
ZURANOLONE (Zurzuvae) Fact Sheet

Bottom Line:

Zuranolone is a novel, fast-acting neurosteroid, similar to brexanolone. Rather than intravenously, it's given orally for patients with severe postpartum depression (PPD). This new drug provides ease of use, good tolerability, rapid action, and significant improvement in patients with PPD. We recommend using it in severe PPD when rapid response is critical.

FDA Indications:

PPD.

Dosage Forms:

Capsules: 20 mg, 25 mg, 30 mg.

Dosage Guidance:

Start 50 mg once daily in the evening, with a fatty meal, for 14 days. May lower to 40 mg if CNS depressant effects occur.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$\$\$\$\$

Side Effects:

- Most common: Somnolence, dizziness, diarrhea, fatigue.
- Serious but rare: Confusional state; CNS depression (patients should not drive or operate heavy machinery for at least 12 hours after taking).
- Pregnancy/breastfeeding: Insufficient data in pregnancy. No clinical data in breastfeeding, but limited data showed low levels in human milk.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Gamma-aminobutyric acid A (GABA_A) modulator.
- Metabolized by CYP3A4; t_{1/2}: 20–25 hours.
- Use caution or avoid use with CNS depressants such as benzodiazepines, which may have additive effects. Use with 3A4 inhibitors or inducers may require dose adjustment.

Clinical Pearls:

- Zuranolone is a neurosteroid that is chemically identical to endogenous allopregnanolone, a hormone whose levels rise during pregnancy and then fall abruptly after childbirth.
- Approval was based on positive results in two trials of 347 pregnant women with moderate to severe PPD. Benefits were evident within three days and sustained for six weeks. Both the 30 mg and the 50 mg daily doses showed moderate effect sizes.
- For women wishing to breastfeed, sparse data involving 14 women indicate that zuranolone transfer to breast milk does occur. While the risks of adverse effects are not known, the concentrations of the drug in breast milk are low. Until more data are available, patients may pump during the 14 days of medication administration to maintain milk supply or feed with caution, particularly monitoring for sedation in infants.
- Taking zuranolone with a high-fat meal is recommended as it increases bioavailability two-fold.
- The DEA designated brexanolone as a Schedule IV controlled substance. Zuranolone will likely receive similar scheduling once it's reviewed.
- Price and access are significant considerations, but when PPD is severe and fast medication action is critical, there are minimal alternatives.

Fun Fact:

Trial results in patients with major depressive disorder were mixed, and the FDA declined to grant that indication to zuranolone without further testing.