

OXAZEPAM



Ms. Holly Golightly (Audrey Hepburn), "Breakfast at Tiffany's", 1961

*She was still hugging the cat. "Poor slob", she said, tickling his head. "poor slob without a name. It's a little inconvenient, his not having a name. But I haven't the right to give him one: he'll have to wait until he **belongs** to somebody. We just sort of took up by the river one day, we don't belong to each other: he's an independent, and so am I. I don't want to own anything until I know I've found the place where me and things belong together. I'm not quite sure where that is just yet. But I know what it's like". She smiled and let the cat drop to the floor. "It's like Tiffany's", she said. "Not that I give a hoot about jewellery. Diamonds yes. But its tacky to wear diamonds before you are forty; and even that's risky. They only look right on the really old girls. Maria Ouspenskaya. Wrinkles and bones, white hair and diamonds: I can't wait. But that's not why I'm mad about Tiffany's. Listen. You know those days when you've got the mean reds?"*

"Same as the blues?"

"No," she said slowly. "No, the blues are because you're getting fat or maybe it's been raining too long. You're sad, that's all. But the mean reds are horrible. You're afraid and you sweat like hell, but you don't know what you're afraid of. Except something bad is going to happen, only you don't know what it is. You've had that feeling?"

*"Quite often. Some people call it **angst**".*

*"All right. **Angst**. But what do you do about it?"*

"Well, a drink helps".

"I've tried that. I've tried aspirin, too. Rusty thinks I should smoke marijuana, and I did for a while, but it only makes me giggle. What I've found does the most good is just to get into a taxi and go to Tiffany's. It calms me down right away, the quietness, and the proud look of it; nothing very bad could happen to you there, not with those kind men in their nice suits, and that lovely smell of silver and alligator wallets. If I could find a real-life place that made me feel like Tiffany's, then I'd buy some furniture and give the cat a name. I've thought maybe after the war, Fred and I -". She pushed up her dark glasses, and her eyes, the differing colours of them, the greys and wisps of blue and green, had taken on a far seeing sharpness. "I went to Mexico once. It's wonderful country for raising horses. I saw one place near the sea. Fred's good with horses..."

Truman Capote, "Breakfast at Tiffany's", 1958.

The "mean reds" (or angst) are a devilish tricky ailment to treat! Ms Holly Golightly, tried all manner of remedies - aspirin, marijuana and champagne, (even before breakfast!), but none seemed to work. Today we have at our disposal the very best agents for the treatment of anxiety, such as oxazepam - but even our most modern drugs have the most significant drawbacks. Perhaps after over half a century, the very best cure, the only real cure, for the mean reds, remains, not drugs - but breakfast at Tiffany's!

OXAZEPAM

Introduction

Oxazepam is a quick onset and *very* short acting benzodiazepine derivative widely used in the **short term** as an anxiolytic agent.

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: 15 mg, 30mg.

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

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

Pharmacokinetics

Absorption:

- Oxazepam is readily absorbed orally.

Distribution:

- At clinically relevant concentrations, oxazepam is 95 to 98% bound to plasma protein.

Metabolism and excretion:

- Oxazepam is 95% metabolized by the liver.
- There are no active metabolites of oxazepam.
- Usual multiple dose therapy does not lead to excessive drug accumulation.
- The half life of oxazepam is around 6 -12 hours.

Pharmacodynamics

As with most other benzodiazepine agents, principle effects include:

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

Indications

The most common indications for oxazepam include the **short-term** (around 2 - 4 weeks) treatment of management of:

1. Anxiety
2. Panic disorder
3. Insomnia
4. Alcohol withdrawal symptoms.

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

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 apnoea.
- 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 oxazepam to individuals known to be **addiction prone**.

Pregnancy

Oxazepam 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

Compatible; but caution with chronic use, monitor infant for drowsiness

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.

2. Physical dependence:

- A benzodiazepine withdrawal syndrome is possible.
- Patients who have been on longer term therapy of benzodiazepines should not have these *abruptly* withdrawn.

3. Psychological dependence:

- Paradoxical hyper-excitement reactions are rarely seen (mainly children or elderly).

4. 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

Standard dosing is:

Anxiety:

Adults: 15 - 30 mg 3 or 4 times daily.

Elderly: Initially 7.5 mg 2 or 3 times daily, to a maximum of 15 mg 3 or 4 times daily.

Insomnia:

Adults: 7.5 - 30 mg nocte.

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.



Ms. Holly Golightly with "Cat", "Breakfast at Tiffany's", 1961

References

1. eTG - July 2013
2. Oxazepam in Australian Medicines Handbook, October 2013
3. Oxazepam in MIMs October 2013.

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