**TEMAZEPAM THERAPEUTICS**

**Brands** • Restoril
see index for additional brand names

**Generic?** Yes

**Class** • Benzodiazepine (hypnotic)

**Commonly Prescribed for**
(bold for FDA approved)
• Short-term treatment of insomnia
• Catatonia

**How the Drug Works**
• Binds to benzodiazepine receptors at the GABA-A ligand-gated chloride channel complex
• Enhances the inhibitory effects of GABA
• Boosts chloride conductance through GABA-regulated channels
• Inhibitory actions in sleep centers may provide sedative hypnotic effects

**How Long Until It Works**
• Generally takes effect in less than an hour, but can take longer in some patients

**If It Works**
• Improves quality of sleep
• Effects on total wake-time and number of nighttime awakenings may be decreased over time

**If It Doesn’t Work**
• If insomnia does not improve after 7–10 days, it may be a manifestation of a primary psychiatric or physical illness such as obstructive sleep apnea or restless leg syndrome, which requires independent evaluation
• Increase the dose
• Improve sleep hygiene
• Switch to another agent

**Best Augmenting Combos for Partial Response or Treatment Resistance**
• Generally, best to switch to another agent
• Trazodone
• Agents with antihistamine actions (e.g., diphenhydramine, tricyclic antidepressants)

**Tests**
• In patients with seizure disorders, concomitant medical illness, and/or those with multiple concomitant long-term medications, periodic liver tests and blood counts may be prudent

**SIDE EFFECTS**

**How Drug Causes Side Effects**
• Same mechanism for side effects as for therapeutic effects – namely due to excessive actions at benzodiazepine receptors
• Actions at benzodiazepine receptors that carry over to the next day can cause daytime sedation, amnesia, and ataxia
• Long-term adaptations in benzodiazepine receptors may explain the development of dependence, tolerance, and withdrawal

**Notable Side Effects**
✽ Sedation, fatigue, depression
✽ Dizziness, ataxia, slurred speech, weakness
✽ Forgetfulness, confusion
✽ Hyperexcitability, nervousness
• Rare hallucinations, mania
• Rare hypotension
• Hypersalivation, dry mouth
• Rebound insomnia when withdrawing from long-term treatment

**Life-Threatening or Dangerous Side Effects**
• Respiratory depression, especially when taken with CNS depressants in overdose
• Rare hepatic dysfunction, renal dysfunction, blood dyscrasias

**Weight Gain**
• Reported but not expected

**Sedation**
• Many experience and/or can be significant in amount
TEMAZEPAM (continued)

What to Do About Side Effects
• Wait
• To avoid problems with memory, only take temazepam if planning to have a full night’s sleep
• Lower the dose
• Switch to a shorter-acting sedative hypnotic
• Switch to a non-benzodiazepine hypnotic
• Administer flumazenil if side effects are severe or life-threatening

Best Augmenting Agents for Side Effects
• Many side effects cannot be improved with an augmenting agent

Long-Term Use
• Not generally intended for long-term use

Habit Forming
• Temazepam is a Schedule IV drug
• Some patients may develop dependence and/or tolerance; risk may be greater with higher doses
• History of drug addiction may increase risk of dependence

How to Stop
• If taken for more than a few weeks, taper to reduce chances of withdrawal effects
• Patients with history of seizure may seize upon sudden withdrawal
• Rebound insomnia may occur the first 1–2 nights after stopping
• For patients with severe problems discontinuing a benzodiazepine, dosing may need to be tapered over many months (i.e., reduce dose by 1% every 3 days by crushing tablet and suspending or dissolving in 100 mL of fruit juice and then disposing of 1 mL while drinking the rest; 3–7 days later, dispose of 2 mL, and so on). This is both a form of very slow biological tapering and a form of behavioral desensitization

Pharmacokinetics
• No active metabolites
• Half-life approximately 8–15 hours

Drug Interactions
• Increased depressive effects when taken with other CNS depressants
• If temazepam is used with kava, clearance of either drug may be affected

Other Warnings/Precautions
• Insomnia may be a symptom of a primary disorder, rather than a primary disorder itself
• Some patients may exhibit abnormal thinking or behavioral changes similar to those caused by other CNS depressants (i.e., either depressant actions or disinhibiting actions)
• Some depressed patients may experience a worsening of suicidal ideation

DOSING AND USE

Usual Dosage Range
• 15 mg/day at bedtime

Dosage Forms
• Capsule 7.5 mg, 15 mg, 30 mg

How to Dose
• 15 mg/day at bedtime; may increase to 30 mg/day at bedtime if ineffective

Dosing Tips
• Use lowest possible effective dose and assess need for continued treatment regularly
• Temazepam should generally not be prescribed in quantities greater than a 1-month supply
• Patients with lower body weights may require lower doses
* Because temazepam is slowly absorbed, administering the dose 1–2 hours before bedtime may improve onset of action and shorter sleep latency
• Risk of dependence may increase with dose and duration of treatment

Overdose
• Can be fatal in monotherapy; slurred speech, poor coordination, respiratory depression, sedation, confusion, coma

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• Use only with extreme caution in patients with impaired respiratory function or obstructive sleep apnea
• Temazepam should only be administered at bedtime

**Do Not Use**
• If patient is pregnant
• If patient has narrow angle-closure glaucoma
• If there is a proven allergy to temazepam or any benzodiazepine

**Breast Feeding**
• Unknown if temazepam is secreted in human breast milk, but all psychotropics assumed to be secreted in breast milk
*) Recommended either to discontinue drug or bottle feed
• Effects on infant have been observed and include feeding difficulties, sedation, and weight loss

**ART OF PSYCHOPHARMACOLOGY**

**Potential Advantages**
• Patients with middle insomnia (nocturnal awakening)

**Potential Disadvantages**
• Patients with early insomnia (problems falling asleep)

**Primary Target Symptoms**
• Time to sleep onset
• Total sleep time
• Nighttime awakenings

**Pearls**
• If tolerance develops, it may result in increased anxiety during the day and/or increased wakefulness during the latter part of the night
*) Slow gastrointestinal absorption compared to other sedative benzodiazepines, so may be more effective for nocturnal awakening than for initial insomnia unless dosed 1–2 hours prior to bedtime
*) Notable for delayed onset of action compared to some other sedative hypnotics
• Though not systematically studied, benzodiazepines have been used effectively to treat catatonia and are the initial recommended treatment

**SPECIAL POPULATIONS**

**Renal Impairment**
• Recommended dose: 7.5 mg/day

**Hepatic Impairment**
• Recommended dose: 7.5 mg/day

**Cardiac Impairment**
• Dosage adjustment may not be necessary
• Benzodiazepines have been used to treat insomnia associated with acute myocardial infarction

**Elderly**
• Recommended dose: 7.5 mg/day

**Children and Adolescents**
• Safety and efficacy have not been established
• Long-term effects of temazepam in children/adolescents are unknown
• Should generally receive lower doses and be more closely monitored

**Pregnancy**
• Risk Category X [positive evidence of risk to human fetus; contraindicated for use in pregnancy]
• Infants whose mothers received a benzodiazepine late in pregnancy may experience withdrawal effects
• Neonatal flaccidity has been reported in infants whose mothers took a benzodiazepine during pregnancy
Suggested Reading


