BREXANOLONE (Zulresso) Fact Sheet

Bottom Line:

Brexanolone is a novel, fast-acting option that is given intravenously for patients with severe postpartum depression. However, its utility is limited by the lengthy infusion (60 hours) in a health care setting, potential for severe reactions and associated need for close monitoring, high cost ($34,000 for the drug alone, plus costs associated with providers and health care facilities), and lack of follow-up data beyond 30 days. Zuranolone, a new orally available neurosteroid, provides a safer and easier option for this indication.

FDA Indications:

Postpartum depression.

Dosage Forms:

Vial for injection: 100 mg/20 mL.

Dosage Guidance:

Dosing is gradually titrated up and then tapered off over a 60-hour administration period. Start 30 mcg/kg/hour for hours 0–4, 60 mcg/kg/hour for hours 4–24, 90 mcg/kg/hour for hours 24–52 (can use 60 mcg/kg/hour for those who don't tolerate 90 mcg/kg/hour), 60 mcg/kg/hour for hours 52–56, and 30 mcg/kg/hour for hours 56–60.

Monitoring: Pulse oximetry.

Cost: $$$$$

Side Effects:

- Most common: Sedation, somnolence, dry mouth, loss of consciousness, flushing.
- Serious but rare: Excessive sedation or loss of consciousness, hypoxia.
- Pregnancy/breastfeeding: Not used in pregnancy (only postpartum); data suggest only low amounts in breast milk and likely safe, but monitor for excessive sedation if breastfeeding during infusion.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Gamma-aminobutyric acid A ($GABA_A$) modulator.
- Metabolized by non-CYP450 pathways; t ½: 9 hours.
- Use caution or avoid use with CNS depressants such as benzodiazepines, which may have additive effects.

Clinical Pearls:

- Brexanolone 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 pregnant women with moderate to severe postpartum depression; a statistically significant higher percentage of brexanolone patients remitted compared to placebo (51% vs 16% with 60 mcg/kg/hour and 61% vs 38% with 90 mcg/kg/hour infusion). In the higher-dose patients, 94% maintained response at 30 days.
- Zulresso's use is restricted to patients and health care facilities enrolled in the Zulresso Risk Evaluation and Mitigation Strategy (REMS) program (www.zulressorems.com). Monitoring for sedation, sudden loss of consciousness, and hypoxia using continuous pulse oximetry with an alarm is required for the duration of the 60-hour infusion.
- If patient experiences excessive sedation during non-sleep periods, the infusion should be stopped and can be resumed at the same or lower dose as clinically appropriate once symptoms resolve.
- For women wishing to breastfeed, sparse data involving 12 women indicate that brexanolone transfer to breast milk is minimal, with a relative infant dose of 1%–2% of maternal weight–adjusted dosage. While the risks of adverse effects are not known, the concentrations of the drug in breast milk are low.
- The DEA has designated brexanolone as a Schedule IV controlled substance.

Fun Fact:

Many psychiatric medications owe their discovery to chance or serendipity. Not so with brexanolone, which was developed by design starting with a series of basic and translational neuroscience studies dating back to the 1980s.