

ABSTRACT

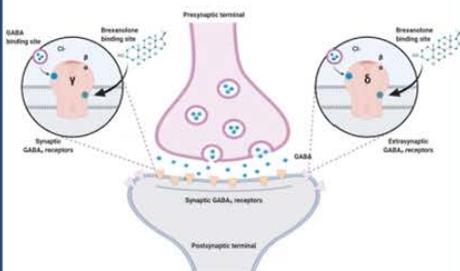
Brexanolone (ZULRESSO™) is a novel approach to treat postpartum depression in adult women as a neuroactive steroid similar in chemical composition to the hormone allopregnanolone. It was approved for use in adult women suffering from postpartum depression by the FDA in March 2019, with emphasis on its potential use in patients who are unresponsive to mainstay interventions. Brexanolone is the only drug currently on the market approved to treat PPD, use of Brexanolone requires patients to be enrolled in the REMS (Risk Evaluation and Mitigation Strategies) ZULRESSO™ program necessitating a 60-hour period of intravenous administration and close monitoring. The pharmacogenomics of this drug have yet to be studied but could potentially aide in determining if Brexanolone administration is an appropriate therapy for a patient. Additional clinical studies with larger sample sizes are necessary in order to evaluate the use of Brexanolone in women with PPD.

Brexanolone: A Review of the Novel Drug Injection for Postpartum Depression

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PHARMACOLOGY



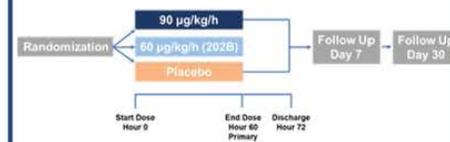
Brexanolone enhances phasic and tonic inhibition in the brain through the positive allosteric modulation of synaptic (left) and extrasynaptic (right) GABA_A receptors.

Table 1. Pharmacokinetic Properties for Brexanolone

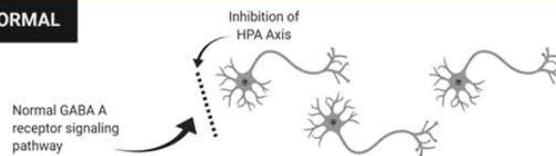
C_{max}	82 ng/mL (90 dose regimen) 54.84 ng/mL (60 dose regimen)
AUC	3980 ng*hr/mL (90 dose regimen) 2867 ng*hr/mL (60 dose regimen)
V_d	3 L/kg (based on a healthy individual)
Metabolism	Keto-reduction, glucuronidation, and sulfation
Half-Life	Biphasic with initial rapid decline half-life of 40 minutes followed by a later terminal half-life of 12 hours
Clearance	0.8 L/hr/kg independent of dose
Special Populations	No evidence showing PK-related differences based on age, ethnicity, BMI, or race
Excretion into Breastmilk	Considered low at < 10 ng/mL in 95% of women 36 hours after infusion was completed
Drug Interactions	No studies conducted to date, unlikely that co-administration of CYP inhibitors or inducers will affect Brexanolone exposure

CLINICAL TRIAL DATA

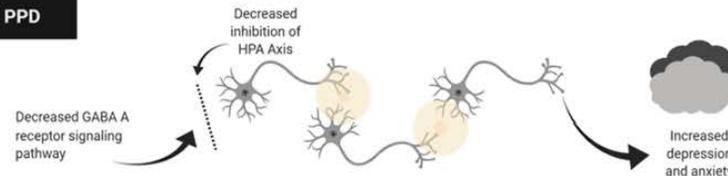
- Phase II study found a greater decrease in HAM-D score for women receiving Brexanolone infusion than the placebo group (Kanes, 2017). It was concluded that women with severe PPD had a significant reduction in their HAM-D score when treated with Brexanolone infusion (Meltzer-Brody et. al, 2018).
- Phase III study found a mean reduction in HAM-D score from baseline of 14.6 points in the BRX90 group and 12.1 points in the placebo group (Meltzer-Brody, et. al, 2018). It was concluded that Brexanolone infusions cause a significant reduction in HAM-D scores when compared to placebo, thus supporting its use in treating PPD (Meltzer-Brody et. al, 2018).



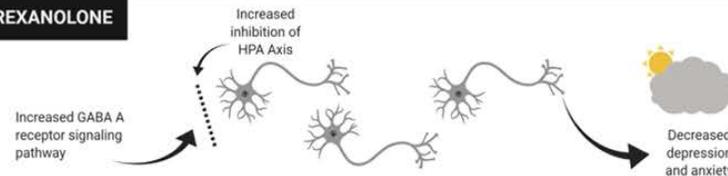
NORMAL



PPD



BREXANOLONE



CONCLUSION

The novel approach of Brexanolone has brought an approved therapy into a previously devoid space of postpartum depression in adult women.

KEY REFERENCES

- Frieder, A., Fersh, M., Hainline, R., & Deligiannis, K. M. (2019). Pharmacotherapy of Postpartum Depression: Current Approaches and Novel Drug Development. *CNS Drugs*, 32(3), 205–262. <https://doi.org/10.1007/s40263-019-00695-7>
- Jamnan, A. F., MacLellan, J. V., Sarson, R. J., Wightman, R. S., & McGregor, A. J. (2020). Brexanolone For Postpartum Depression: A Novel Approach and a Call for Comprehensive Postpartum Care. *Clinical Therapeutics*, 42(1), 231–235. <https://doi.org/10.1016/j.clinthera.2019.11.005>
- Kanes, S., Coquihoun, H., Gunduz-Bruce, H., Raines, S., Arnold, R., Schacterle, A., Doherty, J., Epperson, C. N., Deligiannis, K. M., Riesenberg, R., Hoffmann, E., Rubinow, D., Jonas, J., Paul, S., & Meltzer-Brody, S. (2017). Brexanolone (SAGE-547 injection) in post-partum depression: A randomized controlled trial. *The Lancet*, 391(10050), 460–469. [https://doi.org/10.1016/S0140-6736\(17\)3194-3](https://doi.org/10.1016/S0140-6736(17)3194-3)
- Leader, L. D., O'Connell, M., & VandenBerg, A. (2019). Brexanolone for Postpartum Depression: Clinical Evidence and Practical Considerations. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 39(11), 1105–1112. <https://doi.org/10.1002/phar.2331>
- Levien, T. L., & Baker, D. E. (2019). Formulary Drug Reviews: Brexanolone Injection. *Hospital Pharmacy*, 001857819887895. <https://doi.org/10.1177/001857819887895>
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