Medical Drug Clinical Criteria

Subject:	Zulresso (brexanolone)		
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Overview

This document addresses the use of Zulresso (brexanolone intravenous). Zulresso is FDA approved for the treatment of postpartum depression in women. Zulresso is a positive allosteric modulator of gamma-aminobutyric-acid type A ($GABA_A$) receptors. Postpartum depression is a common complication of childbirth and affects all socioeconomic levels. According to the American College of Obstetricians and Gynecologists (ACOG), perinatal depression (depression occurring either during pregnancy or the first 12 months following childbirth) affects in one in seven women (ACOG 2023).

The 2023 ACOG Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum clinical guidelines recommends psychotherapy as standard therapy for mild to moderate PPD. For moderate to severe PPD, oral antidepressants in combination with psychotherapy may be an option. ACOG also recommends consideration of brexanolone administration in the postpartum period for moderate-to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum. Zulresso is given as a single 60 hour continuous infusion.

In clinical studies, women with moderate to severe post-partum depression showed an improvement compared to placebo at hour 60 (after the infusion time). Trial exclusion parameters included active psychosis and medical history of bipolar disorder, schizophrenia, and/or schizoaffective disorder.

Zulresso has a black box warning regarding the risk for excessive sedation and sudden loss of consciousness during administration. Because of this, individuals must be monitored for these adverse events and must have continuous pulse oximetry monitoring. Individuals must be accompanied during interactions with their child(ren). Zulresso is available only through the Zulresso REMS.

Per the manufacturer website, Zulresso is no longer commercially available in the U.S. as of January 1, 2025. Criteria will remain active until it is considered obsolete in the pharmacy files as claims can adjudicate several years after agent discontinuation.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Zulresso (brexanolone)

Requests for Zulresso (brexanolone) may be approved if the following criteria are met (Meltzer-Brody 2018):

I. Individual is 15 years of age or older; **AND**
II. Individual is 6 months postpartum or less; **AND**
III. Individual has a diagnosis of moderate to severe postpartum depression consistent with a qualifying score using a standardized screening tool for depression (such as, but not limited to, Hamilton Rating Scale for Depression [HAM-D], Patient Health Questionnaire [PHQ-9], Beck Depression Inventory [BDI], Montgomery-Asberg Depression Rating Scale [MADRS], Edinburgh Postnatal Depression Scale [EPDS]).

Requests for Zulresso (brexanolone) may not be approved for the following:

I. Individual has end stage renal disease (ESRD) with eGFR < 15 mL/minute/1.73 m^2; **OR**
II. When the above criteria are not met and for all other indications.

Approval duration: 1 single infusion, 1 time per year

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J1632	Injection, brexanolone, 1 mg [Zulresso]

ICD-10 Diagnosis

F32.0-F32.9	Major depressive disorder
F53.0	Postpartum depression

Document History

Reviewed: 02/21/2025
Document History:

- 02/21/2025 – Annual Review: No changes. Coding Reviewed: Updated description for HCPCS J1632.
- 02/23/2024 – Annual Review: Update approval duration to clarify use as a single infusion per label. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: Wording and formatting updates. Coding Reviewed: No changes.
- 08/19/2022 – Select Review: Update criteria to expand age population per label update. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: Added statement that Zulresso would not be approved for criteria not met and all other indications. Coding Reviewed: No changes.
- 02/21/2020 – Annual Review – No Changes. Coding Reviewed: Added HCPCS C9055 and ICD-10 F32.0-F32.9, F53.0. Deleted C9399 and All Diagnosis. Added HCPCS J3590. Effective 10/1/2020 Added HCPCS J1632, Delete 9/30/2020 J3590, J3490, C9055.
- 05/17/2019 – Selected Review – Add new clinical criteria document for Zulresso (brexanolone). Coding Reviewed: Added HCPCS J3490, C9399 and All Diagnosis.

References

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 10, 2025.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; Updated periodically.
4. 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. Erratum in: Lancet. 2018;392(10153):1116.
5. Screening and Diagnosis of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 4. Obstet Gynecol. June 2023. Vol. 141, No. 6. 1232-1261. Accessed January 10, 2025.
6. Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 5. Obstet Gynecol. 2023;141(6):1262-1288. doi:10.1097/AOG.0000000000005202. Accessed January 10, 2025.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.