

BREXPIPRAZOLE (Rexulti) Fact Sheet

Bottom Line:

Brexpiprazole is a cousin of aripiprazole and is also a partial dopamine agonist. While it has a very similar efficacy profile to aripiprazole, it was recently awarded approval for treatment of agitation in Alzheimer's dementia—the first drug to gain this indication. However, effect sizes were small, and safety in the elderly remains a concern.

FDA Indications:

Schizophrenia (adults, adolescents 13–17 years); **depression adjunct; agitation associated with dementia due to Alzheimer's disease (AD).**

Off-Label Uses:

Borderline personality disorder.

Dosage Forms:

Tablets: 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, 4 mg.

Dosage Guidance:

- Schizophrenia: Start 1 mg/day on days one through four, ↑ to 2 mg/day on days five through seven, then up to max 4 mg/day based on patient response. Usual dose 2–4 mg/day. Children: Start 0.5 mg/day, increase to 1 mg/day on fifth day and 2 mg/day on eighth day; may increase further by 1 mg/day increments weekly to target dose of 2–4 mg/day.
- Depression adjunct: Start 0.5–1 mg/day, ↑ at weekly intervals up to target 2 mg/day; max 3 mg/day.
- Agitation associated with dementia due to AD: Start 0.5 mg QD on days one through seven, ↑ to 1 mg QD on days eight through 14, ↑ to target dose of 2 mg QD on day 15; max 3 mg/day.
- Dose timing: Like aripiprazole, can be taken in the morning or at night; may unpredictably cause drowsiness or insomnia.

Monitoring: Fasting glucose, lipids.

Cost: \$\$\$\$\$

Side Effects:

- Most common: Weight gain, akathisia, somnolence.
- Serious but rare: Rare reports of reversible pathologic gambling and other impulse control problems (eating, spending, sexual).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT1A receptor partial agonist and serotonin 5-HT2A receptor antagonist.
- Metabolized by CYP2D6 and CYP3A4; t_{1/2}: 91 hours.
- Use ½ usual dose in presence of 2D6 or 3A4 inhibitors or in known 2D6 poor metabolizers; ¼ dose if both 2D6 inhibitor/poor metabolizer and 3A4 inhibitor; double dose if also using 3A4 inducer.

Clinical Pearls:

- As the name suggests, brexpiprazole is chemically and structurally related to its manufacturer's previous blockbuster aripiprazole (Abilify).
- Although the FDA-approved target dose for schizophrenia is 2–4 mg/day, 2 mg/day was no better than placebo in one of two preclinical registration studies.
- Unlike aripiprazole, brexpiprazole may not be effective in bipolar mania. It was no better than placebo at reducing symptoms in about 650 patients enrolled in two studies in acute mania. One study compared weight gain from brexpiprazole to aripiprazole and found a similar increase of about 5–10 pounds over a year.
- In the two 12-week trials for agitation related to dementia, the 2 mg and 3 mg doses were shown to be effective but not the 1 mg dose. As-needed dosing is not recommended for this indication.
- Once-a-day dosing with no regard to meals makes this an easy-to-use option.
- Generic/brand name mnemonic: "Brex is Rex" (thanks to Dr. Raj Mago).

Fun Fact:

Plan on seeing more trial results with Rexulti in the future, including those in patients with ADHD and PTSD.