



MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an independent
Licensee of the Blue Cross and Blue Shield Association

Medical Policy

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

Table of Contents

- [Policy: Commercial](#)
- [Policy: Medicare](#)
- [Authorization Information](#)
- [Coding Information](#)
- [Description](#)
- [Policy History](#)
- [Information Pertaining to All Policies](#)
- [References](#)
- [Endnotes](#)

Policy Number: 147

BCBSA Reference Number: N/A

NCD/LCD: N/A

Related Policies

Outpatient Psychotherapy, #423

Policy¹

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

Zulresso™ (brexanolone) for the treatment of post-partum depression in women 18 years and older, may be **MEDICALLY NECESSARY** when the following criteria are met:

1. The prescriber is a specialist in the area of the patient's diagnosis (e.g. psychiatrist) or the prescriber has consulted with a specialist in the area of the patient'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 patient 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) | <ol style="list-style-type: none"> 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 SM | Prior authorization is required* |
| Medicare PPO Blue SM | Prior authorization is required* |

*Prior Authorization Request Form: Zulresso (brexanolone) for the Treatment of Post-partum Depression

This form must be completed and faxed to: Medical and Surgical: 1-888-282-0780; Medicare Advantage: 1-800-447-2994.

[Click here for Zulresso \(brexanolone\) Treatment for Post-partum Depression authorization form #148](#)

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 $\mu\text{g}/\text{kg}/\text{h}$ (n=38), brexanolone 90 $\mu\text{g}/\text{kg}/\text{h}$ (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 |
|---------|---|
| 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

1. Ko JY, Rockhill KM, Tong VT, et al. Trends in Postpartum Depressive Symptoms - 27 States, 2004, 2008, and 2012. *MMWR Morb Mortal Wkly Rep.* Feb 17 2017;66(6):153-158. PMID 28207685
2. Sage Presentations for the November 2, 2018 Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee. <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM629510.pdf>. Accessed February 18, 2019.
3. Sage Briefing Information for the November 2, 2018 Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee. <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM624646.pdf>. Accessed February 19, 2019.
4. A-C Bernard-Bonnin, Canadian Paediatric Society, Mental Health and Developmental Disabilities Committee; Maternal depression and child development, *Paediatrics & Child Health*, Volume 9, Issue 8, 1 October 2004, Pages 575–583, <https://doi.org/10.1093/pch/9.8.575>.
5. Do T, Hu Z, Otto J, et al. Depression and suicidality during the postpartum period after first time deliveries, active component service women and dependent spouses, U.S. Armed Forces, 2007-2012. *MSMR.* Sep 2013;20(9):2-7. PMID 24093957
6. Savitz DA, Stein CR, Ye F, et al. The epidemiology of hospitalized postpartum depression in New York State, 1995-2004. *Ann Epidemiol.* Jun 2011;21(6):399-406. PMID 21549277
7. *American Psychiatric Association. DSM 5. Diagnostic and statistical manual of mental disorders. American Psychiatric Press Inc, (5th edition). 2013; Washington, DC: American Psychiatric Association.*
8. Mauri M, Oppo A, Borri C, et al. SUICIDALITY in the perinatal period: comparison of two self-report instruments. Results from PND-ReScU. *Arch Womens Ment Health.* Feb 2012;15(1):39-47. PMID 22215284
9. Wisner KL, Sit DK, McShea MC, et al. Onset timing, thoughts of self-harm, and diagnoses in postpartum women with screen-positive depression findings. *JAMA Psychiatry.* May 2013;70(5):490-498. PMID 23487258
10. FDA Briefing Information for the November 2, 2018 Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee. <https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/ucm624642.htm>. Accessed February 19, 2019.
11. Farrant M, Nusser Z. Variations on an inhibitory theme: phasic and tonic activation of GABA(A) receptors. *Nat Rev Neurosci.* Mar 2005;6(3):215-229. PMID 15738957
12. Yonkers KA, Vigod S, Ross LE. Diagnosis, pathophysiology, and management of mood disorders in pregnant and postpartum women. *Obstet Gynecol.* Apr 2011;117(4):961-977. PMID 21422871
13. Scope A, Leaviss J, Kaltenthaler E, et al. Is group cognitive behaviour therapy for postnatal depression evidence-based practice? A systematic review. *BMC Psychiatry.* Nov 28 2013;13:321. PMID 24283266
14. Daley A, Jolly K, MacArthur C. The effectiveness of exercise in the management of post-natal depression: systematic review and meta-analysis. *Fam Pract.* Apr 2009;26(2):154-162. PMID 19126829

15. Sado M, Ota E, Stickley A, et al. Hypnosis during pregnancy, childbirth, and the postnatal period for preventing postnatal depression. *Cochrane Database Syst Rev*. Jun 13 2012(6):CD009062. PMID 22696381
16. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. Feb 1960;23:56-62. PMID 14399272
17. Molyneaux E, Telesia LA, Henshaw C, et al. Antidepressants for preventing postnatal depression. *Cochrane Database Syst Rev*. Apr 18 2018;4:CD004363. PMID 29669175
18. Kaner S, Colquhoun H, Gunduz-Bruce H, et al. Brexanolone (SAGE-547 injection) in post-partum depression: a randomised controlled trial. *Lancet*. Jul 29 2017;390(10093):480-489. PMID 28619476
19. Meltzer-Brody S, Colquhoun H, Riesenber R, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. *Lancet*. Sep 22 2018;392(10152):1058-1070. PMID 30177236
20. FDA Presentations for the November 2, 2018 Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee. <https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/UCM629509.pdf>. Accessed February 19, 2019.
21. De Crescenzo F, Perelli F, Armando M, et al. Selective serotonin reuptake inhibitors (SSRIs) for postpartum depression (PPD): a systematic review of randomized clinical trials. *J Affect Disord*. Jan 2014;152-154:39-44. PMID 24139299
22. Wisner KL, Perel JM, Peindl KS, et al. Prevention of recurrent postpartum depression: a randomized clinical trial. *J Clin Psychiatry*. Feb 2001;62(2):82-86. PMID 11247106
23. Wisner KL, Perel JM, Peindl KS, et al. Prevention of postpartum depression: a pilot randomized clinical trial. *Am J Psychiatry*. Jul 2004;161(7):1290-1292. PMID 15229064
24. Practice Guideline for the Treatment of Patients With Major Depressive Disorder (Third Edition). https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf. Accessed February 20, 2019.
25. Spinelli MG, Endicott J. Controlled clinical trial of interpersonal psychotherapy versus parenting education program for depressed pregnant women. *Am J Psychiatry*. Mar 2003;160(3):555-562. PMID 12611838
26. Stuart S, O'Hara MW, Gorman LL. The prevention and psychotherapeutic treatment of postpartum depression. *Arch Womens Ment Health*. Aug 2003;6 Suppl 2:S57-69. PMID 14615924
27. Force USPST, Curry SJ, Krist AH, et al. Interventions to Prevent Perinatal Depression: US Preventive Services Task Force Recommendation Statement. *JAMA*. Feb 12 2019;321(6):580-587. PMID 30747971

Endnotes

¹ Based on expert opinion