MEDICAL COVERAGE POLICY	
SERVICE:	**Brexanolone (Zulresso®)**
Policy Number:	**256**
Effective Date:	**11/01/2024**
Last Review:	**08/12/2024**
Next Review:	**08/12/2025**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

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PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Brexanolone (Zulresso®) may be medically necessary for the treatment of Postpartum Depression when **ALL** of the following criteria are met:

1. Member is ≥ 15 years of age
2. Must be prescribed by a psychiatrist
3. Diagnosis of postpartum depression with a HAM-D total score of at least 20, or as scored by an alternative comparable rating scale that measures depressive symptoms.
4. Onset of the major depressive episode is within the third trimester and no later than the first four weeks postpartum.
5. Six months or less postpartum at screening.
6. No active psychosis or history of bipolar disorder or schizophrenia.
7. Has not received treatment with brexanolone for the current postpartum depressive episode.
8. Have continuous pulse oximetry monitoring during the infusion period due to risk of serious harm and be accompanied when interacting with their child(ren) as the drug can cause loss of consciousness.
9. A health-care provider must be available on site for continuous monitoring of the client for the duration of the infusion.

Only ONE treatment per postpartum period will be authorized for duration of request or 6 months (whichever is less).

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BACKGROUND:

Postpartum depression (PPD) refers to the development of a depressive illness following childbirth. The American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM-5) does not recognize PPD as a separate diagnosis; rather, PPD patients meet the criteria for a major depressive episode and the criteria for peripartum onset. PPD is a serious mood disorder associated with a range of debilitating symptoms that impact a woman's ability to function, and is a leading cause of maternal suicide.

The prevalence of PPD among women residing in high income countries is reported to be approximately 10%. The Centers for Disease Control and Prevention report that PPD estimates in the U.S. vary by state, and can be as high as 1 in 5 women.

Treatment of PPD depends on the severity of symptoms and the level of functional impairment. Psychotherapy is considered first-line treatment for mild-to-moderate postpartum depression; psychotherapy may be combined with medication in patients with more severe symptoms. Use of pharmacotherapy in breastfeeding mothers is a concern, although the risks must be weighed against the risks associated with PPD, including suicide risk and impaired maternal-infant bonding.

Medication options include selective serotonin reuptake inhibitor (SSRI) agents. However, SSRI agents are not specifically FDA-approved for the treatment of PPD, and they can often take weeks to months to be effective in alleviating symptoms of depression. There is a high unmet need for new pharmacotherapy agents for the management of PPD; brexanolone was developed to address this need.

Brexanolone is a sterile solution of allopregnanolone for intravenous (IV) infusion. Allopregnanolone is a positive allosteric modulator of the neurotransmitter gamma-aminobutyric acid (GABAA) receptors. Plasma allopregnanolone concentrations rise in concert with progesterone throughout pregnancy, reaching the highest physiological concentrations in the third trimester. After childbirth, these concentrations decrease abruptly. Failure of GABAA receptors to adapt to these changes may have a role in triggering PPD. Although the cause of PPD is not entirely understood, it is proposed that treatment of women with PPD with doses of allopregnanolone that result in serum concentrations equivalent to those present during the third trimester may lessen PPD symptoms.

The U.S. Food and Drug Administration (FDA) approved brexanolone on March 19, 2019. The efficacy of brexanolone in the treatment of PPD was demonstrated in two multicenter, randomized, double-blind, placebo-controlled studies in women ages 18 to 45 years with PPD who met the Diagnostic and Statistical Manual of Mental Disorders criteria for a major depressive episode (DSM-IV) with onset of symptoms in the third trimester or within 4 weeks of delivery. In both studies, brexanolone titrated to 90 mcg/kg/hour was superior to placebo in improvement of depressive symptoms as measured by the HAM-D total score.

On June 16, 2022, the FDA expanded the age limit to patient 15 years and older based on an open-label study evaluating safety, tolerability, and pharmacokinetics of brexanolone in adolescent females, 15 years to less than 18 years of age, diagnosed with postpartum depression.

Brexanolone is administered as a continuous IV infusion over 60 hours. The recommended dosage and administration is as follows:

0 to 4 hours: initiate with a dosage of 30 mcg/kg/hour

4 to 24 hours: increase dosage to 60 mcg/kg/hour

24 to 52 hours: increase dosage to 90 mcg/kg/hour (a reduction in dosage to 60 mcg/kg/hour may be considered during this time period for patients who do not tolerate 90 mcg/kg/hour)

52 to 56 hours: decrease dosage to 60 mcg/kg/hour

56 to 60 hours: decrease dosage to 30 mcg/kg/hour

If excessive sedation occurs at any time during the infusion, the infusion should be stopped until the symptoms resolve. The infusion may be resumed at the same or lower dose as clinically appropriate.

FDA Label restrictions:

- Patients are at risk of excessive sedation or sudden loss of consciousness during administration of brexanolone.
- 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).
- Brexanolone is available only through a restricted program called the ZULRESSO® REMS.

Brexanolone (Zulresso®) will be available only through a Risk Evaluation and Mitigation Strategy (REMS) program which requires the following:

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

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	
HCPCS Codes:	J1632 - Injection, brexanolone, 1 mg
ICD10 codes:	F53.0 – Postpartum depression
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	07/25/2019	New policy
Updated	06/25/2020	Logo changed to include FC
Reviewed	06/24/2021	Updated HCPCS code
Updated	06/23/2022	Removed Medicaid/CHIP provider and subsequent pregnancy statement, updated auth duration, minor format updates
Updated	12/01/2023	Updated age criterion
Updated	09/28/2023	Updated Medicaid instructions
Updated	08/12/2023	Applied new format and layout

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Kose S, Cetin M. Brexanolone: an allosteric modulatorof GABA-A receptors in the rapid treatment of postpartum depression. Psychiatry and Clinical Psychopharmacology, 2017. 27:4, 326-328, DOI: 10.1080/24750573.2017.1380352
2. Fischer MD, Bernard (2022, June 16). [Letter of supplemental approval/fulfilment of postmarketing requirement from FDA to Sage Therapeutics, Inc.]. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/211371Orig1s007ltr.pdf.
3. Gelaye B, Rondon M, Araya, PhD, Williams M. Epidemiology of maternal depression, risk factors, and child outcomes in low-income and middle-income countries. Lancet Psychiatry. 2016 Oct; 3(10): 973–982. DOI: 10.1016/S2215-0366(16)30284-X
4. Kanes S, Colquhoun H, Gunduz-Bruce H, Raines S, Arnold R, Schacterle A, Doherty J, Epperson CN, Deligiannidis KM, Riesenberg R, Hoffmann E, Rubinow D, Jonas J, Paul S, Meltzer-Brody S. Brexanolone (SAGE-547 injection) in post-partum depression: a randomised controlled trial. Lancet. 2017 Jul 29;390(10093):480-489. DOI: 10.1016/S0140-6736(17)31264-3. Epub 2017 Jun 12.
5. US Food & Drug Administration. (2019, Mach 19). FDA approves first treatment for post-partum depression [Press release]. https://www.fda.gov/news-events/press-announcements/fda-approves-first-treatment-post-partum-depression
6. Zulresso (brexanolone) [prescribing information]. Cambridge, MA: Sage Therapeutics Inc; June 2022.

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Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid plans are offered through Scott and White Health Plan in the Central Managed Care Service Area (MRSA) and STAR and CHIP plans are offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs.