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Section:	Prescription Drugs	**Effective Date:**	January 1, 2025
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	April 12, 2019
Subject:	Zulresso	**Page:**	1 of 4

Last Review Date: December 13, 2024

Zulresso

Description

Zulresso (brexanolone)

Background
Zulresso (brexanolone) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator. The mechanism of action in the treatment of postpartum depression (PPD) is thought to be related to its positive allosteric modulation of $GABA_A$ receptors (1).

Regulatory Status
FDA-approved indication: Zulresso is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of postpartum depression (PPD) in patients 15 years and older (1).

Clinical studies for Zulresso included the diagnosis of PPD with onset of symptoms in the third trimester or within 4 weeks of delivery. Patients had moderate to severe PPD with a baseline Hamilton Depression Rating Scale (HAM-D) score of 20 or greater (1).

Zulresso has a boxed warning regarding excessive sedation and sudden loss of consciousness. 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 child(ren) (1).

Zulresso is only available through a Risk Evaluation and Mitigation Strategy (REMS) drug safety program called the Zulresso REMS because excessive sedation or sudden loss of consciousness can result in serious harm (1).

A healthcare provider must be available on site to continuously monitor the patient, and intervene as necessary, for the duration of the Zulresso infusion. Patients should be monitored for hypoxia using continuous pulse oximetry equipped with an alarm. Patients should also be assessed for excessive sedation every 2 hours during planned, non-sleep periods (1).

The safety and effectiveness of Zulresso in pediatric patients less than 15 years of age have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zulresso may be considered **medically necessary** if the conditions indicated below are met.

Zulresso may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 15 years of age or older

Diagnosis

Patient must have the following:

Postpartum depression (PPD)

AND ALL of the following:

1. Onset of depressive symptoms between the third trimester and 4 weeks postpartum
2. Severe PPD based on the Hamilton Rating Scale for Depression (HAM-D) or another valid scoring tool
   (https://www.psychcongress.com/hamilton-depression-rating-scale-ham-d)
3. A healthcare provider will be available on site for the duration of the infusion
4. Patient will be monitored for hypoxia using continuous pulse oximetry equipped with an alarm

5. Patient will be monitored for excessive sedation every 2 hours during planned, non-sleep periods
6. Healthcare facility and patient are enrolled in the Zulresso REMS program

Prior–Approval *Renewal* Requirements

None

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Duration 30 days
Each additional childbirth is initiation of therapy

Prior–Approval *Renewal* Limits

None

Rationale

Summary

The mechanism of action of Zulresso (brexanolone) is thought to be related to its positive allosteric modulation of $GABA_A$ receptors. It is used for the treatment of postpartum depression (PPD). Due to the risk for excessive sedation and sudden loss of consciousness, Zulresso is only available through the Zulresso REMS program. The safety and effectiveness of Zulresso in pediatric patients less than 15 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Zulresso while maintaining optimal therapeutic outcomes.

References

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; June 2022.

Policy History

Date	Action
April 2019	Addition to PA
June 2019	Annual review. Revised requirement for moderate to severe PPD to just severe PPD per SME
December 2020	Annual review and reference update
December 2021	Annual review
July 2022	Per PI update, decreased age requirement to 15 and older from 18 and older. Updated REMS requirement wording for consistency
September 2022	Annual review
December 2023	Annual review
December 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.