zuranolone (Zurzuvae™)

Policy # 00869
Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of zuranolone (Zurzuvae™)‡ for the treatment of postpartum depression to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for zuranolone (Zurzuvae) will be considered when the following criteria are met:

- Patient is greater than or equal to 18 years of age; AND
- Patient has a diagnosis of postpartum depression; AND
- Patient is not currently pregnant; AND
- Patient is less than or equal to 12 months postpartum; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Duration will not exceed one 14-day treatment course per pregnancy.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of zuranolone (Zurzuvae) in patients who are not less than or equal to 12 months postpartum to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of zuranolone (Zurzuvae) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Zurzuvae is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of postpartum depression (PPD) in adults. Its mechanism of action in the treatment of PPD is not fully understood but is thought to be related to its positive modulation of GABA A receptors. It is the second agent with this mechanism to be approved for PPD with the first being brexanolone (Zulresso®)‡. In contrast to Zulresso, Zurzuvae is administered orally and can be self-administered at home at a dose of 50 mg once daily in the evening for 14 days. Zurzuvae should be administered with a fat-containing food. If patients experience CNS depressant effects within the 14-day period, the dose may be reduced to 40 mg once daily. The safety and effectiveness of Zurzuvae use beyond 14 days in a single treatment course have not been established. Zurzuvae contains a black box warning regarding impaired ability to drive or engage in other potentially hazardous activities. Patients should be advised not to drive or engage in other potentially hazardous activities within 12 hours of dosing for the duration of the treatment course.

Postpartum depression is a major depressive episode with onset during pregnancy or within 4 weeks of delivery that can have serious effects on the maternal-infant bond and later infant development. In the United States, postpartum depression has an overall prevalence of approximately 12%. It is symptomatically indistinguishable from major depression, but the timing of its onset has led to the acknowledgement of it potentially being a unique illness. As with other forms of depression, it is characterized by sadness and/or loss of interest in activities that one used to enjoy and a decreased ability to feel pleasure and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation. Because of the risk of suicide, postpartum depression is considered a life-threatening condition.

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Zulresso and Zurzuvae are currently the only medications approved by the FDA for the treatment of postpartum depression. No other antidepressants are indicated for PPD and data on their effectiveness are limited. Non-drug treatments such as electroconvulsive shock therapy (ECT), repetitive transcranial magnetic stimulation (rTMS), and psychotherapy have been used to treat postpartum depression. Antidepressant medications are the most common treatments for depression in general and among postpartum women with moderate to severe depression. In women who choose to breastfeed, the selective serotonin reuptake inhibitors (SSRIs) sertraline and paroxetine are the recommended initial oral antidepressant therapy unless the woman has a history of efficacy with a different antidepressant. It should be noted that Zurzuvae is contraindicated during pregnancy due to risk of fetal harm and has not been studied in breastfeeding patients.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Zurzuvae was approved in August 2023 for the treatment of postpartum depression in adults.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Zurzuvae for the treatment of postpartum depression in adults was demonstrated in two randomized, placebo-controlled, double-blind, multicenter studies in women with PPD who met the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for a major depressive episode with onset of symptoms in the third trimester or within 4 weeks of delivery. In these studies, concomitant use of existing oral antidepressants was allowed for patients taking a stable dose of oral antidepressant for at least 30 days before baseline. These studies included patients with the 17-item Hamilton Rating Scale for Depression (HAMD) scores $\geq$26 at baseline.

In Study 1, patients received 50 mg of Zurzuvae (n=98) or placebo (n=97) once daily in the evening with fat-containing food for 14 days, with the option to reduce the dosage based on tolerability to 40

mg once daily of Zurzuvae or placebo. The patients were followed for a minimum of 4 weeks after the 14-day treatment course.

In Study 2, patients received another zuranolone capsule formulation (approximately equivalent to 40 mg of Zurzuvae) (n=76) or placebo (n=74) once daily in the evening with food for 14 days. The patients were followed for a minimum of 4 weeks after the 14-day treatment course.

The primary endpoint for Studies 1 and 2 was the change from baseline in depressive symptoms as measured by the HAMD-17 total score at Day 15. In these studies, patients in the Zurzuvae groups experienced statistically significantly greater improvement on the primary endpoint compared to patients in the placebo groups. In Study 1, the least squares mean change from baseline in HAMD-17 score was -15.6 in the Zurzuvae group and -11.6 in the placebo group. In Study 2, the least squares mean change from baseline in the HAMD-17 score was -17.8 in the zuranolone group and -13.6 in the placebo group.

References

1. Zurzuvae [package insert]. Biogen MA, Inc. Cambridge, MA. Updated November 2023.
2. Zurzuvae Drug Evaluation. Express Scripts. Updated August 2023.

Policy History

Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024
03/07/2024 Medical Policy Committee review
03/13/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 03/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.