Zulresso® (Brexanolone)

Policy Number: IEXD0080.06
Effective Date: November 1, 2023

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Related Policies
None

Applicable States

This Medical Benefit Drug Policy applies to Individual Exchange benefit plans in all states except for Massachusetts, Nevada, and New York.

Coverage Rationale

Ü See Benefit Considerations

Zulresso (brexanolone) is proven and medically necessary for the treatment of postpartum depression in patients who meet all of the following criteria:

- Diagnosis of major depressive disorder (MDD) according to the current DSM (i.e., DSM-5), by a mental health professional; **and**
- Onset of current depressive episode was during the third trimester or within 4 weeks postpartum; **and**
- Current depressive episode is considered moderate to severe based on a standardized, validated tool; **and**
- Patient has not previously received Zulresso (brexanolone) for the current postpartum depressive episode from the most recent pregnancy (within 6 months); **and**
- The provider and/or the provider's healthcare setting is certified in the Zulresso REMS program, with ability to support onsite continuous monitoring; **and**
- The provider and/or the provider's healthcare setting is certified in the Zulresso REMS program, with ability to support onsite continuous monitoring; **and**
- Brexanolone is dosed in accordance with the United States Food and Drug Administration approved labeling; **and**
- Approval is for a single 60-hour infusion

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service.

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1632	Injection, brexanolone, 1 mg

Diagnosis Code	Description
F53.0	Postpartum depression

Background

Brexanolone is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator, that is chemically identical to endogenous allopregnanolone.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Meltzer-Brody et al. assessed brexanolone as a treatment for moderate to severe postpartum depression (PPD) in two double-blind, randomized, placebo-controlled, phase 3 trials.[2] Women in the trial were 18-45 years of age, 6 months post-partum or less at screening, and diagnosed with PPD with a Hamilton Rating Scale for Depression (HAM-D) score of ≥ 26 and 20-25 for study 1 and study 2, respectively. Study participants were randomly assigned to receive either brexanolone 90 μg/kg per hr (BRX90), brexanolone 60 μg/kg per hr (BRX60), or matching placebo for a single 60 hour infusion in study 1. In study 2 BRX90 or placebo was infused as a single 60 hour infusion. The primary efficacy endpoint was the change from baseline in the 17-item HAM-D total score at 60 hours. This was assessed in all patients who started infusion of brexanolone or placebo, had a valid HAM-D baseline assessment, and had at least one post-baseline HAM-D assessment. The trials are NCT02942004 (study 1) and NCT02942017 (study 2). In study 1, at 60 hours, the least-squares (LS) mean reduction in HAM-D total score from baseline was 19.5 points (SE 1.2) in the BRX60 group and 17.7 points (1.2) in the BRX90 group compared with 14.0 points (1.1) in the placebo group (difference -5.5 [95% CI -8.8 to -2.2], p = 0.0013 for the BRX60 group; -3.7 [95% CI -6.9 to -0.5], p = 0.0252 for the BRX90 group). In study 2, at 60 hours, the LS mean reduction in HAM-D total score from baseline was 14.6 points (SE 0.8) in the BRX90 group compared with 12.1 points (SE 0.8) for the placebo group (difference -2.5 [95% CI -4.5 to -0.5], p = 0·0160). The authors conclude that brexanolone for PPD resulted in significant and clinically meaningful reductions in HAM-D total score at 60 hours compared with placebo, with rapid onset of action and durable treatment response during the study period. The authors conclude that results suggest that brexanolone injection is a novel therapeutic drug for PPD that has the potential to improve treatment options for women with this disorder.

Professional Societies

The American College of Obstetricians and Gynecologists (ACOG) has published a clinical practice guideline with recommendations on treatment and management of perinatal mental health conditions including depression. ACOG 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. The decision to use brexanolone should balance the benefits (e.g., rapid onset of action) with the risks and challenges (e.g., limited access, high cost, lack of data supporting safety with

breastfeeding, requirement for inpatient monitoring during the infusion, lack of efficacy data beyond 30 days). (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Zulresso is indicated for the treatment of postpartum depression (PPD) in adults.

Zulresso is only available through a restricted program under a REMS called the Zulresso REMS due to the risk of excessive sedation or sudden loss of consciousness that can result in serious harm.

Important requirements of the Zulresso REMS include the following:

- Healthcare facilities must enroll in the program and ensure that Zulresso is only administered to patients who are enrolled in the Zulresso REMS
- Pharmacies must be certified with the program and must only dispense Zulresso to healthcare facilities who are certified in the Zulresso REMS
- Patients must be enrolled in the Zulresso REMS prior to administration of Zulresso
- Wholesalers and distributors must be registered with the program and must only distribute to certified healthcare facilities and pharmacies

References

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics; June 2019.
2. Meltzer-Brody S, Colquhoun H, Riesenberg R, Epperson CN, Deligiannidis KM, Rubinow DR, Li H, Sankoh AJ, Clemson C, Schacterle A, Jonas J, Kanes S. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet. 2018 Sep 22;392(10152):1058-1070.
3. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. 2013. Washington, DC. Pages 451-459.
4. 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.

Policy History/Revision Information

Date	Summary of Changes
11/01/2023	**Coverage Rationale** · Replaced references to “brexanolone” with “Zulresso (brexanolone)” · Revised coverage criteria: o Added criterion requiring the provider and/or the provider’s healthcare setting is certified in the Zulresso REMS program, with ability to support onsite continuous monitoring o Replaced criterion requiring “onset of current depressive episode was during the third trimester *and* 4 weeks postpartum” with “onset of current depressive episode was during the third trimester *or within* 4 weeks postpartum” **Supporting Information** · Updated *Clinical Evidence* and *References* sections to reflect the most current information • Archived previous policy version IEXD0080.05

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this

policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies 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.