Policy Title:	**Zulresso (brexanolone)** (Intravenous)		
		Department:	PHA
Effective Date:	09/01/2019		
Review Date:	10/2020, 7/2021, 4/2022, 4/2023, 12/2023, 01/2024, 2/2024		

Purpose: To support safe, effective, and appropriate use of Zulresso (brexanolone).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Zulresso (brexanolone) is covered under the Medical Benefit when used within the following guidelines. Use outside of these guidelines may result in non-payment unless approved under an exception process.

Procedure:

Coverage of Zulresso (brexanolone) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Clinical trials evaluating the efficacy and safety of Zulresso in the treatment of postpartum depression have demonstrated significant improvement in depressive symptoms compared to placebo, as measured by standardized depression rating scales such as the Hamilton Rating Scale for Depression (HAM-D) and the Edinburgh Postnatal Depression Scale (EPDS). Zulresso acts as a positive allosteric modulator of gamma-aminobutyric acid (GABA) neurotransmission, which is thought to play a role in the pathophysiology of postpartum depression.

Initial Criteria:

Authorization of 1 (one) infusion may be granted for treatment of moderate to severe postpartum depression in members 15 years of age or older when all of the following criteria are met:

A. The requested medication must be prescribed by or in consultation with a psychiatrist.
B. Member has moderate to severe postpartum depression with documentation of diagnosis provided.
C. Member has had a major depressive episode that began no earlier than the third trimester of pregnancy and no later than the first 4 weeks following delivery, documented by standardized rating scales that reliably measure depressive symptoms (e.g., Beck Depression Scale [BDI], Hamilton Depression Rating Scale [HDRS], Montgomery-Asberg Depression Rating Scale [MADRS], etc.)
D. Member is 6 months postpartum or less.
E. Member is not currently pregnant.
F. Lactation has ceased or breastmilk produced will not be used for feedings during the infusion and up to 4 days following infusion completion.
G. Member will not receive more than one infusion per pregnancy/childbirth

H. Member will not use in combination with Zurzuvae and has not received prior treatment with Zurzuvae after the most recent pregnancy.
I. Member has experienced an inadequate treatment response from a 4-week trial of a formulary oral selective serotonin reuptake inhibitor (SSRI) or serotonin-norepinephrine reuptake inhibitor (SNRI) for PPD, if appropriate, with documentation provided.
J. The requested drug will be used in combination with, or a recommendation will be given for psychotherapy, if appropriate.
K. The provider and/or the provider's healthcare setting is certified in the Zulresso REMS program, with ability to support onsite continuous monitoring
L. Authorizations will only be granted if Zulresso is provided at a Neighborhood Health Plan of Rhode Island authorized and approved facility for Zulresso administration.
M. MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements.
N. Dose does not exceed the following:
    a. 0 to 4 hours: Initiate with a dosage of 30 mcg/kg/hour
    b. 4 to 24 hours: Increase dosage to 60 mcg/kg/hour
    c. 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)
    d. 52 to 56 hours: Decrease dosage to 60 mcg/kg/hour
    e. 56 to 60 hours: Decrease dosage to 30 mcg/kg/hour

Approval Duration: Approve to 6 months post delivery date with a limit on the dosage (Approval is for a single 60 hour infusion)

Per §§ 42 CFR 422.101, this clinical medical policy only applies to INTEGRITY in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Zulresso was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Zulresso according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT codes are:

HCPCS/CPT Code	Description
J1632	Injection, brexanolone, 1mg

References:

1. Zulresso [package insert]. Cambridge, MA: Sage Therapeutics, Inc.; June 2022.