_a). This is similar to the chemical-structurally similar benzodiazepines, though benzodiazepines work non-selectively on a variety of subtypes (?1, ?2, ?3, and ?5). Binding of nonbenzodiazepines leads to increased chloride conductance, neuronal hyperpolarization, an inhibition of action potential, and a decrease in neuronal excitability producing sedative effect.

Less dependence
Lifting away Dependence-ball-and-chain
Compared to benzodiazepines, nonbenzodiazepines have overall lower risk of dependence, tolerance and abuse. They cause less day-after psychomotor depression and amnestic effects relative to older sedative-hypnotics.

Drugs

Zolpidem (Ambien)
Z-pigeon
Zolpidem is a commonly used drug of this class, and is also known by the brand name, Ambien. Zolpidem helps to reduce sleep onset latency and may also have some minimal anxiolytic activity. Other nonbenzodiazepine hypnotics are zaleplon and eszopiclone.

Side Effects

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Ataxia, confusion

A-taxi and Confucius

Nonbenzodiazepine hypnotics, commonly known as "Z-drugs" (e.g., zolpidem, zaleplon, eszopiclone), are effective in treating sleep disorders such as insomnia. However, they are associated with central nervous system side effects, including ataxia (impaired coordination) and confusion. These adverse effects can impair cognitive and motor functions, leading to difficulties in performing daily activities and an increased risk of falls, particularly in older adults. Z-drugs selectively bind to the ?1 subunit of the GABA receptor (?1GABA_areceptor), enhancing inhibitory neurotransmission and promoting sedation. This selectivity contributes to their hypnotic effects without significant anxiolytic or muscle relaxant properties.

Antidote

Flumazenil for Overdose

Flute-mace-nail

The sedative and hypnotic effects of nonbenzodiazepine hypnotics—such as zolpidem, zaleplon, and eszopiclone—can be reversed by flumazenil. Flumazenil, a competitive antagonist at this site, can effectively counteract the central nervous system depression caused by these drugs. This reversal is particularly useful in cases of overdose or when rapid awakening is necessary.

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