

Letters of Medical Necessity & Appeal Guide

This guide is for informational purposes only, providing an example of the process and materials that may be required or helpful when responding to a request from a patient's health plan. Use of this information does not constitute medical or legal advice and does not guarantee reimbursement for coverage. It is not intended to be a substitute for the independent clinical decision of the prescribing healthcare professional.

INDICATION

ZURZUVAE® (zuranolone) is indicated for the treatment of postpartum depression (PPD) in adults.

IMPORTANT SAFETY INFORMATION

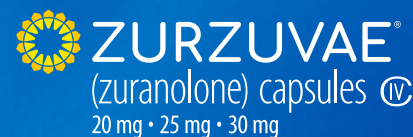
WARNING: IMPAIRED ABILITY TO DRIVE OR ENGAGE IN OTHER POTENTIALLY HAZARDOUS ACTIVITIES

ZURZUVAE causes driving impairment due to central nervous system (CNS) depressant effects.

Advise patients not to drive or engage in other potentially hazardous activities until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course. Inform patients that they may not be able to assess their own driving competence, or the degree of driving impairment caused by ZURZUVAE.

Please see additional Important Safety Information throughout and full [Prescribing Information](#), including **Boxed Warning**.

Letter of Medical Necessity



A Letter of Medical Necessity is a patient-specific document used to support your determination that ZURZUVAE is a medically necessary treatment for your adult patients with postpartum depression (PPD) by explaining the rationale supporting your treatment decision. It is important to tailor the letter to the specific needs of your patient and address the reason(s) why you believe ZURZUVAE is the most appropriate treatment option.

Review & Prepare



1. Review the health plan's coverage policy



2. Provide background on your patient's condition and clearly state your patient's individual circumstances to justify why, in your opinion, the prescribed therapy is the most appropriate choice. Provide all required information, including documentation of all criteria your patient meets and a clear explanation for any they do not meet



3. Include clinical justification and copies of relevant clinical data to support your decision (eg, the Prescribing Information for ZURZUVAE, depression screening results from the EPDS [Edinburgh Postnatal Depression Scale] or PHQ-9 [Patient Health Questionnaire], comorbidities, prior therapies, contraindications, tolerability issues)

Submit & Follow Up



4. Consider requesting the health plan provide a psychiatrist to review the patient's case



5. Submit the letter (on your practice letterhead) as required by the patient's health plan along with the prior authorization or medical exception request



6. Track the status of your request and follow up with the health plan as needed

[Click to access the ZURZUVAE Sample Letter of Medical Necessity.](#)

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Impaired Ability to Drive or Engage in Other Potentially Hazardous Activities

- ZURZUVAE causes driving impairment due to central nervous system (CNS) depressant effects
- Advise patients not to drive a motor vehicle or engage in other potentially hazardous activities requiring complete mental alertness, such as operating machinery, until at least 12 hours after ZURZUVAE administration for the duration of the 14-day treatment course. Inform patients that they may not be able to assess their own driving competence or the degree of driving impairment caused by ZURZUVAE

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Letter of Appeal

A Letter of Appeal is a patient-specific document that requests a health plan reconsider its initial decision to deny coverage for a medication. It is important to tailor the letter to the specific needs of your patient and address the reason(s) why you believe ZURZUVAE is the most appropriate treatment option.

Review & Prepare

1. Review the health plan's denial and state the reason(s) you disagree with the denial. The denial letter may also include instructions detailing the appeals process

2. Provide background on your patient's condition and clearly state your patient's individual circumstances to justify why, in your opinion, the prescribed therapy is the most appropriate choice. Provide all required information, including documentation of all criteria your patient meets and a clear explanation for any they do not meet

3. Include clinical justification and copies of relevant clinical data to support your decision (eg, the Prescribing Information for ZURZUVAE, depression screening results from the EPDS or PHQ-9, comorbidities, prior therapies, contraindications, tolerability issues)

Submit & Follow Up

4. Consider requesting a peer-to-peer consult to discuss the patient's case

5. Submit the letter (on your practice letterhead) as required by the patient's health plan

6. Track the status of your appeal and follow up with the health plan as needed

[Click to access the ZURZUVAE Sample Letter of Appeal.](#)

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Central Nervous System Depressant Effects

- ZURZUVAE can cause CNS depressant effects such as somnolence and confusion
- Somnolence developed in 36% of patients who received ZURZUVAE (50 mg) and in 6% of patients who received placebo daily. Some ZURZUVAE-treated patients developed confusional state. One of these cases was severe, and was also associated with somnolence, dizziness, and gait disturbance

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Central Nervous System Depressant Effects (continued)

- A higher percentage of ZURZUVAE-treated patients, compared to placebo-treated patients, experienced somnolence, dizziness, or confusion that required dosage reduction, interruption, or discontinuation
- Because ZURZUVAE can cause CNS depressant effects, patients may be at higher risk of falls
- Other CNS depressants such as alcohol, benzodiazepines, opioids, tricyclic antidepressants, or drugs that increase zuranolone concentration, may increase impairment of psychomotor performance or CNS depressant effects such as somnolence, cognitive impairment, and the risk of respiratory depression in ZURZUVAE-treated patients
- To reduce the risk of CNS depressant effects and/or mitigate CNS depressant effects that occurs with ZURZUVAE treatment:
 - If patients develop CNS depressant effects, consider dosage reduction or discontinuation of ZURZUVAE
 - If use with another CNS depressant is unavoidable, consider dosage reduction
 - Reduce the ZURZUVAE dosage in patients taking strong CYP3A4 inhibitors

Suicidal Thoughts and Behavior

- In pooled analyses of placebo-controlled trials of chronically administered antidepressant drugs (SSRIs and other antidepressant classes) that included 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)
- ZURZUVAE does not directly affect monoaminergic systems. Consider changing the therapeutic regimen, including discontinuing ZURZUVAE, in patients whose depression becomes worse or who experience emergent suicidal thoughts and behaviors

Embryo-fetal Toxicity

- Based on findings from animal studies, ZURZUVAE may cause fetal harm when administered to a pregnant woman
- Advise a pregnant woman of the potential risk to an infant exposed to ZURZUVAE in utero. Advise females of reproductive potential to use effective contraception during treatment with ZURZUVAE and for one week after the final dose

ADVERSE REACTIONS

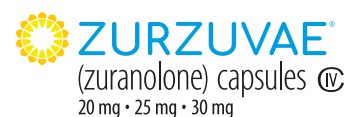
- The most common adverse reactions ($\geq 5\%$ and greater than placebo) in ZURZUVAE-treated patients were somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection

DRUG INTERACTIONS

CNS Depressant Drugs and Alcohol

- Caution should be used when ZURZUVAE is administered in combination with other CNS drugs or alcohol. If use with another CNS depressant is unavoidable, consider dosage reduction

Please see additional Important Safety Information throughout and full [Prescribing Information](#), including **Boxed Warning**.



IMPORTANT SAFETY INFORMATION (continued)

DRUG INTERACTIONS (continued)

Strong CYP3A4 Inhibitors

- Reduce the ZURZUVAE dosage when used with a strong CYP3A4 inhibitor

CYP3A4 Inducers

- Avoid concomitant use of ZURZUVAE with CYP3A4 inducers

USE IN SPECIFIC POPULATIONS

Pregnancy

- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to antidepressants, including ZURZUVAE, 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/research/pregnancyregistry/antidepressants/>
- Based on findings from animal studies, ZURZUVAE may cause fetal harm. Advise pregnant women of the potential risk to a fetus. Available data on ZURZUVAE use in pregnant women from the clinical development program are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes

Lactation

- Available data from a clinical lactation study in 14 women indicate that zuranolone is present in low levels in human milk. There are no data on the effects of zuranolone on a breastfed infant and limited data on the effects on milk production
- The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZURZUVAE and any potential adverse effects on the breastfed child from ZURZUVAE or from the underlying maternal condition

Hepatic Impairment

- The recommended ZURZUVAE dosage in patients with severe hepatic impairment (Child-Pugh C) is lower than patients with normal hepatic function

Renal Impairment

- The recommended ZURZUVAE dosage in patients with moderate and severe renal impairment is lower than those with normal renal function

DRUG ABUSE AND DEPENDENCE

- ZURZUVAE contains zuranolone, a Schedule IV controlled substance
- Zuranolone has abuse potential with associated risks of misuse, abuse, and substance use disorder including addiction
- ZURZUVAE may produce physical dependence

Please see full [Prescribing Information](#), including **Boxed Warning**.

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