CARECONTINUUM™

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Psychiatry – Zulresso Utilization Management Medical Policy
- Zulresso® (brexanolone intravenous infusion – Sage Therapeutics)

REVIEW DATE: 06/12/2024

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]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Zulresso. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Zulresso as well as the monitoring required for adverse events and long-term efficacy, approval requires Zulresso to be prescribed by or in consultation with a physician who specializes in the condition being treated.
Note: A 1-month (30 days) approval duration is applied to allow for the scheduling and administration of the one-time, 60-hour infusion of Zulresso.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Zulresso is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Postpartum Depression.** Approve for 1 month if the patient meets the following (A, B, C, D, and E):
   - **A)** Patient is ≥ 15 years of age; AND
   - **B)** Patient has been diagnosed with moderate to severe depression with symptom onset during the third trimester of pregnancy or up to 4 weeks post-delivery; AND
   - **C)** Patient is ≤ 6 months postpartum; AND
   - **D)** Patient is not currently pregnant; AND
   - **E)** Zulresso is being prescribed by or in consultation with a psychiatrist or an obstetrician-gynecologist.

   Dosing. Approve up to 90 mcg/kg/hour given intravenously as a one-time, 60-hour infusion once per postpartum period.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Zulresso is not recommended in the following situations:

1. **Previous Treatment with Zulresso during the Current Episode of Postpartum Depression**.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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 June 6, 2024.
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 6, 2024.
5. Food and Drug Administration. Zulresso Risk Evaluation and Mitigation Strategy (REMS). Last updated: October 17, 2023. Available at: https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=387. Accessed on June 6, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/07/2023
Annual Revision	No criteria changes.	06/12/2024