Brexanolone Injection for Postpartum Depression

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Q: What is brexanolone injection?

A: Brexanolone is a novel, rapid-acting antidepressant, and is the first medication specifically indicated for the treatment of postpartum depression (PPD). Brexanolone injection was approved by the U.S. Food and Drug Administration (FDA) in early 2019 under the brand name Zulresso for the treatment of PPD in adults. Administration is done intravenously over the course of 60 hours (2.5 days) and requires an on-site healthcare provider to monitor the patient during the infusion.

Q: What is the potential mechanism of action underlying brexanolone?

A: Brexanolone is a y-Aminobutric acid (GABA-A) receptor modulator and is chemically identical to the progesterone metabolite allopregnalone, an endogenous neurosteroid. During pregnancy, allopregnalone levels rise, peaking in the third trimester. Postpartum, levels of allopregnalone decrease rapidly, and this rapid decline in hormones results in downregulation of GABA-A receptors, which is thought to be related to the development of PPD in some women (Osborne et al., 2017). The exact mechanism of action of brexanolone as a treatment for PPD is not fully understood, but it is proposed to occur by "resetting" dysregulated brain function via modulation of GABA-A receptor activity (Sage Therapeutics, 2018).

Q: Is brexanolone recommended as a treatment for PPD in the Military Health System (MHS)?

A: No. The 2022 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder does not have a recommendation for the use of brexanolone in postpartum depression, despite FDA approval.

The MHS relies on the VA/DOD clinical practice guidelines (CPGs) to inform best clinical practices. The CPGs are developed under the purview of clinical experts and are derived through a transparent and systematic approach that includes, but is not limited to, systematic reviews of the literature on a given topic and development of recommendations using a graded system that takes into account the overall quality of the evidence and the magnitude of the net benefit of the recommendation. Recommendations for or against a treatment may be characterized as strong or weak based on a variety of factors (e.g., confidence in the quality of the evidence, weight of treatment benefits versus risks, feasibility). The CPGs also state if there is insufficient evidence to develop a recommendation. A further description of this process and CPGs on specific topics can be found on the VA clinical practice guidelines website.

Q: Do other authoritative reviews recommend brexanolone as a treatment for PPD?

A: No. Other authoritative reviews have not substantiated the use of brexanolone for PPD.

Other recognized organizations conduct systematic reviews and evidence syntheses on psychological health topics using grading systems similar to the VA/DOD CPGs. Notable among these is Cochrane, an international network that conducts high-quality reviews of healthcare interventions.

- Cochrane: No systematic reviews of brexanolone for PPD were identified.

Q: What conclusions can be drawn about the use of brexanolone as a treatment for PPD in the MHS?

A: The 2022 VA/DoD Clinical Practice Guideline for the Management of Major Depressive Disorder does not include brexanolone as a treatment PPD. There is an FDA Black Box Warning for Zulresso for excessive sedation and sudden loss of consciousness. As a result, healthcare facilities must enroll in the FDA's REMS (Risk Evaluation and Management Strategy) for Zulresso, which requires monitoring by a healthcare professional every two hours during the infusion, treatment initiation early in the day to avoid excessive sedation, and pulse oximetry monitoring (Sage Therapeutics, 2019). More research is needed to assess the comparative effectiveness of brexanolone against the current standard of care, the long-term efficacy and safety, and the optimal delivery and treatment combination.

References

Brexanolone (Zulresso) for postpartum depression. (2019). JAMA, 322(1), 73–74.

Department of Veterans Affairs/Department of Defense. (2016). VA/DoD clinical practice guideline for management of major depressive disorder. Version 3.0. Washington (DC): Department of Veterans Affairs/Department of Defense.

Osborne, L. M., Gispen, F., Sanyal, A., Yenokyan, G., Meilman, S., & Payne, J. L. (2017). Lower allopregnalone during pregnancy predicts postpartum depression: An exploratory study. Psychoneuroendocrinology, 79, 116–121.

Sage Therapeutics. (2018). Brexanolone injection, for intravenous use (Brexanolone injection, IV sponsor briefing document). Joint Meeting of the Psychopharmacologic Drug Advisory Committee and Drug Safety and Risk Management Advisory Committee. Retrieved from https://www.fda.gov/media/121348/download

Sage Therapeutics. (March 2019). Zulresso. Retrieved from https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/211371lbl.pdf