

# **ICD-10-PCS Code Proposal: ZULRESSO™ (brexanolone) CIV, injection for Postpartum Depression (PPD) in Adults**

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# PPD Is One of the Most Common Complications During and After Pregnancy<sup>1-3</sup>

- In the United States, CDC estimates new mothers diagnosed with PPD each year vary by state, ranging from **8%** to **20%** with an overall average of **11.5%**.<sup>12</sup>
- Timing of the onset of symptoms varies, <sup>13,14</sup> and symptoms may persist throughout the first postnatal year.<sup>8-10</sup>
- PPD has been associated with negative effects, including:

- Mother experiences breastfeeding complications<sup>4</sup>
- Disruption in sleep routines for the infant and mother<sup>4</sup>
- Impaired mother-infant bonding<sup>5</sup>

Mothers experience thoughts of self-harm or suicide<sup>6</sup>

- Negative parenting practices<sup>4,5</sup>
- Fathers may experience depression in the postnatal period, correlated with maternal PPD<sup>7</sup>
- Women with PPD have higher health services expenditures than non-PPD mothers<sup>11</sup>

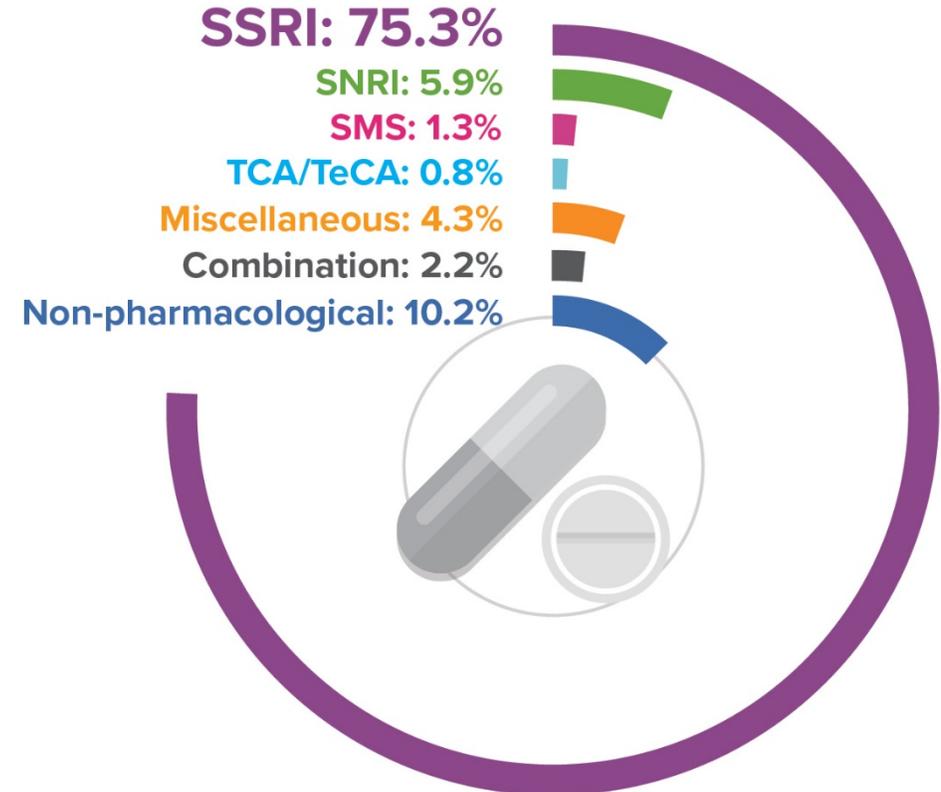
1. Ko JY et al. MMWR Morb Mortal Wkly Rep. 2017;66:153-158. 2. DeSisto CL et al. Prev Chronic Dis. 2014;11:E10. 3. Centers for Disease Control and Prevention. <https://www.cdc.gov/reproductivehealth/maternalinfanthealth/pregnancy-complications-data.htm>. Updated February 28, 2019. Accessed July 15, 2019. 4. Field T. *Infant Behav Dev*. 2010;33(1):1. 5. O'Hara MW et al. *Annu Rev Clin Psychol*. 2013;9:379-407. 6. Georgiopoulos AM et al. *Obstet Gynecol*. 1999;93(5):653-657. 7. Paulson JF et al. *JAMA*. 2010;303(19):1961-1969. 8. Vliegen N et al. *Harv Rev Psychiatry*. 2014;22(1):1-22. 9. Netsi E et al. *JAMA Psychiatry*. 2018;75(3):247-253. 10. Mayberry LJ et al. *J Obstet Gynecol Neonatal Nurs*. 2007;36(6):542-549. 11. Data on file, Analysis Group Report: December 12, 2017. 12. Ko JY et al. <https://www.cdc.gov/mmwr/volumes/66/wr/mm6606a1.htm>. Accessed February 12, 2018. 13. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: American Psychiatric Association; 2013. 14. Committee on Obstetric Practice. *Obstet Gynecol*. 2018;132(5):e208-e212

# Treatment Practices for PPD

Before ZULRESSO, treatment recommendations for PPD depended on the severity of the patient's symptoms<sup>2,3,4</sup>

- Mild-Moderate patients were treated with non-pharmacological therapies (interpersonal psychotherapy, cognitive behavioral therapy)
- Moderate-Severe patients were treated with pharmacological treatment such as antidepressants or antidepressant plus psychotherapy

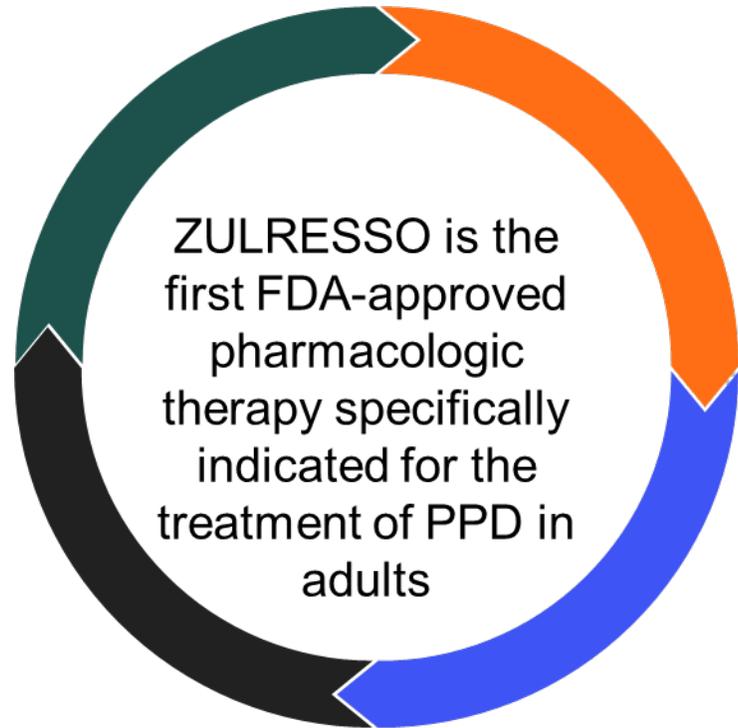
## Therapies Used for PPD<sup>1\*</sup>:



# Through Market Research, Patients have Identified Potential Challenges with the Current Standard of Care<sup>1</sup>

- Long wait times for an appointment/difficulties scheduling follow-up appointment
- Insurance coverage
- Delays in treatment or interruption in treatment
- Multiple dose changes, changes in medications, or doses not changing at all to meet patient needs
- Length of treatment plan is longer than expected

# ZULRESSO Overview<sup>1</sup>



**ZULRESSO** contains brexanolone, a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator and schedule IV controlled substance that is chemically identical to endogenous allopregnanolone.

**ZULRESSO** injection is supplied as 100 mg brexanolone in 20 ml (5 mg/ml) single-dose vials containing a sterile, preservative-free, clear, colorless solution.

**ZULRESSO** is administered as a continuous intravenous (IV) infusion over a total of 60 hours requiring titration.

**ZULRESSO** is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (**ZULRESSO** REMS) because excessive sedation and sudden loss of consciousness can result in serious harm.

# Summary of 3 Studies of ZULRESSO in PPD\*

Table 1. Summary of ZULRESSO studies

	547-PPD-202A <sup>1</sup>	Study 1: 547-PPD-202B <sup>2,3</sup>	Study 2: 547-PPD-202C <sup>2,3</sup>
<b>Type</b>	Phase 2, randomized, placebo-controlled study	Phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled study	Phase 3, multicenter, randomized, double-blind, parallel-group, placebo-controlled study
<b>Dosing and Randomization</b>	Placebo-controlled, 2 treatment arms: <ul style="list-style-type: none"> <li>• ZULRESSO: 90 µg/kg/hr (n=10)</li> <li>• Placebo (n=11)</li> </ul>	Placebo-controlled, 3 treatment arms: <ul style="list-style-type: none"> <li>• ZULRESSO: 60 µg/kg/hr (n=38)</li> <li>• ZULRESSO: 90 µg/kg/hr (n=41)</li> <li>• Placebo (n=43)</li> </ul>	Placebo-controlled, 2 treatment arms: <ul style="list-style-type: none"> <li>• ZULRESSO: 90 µg/kg/hr (n=51)</li> <li>• Placebo (n=53)</li> </ul>
<b>PPD Severity</b>	Severe: HAM-D ≥26	Severe: HAM-D ≥26	Moderate: 20 ≤ HAM-D ≤25
<b>Follow-up Duration</b>	30 days	30 days	30 days
<b>Number of Patients</b>	21	122	104
<b>Primary Endpoint</b>	<b>Change From Baseline in the 17-Item Hamilton Rating Scale for Depression (HAM-D) Total Score at Hour 60</b>	<b>Change From Baseline in the 17-Item Hamilton Rating Scale for Depression (HAM-D) Total Score at Hour 60</b>	<b>Change From Baseline in the 17-Item Hamilton Rating Scale for Depression (HAM-D) Total Score at Hour 60</b>
<b>LS Mean CFB (SE)</b>	<ul style="list-style-type: none"> <li>• ZULRESSO: (90 µg/kg/hr): -21.0 (2.9)</li> <li>• Placebo: -8.8 (2.8)</li> </ul>	<ul style="list-style-type: none"> <li>• ZULRESSO (60 µg/kg/hr): -19.5 (1.2)</li> <li>• ZULRESSO (90 µg/kg/hr): -17.7 (1.2)</li> <li>• Placebo: -14.0 (1.1)</li> </ul>	<ul style="list-style-type: none"> <li>• ZULRESSO (90 µg/kg/hr): -14.6 (0.8)</li> <li>• Placebo: -12.1 (0.8)</li> </ul>
<b>P value**</b>	0.008	0.0013 (60 µg/kg/hr) 0.0252 (90 µg/kg/hr)	0.0160
<b>Most Common Adverse Reactions</b>	(≥ 5% and at least twice rate of placebo) sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush	(≥ 5% and at least twice rate of placebo) sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush	(≥ 5% and at least twice rate of placebo) sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush

CFB=change from baseline; HAM-D=Hamilton Rating Scale for Depression; LS=least squares; SE=standard error.



1. Kanes S et al. *Lancet*. 2017;390(10093):480-489. 2. ZULRESSO™ (brexanolone) injection Prescribing Information. Cambridge, MA: Sage Therapeutics, Inc; 2019. 3. Meltzer-Brody et al. *Lancet*. 2018;392(10152):1058-1070.

\* Safety data was pooled from the 3 placebo-controlled PPD trials (202A, 202B, 202C total N=140), whereas the efficacy information is only inclusive of patients in the 2 pivotal trials: 202B and 202C.

\*\*Statistically significant after multiplicity adjustments

## Administration of ZULRESSO involves a Multidisciplinary Approach to Treatment

- Given the important considerations that may be applicable to administering ZULRESSO to adult women with PPD, a multidisciplinary stakeholder approach may be necessary for the site of care
- Since the inception of the ZULRESSO REMS program, we have seen a number of sites complete the enrollment process: 59% Hospital (even split between usage in the inpatient and outpatient setting) and 41% Non-Hospital sites

### REMS

- Certified healthcare setting
- Monitoring for the duration of the infusion
- Implement the processes and procedures necessary to comply with REMS requirements

### PHARMACY AND INFUSION SERVICES

- The ability to procure and prepare ZULRESSO
- Meet the requirements to properly store and handle ZULRESSO

### APPROPRIATE SITE(S) OF CARE

- Identifying an appropriate setting for patients with PPD receiving a 60+ hour infusion

# Rationale for New ICD-10-PCS Code for ZULRESSO Administration

- There are currently no ICD-10-PCS codes that uniquely describe ZULRESSO administration or supervision associated with its administration.
- A unique ICD-10-PCS code is needed to identify ZULRESSO in order to identify ZULRESSO cases in claims data.
- A unique code will also allow for the identification, tracking and capturing of outcomes data for ZULRESSO.

# Questions?



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