Rexulti® (brexpiprazole) – New indication

- On May 11, 2023, the FDA announced the approval of Otsuka and Lundbeck's Rexulti (brexpiprazole), for treatment of agitation associated with dementia due to Alzheimer's disease.
    - Rexulti is not indicated as an as needed ("prn") treatment for agitation associated with dementia due to Alzheimer's disease.
- Rexulti is also approved for:
    - Adjunctive treatment of major depressive disorder in adults
    - Treatment of schizophrenia in adults and pediatric patients ages 13 years and older.
- Alzheimer's disease is the most common cause of dementia, affecting more than 6.5 million people in the U.S. Patients with dementia often have behavioral and psychological disturbances. Agitation is among the most persistent, complex, stressful, and costly aspects of care among patients with behavioral and psychological symptoms of dementia.
- Rexulti is the first FDA-approved treatment for this specific indication of agitation associated with dementia.
- The approval of Rexulti for the new indication was based on two 12-week, randomized, double-blind, placebo-controlled studies (Study 6 and 7) in patients with agitation associated with dementia due to Alzheimer's disease. In Study 6, patients were randomized to an oral dosage of either Rexulti 1 mg once a day, Rexulti 2 mg once a day, or placebo. In Study 7, patients were randomized to either Rexulti 2 mg or 3 mg once a day (combined treatment arm) or placebo. The primary endpoint in the two studies was the change from baseline in the Cohen-Mansfield Agitation Inventory total (CMAI) score at week 12. The total CMAI scores range from 29 (best) to 203 (worst) (a negative change indicates improvement).
    - In Study 6, patients in the Rexulti 2 mg group showed improved total CMAI scores compared to patients in the placebo group at week 12. In Study 7, patients in the Rexulti 2 mg/3 mg group showed improved total CMAI scores compared to patients in the placebo group at week 12.
    - The 1 mg Rexulti group did not demonstrate significantly greater mean changes at baseline from the placebo group in the total CMAI score. The 1 mg once day Rexulti dosage is not approved and is not recommended for the treatment of agitation associated with dementia due to Alzheimer's disease.

Study	Treatment group	N	Mean baseline score (SD)	LS mean change from baseline (SE)	Placebo-subtracted difference (95% CI)
6	Rexulti 1 mg	134	70.5 (16.0)	-17.6 (1.3)	0.2 (-3.4, 3.9)
	Rexulti 2 mg*	138	71.0 (16.6)	-21.6 (1.3)	-3.8 (-7.4, -0.2)
	Placebo	131	72.2 (17.9)	-17.8 (1.3)	--
7	Rexulti 2 mg/3 mg*	225	80.6 (16.6)	-22.6 (1.1)	-5.3 (-8.8, -1.9)
	Placebo	116	79.2 (17.5)	-17.3 (1.4)	--

* Dosages statistically significantly superior to placebo

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- Rexulti carries a boxed warning for increased mortality in elderly patients with dementia-related psychosis.
- The most common adverse reactions (≥ 4% and at least twice the rate for placebo) with Rexulti use for agitation associated with dementia were nasopharyngitis and dizziness.
- The recommended starting Rexulti dosage for the treatment of agitation associated with dementia due to Alzheimer's disease is 0.5 mg taken orally once daily on days 1 to 7. The dosage should be increased on days 8 through 14 to 1 mg once daily, and on day 15 to 2 mg once daily. The recommended target dose is 2 mg once daily. The dosage can be increased to the maximum recommended daily dosage of 3 mg once daily after at least 14 days, based on clinical response and tolerability.
    - Refer to the Rexulti drug label for dosing for its other indications.

Optum