
PITOLISANT (Wakix) Fact Sheet

Bottom Line:

Pitolisant is the only non-DEA-scheduled treatment option approved for patients with narcolepsy, but limited experience and data, plus a higher price tag, make it a second-line option after the “vigil” drugs. However, for patients with both cataplexy and excessive daytime sleepiness (EDS), it may be a better option than Xyrem, Lumryz, or Xywav.

FDA Indications:

Cataplexy or excessive sleepiness associated with narcolepsy.

Off-Label Uses:

ADHD; fatigue; treatment-resistant depression.

Dosage Forms:

Tablets: 4.45 mg, 17.8 mg.

Dosage Guidance:

Start 8.9 mg QAM for week one. If tolerated, may increase to 17.8 mg QAM for week two. If needed, in week three or beyond, may increase to maximum dose of 35.6 mg QAM. Use lower doses in hepatic or renal impairment.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

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

Side Effects:

- Most common: Insomnia, nausea, anxiety.
- Serious but rare: QT interval prolongation (4.2 msec at therapeutic doses; 16 msec at doses greater than maximum recommended).
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Antagonist/inverse agonist of the histamine-3 (H3) receptor.
- Metabolized primarily by CYP2D6 and, to a lesser extent, CYP3A4; $t_{1/2}$: 20 hours.
- Strong CYP2D6 inhibitors or in poor metabolizers: Maximum recommended dosage is 17.8 mg once daily. Strong CYP3A4 inducers may reduce pitolisant levels by 50%; adjust dose. Avoid H1 antihistaminergic agents, which may decrease effectiveness of pitolisant.

Clinical Pearls:

- Not a controlled substance.
- The H3 receptor is mainly found in the brain, where it regulates wakefulness, appetite, and memory. Pitolisant blocks the H3 receptor, which has downstream effects of increased dopamine and acetylcholine in the prefrontal cortex.
- A head-to-head “non-inferiority” study with modafinil found pitolisant had nearly similar efficacy but was better tolerated.
- A study in kids ages 6 and up showed good results for narcolepsy-related cataplexy and EDS. While the FDA has not yet given its blessing for use in kids, it already has that approval in Europe.

Fun Fact:

Pitolisant is also being studied for efficacy in ADHD, dementia, obesity, and cognitive symptoms of schizophrenia.