Harvard Pilgrim Health Care | TUFTS Health Plan

Medical Necessity Guidelines

Medical Benefit Drugs

Zulresso® (brexanolone) Injection

Effective: January 1, 2026

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Public Plans Products

☒ 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

Post partum depression (PPD) is the most common postnatal psychiatric complication with recent prevalence estimates in the United States ranging between 9% and 12% (about 400,000 cases per year). PPD has a significant impact on maternal-infant interactions (e.g. feelings of disengagement, hostility, intrusion), family relationships, and occupational and social functioning. Despite the potential consequences of untreated PPD, fewer than half of PPD cases are diagnosed in clinical practice. For this reason, there has been a more intense focus on screening and prevention with a recent updated recommendation statement from the US Preventive Services Task Force (Interventions to Prevent Perinatal Depression).

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

Zulresso is a one-time treatment administered by continuous intravenous infusion over 60 hours (2.5 days). Administration of Zulresso is complex. Due to limited stability of the product (12 hours at room temperature), a minimum of 5 infusion bag changes are required. Recommended dosing also requires several infusion rate changes.

Zulresso was studied in 2 multicenter, randomized, double-blind, placebo-controlled studies in women aged 18 to 45 years with PPD who were <6 months postpartum at screening and met the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for a major depressive episode with onset of symptoms in the third trimester or within 4 weeks of delivery. Zulresso treated patients experienced rapid improvement of depressive symptoms vs placebo measured as change from baseline in HAM-D total score over time. At hour 60, a 62.3% reduction for patients on Zulresso vs a 49% reduction on placebo (p=0.0252).

Zulresso is available only through a restricted program under a REMS program because excessive sedation or sudden loss of consciousness can result in serious harm.

Food and Drug Administration (FDA) Approved Indications:

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

The FDA requires that Zulresso be managed under a Risk Evaluation and Mitigation Strategy (REMS) program. The REMS is required by the U.S. Food and Drug Administration (FDA) to ensure the potential benefits of ZULRESSO outweigh its risks.

Clinical Guideline Coverage Criteria

The plan may authorize coverage of Zulresso when all the following clinical criteria is met:

1. Documented diagnosis of postpartum depression

Limitations

- Approval is limited to one single 60-hour infusion per postpartum period.
- Any indications other than FDA-approved indications are considered experimental or investigational and will not be approved by the Plan

Codes

The following code(s) require prior authorization:

Table 1: HCPCS Codes

HCPCS Codes	Description
J1632	Injection, brexanolone, 1 mg

References:

1. Zulresso (brexanolone). Cambridge, MA: Sage Therapeutics, Inc.; June 2022.
2. 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.

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.
- August 2023: Administrative update to rebrand Tufts Health Unify to Tufts Health One Care for 2024.
- November 2023: Administrative Update in support of calendar year 2024 Medicare Advantage and PDP Final Rule.
- November 12, 2024: Minor wording updates. Removed “The Member will be receiving their Zulresso infusion at a REMS certified health care facility” (eff 1/1/25).
- December 2024: Joint Medical Policy and Health Care Services UM Committee review (eff 1/1/25).
- July 2025: Administrative update to remove Harvard Pilgrim Health Care Stride Medicare Advantage from the Medical Necessity Guideline template.
- December 9, 2025: No changes (eff 1/1/26)
- December 2025: Joint Medical Policy and Health Care Services UM Committee review (effective 1/1/26)

Background, Product and Disclaimer Information

Point32Health prior authorization criteria to be applied to Medicare Advantage plan members is based on guidance from Medicare laws, National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). When no guidance is provided, Point32Health uses clinical practice guidance published by relevant medical societies, relevant medical literature, Food and Drug Administration (FDA)-approved package labeling, and drug compendia to develop prior authorization criteria to apply to Medicare Advantage plan members. Medications that require prior authorization generally meet one or more of the following criteria: Drug product has the potential to be used for cosmetic purposes; drug product is not considered as first-line treatment by medically accepted practice guidelines, evidence to support the safety and efficacy of a drug product is poor, or drug product has the potential to be used for indications outside of the indications approved by the FDA. Prior authorization and use of the coverage criteria within this Medical Necessity Guideline will ensure drug therapy is medically necessary, clinically appropriate, and aligns with evidence-based guidelines. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests revisions.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guidelines 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.