SmartPA Criteria Proposal

Drug/Drug Class:	Zulresso Clinical Edit
First Implementation Date:	July 1, 2020
Revised Date:	July 20, 2023
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	☒Existing Criteria ☐Revision of Existing Criteria ☐New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of Zulresso™ (brexanolone)

Why Issue Selected: On March 19, 2019, the FDA approved Zulresso™ (brexanolone) for the treatment of postpartum depression (PPD). Brexanolone is an analog of allopregnanolone, an endogenous steroid hormone metabolite that increases during pregnancy and then declines abruptly after birth; it is thought this decline may trigger depression and anxiety in some women. PPD is the most common postnatal psychiatric complication affecting an estimated 9-12% of postpartum women in the US (approximately 400,000 cases annually). It is well established that PPD can result in adverse short and long term effects on both the mother and the child; treatment focuses on cognitive-behavioral therapy and antidepressant medications. Zulresso, however, can improve symptoms of PPD in as little as 24 hours, while improvement with oral antidepressants may take weeks. Zulresso is a one-time treatment administered by continuous infusion over 60 hours; administration is complex as the product has limited stability (12 hours at room temperature) requiring a minimum of 5 infusion bag changes and recommended dosing requires several changes in infusion rates. There is also a risk of serious harm resulting from excessive sedation and loss of consciousness during the infusion, prompting the FDA to add a Boxed warning to the label and require a REMS program. Sage Therapeutics, the makers of Zulresso, are identifying "Centers of Excellence" that will be able to meet REMS requirements, have the capability to prepare and administer Zulresso, and can provide a positive patient experience. Due to the high cost, possible adverse events, and specific approved indications, MO HealthNet will impose clinical criteria to ensure appropriate utilization of Zulresso.

Program-Specific Information:

Drug	Cost per treatment – 5 vials
ZULRESSO 100 MG/20 ML VIAL	$37,250 MAC

Type of Criteria:
☒ **Increased risk of ADE**
☒ **Appropriate Indications**
☐ **Preferred Drug List**
☒ **Clinical Edit**

Data Sources:
☐ **Only Administrative Databases**
☒ **Databases + Prescriber-Supplied**

Setting & Population

- Drug class for review: Zulresso™ (brexanolone)
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Documented diagnosis of moderate to severe postpartum depression:
  - Participant meets DSM-5 criteria for major depressive disorder (single or recurrent episode) **AND**
  - Participant has a clinical diagnosis, made by a psychiatrist or other specialist in the field of psychiatry, of moderate to severe postpartum depression **AND**
  - Diagnosis and severity of depression is supported by a validated rating scale **AND**
  - Onset of symptoms occurred in the third trimester of pregnancy or within 6 months of delivery **AND**
- Documentation of administration in a facility enrolled in the Zulresso REMS program **AND**
- Quantity limit of 5 vials per treatment – approval for a larger quantity requires documentation of appropriate dosing and participant weight above 90 kg

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Previous history of Zulresso therapy in the past 9 months
- Documented history of end-stage renal disease

Billing Information

- Utilize the following codes so that MO HealthNet will know the billing is for additional hours for the administration of Zulresso under the MO HealthNet FFS Program (You must ensure a Prior Authorization is on file for the medication prior to administering to the participant):
  - First 24 hours of observation
    - Revenue code 762 (Observation Room) **AND**
    - Procedure code G0378 (Hospital Observation per Hour)
  - Subsequent hours of observation
    - Revenue code 769 (Other Treatment/Observation) **AND**
    - Procedure code G0378 (Hospital Observation per Hour)
    - The above combination of billing codes has only been approved for the administration and monitoring of Zulresso.

Required Documentation

Laboratory Results:		Progress Notes:	
MedWatch Form:		Other:	**X**

Disposition of Edit

Denial: Exception code “0682” (Clinical Edit)
Rule Type: CE

Default Approval Period

1 month

References

- ZULRESSO™ (brexanolone) injection, [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; June 2022.
- US Preventive Services Task Force. Interventions to Prevent Perinatal Depression. JAMA. 2019;321(6):580-587. doi:10.1001/jama.2019.0007
- IPD Analytics. New Drug Approval: Zulresso (brexanolone) injection, for intravenous use. March 2019.
- IPD Analytics. Behavioral Health: Depression. Accessed February 2, 2022.
- Clinical Pharmacology. Brexanolone. Accessed January 24, 2023.
- American Psychiatric Association. Practice Guideline for the Treatment of Patients with Major Depressive Disorder. Publication Date: 2010. PG_Depression3e.book(PG_Depression_3e00Pre.fm) (psychiatryonline.org)
- Drug Monograph: “Zulresso (brexanolone)”, Gainwell Technologies; Last updated February 21, 2023.