

TEMAZEPAM



"Jasmine", oil on canvas, Albert Joseph Moore, (1841-1883).

"Blessings on him who invented sleep, the mantle that covers all human thoughts, the food that satisfies hunger, the drink that slates thirst, the fire that warms cold, the cold that moderates heat, and lastly, the common currency that buys all things, the balance and weight that equalizes the shepherd and the king, the simpleton and the sage".

Miguel de Cervantes, "Don Quixote", 1605-1615.

TEMAZEPAM

Introduction

Temazepam is a quick onset and short acting benzodiazepine derivative widely used in the **short term** as a hypnotic agent to assist sleep.

As with all benzodiazepines this agent has potential for abuse and both psychological and physical dependence.

Flumazenil is the specific antidote to overdose of benzodiazepines.

See also separate Documents on:

- **Benzodiazepine overdose, (in Toxicology folder)**
- **Benzodiazepine withdrawal syndrome, (in Toxicology folder)**
- **Flumazenil, (in Drugs folder)**

Preparation

Tablets: 10 mg

Mechanism of Action

The exact mechanism of action of the benzodiazepines is incompletely understood, but most current theories hold that they potentiate the action of the endogenous CNS inhibitory neurotransmitter gamma-aminobutyric acid (or **GABA**)

There are GABA A and GABA B receptors.

Classification

Temazepam is classified as a **short acting** benzodiazepine,(see **Appendix 1 below**).

Pharmacokinetics

Absorption:

- Temazepam is given orally
- It is well absorbed orally
- On average, peak plasma concentrations are reached about two hours after administration.
- It has a quick onset of action (within 1 hour).
- With multiple dosing, steady state is obtained by the third day and there is little or no accumulation of parent drug or metabolites.

Distribution:

- Approximately 96% is bound to plasma proteins.
- Benzodiazepines cross the placenta and may cause effects on the fetus.

Metabolism and excretion:

- Temazepam is metabolized principally in the liver where most of the drug is directly conjugated to the glucuronide and excreted in the urine.

Some drug is demethylated to **oxazepam** and eliminated as the glucuronide.

The glucuronides of temazepam have no demonstrable CNS activity.

- Temazepam has a (relatively) short elimination half-life of approximately ten hours

Pharmacodynamics

As with most other benzodiazepine agents, principle effects include:

- Anxiolysis
- Sedation
- Hypnotic
- Skeletal muscle relaxant
- Antiepileptic effects.

Indications

Temazepam indications include:

1. Hypnotic agent:

Temazepam's principle indication is for the **short-term** (around 2 - 4 weeks) treatment of insomnia.

Continuous *long-term* use of temazepam is *not* recommended.

Most commonly insomnia associated with jet lag, shift workers, acute grief reactions, acute stress situation, (including hospitalised patients), acute severe anxiety.

- Induces the onset of sleep
- Increases the length of sleep time

2. Premedication and sedation
 - For minor procedures or prior to anesthesia
3. Alcohol withdrawal

Contraindications/ Precautions

Contraindications and Precautions include:

- CNS depressant effects are synergistic with other CNS depressants including alcohol.
- Chronic obstructive airways disease with incipient respiratory failure, particularly those who are CO₂ retainers.
- Sleep apnea.
- Contraindicated in myasthenia gravis.
- Children and the elderly are more susceptible to the effects of benzodiazepines in general
- Contraindicated in severe hepatic impairment, particularly when hepatic encephalopathy is present. In mild-to-moderate impairment, use lower doses of a short-acting benzodiazepine to reduce risk of precipitating coma.
- There is increased sensitivity to CNS effects in patients with severe renal impairment; use lower doses in severe impairment.
- Known hypersensitivity to benzodiazepines or any of the components of the formulation
- Caution must be exercised in prescribing temazepam to individuals known to be **addiction prone**.

Pregnancy

Temazepam is a category **C drug** with respect to pregnancy.

Category C drugs are classified as those drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Specialised texts should be consulted for further details.

However there have been some reports that benzodiazepines may have an increased risk of congenital malformations if taken in the first trimester.³

Breastfeeding

Avoid repeated doses; this may cause lethargy and poor feeding in the infant.

Adverse Effects

1. Excessive respiratory depression:
 - This is usually seen in association with other factors that impair respiratory drive, (e.g. COPD, other CNS depressants, sleep apnea).
2. Excessive somnolence/ CNS depression:
 - Usually in the setting of excessive dosing or when used in association with other CNS depressants.
3. Physical dependence:
 - A benzodiazepine withdrawal syndrome is possible.
 - Patients who have been on longer term therapy of benzodiazepines should not have these *abruptly* withdrawn.
4. Psychological dependence:
 - Paradoxical hyper-excitement reactions are rarely seen, (mainly children or elderly).
5. Tolerance:
 - Tolerance, as defined by a need to increase the dose in order to achieve the same therapeutic effect, rarely occurs in patients receiving recommended doses under medical supervision.
 - Tolerance may occur with longer term use, especially in those with drug seeking behaviour.

Dosing

The standard dose is **10 mg orally** (with a range of 5 - 30 mg), taken one hour before bed.

Reversal of effects:

Flumazenil is a specific benzodiazepine antagonist and will rapidly reverse the effects of benzodiazepines including depression of respiration and conscious state.

Appendix 1

Classification of Benzodiazepines:

Length of Action	Half-life	Drugs
Very short	< 6 Hours	Midazolam, Triazolam.
Short	6-12 Hours	Temazepam, Oxazepam, Alprazolam.
Medium	12-24 Hours	Lorazepam, Bromazepam.
Long	> 24 Hours	Diazepam, Nitrazepam, Flunitrazepam, Clobazam, Clonazepam.



"Dreamers", (Detail), oil on canvas, 1882, Albert Joseph Moore.

References

1. eTG - November 2013
2. Temazepam in Australian Medicines Handbook, October 2013
3. Temazepam in MIMs October 2013.

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