Zulresso (brexanolone)
PAM – 037

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2021
Revision Number	4	**Last Reviewed**	01/17/2025
Reviewed By	Medicaid Medical Director	**Next Review**	01/16/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	10/15/2021

Overview

Medication: [1]	brexanolone
Brand Name:	Zulresso®
Pharmacologic Category:	Gamma-aminobutyric acid (GABA) A receptor positive modulator
FDA-Approved Indication(s):	Treatment of postpartum depression (PPD) in patients 15 years of age and older
How Supplied:	Single-dose vial containing 100 mg brexanolone in 20 mL (5 mg/mL)
Dosage and Administration:	A healthcare provider must be available on site to continuously monitor the patient, and intervene as necessary, for the duration of the infusion. Administer as a continuous intravenous (IV) infusion over a total of 60 hours (2.5 days) as follows:
Benefit Category:	Medical

Time	Dose	Hours at this dose
0 – 4 hours	30 mcg/kg/hour	4
4 – 24 hours	60 mcg/kg/hour	20
24 – 52 hours	90 mcg/kg/hour	28
52 – 56 hours	60 mcg/kg/hour	4
56 – 60 hours	30 mcg/kg/hour	4

BOXED WARNING: Excessive sedation and sudden loss of consciousness

- Patients treated with Zulresso® are at risk of excessive sedation or sudden loss of consciousness during administration.
- Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren).
- Because of these risks, Zulresso® is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ZULRESSO REMS.

Descriptive Narrative

There is no established consensus as to what time frame constitutes the postpartum period. According to the American Psychiatric Association's Diagnostic and Statistical Manual, Fifth Edition (DSM-5), onset of postpartum major depression can occur prior to or after parturition. The DSM-5 specifier "with peripartum onset" is used when onset of major depression occurs either during pregnancy or in the four weeks following delivery.

For depressive "episodes that are associated with the puerperium," the World Health Organization's International Classification of Diseases – 10th Rev. (ICD-10) requires onset of the episode within six weeks of delivery. Other definitions of the puerperium range from the first 3 to 12 months following a live birth.

Globally, the prevalence of depression among postpartum women is approximately 10 to 15 percent. In the United States, the 12-month prevalence of unipolar major depression in postpartum women is approximately 9 percent (similar to the rate in non-postpartum women, which is 8 percent). The highest risk factor for postpartum depression (PPD) is a prior history of depression, but other risk factors include stressful life events during pregnancy or after delivery, as well as poor social and financial support in the 6 weeks following giving birth. Untreated PPD may resolve spontaneously or with treatment or may develop into a persistent (chronic) depressive disorder.

A review of clinical and community samples of treated and untreated patients concluded that episodes of postpartum major depression last at least one year in 30 to 50 percent of patients and have several adverse consequences.

PPD impairs maternal functioning, is associated with poor nutrition and health in the offspring, and can interfere with breastfeeding, maternal-infant bonding, care of the infant and other children, and the woman's relationship with her partner. In addition, it is associated with abnormal development, cognitive impairment, and psychopathology in the children.[2] Among the most serious consequences of maternal depression is maternal suicide, which has been estimated at between 1.5 and 4.5 per 100,000.[3]

DSM-5-TR Diagnostic Criteria for a Major Depressive Episode[4]

(DSM V: Diagnostic and Statistical Manual of Mental Disorders)

A. Five or more of the following symptoms have been present during the same two-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
(NOTE: Do not include symptoms that are clearly attributable to another medical condition).
   1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad, empty, hopeless) or observations made by others (e.g., appears tearful) (NOTE: In children and adolescents, can be irritable mood).
   2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation).
   3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month) or decrease or increase in appetite nearly every day (NOTE: In children, consider failure to make expected weight gain).
   4) Insomnia or hypersomnia nearly every day.
   5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).
   6) Fatigue or loss of energy nearly every day.
   7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).
   8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by their subjective account or as observed by others).
   9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

C. The episode is not attributable to the direct physiological effects of a substance or to another medical condition.
   NOTE: Criteria A through C represent a major depressive episode.
   NOTE: Responses to a significant loss (e.g., bereavement, financial ruin, losses from a natural disaster, a serious medical illness or disability) may include the feelings of intense sadness, rumination about the loss, insomnia, poor appetite, and weight loss noted in Criterion A, which may resemble a depressive episode. Although such symptoms may be understandable or considered appropriate to the loss, the presence of a major depressive episode in addition to the normal response to a significant loss should also be carefully considered. This decision inevitably requires the exercise of clinical judgement based on the individual's history and the cultural norms for the expression of distress in the context of loss.

D. The occurrence of the major depressive episode is not better explained by schizoaffective disorder, schizophrenia, schizophreniform disorder, delusional disorder, or other specified and unspecified schizophrenia spectrum and other psychotic disorders.

E. There has never been a manic or hypomanic episode.
   NOTE: This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition.

Guidelines

Practice guidelines issued by the U.S. Preventive Services Task Force (USPSTF) recommend screening all pregnant and postpartum women for depression. Screening for depression during pregnancy and the puerperium should be implemented with services in place to ensure follow-up for diagnosis and treatment (treatment protocols, care management, and availability of specially trained depression care providers).[5] Statement from the American College of Obstetricians and Gynecologists (ACOG):

> *The American College of Obstetricians and Gynecologists (ACOG) is pleased that the USPSTF recognizes that screening for depression is appropriate for all adults, including pregnant and postpartum women. ACOG has long recommended depression screening for all women, both as a part of the well-woman visit and during the perinatal period. Specifically, ACOG's Committee Opinion on Screening for Perinatal Depression recommends routine screening for depression for all women at least once during the perinatal period.* [6]

Criteria

Prior authorization is required.

Zulresso® is considered medically necessary for the treatment of moderate to severe postpartum depression (PPD) when **ALL** of the following are met:

1. Member meets the Diagnostic and Statistical Manual of Mental Disorders (DSM-5 or DSM-5-TR) criteria for a major depressive episode with onset of symptoms in the third trimester or within the first 4 weeks of delivery; **AND**
2. Member is 15 years of age or older; **AND**
3. Member is 6 months postpartum or less; **AND**
4. Member diagnosed with moderate to severe depression, as assessed using one or more of the following (a, b, or c):
    a. Beck Depression Scale (BDI) score $\geq$ 19; or
    b. Hamilton Depression Rating Scale (HAM-D) score $\geq$ 20; or
    c. Montgomery-Asberg Depression Rating Scale (MADRS) score $\geq$ 30; **AND**
5. Documentation of negative pregnancy test; **AND**
6. Prescribed by, or in consultation with, a psychiatrist; **AND**
7. Member's weight is provided, and dosing is appropriate for the given weight (see dosing schedule above in "Overview" section).

Reauthorization is not appropriate; coverage may only be authorized for a one-time infusion per pregnancy.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent
Approval Duration	30 days (allows for a one-time infusion per pregnancy)	Not applicable. One-time infusion per pregnancy only.
Quantity Limits	one 60-hour infusion per pregnancy (dosing is weight-based)	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J1632	Injection, brexanolone, 1 mg

ICD-10	Description
F32.0-F32.9	Major depressive disorder
F53.0	Postpartum depression

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/ Pkg
72152-0547-20 (100 mg/20 mL)	Sage Therapeutics (72152)	1 mg	1	EA	100

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations.

Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Zulresso® prescribing information (07/2024). Sage Therapeutics, Inc.: Cambridge, MA. Available online: www.zulressohcp.com. Accessed November 3, 2024.

[2] Viguera A. Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis. Solomon D, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed December 16, 2024.

[3] M.E. Wallace, D. Hoyert, C. Williams, P. Mendola. Pregnancy-associated homicide and suicide in 37 US states with enhanced pregnancy surveillance. Am J Obstet Gynecol, 215 (2016), pp. 364.e1-364.e10.

[4] Rush AJ. Major depressive disorder in adults: Approach to initial management. Swenson S, Solomon D, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed December 16, 2024.

[5] O'Connor E, Rossom RC, Henninger M, Groom HC, Burda BU, Henderson JT, Bigler KD, Whitlock EP. Screening for Depression in Adults: An Updated Systematic Evidence Review for the U.S. Preventive Services Task Force. Evidence Synthesis No. 128. AHRQ Publication No. 14-05208-EF-1. Rockville, MD: Agency for Healthcare Research and Quality; 2016.

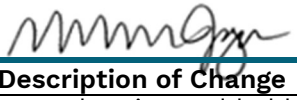
[6] The American College of Obstetricians and Gynecologists (ACOG). ACOG statement on depression screening. Available online at www.acog.org/news/news-releases/2016/01/acog-statement-on-depression-screening. Accessed June 24, 2021.

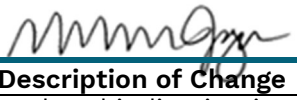
Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
01/17/2025	CAC	Annual review. Updated statistics in Descriptive Narrative. Updated DSM-5 table to DSM-5-TR. Updated references where applicable.	4
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/20/2023	CAC	Annual review. Added boxed warning (excessive sedation and sudden loss of consciousness) to Overview section. Added criterion “Documentation of negative pregnancy test.”	3
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/21/2022	CAC	Updated indication in Overview table: now indicated in ages 15 years and above (previously only indicated for use in adults). Cricriteria also updated to reflect change in age restriction.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
10/15/2021	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee