Effective Date.....**11/15/2023**
Next Review Date.....**11/15/2024**
Coverage Policy Number.....**IP0270**

Brexanolone

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for brexanolone (Zulresso™).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Brexanolone (Zulresso) is considered medically necessary when the following are met:

1. **Postpartum Depression.** Individual meets **ALL** of the following criteria (A, B, C, and D):
   A. Individual is 15 years of age or older
   B. Documented diagnosis of moderate to severe postpartum depression with symptom onset during third trimester of pregnancy up to 4 weeks post-delivery
   C. Individual is postpartum, 6 months or less.

D. The medication is being prescribed by, or in consultation with, a psychiatrist or an obstetrician-gynecologist

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Only one course of treatment will be approved per pregnancy. Not applicable for continuation beyond initial approval duration.

Authorization Duration

Initial approval duration: up to 30 days

Reauthorization approval duration: Not applicable

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven including the following (this list may not be all inclusive):

1. **Retreatment with Zulresso During the Current Episode of Postpartum Depression**.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J1632	Injection, brexanolone, 1 mg

Background

OVERVIEW
Zulresso, a neuroactive steroid gamma-aminobutric acid (GABA) A receptor positive modulator, is indicated for the **treatment of postpartum depression** in patients ≥ 15 years of age.[1]

Disease Overview
Postpartum (or peripartum) 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.[3] Approximately 40% to 80% of cases of postpartum depression are considered moderate to severe.[2]

Clinical Efficacy
The efficacy of Zulresso was established in two Phase III, US-only, randomized, double-blind, placebo-controlled, multicenter, pivotal studies in patients with moderate to severe postpartum depression initiating treatment within 6 months of delivery.[2] Eligible patients were diagnosed with a major depressive episode, which had an onset no earlier than the third trimester of pregnancy and no later than 4 weeks after delivery.

Dosing Information
Zulresso is administered as a continuous intravenous infusion over 60 hours.[1] If excessive sedation occurs during the infusion, the infusion should be stopped until the symptoms resolve, then the infusion may be restarted at the same or a lower dose as clinically appropriate. The dose titration schedule for Zulresso is provided in Table 1.

Table 1. Dose Titration Schedule of Zulresso.[1]

Time	Infusion rate
0 to 4 hours	30 mcg/kg/hour
4 to 24 hours	60 mcg/kg/hour
24 to 52 hours	90 mcg/kg/hour (a reduction in dose to 60 mcg/kg/hour may be considered during this time period for patients who do not tolerate 90 mcg/kg/hour)
52 to 56 hours	60 mcg/kg/hour
56 to 60 hours	30 mcg/kg/hour

Safety
Based on findings from animal studies of other drugs that enhance GABAergic inhibition, Zulresso may cause fetal harm.[1] Currently, there are no available data on Zulresso use in pregnant women to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. A pregnancy exposure registry is available to monitor pregnancy outcomes in women exposed to antidepressants during pregnancy.

Zulresso has a Boxed Warning regarding excessive sedation and sudden loss of consciousness.[1] Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their children. During the infusion, patients must be monitored for sedative effects every 2 hours during planned non-sleep periods. If there are signs or symptoms of excessive sedation, the infusion must be stopped immediately. After symptom resolution, the infusion may be restarted at the same or a lower dose. Due to the risks of serious adverse events resulting from excessive sedation and sudden loss of consciousness, Zulresso is only available through a restricted distribution system under a Risk Evaluation and Mitigation Strategy program.[1,5]

References

1. Zulresso® intravenous infusion [prescribing information]. Cambridge, MA: Sage Therapeutics; June 2022.
2. Meltzer-Brody S, Colquhoun H, Riesenberg R, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet*. 2018;392(10152):1058-1070.
3. FDA briefing document for Zulresso. Psychopharmacologic Drugs Advisory Committee (PDAC) and Drug Safety and Risk Management (DSaRM) Advisory Committee Meeting on November 2, 2018. Available at: https://www.fda.gov/advisory-committees/human-drug-advisory-committees/psychopharmacologic-drugs-advisory-committee. Accessed on May 23, 2022.
4. FDA News Release. FDA approves first treatment for post-partum depression. Published on March 19, 2019. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633919.htm. Accessed on June 2, 2023.
5. Food and Drug Administration. Zulresso Risk Evaluation and Mitigation Strategy (REMS). March 3, 2023. Available at: https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=387. Accessed on June 2, 2023.