MASSACHUSETTS

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Medical Policy

Zulresso™ (Brexanolone) for the Treatment of Post-Partum Depression

Table of Contents

Policy Number: 147

BCBSA Reference Number: N/A
NCD/LCD: N/A

Related Policies

Outpatient Psychotherapy, #423
Prior Authorization Request Form for Zulresso (Brexanalone) for the Treatment of Postpartum Depression (148)

Policy[1]

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Zulresso™ (brexanolone) for the treatment of post-partum depression in individual 15 years and older, may be **MEDICALLY NECESSARY** when the following criteria are met:

1. The prescriber is a specialist in the area of the individual's diagnosis (e.g. psychiatrist) or the prescriber has consulted with a specialist in the area of the individual's diagnosis, **AND**
2. The patient meets the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria for major depressive disorder*, moderate to severe, **AND**
3. Peripartum onset (onset of depressive episode between 3rd trimester through 4 weeks postpartum), **AND**
4. Must be administered in the inpatient setting, **AND**
5. The individual does NOT have any FDA labeled contraindications to the requested agent and is intended to be used consistently with the FDA approved label.

Zulresso (brexanolone) is considered **INVESTIGATIONAL** in all other situations.

Note: Zulresso must be administered to patients through a certified REMS program as part of the FDA approval regulations. Providers and facilities administering Zulresso, must be registered with the REMS program.

***Table 1. Diagnostic Criteria for a Major Depressive Episode Criteria**

A	Five or more symptoms for 2 weeks (one of which must be either depressed mood or anhedonia)	1. Depressed mood most of the day nearly every day 2. Anhedonia most of the day nearly every day 3. Significant weight loss or gain 4. Insomnia or hypersomnia 5. Psychomotor agitation or retardation 6. Fatigue or loss of energy 7. Feelings of worthlessness or excessive guilt 8. Diminished ability to think or concentrate; indecisiveness 9. Recurrent thoughts of death; suicidal ideation or attempt
B	Symptoms cause clinically significant distress or functional impairment	
C	The episode is not attributable to the physiological effects of a substance or another medical condition	
D	The episode is not better explained by a psychotic illness	
E	There has never been a manic or hypomanic episode	

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **required.**
Commercial PPO and Indemnity	Prior authorization is **required.**
Medicare HMO Blue℠	Prior authorization is **required.**
Medicare PPO Blue℠	Prior authorization is **required.**

Requesting Prior Authorization Using Authorization Manager

Providers will need to use Authorization Manager to submit initial authorization requests for services. Authorization Manager, available 24/7, is the quickest way to review authorization requirements, request authorizations, submit clinical documentation, check existing case status, and view/print the decision letter. For commercial members, the requests must meet medical policy guidelines.

To ensure the request is processed accurately and quickly:

- Enter the facility's NPI or provider ID for where services are being performed.
- Enter the appropriate surgeon's NPI or provider ID as the servicing provider, *not* the billing group.

Authorization Manager Resources

- Refer to our Authorization Manager page for tips, guides, and video demonstrations.

Complete Prior Authorization Request Form for Zulresso (Brexanalone) for the Treatment of Postpartum Depression (148) using Authorization Manager.

For out of network providers: Requests should still be faxed to 888-641-5199.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

HCPCS Codes

HCPCS codes:	Code Description
C9399	Unclassified drugs or biologicals
J1632	Injection, brexanolone, 1 mg
J3490	Unclassified drugs

ICD-10 Procedure Codes

ICD-10-PCS codes:	Code Description
XW03306	Introduction of Brexanolone into Peripheral Vein, Percutaneous Approach, New Technology Group 6
XW04306	Introduction of Brexanolone into Central Vein, Percutaneous Approach, New Technology Group 6

The following ICD Diagnosis Code is considered medically necessary when submitted with the codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
F53.0	Postpartum depression

Description

Postpartum depression is a serious and debilitating condition that is characterized by a major depressive episode temporally and pathophysiologically related to pregnancy. It is similar to other forms of depression and characterized by sadness and/or anhedonia and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation. Brexanolone is chemically similar to endogenous hormone allopregnanolone, which is a positive allosteric modulator of GABAA (γ aminobutyric acid-ligand gated chloride channel) receptors. The levels of endogenous allopregnanolone increases during pregnancy, reach a peak during the third trimester but fall abruptly after delivery. It is hypothesized that a one-time administration of brexanolone infusion ameliorates symptoms of postpartum depression via positive allosteric modulation of both synaptic and extrasynaptic GABAA receptors. The number of patients who may qualify to receive brexanolone is currently unknown.

Summary

For individuals with postpartum depression who receive brexanolone, the evidence includes 3 randomized, placebo-controlled trials in which 247 patients were randomized to brexanolone 60 µg/kg/h (n=38), brexanolone 90 µg/kg/h (n=102) and placebo (n=107). The relevant outcomes are change in disease status, quality of life, and treatment-related mortality and morbidity. The primary efficacy endpoint of change from baseline in the 17-item Hamilton Depression Rating Scale total score at 60 hours resulted in significant and clinically meaningful reductions in the 17-item Hamilton Depression Rating Scale total

score compared with placebo. Brexanolone was associated with a greater frequency of sedation-related side effects than placebo including sudden loss of consciousness in six patients. Characterization of the safety of brexanolone was inadequate due to notable study limitations. These include exposure to study drug in a limited number of patients in a controlled setting and a relatively short follow-up of 30 days. The observed loss of consciousness during drug infusion is part of the basis for a Risk Evaluation and Mitigation Strategy requirement. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Policy History

Date	Action
9/2023	Policy clarified to include prior authorization requests using Authorization Manager.
1/2023	Policy revised to include adults 15 years or older as per the United States Food and Drug Administration expansion in the prescribing label. Effective 1/1/2023.
10/2020	Clarified coding information.
1/2020	Clarified coding information.
9/2019	Policy clarified to state that Zulresso™ must be administered in the inpatient setting.
8/2019	New medical policy describing medically necessary and investigational indications. Effective 8/1/2019.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

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Endnotes

[1] Based on expert opinion