Pharmacy Management Drug Policy

SUBJECT: Zulresso ® (brexanolone injection) – for Postpartum Depression
POLICY NUMBER: PHARMACY- 82
EFFECTIVE DATE: 6/20/2019
LAST REVIEW DATE: 01/13/2020

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

Description:

Zulresso™ (brexanolone), a neuroactive steroid gamma-aminobutyric acid A (GABA-A) receptor positive modulator, is the first FDA-approved treatment specifically for postpartum depression (PPD) in adults. No other antidepressants are indicated for postpartum depression, and data on their effectiveness are limited. Zulresso™ is administered as a continuous intravenous (IV) infusion over 60 hours.

Postpartum (or peripartum) depression is a major depressive episode with onset during pregnancy or within 4 weeks of delivery that is thought to affect 10% to 20% of women who give birth worldwide. As with other forms of depression, PPD is characterized by sadness and/or loss of interest in activities that one used to enjoy and a decreased ability to feel pleasure and may present with symptoms such as cognitive impairment, feelings of worthlessness or guilt, or suicidal ideation.

The active ingredient of Zulresso™, brexanolone, is chemically identical to allopregnanolone, an endogenous metabolite of progesterone. During pregnancy, plasma concentrations of allopregnanolone increase, then subsequently decrease substantially after childbirth. These changes are thought to contribute to PDD as fluctuations in allopregnanolone levels have demonstrated effects on anxiety and depression in animal studies.

According to the American College of Obstetricians and Gynecologists (ACOG) Committee Opinion on screening for perinatal depression (2019), clinicians should screen patients at least once during the perinatal period (defined as the period during pregnancy or within 12 months following delivery) for depression and other mood disorders using a standardized, validated tool. Each patient should also be assessed for mood and emotional well-being (including assessing for depression and anxiety) during the comprehensive postpartum appointment. There is evidence that screening alone can benefit patients; however, treatment initiation or referral to a mental health provider provides maximum benefit. ACOG also recommends that postpartum care should be considered an ongoing process with comprehensive assessment of physical, social and psychological well-being within 12 weeks of birth (2018).

The U.S. Preventative Services Task Force (USPSTF) recommends depression screening in the general adult population, including pregnant and postpartum women (B recommendation, 2019). Clinicians should provide or refer pregnant women and women less than 1 year postpartum who are at increased risk of perinatal depression to counseling recommendations.

The American Academy of Pediatrics (AAP) recommends that pediatricians integrate surveillance and screening at the 1-, 2-, 4-, and 6-month visits using the Edinburgh scale as unrecognized maternal depression can cause failure-to-thrive and other pediatric issues (2019).

Policy:

Postpartum Depression Zulresso (brexanolone injection) (Medical Benefit)
1. Zulresso must be prescribed by a psychiatrist or an obstetrician-gynecologist in consultation with a psychiatrist **2.** The patient must be at least 18 years of age **3.** The patient must have a diagnosis, confirmed by a psychiatrist or an obstetrician-gynecologist in consultation with a psychiatrist, of **severe** Postpartum Depression (PPD), based on an ACOG supported validated tool (See Supplemental Information), with documentation of a major depressive episode that occurred between the 3rd trimester through 4 weeks postpartum. There must also be documentation of serious functional decline or an inability to function with potential for harm to themselves or others. a. The major depressive episode must meet the Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) criteria for a major depressive episode as outlined in table 1 (See Supplemental Information) **4.** Documentation must be submitted which confirms the treatment facility and patient are registered through the Zulresso REMS program **5.** The patient must be no more than 6 months postpartum and not currently pregnant **6.** Approval will be for 1 month to allow for a one-time administration of Zulresso over 60 hours **7.** FDA approved dosing for Zulresso (as a continuous IV infusion): 0 to 4 hours: 30 mcg/kg/hour 4 to 24 hours: 60 mcg/kg/hour 24 to 52 hours: 90 mcg/kg/hour OR 60 mcg/kg/hour for those who do not tolerate 90 mcg/kg/hour 52 to 56 hours: 60 mcg/kg/hour 56 to 60 hours: 30 mcg/kg/hour

Supplemental Information:

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	

Adapted from FDA Briefing Document[10] and Diagnostic and Statistical Manual of Mental Disorders: DSM-5. 5th ed., American Psychiatry Association, 2013.[7]

Validated tools supported by the American College of Obstetricians and Gynecologists (ACOG) committee:

- Edinburgh Postnatal Depression Scale
- Postpartum Depression Screening Scale
- PHQ-9 depression questionnaire
- Beck Depression Inventory
- Beck Depression Inventory-II
- Center for Epidemiologic Studies Depression Scale
- Zung Self-Rating Depression Scale

The Edinburgh Postnatal Depression Scale is the most frequently used and has the most support from the American College of Obstetricians and Gynecologists committee due to its specificity.

Policy Guidelines:

1. Non-FDA approved indications for Zulresso will not be approved.
2. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
3. This policy is subject to frequent revisions as new medications come onto the market. Some drugs will require prior authorization prior to approved language being added to the policy.
4. Prior-authorization is contract dependent.
5. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. Codes may not be covered under all circumstances. Please read the policy and guideline statements carefully. Codes may not all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
Code Key: Experimental/Investigational = (E/I). Not medically necessary/appropriate = (NMN).

HCPCS:

Description (Number): **Zulresso (C9055)**

Updates:

Date	Revision
01/2020	Revised
10/2019	Revised
09/2019	P&T Approval
06/2019	Created

References:

1. Zulresso™ injection for intravenous use [prescribing information]. Cambridge, MA: Sage Therapeutics; March 2019. FDA News Release.

2. FDA approves first treatment for post-partum depression. Published on March 19, 2019. Available at: https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm633919.htm. Accessed on June 26, 2019.

3. Meltzer-Brody S, Colquhoun H, Riesenberg R, et al. Brexanolone injection in post-partum depression: two multicentre, double-blind, randomised, placebo-controlled, phase 3 trials. Lancet. 2018;392(10152):1058-1070.

4. American College of Obstetricians and Gynecologists Committee on Obstetric Practice. Screening for perinatal depression. ACOG Committee opinion No. 757. American College of Obstetricians and Gynecologists. Obstet Gynecol. 2018;132:e208-e212

5. Marian F. Earls, Michael W. Yogman, Gerri Mattson, Jason Rafferty, Committee on Psychosocial Aspects of Child and Family Health. Incorporating Recognition and Management of Perinatal and Postpartum Depression into Pediatric Practice. Pediatrics. 2019;143(1):e2018-e3259

6. Zulresso (brexanolone) Injection for intravenous use [prescribing information]. Cambridge, MA: Sage Therapeutics, Inc. March 2019

7. Optimizing postpartum care. ACOG Committee Opinion No. 736. American College of Obstetricians and Gynecologists. Obstet Gynecol 2018;131:e140–50.