UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

# THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

## TODAY'S TOPIC:

### Benzodiazepine Class Review

### Background:

Benzodiazepines have been used for many years to treat anxiety. Generally, their mechanism is through GABA modulation. Many different guidelines do not suggest long-term use of benzodiazepines, given long-term dependence (black box warning) and other side effects such as: cognitive impairment, sleep disturbances, and depression. Benzodiazepines are often utilized in the palliative care population to help mitigate symptoms of anxiety, agitation, seizures, and insomnia to name a few.

### Importance:

We can utilize benzodiazepine pharmacokinetics to help guide our benzodiazepine selection, while also considering patient-specific factors. Palliative care clinicians should be aware of the individual benzodiazepine characteristics to help select the most appropriate benzodiazepine for each individual patient.

### The Literature:

Several resources exist that review benzodiazepine pharmacokinetics (PK). Table below can be utilized as a guide, as variability exists in the literature for PK. References accessed listed at the end of this issue.

- In general, short-acting benzodiazepines are alprazolam, temazepam, and midazolam
- Onset of action below indicates onset for sedation effect
- Would favor the use of lorazepam and temazepam in setting of liver impairment

| Benzodiazepine | Onset of Action* | Time to Peak | Half Life | Metabolism | Dosing Adjustments |
|---|---|---|---|---|---|
| **Alprazolam** | PO: 1 hr | PO: 1-2 hrs | ~6-24 hrs | Hepatic; CYP3A4 | Dose adjust or avoid in liver impairment |
| **Chlordiazepoxide** | PO: 1 hr | PO: 0.5-2 hrs | ~24-84 hrs | Hepatic; CYP3A4 | Dose adjust or avoid in liver impairment |
| **Clonazepam** | PO: ~0.5-1 hr | PO: 1-2 hrs | ~18-50 hrs | Hepatic; CYP3A4, glucuronidation | Dose adjust or avoid in liver impairment |
| **Diazepam** | IV: ~3-5 mins<br>PO: ~30-60 mins | IV: 8-15 mins<br>PO: 1-2 hrs | ~20-80 hrs | Hepatic; CYP3A4, CYP2C19 | Dose adjust or avoid in liver impairment |
| **Lorazepam** | IV: 15-20 mins<br>PO: ~30 mins | IV: ~20 mins<br>PO: 1-4 hrs | ~10-20 hrs | Glucuronidation | None |
| **Midazolam** | IV: ~5 mins<br>PO: 10-20 mins | IV: 10-15 mins<br>PO: 1.5 hrs | ~6 hrs | Hepatic; CYP3A4 | Dose adjust in liver impairment |
| **Temazepam** | PO: ~0.5-1 hr | PO: ~1.5 hrs | ~8-15 hrs | Glucuronidation | None |

***Approximate* Dose Equivalencies**

| Benzodiazepine | Dose (PO) |
|---|---|
| Alprazolam | 0.5mg |
| Chlordiazepoxide | 25mg |
| Clonazepam | 0.25mg |
| Diazepam | 5mg |
| Lorazepam | 1mg |
| Midazolam | 5mg |
| Temazepam | 10mg |

**Formulations and Cost**

From Lexicomp® Medication Database:
In general, IN solutions, rectal gels, and ER products are most expensive formulations

| Benzodiazepine | Available Formulations in the U.S. | *Cost* |
|---|---|---|
| **Alprazolam** | PO concentrate (1mg/mL), PO tablet (IR/ER), ODT | $-$$$ |
| **Chlordiazepoxide** | PO capsule | $$ |
| **Clonazepam** | PO tablet, ODT | $-$$ |
| **Diazepam** | PO concentrate (5mg/mL), Rectal gel, IN liquid, IV injection, PO solution, PO tablet | $-$$$ |
| **Lorazepam** | PO ER Capsule, PO concentrate (2mg/mL), IV injection, PO tablet | $-$$ |
| **Midazolam** | IV injection, IN solution, PO syrup | $-$$$ |
| **Temazepam** | PO capsule | $$ |

PO: oral, ER: extended release, IR: immediate release, ODT: oral disintegrating tablet, IN: intranasal, IV: Intravenous

### Bottom Line:

You can utilize pharmacokinetics, available formulations to help assist with your benzodiazepine Selection.

### References:

1. Howard P, Twycross R, Shuster J et al. Benzodiazepines. J Pain Symptom Manage. 2014 May;47(5):955-64.
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3. Greenblatt DJ, Shader RI, Divoll M et al. Benzodiazepines: a summary of pharmacokinetic properties. Br J Clin Pharmacol. 1981;11 Suppl 1:11S-16S.
4. Garzone PD, Kroboth PD. Pharmacokinetics of the newer benzodiazepines. Clin Pharmacokinet. 1989 Jun;16(6):337-64.
5. Geier C. Aliem Cards Benzodiazepine (and barbiturate) Comparison. Updated 1/15/20. Available at: https://aliemcards.com/cards/benzodiazepine-and-barbiturate-comparison/.
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**CLINICAL PEARL: Utilize pharmacokinetics, available formulations to help assist with your benzodiazepine selection**