Medical Policy:

ZULRESSO® (brexanolone)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.197	January 2, 2024	

Definitions

Zulresso, a neuroactive steroid gamma-aminobutric acid (GABA) A receptor positive modulator, is indicated for the treatment of postpartum depression in adults. Zulresso was approved under a priority review by the FDA and was granted a breakthrough therapy designation. The active ingredient of Zulpressa, brexanolone, is chemically identical to endogenous allopregnanolone. Plasma concentrations of allopregnanolone increase during pregnancy and decrease substantially after childbirth in both rodents and humans, and fluctuations in allopregnanolone have demonstrated effects on anxiety and depression in animal models. The mechanism of action of Zulresso is not fully understood but it has been shown to modulate GABA-mediated currents from recombinant human GABAA receptors in mammalian cells expressing α1β2γ2, α4β3δ, and α6β3δ receptor subunits.

Length of Authorization

Coverage will be provided for 1 treatment session (60-hour infusion) and may not be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

- 5 vials of 20mL (100mg/20mL) per treatment.
- Each 60-hour infusion will generally require preparation of 5 infusion bags; additional bags may be required for patients weighing ≥90 kg.

Guideline

I. Initial Approval Criteria

Zulresso *may be considered medically necessary if ALL of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

Postpartum Depression

1. The patient has a diagnosis of postpartum depression
2. The patient is 15 years of age or older
3. The patient has moderate to severe postpartum depression with a HAM-D total score of ≥20, or Montgomery-Åsberg depression rating scale (MADRS) with a score of ≥20, or as scored by a comparable standardized rating scale that reliably measures depressive symptoms. Scores must be documented by a psychiatrist.
4. The patient has onset of depressive symptoms no sooner than the third trimester of pregnancy and no later than within 4 weeks after delivery
5. The patient is ≤ 6 months postpartum at screening
6. Brexanolone is prescribed by or in consultation with a psychiatrist or an obstetrician-gynecologist.
7. The patient is not currently pregnant
8. Brexanalone (Zulresso) will be administered at a brexanalone (Zulresso) Center of Excellence

Limitations/Exclusions

Zulresso is not considered medically necessary for when any of the following selection criteria is met:

1. Repeat administration
2. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

1. Coverage may not be renewed. Limited to one infusion per pregnancy or postpartum period.

Dosage/Administration

Indication	Dose
Postpartum Depression	Administer ZULRESSO as a continuous intravenous (IV) infusion over a total of 60 hours (2.5 days) as follows: • 0 to 4 hours: Initiate with a dosage of 30 mcg/kg/hour • 4 to 24 hours: Increase dosage to 60 mcg/kg/hour • 24 to 52 hours: Increase dosage to 90 mcg/kg/hour (a reduction in dosage 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: Decrease dosage to 60 mcg/kg/hour • 56 to 60 hours: Decrease dosage to 30 mcg/kg/hour

Applicable Procedure Codes

Code	Description
J1632	Injection, brexanolone, 1 mg (Zulresso)

Applicable NDCs

Code	Description
72152-0547-20	Brexanolone (Zulresso) 100 mg/20 mL Intravenous Solution

ICD-10 Diagnoses

Code	Description
F53.0	Postpartum depression

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: No criteria changes
EmblemHealth & ConnectiCare	3/3/2023	Annual Review- The age restriction was lowered from 18 years of age to 15 years of age; Removed both of the following from initial criteria: "The patient has a confirmed diagnosis of a major depressive episode using DSM criteria" and "The patient does not have active psychosis, or history of seizure, or schizophrenia, or bipolar disorder, or schizo affective disorder."
EmblemHealth & ConnectiCare	09/28/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	09/11/2020	Added J-Code (J1632) Injection, brexanolone, 1 mg (Zulresso). J-Code effective date: 10/01/2020
EmblemHealth & ConnectiCare	01/01/2020	Added C9055, Injection, brexanolone, 1mg (effective 01/01/2020)

References

1. Product Information: ZULRESSO™ intravenous injection, brexanolone intravenous injection. Sage Therapeutics, Inc (per FDA), Cambridge, MA, 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2018.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2018.
4. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2018.