ZULRESSO™ (BREXANOLONE)

Policy Number: PHARMACY 319.1 T2 **Effective Date**: August 1, 2019

Instructions for Use

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Related Policy

- Acquired Rare Disease Drug Therapy Exception Process

CONDITIONS OF COVERAGE

Applicable Lines of Business/Products	This policy applies to Oxford Commercial plan membership.
Benefit Type	General Benefits Package
Referral Required (Does not apply to non-gatekeeper products)	No
Authorization Required (Precertification always required for inpatient admission)	No
Precertification with Medical Director Review Required	No
Applicable Site(s) of Service (If site of service is not listed, Medical Director review is required)	Inpatient

COVERAGE RATIONALE

See Benefit Considerations

Brexanolone is proven for the treatment of postpartum depression.

Brexanolone is 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 and 4 weeks postpartum; **and**
- Current depressive episode is considered moderate to severe based on a standardized, validated tool; **and**
- Patient has not previously received 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**
- 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 may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics

ICD-10 Diagnosis Code	Description
F53.0	Postpartum depression

BACKGROUND

Brexanolone is a neuroactive steroid 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. See the Administrative Policy titled Acquired Rare Disease Drug Therapy Exception Process for additional details.

CLINICAL EVIDENCE

Meltzer-Brody et al assessed brexanolone as a treatment for moderate to severe postpartum depression (PPD) in two double-blind, randomised, 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.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

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 that 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

The foregoing Oxford policy has been adapted from an existing UnitedHealthcare Pharmacy, Clinical Pharmacy Program that was researched, developed and approved by the UnitedHealth Group National Pharmacy & Therapeutics Committee. [2019D0080A]

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics; March 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. 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.
4. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition. 2013. Washington, DC. Pages 451-459.

POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
08/01/2019	• New Clinical Policy

INSTRUCTIONS FOR USE

This Clinical Policy provides assistance in interpreting UnitedHealthcare Oxford standard 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 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 Oxford reserves the right to modify its Policies as necessary. This Clinical Policy is provided for informational purposes. It does not constitute medical advice.

The term Oxford includes Oxford Health Plans, LLC and all of its subsidiaries as appropriate for these policies. Unless otherwise stated, Oxford policies do not apply to Medicare Advantage members.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Oxford Clinical 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.