Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines

Medical Benefit Drugs

Zulresso (brexanolone)

Effective: June 9, 2026

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	Yes ☒ No ☐

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax 617-673-0988

☒ Tufts Health Plan Commercial products; Fax 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax 617-673-0988

☐ Tufts Health Together – MassHealth Accountable Care Partnership Plans; Fax 617-673-0939

☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax 617-673-0939

☐ Tufts Health One Care* – A Medicare-Medicaid Plan (a dual eligible product); Fax 617-673-0956

*The MNG applies to Tufts Health One Care members unless a less restrictive LCD or NCD exists.

Senior Products

☐ Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product); Fax 617-673-0956

☐ Tufts Medicare Preferred HMO, (a Medicare Advantage product); Fax 617-673-0956

☐ Tufts Medicare Preferred PPO, (a Medicare Advantage product); Fax 617-673-0956

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Food and Drug Administration (FDA) Approved Indications:

Zulresso (brexanolone) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator indicated for the treatment of postpartum depression in patients 15 years and older.

Effective April 14, 2025, the FDA withdrew approval of Zulresso (brexanolone) solution. Per FDA notice, any Zulresso (brexanolone) solution, 100 mg/20 mL, that is in inventory on April 14, 2025 may continue to be dispensed until the inventories have been depleted or the drug products have reached their expiration dates or otherwise become violative, whichever occurs first.

Clinical Guideline Coverage Criteria

The Plan may authorize coverage of Zulresso when **ALL** of the following criteria are met:

1. The medication is being administered at an acute inpatient or psychiatric hospital

AND

2. Documentation of moderate to severe postpartum depression (PPD)

AND

3. Documentation that patient is postpartum for 6 months or less at the time of request

AND

4. Onset of depressive episode is between 3rd trimester and 4 weeks following delivery, that has been documented by standardized rating scales such as the Beck Depression Scale (BDI), Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS), Quick Inventory of Depressive Symptomatology (QIDS, also known as QIDS-SR-16), or the Diagnostic and Statistical Manual of Mental Disorders (DSM 5) criteria.

AND

5. The prescriber is a mental health specialist (e.g., psychiatrist, nurse practitioner with a specialty in behavioral health)

AND

6. Documentation that the patient has not responded adequately to a trial of an oral antidepressant, or clinical rationale that trial of an oral antidepressant is not appropriate due to severity of depression (clinical documentation required)

Limitations

- Approval is limited to one single 60-hour infusion per postpartum period. Approval will not be authorized in patients who have previously received Zulresso (brexanolone) or Zurzuvae (zuranolone) for the current postpartum depressive episode from the most recent pregnancy.
- Samples, free goods, or similar offerings of the requested medication do not qualify for an established clinical response or exception but will be considered on an individual basis for prior authorization.

Codes

The following code(s) require prior authorization:

Table 1: Codes

Codes	Description
J1632	INJECTION BREXANOLONE 1 MG

References:

1. Amick HR, Gartlehner G, Gaynes BN et al. Comparative benefits and harms of second-generation antidepressants and cognitive behavioral therapies in initial treatment of major depressive disorder: systematic review and meta-analysis. BMJ. 2015; 351:h6019.
2. Brexanolone (Zulresso) for Postpartum Depression. Accessed online March 1, 2022 at https://jamanetwork.com/journals/jama/article-abstract/2737169#:~:text=JAMA.%202019%3B322(1)%3A73%2D74.%20doi%3A10.1001/jama.2019.6622
3. Food and Drug Administration. FDA approves first treatment for post-partum depression. 2019d March. URL: /NewsEvents/Newsroom/PressAnnouncements/ucm633919.htm. Available from Internet. Accessed 2019 April 1.
4. Gartlehner G, Gaynes BN, Amick HR et al. Comparative benefits and harms of antidepressant, psychological, complementary, and exercise treatments for major depression: an evidence report for a clinical practice guideline from the American College of Physicians. Ann Intern Med. 2016; 164(5):331-41.
5. Gautam S, Jain A, Gautam M et al. Clinical practice guidelines for the management of depression. Indian J Psychiatry. 2017; 59(Suppl 1):S34-S50.
6. 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):1058-70.
7. Molyneaux E, Telesia LA, Henshaw C et al. Antidepressants for preventing postnatal depression. Cochrane Database Syst Rev. 2018; 4:CD004363.
8. Stewart D, Vigod S. Postpartum depression. N Engl J Med. 2016; 375:2177-86.
9. Zulresso prescribing information. Cambridge, MA: Sage Therapeutics; June 2022.
10. Food and Drug Administration, HHS. Sage Therapeutics, Inc.; Withdrawal of Approval of a New Drug Application for ZULRESSO (Brexanolone) Solution, 100 Milligrams/20 Milliliters. 90 FR 12162. Published 3/14/25.

Approval And Revision History

May 17, 2023: Reviewed by the Medical Policy Approval Committee (MPAC)

June 13, 2023: Reviewed by Pharmacy and Therapeutics Committee (P&T)

Subsequent endorsement date(s) and changes made:

- Originally approved September 13, 2022 by P&T and September 21, 2022 by MPAC committees effective January 1, 2023
- Administrative update: April 2023 added Medical Benefit Drugs to title, updated MATogether and RITogether fax numbers to 617-673-0939
- May 17, 2023: Annual review, no change, effective July 1, 2023
- June 11, 2024: Updated criterion for documentation that the patient has not responded adequately to a trial of an oral antidepressant, or clinical rationale that trial of an oral antidepressant is not appropriate due to severity of depression (clinical documentation required). Added the Limitation that approval will not be authorized in patients who have previously received Zulresso (brexanolone) or Zurzuvae (zuranolone) for the current postpartum depressive episode from the most recent pregnancy. Removed the Limitation the Plan does not cover Zulresso for any indications other than those listed on this Medical Necessity Guideline. Minor wording edits (effective September 1, 2024).
- May 2024: Administrative Updates: Rebranded from Tufts Health Unify to Tufts Health One Care for 2024
- June 10, 2025: Updated overview to indicate that FDA withdrew approval of Zulresso effective April 14, 2025. Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template. (eff 6/10/25).

- June 9, 2026: Administrative updates: Template updated to remove CareLink from the Medical Necessity Guideline template. Template updated from “Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans” to “Tufts Health Together- MassHealth Accountable Care Partnership Plans.” (eff 6/9/26).

Background, Product and Disclaimer Information

Medical Necessity Guidelines are developed to determine coverage for benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member’s benefit document, and in coordination with the Member’s physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern. For Tufts Health Together (Medicaid), coverage may be available beyond these guidelines for pediatric members under age 21 under the Early and Periodic Screening, Diagnostic and Treatment (EPSDT) benefits of the plan in accordance with 130 CMR 450.140 and 130 CMR 447.000, and with prior authorization.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.