Zuranolone for Postpartum Depression in Real-World Clinical Practice

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Zuranolone was US Food and Drug Administration (FDA)-approved in August 2023 as the first oral medication for adults with postpartum depression (PPD), which is administered nightly with a fat-containing meal for 2 weeks within the year of delivery.[1] Zuranolone is an allopregnanolone analogue that acts as a positive allosteric modulator of GABA-A receptors at the nonbenzodiazepine site, exhibiting rapid, phasic effects synaptically and sustained, tonic effects extra-synaptically.[2] Despite FDA approval and demonstration of efficacy in clinical trials, real-world experience is still necessary to understand the appropriate uses of this new medication. The following are representative cases drawn from a cohort of 30 outpatients treated with zuranolone to date in our Hudson Valley, New York, psychiatry practice.

Case 1

Ms A is a 21-year-old first-time mother, who is not breastfeeding, with a history of premenstrual dysphoric disorder (PMDD) and not using any form of hormonal contraception. She presented 2 weeks following childbirth. She presented with acute postpartum psychosis, with symptoms of delusions that a devil was harming her baby, depressed mood, pathological guilt, panic attacks, and insomnia. Although psychiatric hospitalization is the standard of care for postpartum psychosis, there was a community option that was appropriate to meet the safety needs of postpartum psychosis as an alternative. Hence, she opted for a medically supervised mother-baby community rest home with substantial monitoring. For 2 weeks, she was treated with clonazepam 1–2 mg nightly plus aripiprazole 15 mg with limited effect, but declined an extended course of a selective serotonin reuptake inhibitor (SSRI) due to potential sexual side effects. We switched clonazepam to zuranolone. After 3 days, her symptoms completely resolved with improved sleep and panic, followed by better mood and cessation of psychosis. Since return of menses, she has not reported PMDD symptoms for over 6 months now, tapering off aripiprazole 2 weeks after completing zuranolone. Two 25 mg zuranolone capsules nightly were sedating, which tends to lessen gradually[3] and was mitigated by taking 1 capsule with dinner and another at bedtime with a snack.

Case 2

Ms B is a 30-year-old married mother of 4 children, with bipolar II depression and obsessive-compulsive disorder (OCD), taking lamotrigine 400 mg, sertraline 200 mg, and adjunctive risperidone 2 mg for 3 years with partial response despite cognitive-behavioral therapy, which she discontinued. She reported her third PPD episode at 10 months postpartum with onset during the third trimester, including worsening cognition and agitation, making it challenging to breastfeed. She added zuranolone 50 mg, continued nursing without sedation for either or her infant, and felt her depression and OCD dramatically improve at day 14. For the past 8 months, she has been feeling better than baseline in terms of anhedonia, cognition, and obsessive thoughts, subsequently enabling her to taper off risperidone, which had caused her weight gain.

Case 3

Ms C is a 38-year-old single woman with history of bipolar I disorder with psychosis, previously stable on olanzapine plus fluoxetine (a CYP3A4 inhibitor), who had severe PPD with suicidal ideation following miscarriage after a 4-month unintended pregnancy. She declined another psychiatric hospitalization for fear of losing her 2 young children to Protective Services, so we developed a safety plan for outpatient care. She added zuranolone 30 mg with complete resolution of depression and suicidality after 1 day, able to continue caring for her children. Ms C has remained stable for over a year with regular, monthly psychiatric visits and ongoing psychosocial support.

Discussion

Zuranolone is an exciting antidepressant, representing the first oral medication in the class of neurosteroids approved for one mood disorder, postpartum depression. Here, we illustrate clinical situations in which there are unmet needs in our field, such as postpartum psychosis, postpartum bipolar mood episodes, and PMDD. Zuranolone is a rapidly acting antidepressant approved for PPD that occurs in the third trimester

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or within 1 month postpartum, with or without SSRI treatment,[4,5] and appears to alleviate associated insomnia and anxiety.[6] We have found it well tolerated in 25 nursing children. This is consistent with the reported relative infant dose below 1%.[7] For women with a history of major depressive disorder (MDD)[8] or bipolar depression[9] who experience a PPD exacerbation, we add zuranolone to their current regimen, bearing in mind that CYP3A4 inhibitors can raise zuranolone levels, necessitating a lower zuranolone dose.[1] We switch benzodiazepines to zuranolone as we find that the combination can attenuate zuranolone's antidepressant effects and exacerbate sedation.[10] Driving is prohibited for at least 12 hours following administration, and it is contraindicated in pregnancy.[1] Given our experience, we support initiating zuranolone as first-line PPD treatment at postpartum screening visits for uncomplicated PPD. In combination with antimanic medication, we have not encountered induced mania, hypomania, rapid cycling, or mixed symptomatology utilizing zuranolone to treat postpartum exacerbation of bipolar depression. Based on our clinical experience, we believe that there may be a role for zuranolone for other disorders, such as postpartum psychosis, postpartum anxiety, bipolar mood episodes occurring in the postpartum period, and PMDD. We encourage repeat studies[11–13] utilizing 50 mg for adjunctive MDD in its current formulation, since some previous trials were possibly underdosed.[14] The effects of neurosteroids on neuroplasticity, neuroinflammation, network regulation, and stress responses[8] warrant further investigation for a range of affective, anxiety, and obsessive disorders, potentially in conjunction with psychotherapy as augmentation.

Article Information

Published Online: July 2, 2025. https://doi.org/10.4088/JCP.25cr15876

J Clin Psychiatry 2025;86(3):25cr15876

Submitted: March 14, 2025; accepted April 23, 2025.

To Cite: Price MZ, Price RL. Zuranolone for postpartum depression in real-world clinical practice. *J Clin Psychiatry* 2025;86(3):25cr15876.

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Relevant Financial Relationships: Dr Price has received speaker honoraria from Abbvie, Alkermes, Allergan, Axsome, Biogen, Bristol Myers Squibb, Idorsia, Intracellular, Janssen, Jazz, Lundbeck, Neuronetics, Otsuka, Sage/Biogen (manufacturer of Zurzuvae), Supernus, Teva, and Vanda. **Mr Price** reports no financial relationships with any companies whose products are mentioned in this article, or with manufacturers of competing products.

Funding/Support: None. Funding for publication fees is solely the responsibility of the authors.

Patient Consent: Written consent was obtained from each patient to publish the case reports, and information has been de-identified to protect anonymity.

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References

1. Zurzuvae (zuranolone) capsules, for oral use, CIV. Accessed March 14, 2025. https://documents.sage-biogen.com/us/zurzuvae/pi.pdf
2. Antonoudiou P, Colmers PLW, Walton NL, et al. Allopregnanolone mediates affective switching through modulation of oscillatory states in the basolateral amygdala. *Biol Psychiat*. 2022;91(3):283–293.
3. Meltzer-Brody S, Shirikjian L, Cooke J, et al. Zuranolone safety and tolerability in adults with postpartum depression: analyses from SKYLARK, a 50 mg placebo-controlled study. In: Poster presented at: Psych Congress; September 6–9, 2023; Nashville, TN.
4. Deligiannidis KM, Meltzer-Brody S, Gunduz-Bruce H, et al. Effect of zuranolone vs placebo in postpartum depression: a randomized clinical trial. *JAMA Psychiatry*. 2021;78(9):951–959.
5. Deligiannidis KM, Meltzer-Brody S, Maximos B, et al. Zuranolone for the treatment of postpartum depression. *Am J Psychiatry*. 2023;180(9):668–675.
6. Deligiannidis KM, Citrome L, Huang M-Y, et al. Effect of zuranolone on concurrent anxiety and insomnia symptoms in women with postpartum depression. *J Clin Psychiatry*. 2023;84(1):22m14475.
7. Deligiannidis KM, Bullock A, Nandy I, et al. Zuranolone concentrations in the breast milk of healthy, lactating individuals: results from a phase 1 open-label study. *J Clin Psychopharm*. 2024;44(4):337–344.
8. Cutler AJ, Mattingly GW, Maletic V. Understanding the mechanism of action and clinical effects of neuroactive steroids and GABAergic compounds in major depressive disorder. *Transl Psychiatry*. 2023;13(1):228.
9. Gunduz-Bruce H, Lasser R, Nandy I, et al. Open-label, phase 2 trial of the oral neuroactive steroid GABAA receptor positive allosteric modulator zuranolone in bipolar disorder I and II. In: Poster presented at: Psych Congress; September 10–13, 2020; virtual.
10. Dunbar J, Walling DP, Hassman HA, et al. Cognitive effects, pharmacokinetics, and safety of zuranolone administered alone or with alprazolam or ethanol in healthy adults in a phase 1 trial. *J Psychopharmacol*. 2024;38(12):1122–1136.
11. Gunduz-Bruce H, Silber C, Kaul I, et al. Trial of SAGE-217 in patients with major depressive disorder. *N Engl J Med*. 2019;381(10):903–911.
12. Parikh SV, Aaronson ST, Mathew SJ, et al. Efficacy and safety of zuranolone co-initiated with an antidepressant in adults with major depressive disorder: results from the phase 3 CORAL study. *Neuropsychopharmacol*. 2024;49(2):467–475.
13. Cutler AJ, Mattingly GW, Kornstein SG, et al. Long-term safety and efficacy of initial and repeat treatment courses with zuranolone in adult patients with major depressive disorder: interim results from the open-label, phase 3 SHORELINE study. *J Clin Psychiatry*. 2023;85(1):23m14845.
14. Clayton AH, Lasser R, Nandy I, et al. Zuranolone in major depressive disorder. *J Clin Psychiatry*. 2023;84(2):22m14445.