

Medical Policy:

ZULRESSO® (brexanolone)

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

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Zulresso, a neuroactive steroid gamma-aminobutyric 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 GABA_A receptors in mammalian cells expressing $\alpha 1\beta 2\gamma 2$, $\alpha 4\beta 3\delta$, and $\alpha 6\beta 3\delta$ 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. Brexanolone (Zulresso) will be administered at a brexanolone (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: <ul style="list-style-type: none"> • 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.