

CLINICAL **ADVISORY**

June | 2024

PharMerica

Lorazepam Injection Drug Shortage

Issue

A disruption in the dependable supply of lorazepam products was first noted by the [ASHP Drug Shortages Bulletin](#) in 2015. The issue has persisted, culminating in current shortages of **lorazepam injections, oral tablets, and oral solutions**. This benzodiazepine carries FDA labeled indications for *anxiety* (oral), *status epilepticus* (injection), and as a pre-op medication for the relief of *procedural anxiety* and *tension* (injection).

Products Affected

All NDCs of lorazepam are sporadically affected, as intermittent shortages of any one product begets shortages of others. There may be insufficient supply of these products as this shortage has been ongoing.

Estimated Resupply Date(s)

No definitive resupply date(s) have been provided.

Action Steps

PharMerica Pharmacies

- Monitor for availability of product and complete orders when possible.
- Promptly notify serviced facilities when prescription orders are unable to be fulfilled due to the drug shortage(s).

Facilities

- Solicit recommendations from prescribers and obtain prescriptions for alternative therapy to switch patients to alternative agents for their treated indication when notified by PharMerica pharmacies of drug shortages.
 - There are no direct dosage conversions between the benzodiazepines because each has a distinct pharmacokinetic profile that dictates the agent's therapeutic use and dosing (see following comparison chart).

Abridged Clinical Considerations

If **LORAZEPAM INJECTION** ordered for **STATUS EPILEPTICUS** is unavailable, consider this [UpToDate Summary](#)

- **Benzodiazepines** — 1st line treatment for convulsive status epilepticus because they control seizures rapidly.
- 3 most commonly used benzodiazepines for status epilepticus are **diazepam, lorazepam, and midazolam**.
- In adults, choice of benzodiazepine medication varies by route of administration:
 - **Diazepam** is preferred for rectal administration.
 - Rectal diazepam is given in doses of 0.2 mg/kg up to 20 mg for an adult.
 - Intranasal diazepam given at 0.2 mg/kg is an alternative.
 - **Lorazepam** is preferred for the intravenous (IV) route.
 - 4 mg IV is the best-studied dose in this setting.
 - **Midazolam** is preferred for intramuscular (IM), intranasal, or buccal administration.
 - 10 mg IM is the best studied dose in this setting.
 - The typical dose of buccal midazolam is 0.2 mg/kg, or 10 mg in adolescents and adults. The dose of intranasal midazolam using the nasal spray formulation (5 mg/0.1 mL) is one spray (5 mg) in each nostril to give 10 mg.

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Benzodiazepine Comparison Chart

Agent	FDA-Approved Indication	Dosage Forms	Approximate Dose Equivalence ^a	Protein Binding (%)	Volume of Distribution (L/kg)	Major Active Metabolite	Onset (oral) ^b	Peak Blood Levels (hours)	Metabolism	Half-Life (parent) (hours)	Half-Life (metabolite) (hours)	Elimination
ALPRAZolam (ALPRAZolam Intenso!; Xanax; Xanax XR)	Anxiety; panic disorder	Extended release tablet; immediate release tablet; oral concentrate; orally disintegrating tablet	0.5	80	0.84 to 1.2	No	Intermediate	Immediate release: 1 to 2 Extended release: 9	Hepatic via CYP3A4	6 to 27	N/A	Urine (as unchanged drug and metabolites)
ChlordiazepOXIDE	Acute alcohol withdrawal; anxiety; preoperative anxiety	Capsule	10	96	3.3	Yes	Intermediate	0.5 to 2	Hepatic	24 to 48	Demoxepam: 14 to 95	Urine (1% to 2% unchanged; 3% to 6% as metabolite)
CloBAZam (Onfi)	Adjunct in Lennox-Gastaut syndrome	Oral suspension; tablet	N/A	80 to 90	100 L	Yes	N/A	0.5 to 4	Hepatic via CYP3A4 (primary), 2C19, 2B6	36 to 42	N-desmethy!clobazam: 71 to 82	Urine (primarily as active and inactive metabolites) and feces
ClonazepAM (KlonoPIN)	Alone or as an adjunct in Lennox-Gastaut syndrome, akinetic seizures, myoclonic seizures, absence seizures, panic disorder	Orally disintegrating tablet; tablet	0.25	85	1.5 to 6.4	No	Intermediate	1 to 4	Hepatic via glucuronide and sulfate conjugation	17 to 60	N/A	Urine (primary metabolites)
Clorazepate (Tranxene-T)	Adjunct in partial seizures; alcohol withdrawal ^c ; anxiety	Tablet	7.5	97 to 98	0.7 to 2.2	Yes	Rapid	0.5 to 2	Decarboxylated in acidic stomach prior to absorption to nordiazepam; hepatic hydroxylation via CYP3A4 and 2C19 and glucuronidation	Not significant	Nordiazepam: 20 to 160 Oxazepam: 6 to 24	Urine (primarily as conjugated metabolites) and feces

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Benzodiazepine Comparison Chart (cont.)

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DiazePAM (Diasat AcuDial; Diasat Pediatric; DiazePAM Intenso; Valium, Valtoco)	Alcohol withdrawal; anxiety; preoperative anxiety and amnesia (IV); status epilepticus (IV); seizures; skeletal muscle spasms	Injection; intramuscular solution auto-injector; nasal spray; oral concentrate; oral solution; rectal gel; tablet	5	95 to 98	0.8 to 1.2	Yes	Rapid	IM: 1 Intranasal: 1.5 IV: 0.01 Oral: 0.25 to 2.5 Rectal: 1.5	Hepatic via 2C19 and 3A4	IM: ~60 to 72 Intranasal: 49 IV: 33 to 45 Oral: 44 to 48 Rectal: 45	Desmethyldiazepam: IM: ~152 to 174 IV: 87 Oral: 100 Rectal: 71 to 99	Urine (predominantly as glucuronide conjugates)
Estazolam	Insomnia	Tablet	N/A	93	N/A	No	N/A	~2	Hepatic via CYP3A4	10 to 24	N/A	Urine (as unchanged drug and inactive metabolites) and feces (minimal)
Flurazepam	Insomnia	Capsule	30	97	3.4	Yes	Rapid to intermediate	0.5 to 1	Hepatic	2.3	N-desalkylflurazepam: 74 to 113	Urine (as active and inactive metabolites)
LORazepam (Ativan; LORazepam Intenso; Loreev XR)	Adjunct to anesthesia (IM/IV); anxiety; status epilepticus (IV)	Capsule; injection; oral concentrate; tablet	1	85 to 91	1.3	No	Intermediate	IM: ≤3 Oral (extended release): ~14 Oral (immediate release): ~2	Hepatic	IM: 13 to 18 IV: 14 Oral (extended release): ~20.2 ± 7.2 Oral (immediate release): 12	N/A	Urine (predominantly as inactive metabolites) and feces (minimal)

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Midazolam	Anesthesia (IV); sedation/anolysis/amnesia (preoperative/procedural) (IM, IV, oral); sedation for mechanically ventilated patients (IV); acute intermittent seizures (intranasal); status epilepticus (IM)	Injection; nasal spray; oral suspension; oral syrup	2	97	1 to 3.1	Yes	N/A	IM: ~0.5 Intranasal: 0.13 to 0.46 Oral: 0.17 to 2.65	Hepatic via CYP3A4	1.8 to 6.4	N/A	Urine (primarily as glucuronide conjugates) and feces (minimal)
Oxazepam	Alcohol withdrawal; anxiety	Capsule	15	96 to 98	0.6 to 2	No	Intermediate to slow	~3	Hepatic via glucuronide conjugation	~8	N/A	Urine (as inactive glucuronide conjugate)
Quazepam (Doral)	Insomnia	Tablet	N/A	>95	5 to 8.6	Yes	N/A	2	Hepatic via CYP3A4, 2C9, 2C19	39	2-oxoquazepam: 39 N-desalkyl-2-oxoquazepam: 73	Urine (primarily metabolites) and feces
Temazepam (Restoril)	Insomnia	Capsule	30	96	1.4	No	Intermediate to slow	1.2 to 1.6	Hepatic	3.5 to 18.4	N/A	Urine (as inactive metabolites)
Triazolam (Halcion)	Insomnia	Tablet	0.25	89	0.6 to 1.7	No	Intermediate	2	Hepatic via CYP3A4 and glucuronide conjugation	1.5 to 5.5	N/A	Urine (primarily metabolites)