Zurzuvae (zuranolone)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations, or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Zurzuvae drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. Zurzuvae is a neuroactive steroid GABA A receptor positive modulator, that is chemically identical to endogenous allopregnanolone. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met, and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications
Treatment of postpartum depression (PPD) in patients 18 years of age and older.

Limitations of Use

- The safety and effectiveness of Zurzuvae use beyond 14 days in a single treatment course have not been evaluated.
- The use of Zurzuvae (zuranolone) for any other indication has not been evaluated.

POLICY

Required Documentation
The following information is necessary to initiate the prior authorization review:

1. Medical records (e.g. office notes) documenting relevant history, physician evaluation information, and rating scale/diagnostic criteria for major depression with peripartum onset
2. Medical records documenting inadequate response with antidepressant or intolerance or contraindication to antidepressants (if applicable)
3. Medical records documenting urgent need for treatment negating the step through antidepressant agent (if applicable)

Criteria for Approval

A. Authorization of 1 month may be granted for treatment of moderate to severe postpartum depression in members 18 years of age or older when all of the following criteria are met:
    1. Member has had a major depressive episode that began no earlier than the third trimester of pregnancy and no later than the first 4 weeks following delivery, documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
    2. Member is 6 months postpartum or less
    3. Member is not currently pregnant
    4. Member will not receive more than one 14-day course per 12 months
    5. Member's current episode of depression is moderate to severe
    6. Member meets one of the following:
        a) Has tried and had an inadequate response to at least one antidepressant agent (i.e. SSRIs, SNRIs, TCAs, bupropion, or mirtazapine) at a maximally tolerated therapeutic dose for a minimum duration of 2 months

        OR

        b) Has a documented intolerance or FDA labeled contraindication, to ALL classes of antidepressant agents

        OR

        c) Shows a potential risk of harm to self and/or others as determined by the treating provider and supported by documentation

All other uses of Zurzuvae (zuranolone) for conditions not outlined in this policy are considered **not medically necessary**.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limit

Medication	Standard Limit	FDA-recommended dosing
Zurzuvae (zuranolone) 20 mg capsule	28 capsules per 365 days	Dose modification: • CNS depressant effects 40 mg every evening for 14 days
Zurzuvae (zuranolone) 25 mg capsule	28 capsules per 365 days	50 mg every evening for 14 days
Zurzuvae (zuranolone) 30 mg capsule	14 capsules per 365 days	Dose modification: • Moderate or severe renal impairment (eGFR <30 mL/min/1.73 m^2): 30 mg every evening for 14 days

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

REFERENCES

- Zurzuvae [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; July 2024.
- American Psychiatric Association (APA). Postpartum depression: What is postpartum depression? Washington, DC: APA; reviewed March 2017.
- American Psychiatric Association (APA). Depressive Disorders. In: Diagnostic and statistical manual of mental disorders: 5th edition text revision DSM-5-TR. 2022. Accessed August 23, 2023. https://ebooks.appi.org/epubreader/diagnostic-statistical-manual-mental-disorders-fifth-edition-text-revision-dsm5tr
- Centers for Disease Control and Prevention (CDC). Reproductive health: Depression among women. CDC [online]. Atlanta, GA: CDC; reviewed May 2023.
- American College of Obstetricians and Gynecologists (ACOG). Treatment and management of mental health conditions during pregnancy and postpartum: ACOG Clinical Practice Guideline No. 5. Obstet Gynecol. 2023b;141(6):1262-1288. doi:10.1097/AOG.0000000000005202
- Deligiannidis KM, Meltzer-Brody S, Maximos B, et al. Zuranolone for the treatment of postpartum depression. Am J Psychiatry. 2023;180:668-675. doi: 10.1176/appi.ajp.20220785
- 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. doi:10.1001/jamapsychiatry.2021.1559
- Stewart DE, Vigod S. Postpartum depression. N Engl J Med. 2016;375(22):2177-2186. doi:10.1056/NEJMcp1607649
- U.S. Food and Drug Administration (FDA). FDA Approves First Oral Treatment for Postpartum Depression. FDA News Release. Silver Spring, MD: FDA; August 04, 2023.

*Some content reprinted from CVSHealth

POLICY HISTORY

Policy #: 05.05.21
Policy Creation: October, 2023
Reviewed: June 2025
Revised: June 2025
Current Effective Date: August 19, 2025