For US healthcare professionals only

Zulresso®
(brexanolone) injection IV
for intravenous use 100mg/20mL

Starting your patient on the ZULRESSO® treatment journey

What to expect: a guide for you and your patient

This guide provides an overview of your role and some of your responsibilities, along with helpful information you can share with your patient about ZULRESSO.

The ZULRESSO REMS program requirements

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

Notable requirements of the ZULRESSO REMS include:

- Healthcare facilities must enroll in the program and ensure that ZULRESSO is only administered to patients who are enrolled in the ZULRESSO REMS
- Pharmacies must be certified with the program and must only dispense ZULRESSO to healthcare facilities who are certified in the ZULRESSO REMS
- **Patients must be enrolled in the ZULRESSO REMS prior to administration of ZULRESSO**
- Wholesalers and distributors must be registered with the program and must only distribute to certified healthcare facilities and pharmacies

Be sure to counsel your patients using the Patient Information Guide, which can be found at ZulressoREMS.com, and ensure they are enrolled in the ZULRESSO REMS prior to infusion. Further information, including a list of certified healthcare facilities, is available at ZulressoREMS.com or by calling 1-844-472-4379. Healthcare settings, also known as Treating Centers, included in the locator tool have completed the requirements to enroll and certify in the ZULRESSO REMS; however, not all healthcare settings listed are accepting new patients. Please call the healthcare setting to confirm.

INDICATION

ZULRESSO® is indicated for the treatment of postpartum depression (PPD) in patients 15 years and older

ZULRESSO IMPORTANT SAFETY INFORMATION

WARNING: EXCESSIVE SEDATION AND SUDDEN LOSS OF CONSCIOUSNESS

Patients treated with ZULRESSO are at risk of excessive sedation or sudden loss of consciousness during administration.

Because of the risk of serious harm, patients must be monitored for excessive sedation and sudden loss of consciousness and have continuous pulse oximetry monitoring. Patients must be accompanied during interactions with their child(ren).

Because of these risks, ZULRESSO is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ZULRESSO REMS.

Please see additional Important Safety Information throughout and click for full Prescribing Information, including Boxed Warning.

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Putting your patient on the path to treatment

STEP 1

PRESCRIBING PHYSICIAN
(Affiliated with REMS-certified Healthcare Setting (HCS))

- If you are the **PRESCRIBING PHYSICIAN**, then you are responsible for completing the required REMS forms to enroll your patient into ZULRESSO REMS
- You can find the required ZULRESSO REMS forms on ZulressoREMS.com
- A prior authorization (PA) is often required. As the **PRESCRIBING PHYSICIAN**, you may be responsible for submitting the PA and/or the patient documentation needed to complete the PA

REFERRING PROVIDER
(Not affiliated with REMS-certified Healthcare Setting (HCS))

- If you are the **REFERRING PROVIDER**, then you are responsible for providing any required patient documentation to the HCS where your patient will be treated with ZULRESSO
- A prior authorization (PA) is often required. As the **REFERRING PROVIDER**, you may be responsible for submitting the PA and/or the patient documentation needed to complete the PA. If the HCS selected uses a specialty pharmacy, additional documentation may be required
- You can use the Locator Tool for Treating Centers on ZulressoHCP.com to find HCSs currently accepting patients

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OPTIONAL STEP – ENROLLING INTO SAGE CENTRAL

If you choose to enroll your patient into Sage Central Patient Support, you and your patient must complete and submit the Sage Central Enrollment form. You will be notified when the form is received. You can find the Sage Central Enrollment Form at ZulressoHCP.com and SageCentralSupport.com.

Sage Central provides patient support services during the treatment journey, including:

- Welcome call with you and your patient
- Evaluation of patient's financial assistance eligibility
- Treatment scheduling updates and timelines

2 If a PA is required and completed, the HCS will work with the patient to schedule the infusion.

3 Once the REMs paperwork is completed, your patient will be enrolled into ZULRESSO REMS and can begin treatment.

IF ENROLLED INTO SAGE CENTRAL: Sage Central will follow up once your patient has completed treatment with ZULRESSO.

WARNINGS AND PRECAUTIONS

Excessive Sedation and Sudden Loss of Consciousness
In clinical studies in adults, 5% of ZULRESSO-treated patients compared to 0% of placebo-treated patients experienced sedation and somnolence that required dose interruption or reduction during the infusion. Loss of consciousness or altered state of consciousness was reported in 4% of ZULRESSO-treated patients compared with 0% of placebo-treated during the infusion.

In an open-label clinical study in 20 patients ages 15 to 17 years, one patient experienced dizziness and loss of consciousness

During the infusion, monitor patients for sedative effects every 2 hours during planned, non-sleep periods. Immediately stop the infusion if there are signs or symptoms of excessive sedation. After symptoms resolve, the infusion may be resumed at the same or lower dose as clinically appropriate. Immediately stop the infusion if pulse oximetry reveals hypoxia. After hypoxia, the infusion should not be resumed.

Concomitant use of opioids, antidepressants, or other CNS depressants such as benzodiazepines or alcohol may increase the likelihood or severity of adverse reactions related to sedation. Patients must be accompanied during interactions with their child(ren) while receiving the infusion because of the potential for excessive sedation and sudden loss of consciousness.

Patients should be cautioned against engaging in potentially hazardous activities requiring mental alertness, such as driving, after infusion until any sedative effects of ZULRESSO have dissipated.

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Preparing your patient for ZULRESSO treatment

Share this information with your patient to help set expectations for their ZULRESSO treatment journey.

Treatment initiation and duration

ZULRESSO is administered as a continuous intravenous infusion into the arm over 60 hours (2.5 days). Patients can only be treated in a ZULRESSO REMS-certified healthcare setting. Timing to treatment may vary by healthcare setting.

Review Important Safety Information described in this brochure with your patient

Inform your patient of serious side effects including the risk of excessive sedation or sudden loss of consciousness and the increased risk of suicidal thoughts or actions. Patients should be cautioned against engaging in potentially hazardous activities requiring mental alertness, such as driving, after infusion until any sedative effects of ZULRESSO have dissipated. The most common side effects of ZULRESSO include sleepiness, dry mouth, passing out, and flushing of the skin or face.

Childcare during treatment

While each REMS-certified Healthcare Setting may have different rules, your patient typically will be able to receive visits from their family and baby. Your patient needs to arrange full-time childcare for the duration of treatment. While receiving the infusion, patients must be accompanied during interactions with their child(ren) because of the potential for excessive sedation and sudden loss of consciousness.

Connect your patients to the Sage Central® Patient Support program

Sage Central is a support program that offers a range of resources to support patients and their families. Once enrolled, your patients will have a dedicated team of case managers—known as Sage Central Navigators—who can provide information to help them no matter where they are on the path to treatment.

Enroll your patient in the Sage Central program to provide them with support throughout their PPD treatment journey. Once you have completed and submitted the enrollment form to Sage Central, a Sage Central Navigator will call your patient within 1 to 2 business days to welcome them to the program.

Sage Central provides:

- Dedicated case managers
- Personalized support
- Financial assistance for eligible patients
- Additional resources

Visit SageCentralSupport.com or call
1-844-4-SAGERX (844-472-4379)
Monday–Friday, 8AM–6PM ET

ZULRESSO IMPORTANT SAFETY INFORMATION (CONT'D)

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

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ZULRESSO IMPORTANT SAFETY INFORMATION (CONT'D)

Suicidal Thoughts and Behaviors
In pooled analyses of placebo-controlled trials of chronically administered antidepressant drugs (SSRIs and other antidepressant classes) that include approximately 77,000 adult patients and 4,500 pediatric patients, the incidence of suicidal thoughts and behaviors in antidepressant-treated patients age 24 years and younger was greater than in placebo-treated patients. There was considerable variation in risk of suicidal thoughts and behaviors among drugs, but there was an increased risk identified in young patients for most drugs studied. There were differences in absolute risk of suicidal thoughts and behaviors across the different indications, with the highest incidence in patients with major depressive disorder (MDD).

ZULRESSO does not directly affect monoaminergic systems. Because of this and the comparatively low number of exposures to ZULRESSO, the risk of developing suicidal thoughts and behaviors with ZULRESSO is unknown. If depression becomes worse or patients experience emergent suicidal thoughts and behaviors, consider changing the therapeutic regimen, including discontinuing ZULRESSO.

Adverse Reactions
The most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) were sedation/somnolence, dry mouth, loss of consciousness, and flushing/hot flush. Adverse reactions reported in an open-label study in patients 15 to 17 years were generally similar to those observed in clinical studies of ZULRESSO in adults with PPD.

Use in Specific Populations
- **Pregnancy:** Based on findings from animal studies of other drugs that enhance GABAergic inhibition, ZULRESSO may cause fetal harm There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including ZULRESSO, during pregnancy. Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/antidepressants/.
- **Lactation:** Brexanolone is transferred to breastmilk in nursing mothers. There are no data on the effects of ZULRESSO on a breastfed infant. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZULRESSO and any potential adverse effects on the breastfed child from ZULRESSO or from the underlying maternal condition
- **Pediatric Use:** The safety and effectiveness of ZULRESSO for the treatment of PPD have been established in patients 15 to 17 years. The safety and effectiveness of ZULRESSO in patients less than 15 years of age have not been established
- **Renal Impairment:** No dosage adjustment is recommended in patients with mild, moderate, or severe renal impairment. Avoid use of ZULRESSO in patients with end stage renal disease (ESRD)

Controlled Substance
ZULRESSO contains brexanolone, a Schedule IV controlled substance under the Controlled Substances Act.

To report SUSPECTED ADVERSE REACTIONS, contact Sage Therapeutics, Inc. at 1-844-4-SAGERX (1-844-472-4379) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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