

Expect a Limited Role for Zurzuvae for Postpartum Depression

New Rx zuranolone (*Zurzuvae*) will be the first ORAL med approved for treatment of postpartum depression.

Think of it as similar to IV brexanolone (*Zulresso*).

Both mimic the hormone allopregnanolone, which interacts with GABA receptors. This hormone abruptly dips around childbirth...possibly leading to major depression.

Zuranolone is dosed orally once daily for 14 days. Brexanolone is a 60-hour continuous infusion given in a REMS-certified healthcare facility. Both are C-IV meds.

These GABA modulators start to improve depression symptoms within days. In contrast, SSRIs take at least 1 to 2 weeks to start working.

Current evidence supports one 14-day course of zuranolone within 12 months after delivery...given alone or with a daily antidepressant...if symptoms start in the 3rd trimester or within 4 weeks postpartum.

Efficacy past 45 days is unknown...longer-term data are lacking.

Zuranolone hasn't been compared to other meds...and patients at risk for suicide or with a psychosis history were excluded from studies.

Continue to recommend SSRIs (sertraline, etc) for most patients...and expect zuranolone to have a limited role.

Zuranolone is a specialty med and costs about \$16,000/14 days. Brexanolone is around \$30,000 plus infusion-related costs. SSRIs cost about \$10/month.

If patients get zuranolone, advise taking it with a fatty meal to improve absorption.

Warn patients of CNS effects (drowsiness, confusion, etc). Advise taking zuranolone in the evening...and to avoid driving for at least 12 hours after each dose.

Watch for interactions. For example, avoid zuranolone with CYP3A4 inducers (phenytoin, rifampin, etc)...and if possible, other CNS depressants (alcohol, opioids, etc).

Weigh the risks and benefits of breastfeeding. Exposure to the infant is expected to be low, but it's too soon to know the actual risk. Suggest monitoring the baby for excessive sedation if the mother takes zuranolone.

Don't recommend zuranolone to treat or prevent depression before childbirth. Advise using effective contraception while on zuranolone and for one week after the last dose...due to possible fetal harm.

Review our resource, *Choosing and Switching Antidepressants*, to weigh pros and cons, for advice on tapering, and more.

Key References:

- The American College of Obstetricians and Gynecologists. Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 5. *Obstet Gynecol*. 2023 Jun 1;141(6):1262-1288.
- The American College of Obstetricians and Gynecologists. Zuranolone for the Treatment of Postpartum Depression. August 2023. <https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2023/08/zuranolone-for-the-treatment-of-postpartum-depression> (Accessed January 2, 2024).

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-Deligiannidis KM, Meltzer-Brody S, Maximos B, et al. Zuranolone for the Treatment of Postpartum Depression. Am J Psychiatry. 2023 Sep 1;180(9):668-675.

-Medication pricing by Elsevier, accessed Jan 2024.

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