Optum Rx®

Zurzuvae™ (zuranolone) – New drug approval

- On August 4, 2023, the FDA announced the approval of Biogen and Sage Therapeutics' Zurzuvae (zuranolone), for the treatment of postpartum depression (PPD) in adults.

- The FDA also reviewed Zurzuvae for treatment of adults with major depressive disorder (MDD); however, Sage and Biogen announced they received an FDA Complete Response Letter (CRL) for the MDD indication. The CRL stated that the application did not provide substantial evidence of effectiveness to support the approval of zuranolone for the treatment of MDD and that an additional study or studies will be needed.

- PPD is a major depressive episode that typically occurs after childbirth but can also begin during the later stages of pregnancy. It is estimated approximately 1 in 8 women experience symptoms of PPD.

- Zurzuvae is the first oral treatment approved for PPD.

    — Zurzuvae is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator. The mechanism of action of zuranolone in the treatment of PPD is not fully understood, but is thought to be related to its positive allosteric modulation of $GABA_A$ receptors.

- The efficacy of Zurzuvae was established in a two randomized, placebo-controlled, double-blind studies in women with PPD with onset of symptoms in the third trimester or within 4 weeks of delivery. Patients received Zurzuvae or placebo for 14 days. In these studies, concomitant use of existing oral antidepressants was allowed for patients taking a stable dose of oral antidepressant for at least 30 days before baseline. The primary endpoint was the change from baseline in depressive symptoms as measured by the 17-item Hamilton depression rating scale (HAMD-17) total score at day 15.

    — In both studies, patients in the Zurzuvae groups experienced statistically significantly greater improvement on the primary endpoint compared to patients in the placebo groups.

Study number	Treatment group	Mean baseline score	Least squares mean change from baseline	Placebo-subtracted difference
1	Zurzuvae (N = 98)	28.6	-15.6	-4.0 (-6.3, -1.7)
	Placebo (N = 97)	28.8	-11.6	
2	Zurzuvae (N = 76)	28.4	-17.8	-4.2 (-6.9, -1.5)
	Placebo (N = 74)	28.8	-13.6	

- Zurzuvae carries a boxed warning for impaired ability to drive or engage in other potentially hazardous activities.

- Additional warnings and precautions for Zurzuvae include central nervous system (CNS) depressant effects; suicidal thoughts and behavior; and embryo-fetal toxicity.

- The most common adverse reactions (≥ 5% and greater than placebo) with Zurzuvae use were somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infection.

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- The recommended dosage of Zurzuvae is 50 mg taken orally once daily in the evening for 14 days. If patients experience CNS depressant effects within the 14-day period, reducing the dosage should be considered to 40 mg once daily in the evening within the 14-day period.
    - Zurzuvae can be used alone or as an adjunct to oral antidepressant therapy.
    - The safety and effectiveness of Zurzuvae use beyond 14 days in a single treatment course have not been established.

- Zurzuvae is expected to launch in the fourth quarter of 2023 shortly following scheduling as a controlled substance by the DEA, which is anticipated to occur within 90 days. Zurzuvae will be available as a 20 mg, 25 mg, and 30 mg capsule.

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