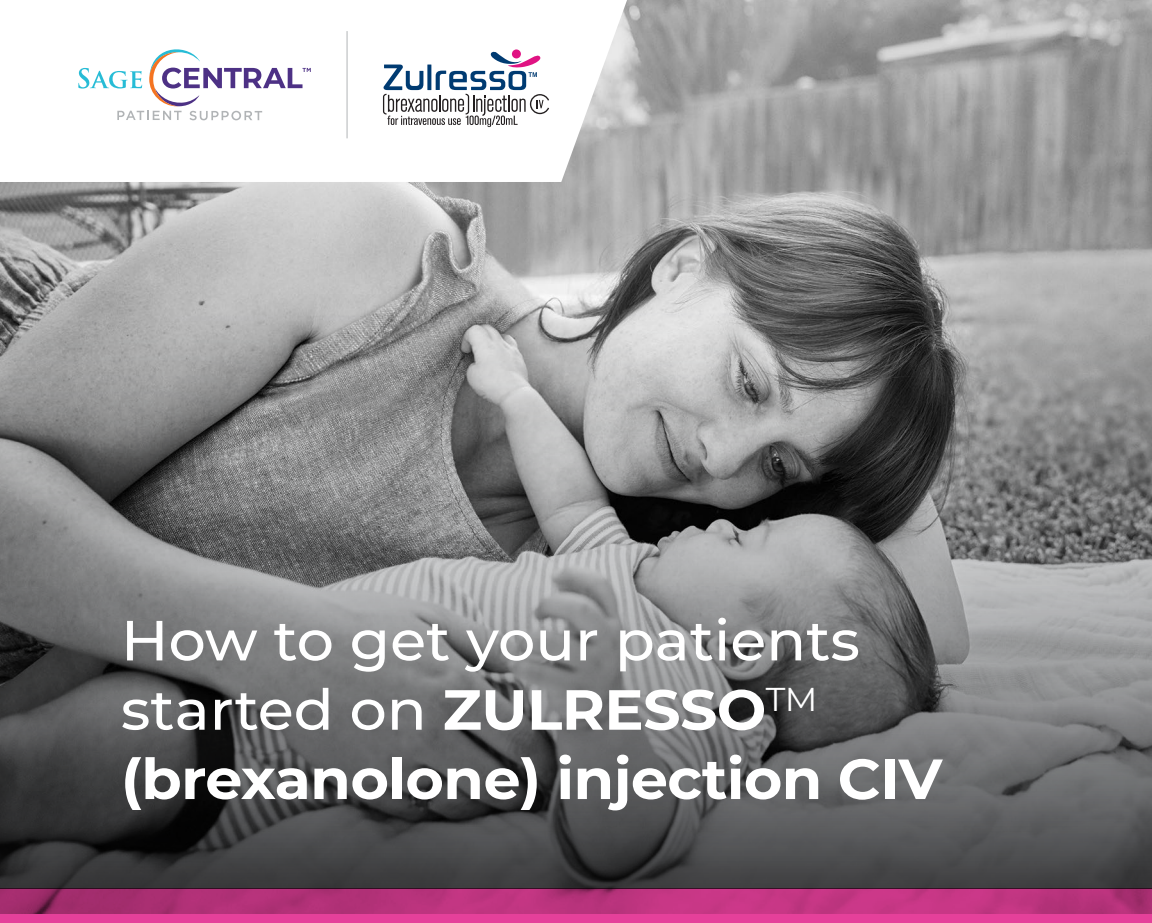
SAGE CENTRAL™ PATIENT SUPPORT

Zulresso™ (brexanolone) Injection IV for intravenous use 100mg/20mL



How to get your patients started on **ZULRESSO**™ **(brexanolone) injection CIV**

INDICATION

ZULRESSO™ (brexanolone) CIV is indicated for the treatment of postpartum depression (PPD) in adults.

IMPORTANT SAFETY INFORMATION for ZULRESSO

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 Important Safety Information throughout brochure and accompanying Full Prescribing Information including Boxed Warning and Medication Guide in pocket.

The ZULRESSO REMS

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

Notable requirements of the ZULRESSO REMS include the following:

- 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 and ensure they are enrolled in the ZULRESSO REMS prior to infusion.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Excessive Sedation and Sudden Loss of Consciousness

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

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.

Further information is available at www.zulressorems.com or 844-472-4379.

Please see Important Safety Information throughout brochure and accompanying Full Prescribing Information including Boxed Warning and Medication Guide in pocket.

Enrolling your patient in Sage Central

Sage Central offers additional support and resources to your patient. Enrollment in Sage Central is optional and can be completed by following the steps below. Your patient will be enrolled in the program once the Sage Central Enrollment Form is received.

Are you trained by the Authorized Representative within the certified Healthcare Setting where you want this patient treated?

YES

You are the patient's **PRESCRIBING PHYSICIAN** and are responsible for completing both the *Sage Central Enrollment Form* and the *ZULRESSO REMS Patient Enrollment Form.*

NO

You are the patient's **REFERRING PHYSICIAN** and are responsible for completing only the *Sage Central Enrollment Form.*

If you refer the patient to a specific certified Healthcare Setting on the form, the REMS enrollment process will begin.

If you do not know the certified Healthcare Setting, Sage Central can provide options for you and your patient to decide.

Once the necessary paperwork is completed:

- The patient is enrolled in Sage Central and the ZULRESSO REMS
- Evaluation of financial assistance eligibility begins
- Sage Central Navigators assist with logistical support and offer treatment preparation information
- Patient is notified of the scheduled infusion date

PATIENT CAN BEGIN TREATMENT

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Personalized support for your patients treated with ZULRESSO

Sage Central is a source for support resources and programs for your patients with postpartum depression and their families, including financial assistance programs for eligible patients, educational materials, and information about potential sources of support within their communities. Our dedicated case managers—Sage Central Navigators—can help your patients throughout the treatment journey.

SAGE CENTRAL™ PATIENT SUPPORT

To learn more about Sage Central Support, call

844-4-SAGERX

(844-472-4379) M-F, 8AM-8PM ET

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

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.

Please see Important Safety Information throughout brochure and accompanying Full Prescribing Information including Boxed Warning and Medication Guide in pocket.

Sage Central offers the following resources and support for your patients

Live support
- Dedicated Sage Central Navigators help patients throughout the treatment journey

Logistical support
- Assistance with finding options for a ZULRESSO REMS certified Healthcare Setting

Financial assistance
- Helping patients understand their insurance coverage and options
- Financial assistance programs for eligible patients

Additional resources
Support in the days leading up to treatment, including:
- Educational resources and helpful treatment preparation tips
- Assistance with connecting to potential sources of support within their communities

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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

Further information, including a list of certified healthcare facilities, is available at www.zulressorems.com or call 1-844-472-4379.

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Be sure to tell your patients:
- Sage Central can be a resource to provide support throughout the treatment process
- Dedicated Sage Central Navigators will be there to answer questions about the treatment process and assist with understanding insurance and coverage options

Sage Central financial assistance programs

We understand that paying for treatment can sometimes be challenging. That's why Sage Central has financial assistance programs for eligible patients to help reduce their out-of-pocket cost related to ZULRESSO. Once patients are enrolled in Sage Central, they will be automatically enrolled in the financial assistance programs for which they may be eligible. A patient's continued eligibility is subject to the satisfaction of the terms and conditions of the financial assistance programs.

Be sure to tell your patients:

There are financial assistance programs in place that may help reduce their out-of-pocket costs related to their treatment with ZULRESSO if they are eligible.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (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).

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1. The **ZULRESSO Drug Copay Assistance Program** is designed to help reduce a patient's eligible out-of-pocket copay costs related to the drug. Subject to certain terms and conditions, commercially insured patients may be eligible for copay assistance to reduce their out-of-pocket, drug-related copay costs up to $15,000—regardless of income level.*

2. The **ZULRESSO Infusion Copay Assistance Program** is designed to help reduce a patient's eligible out-of-pocket copay costs related to the infusion. Subject to certain terms and conditions, commercially insured patients may be eligible for copay assistance to reduce their out-of-pocket, infusion-related copay costs up to $2,000—regardless of income level.*

   (Residents of Michigan, Minnesota, Massachusetts, and Rhode Island are not eligible for infusion copay assistance.)

3. **Free Drug Program** provides ZULRESSO at no cost for eligible patients who would not otherwise have access to ZULRESSO and who meet certain income criteria. If a patient is uninsured or underinsured and meets the financial eligibility criteria, the patient may qualify for the Free Drug Program.

   The healthcare setting will be required to provide an attestation that it will not bill the patient or the patient's insurer for any costs associated with ZULRESSO.

For patients enrolled in the ZULRESSO Drug Copay and Infusion Copay Assistance Programs: Following treatment, the healthcare setting will need to submit an Explanation of Benefits and a copy of the ZULRESSO Copay Reimbursement Request Form to Sage Central in order to identify the amount billed for infusion and drug related costs and the patient's out-of-pocket responsibility.

Please open flap to see Terms and Conditions

*ZULRESSO Drug Copay Assistance Program and ZULRESSO Infusion Copay Assistance Program are not available for prescriptions covered by Medicare, Medicaid, TRICARE, or other federal- and state-funded programs.

Terms and Conditions

Combined Copay Programs

The ZULRESSO Drug and Infusion Copay Assistance Programs (the "Copay Programs") help eligible patients with private, commercial health insurance reduce their out-of-pocket costs associated with the drug, up to a maximum of $15,000, and out-of-pocket, infusion-related costs, up to a maximum of $2,000. Cash paying patients and patients eligible for a state or federally funded insurance program, including but not limited to Medicare, Medicaid, TRICARE, Veterans Affairs health care, a state prescription drug assistance program, or the Government Health Insurance Plan available in Puerto Rico (formerly known as "La Reforma de Salud"), are not eligible to participate in the Copay Programs. Residents of Massachusetts, Michigan, Minnesota and Rhode Island are not eligible to receive assistance for out-of-pocket infusion related costs. Sage Therapeutics, Inc. may rescind, revoke or amend the Copay Programs at any time. For full patient eligibility requirements and program terms and conditions, visit SageCentralSupport.com.

Free Drug Program

To be eligible to participate in the ZULRESSO™ Free Drug Program (the "FDP"), the patient must: (i) Be prescribed ZULRESSO™ for an on-label diagnosis; (ii) Have household income less than or equal to 500% of the Federal Poverty Level (FPL); (iii) Be uninsured or rendered uninsured under any of the following circumstances: (a) Patient has no healthcare insurance, (b) Patient is insured but such insurance does not cover ZULRESSO, or (c) Patient is insured with coverage for ZULRESSO, but is ineligible for the ZULRESSO Copay Assistance Programs, and cannot afford the medication (patient out-of-pocket costs are greater than $25); (iv) Reside in the United States or a U.S. territory; (v) Be treated by a healthcare professional in the United States or a U.S. territory; and (vi) Be 18 years of age or older. Patients enrolled in Medicare, Medicaid or any other federal or state funded health plan may participate in the FDP if they receive the free product outside of their government-funded benefits. The treating healthcare provider must certify that based on his/her independent medical judgment, ZULRESSO is a medically appropriate treatment for the patient. The healthcare provider must agree not to bill the patient or the patient's insurer for any costs associated with ZULRESSO and the corresponding treatment, including costs associated with the infusion of ZULRESSO (administration, needles, tubing, infusion bags, syringes, infusion pump, preparation of medication, and IV access) and hospital room and board costs. The healthcare provider must certify that he/she will not seek reimbursement from any third-party payer or government program for the cost of ZULRESSO or any costs associated with the infusion of ZULRESSO. The patient will be informed that she must not (i) seek reimbursement for the free drug from their health plan, and (ii) count the cost of the free drug towards her out-of-pocket spending requirements, if any, under her insurance. The free drug provided under the FDP is not conditioned on any past or future purchases. For any patient enrolled in a readily identifiable Medicare, Medicaid or other government funded plan, Sage will send a letter to the plan informing it that: (i) the patient is receiving free product from the ZULRESSO FDP outside of the patient's Medicare/Medicaid plan benefit, (ii) the patient and her physician have been informed that they must not seek reimbursement for the free drug from their health plan or count the cost of the free product towards the patient's out-of-pocket spending requirements, and (iii) the plan should discontinue any pending prior authorization or coverage appeal associated with the patient.

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Support for your patients throughout the treatment journey, from start...

Welcoming your patient

One to two business days after her enrollment, your patient will receive a welcome call from a dedicated Sage Central Navigator.

This call will include:

- An overview of the treatment process
- What to expect from Sage Central
- Details of insurance coverage and an overview of possible financial assistance programs

Following enrollment, Sage Central Navigators can provide support to your patient in the days leading up to treatment.

Preparing for treatment

Once a patient has been prescribed ZULRESSO and enrolled in Sage Central, Sage Central Navigators are there to answer questions. We want patients to have a positive experience during treatment, and being prepared ahead of time can certainly help.

We also understand that many patients may not have experience with an infusion treatment, so our Sage Central Navigators can provide helpful preparation tips and support resources in the days leading up to treatment. In addition, Sage Central Navigators can assist with connecting patients to potential sources of support within their communities.

Your patient can also download the Treatment Preparation Resource at SageCentralSupport.com.

Be sure to tell your patients:

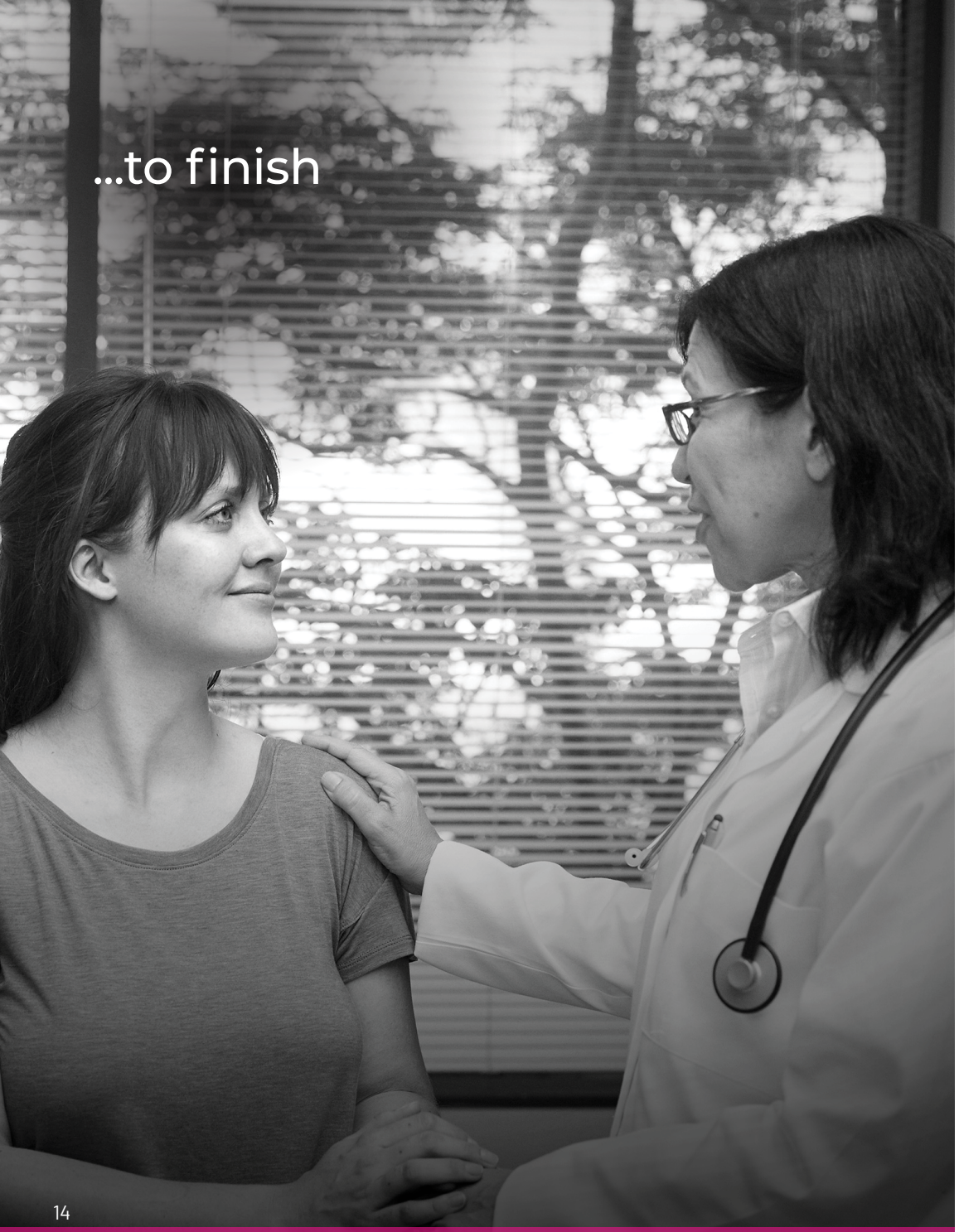
- Sage Central Navigators are available to answer their questions and help throughout the treatment journey
- SageCentralSupport.com is a valuable source of information about preparing for treatment with ZULRESSO
- They must sign and indicate their consent on the Sage Central Enrollment Form to be enrolled in Sage Central
- They must check the *Consent for Marketing Calls and Text Messages* box when enrolling in Sage Central if they would like to receive pre-treatment emails and text messages

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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.

Please see Important Safety Information throughout brochure and accompanying Full Prescribing Information including Boxed Warning and Medication Guide in pocket.



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Completing treatment

2.5 DAYS

Your patient will receive a continuous IV infusion over the course of 2.5 days. A REMS-trained Healthcare Provider must be available on site to continuously monitor your patient, and intervene as necessary, for the duration of the ZULRESSO infusion

A Sage Central Navigator will continue to be available to address questions or concerns throughout your patient's treatment journey and will follow up once treatment is completed

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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/

Please see Important Safety Information throughout brochure and accompanying Full Prescribing Information including Boxed Warning and Medication Guide in pocket.

Additional support

Sage Central may be able to provide assistance with connecting to local community-based resources for women with PPD and their families. Each group may have different types of support available. There are also helplines available that your patients can connect to.

Our community resource locator tool is available at SageCentralSupport.com

Be sure to tell your patients:

- A healthcare provider will be there to monitor them for the duration of the infusion
- Sage Central may provide assistance with connecting to local community-based support resources

IMPORTANT SAFETY INFORMATION (CONT'D)

Use in Specific Populations (cont'd)

- **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 in pediatric patients 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)

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SAGE CENTRAL™ PATIENT SUPPORT

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For your patients with **postpartum depression**...

Take advantage of Sage Central Patient Support

LIVE SUPPORT

LOGISTICAL SUPPORT

FINANCIAL ASSISTANCE

ADDITIONAL RESOURCES

SAGE CENTRAL™ PATIENT SUPPORT

For more information, call

844-4-SAGERX

(844-472-4379) M-F, 8AM-8PM ET, and one of our Sage Central Navigators will assist you.

IMPORTANT SAFETY INFORMATION (CONT'D)

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*.

Please also see **Full Prescribing Information including Boxed Warning** and **Medication Guide** for ZULRESSO.

Sage Therapeutics™