PROVIDER POLICIES & PROCEDURES

ZULRESSO™ (BREXANOLONE)

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for Zulresso (brexanolone) therapy. By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Zulresso (brexanolone, allopregnanolone) is a neuroactive steroid related to progesterone with activity on the gamma-aminobutyric acid (GABA) receptor where it functions as a positive modulator. Zulresso is indicated for the treatment of postpartum depression (an episode of major depression starting in the third trimester of pregnancy or within 4 weeks after delivery) in individuals 15 years of age and older.

Zulresso is only available through a restricted program under a Risk Evaluation and Mitigation Strategy called the Zulresso REMS. The REMS requires that the drug be dispensed by a certified pharmacy and administered by a health care provider in a certified health care facility that provides inpatient monitoring while Zulresso is administered. Zulresso is administered as a continuous IV infusion and requires a 60-hour inpatient admission.

CLINICAL GUIDELINE

Coverage guidelines for Zulresso are made in accordance with the Department of Social Services (DSS) definition of Medical Necessity. The following criteria are guidelines *only*. Coverage determinations are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail.

Zulresso may be considered medically necessary in the treatment of postpartum depression (PPD) when the following criteria are met:

A. The individual is 15 years of age or older; **AND**
B. The individual has been diagnosed with moderate to severe PPD, and has had a major depressive episode with onset no earlier than the third trimester, and no later than 4 weeks after delivery; **AND**
C. No history of active psychosis, schizophrenia, bipolar disorder, or schizoaffective disorder; no suicide attempt during the current episode of postpartum depression; no history of alcohol or substance use disorder in the previous 12 months; no history of seizure disorder; **AN**D
D. Results from validated diagnostic tests for depression that reliably measure depressive symptoms such as the Hamilton Rating Scale for Depression, [HRSD], Patient Health Questionnaire [PHQ-9], and Montgomery-Asberg Depression Rating Scale [MADRS] have been provided and show moderate to severe depression. Results from screening tools such as the Edinburgh Depression Scale are not sufficient; **AND**
E. Diagnosis has been confirmed by a psychiatrist; **AND**
F. The individual is not currently pregnant; **AND**

G. Treatment is occurring in the postpartum period within six months of last delivery; **AND**
H. Lactation has ceased or breastmilk produced during the infusion and up to 4 days following infusion completion will not be used for feedings; **AND**
I. The individual does not have end stage renal disease (ESRD) with eGFR <15mL/min/1.73m^2; **AND**
J. All other medical and behavioral conditions have been addressed and deemed stable by the ordering provider; **AND**
K. Zulresso administration will follow the current FDA Zulresso labeling for dosing protocol; **AND**
L. The provider or provider's healthcare setting is certified in the Zulresso REMS program, with the ability to support ongoing monitoring; **AND**
M. A documented description of the benefits, risks and treatment expectations has been provided to the individual, which the individual has signed acknowledging receipt of this information (this documentation of the description of risks versus benefits may be requested prior to approval).

The use of more than one Zulresso infusion in the postpartum period following a pregnancy/childbirth is considered experimental and investigational because the safety and efficacy have not been established in the peer-reviewed published literature.

The use of Zulresso for all other indications is considered experimental and investigational as the safety and efficacy have not been established in the peer-reviewed published literature.

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of Zulresso is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for Zulresso:
1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program Zulresso Prior Authorization Request form (to include physician's order and signature);
2. Clinical information supporting the medical necessity of the treatment as outlined above;
3. Documentation of the provider's compliance with the Zulresso REMS requirements, as well as documentation of a full discussion of the benefits, risks and treatment expectations signed by the individual may be requested; and
4. Other information as requested.

EFFECTIVE DATE
This Policy is effective for prior authorization requests for Zulresso for HUSKY Health Program individuals on or after November 1, 2019.

LIMITATIONS
N/A

CODE

Code	Description
J1632	Injection, brexanolone, 1 mg

DEFINITIONS

1. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
2. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

RESOURCES AND REFERENCES:

1. Kanes SJ, Colquhoun H, Gunduz-Bruce H, et al. Brexanolone (SAGE-547 injection) in post-partum depression: A randomised controlled trial. Lancet. 2017b;390(10093):480-489.
2. Kanes SJ, Colquhoun H, Doherty J, et al. Open-label, proof-of-concept study of brexanolone in the treatment of severe postpartum depression. Hum Psychopharmacol. 2017a;32(2):e2576.
3. Meltzer-Brody S, Colquhoun H, Riesenberg, 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. Sage Therapeutics. (2022, August 11). A study to assess the safety of Brexanolone in the treatment of adolescent female participants with postpartum depression (PPD) - full text view. ClinicalTrials.gov. https://classic.clinicaltrials.gov/ct2/show/study/NCT03665038. Accessed on August 2, 2023
5. U.S. Food and Drug Administration (FDA). FDA approves first treatment for post-partum depression. FDA News Release. Silver Spring, MD: FDA; March 19, 2019.
6. US Food and Drug Administration: NDA 211371/S-007. Supplement approval/ Fulfillment of postmarketing requirement. Accessed July 26, 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2022/211371Orig1s007ltr.pdf

7. Zulresso Full Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc.; Revised June 2022. Available at: https://assets.sagerx.com/zulresso/prescribing-information.pdf

PUBLICATION HISTORY

Date		Action Taken
Original Publication		Approved at the June 26, 2019 CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on September 16, 2019. Approved by DSS on September 23, 2019.
Updated	August 2020	Updated introduction section to further describe chemical makeup of Zulresso as well as further defining postpartum depression. Updated Policy section to more closely align with inclusion and exclusion criteria of clinical study and FDA recommendations. Approved at the August 12, 2020 Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on September 21, 2020. Approved by DSS on October 7, 2020.
Update	September 2021	Changed “drug abuse” to “substance use disorder’ Added requirement that facility administering Zulresso must be certified in the Zulresso REMS program with ability to support ongoing monitoring. Changes approved at the August 11, 2021 CHNCT Medical Reviewer meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on September 20, 2021. Changes approved by DSS on September 30, 2021.
Update	September 2022	Update to criteria section. Added “moderate to severe” post-partum depression and quantified eGFR for ESRD. Changes approved at the August 10, 2022 CHNCT Medical Reviewer Meeting. Changes approved by the CHNCT Clinical Quality Subcommittee on September 19, 2022. Approved by DSS on September 28, 2022.
Update	September 2023	Updated age requirement to “15 years or older” as per the updated FDA indication. Clarified some verbiage and added additional references. Changes approved at the August 9, 2023, CHNCT Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on September 18, 2023. Approved by DSS on October 2, 2023.