Optum Rx®

Exxua (gepirone) – New drug approval

- On September 22, 2023, the FDA approved Fabre-Kramer Pharmaceuticals' Exxua (gepirone), for the treatment of major depressive disorder (MDD) in adults.

- The mechanism of the antidepressant effect of Exxua is not fully understood but is thought to be related to its modulation of serotonergic activity in the central nervous system through selective agonist activity at 5HT1A receptors.

- The efficacy of Exxua was established in two randomized, double-blind, placebo-controlled, flexible-dose studies in adults with MDD. In both studies, patients were randomized to Exxua or placebo. The primary endpoint was the change from baseline in the Hamilton Depression Rating Scale (HAMD-17) total score at week 8.

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

Study	Treatment group	N	Least squares mean change from baseline	Placebo-adjusted difference (95% CI)
1	Exxua	101	-9.04	-2.47 (-4.41, -0.53)
	Placebo	103	-6.75	--
2	Exxua	116	-10.22	-2.45 (-4.47, -0.43)
	Placebo	122	-7.96	--

- Exxua carries a boxed warning for suicidal thoughts and behaviors.

- Exxua is contraindicated in patients:

    — With known hypersensitivity to gepirone or components of Exxua
    — With prolonged QTc interval > 450 msec at baseline
    — With congenital long QT syndrome
    — Receiving concomitant strong CYP34A inhibitors
    — With severe hepatic impairment
    — Taking, or within 14 days of stopping, monoamine oxidase inhibitors (MAOIs) due to the risk of serious and possibly fatal drug interactions, including hypertensive crisis and serotonin syndrome.

- Additional warnings and precautions for Exxua include QT prolongation, serotonin syndrome, and activation of mania/hypomania.

- The most common adverse reactions (≥ 5% and at least twice incidence of placebo) with Exxua use were dizziness, nausea, insomnia, abdominal pain, and dyspepsia.

- The recommended starting dosage of Exxua is 18.2 mg orally once daily. Based on clinical response and tolerability, the dosage may be increased to 36.3 mg once daily on day 4 and further titrated to 54.5 mg once daily after Day 7 and to 72.6 mg once daily after an additional week. The maximum recommended daily dosage of Exxua is 72.6 mg once daily.

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- Fabre-Kramer Pharmaceuticals' launch plans for Exxua are pending. Exxua will be available as 18.2 mg, 36.3 mg, 54.5 mg, and 72.6 mg extended-release tablets.