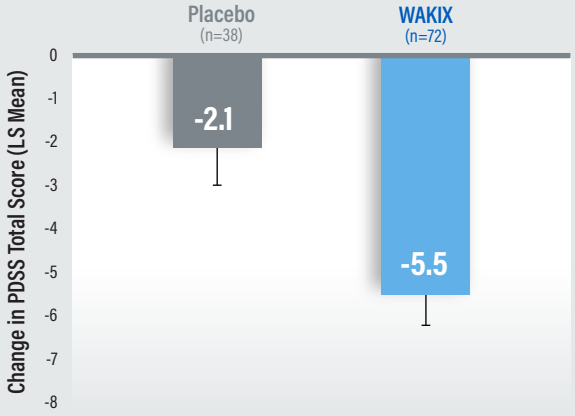
WAKIX Significantly Reduced EDS Versus Placebo

Significant improvement in LS mean change from baseline to end of treatment in the final PDSS total score with WAKIX versus placebo: -3.41 points (*P*=0.002)[1,*]

Reduction in PDSS Total Score From Baseline[1,†]



- WAKIX demonstrated a 5.5-point mean reduction in PDSS total score from baseline versus 2.1 points with placebo[†]
- Mean PDSS total scores at baseline[‡]
  - Placebo: 20.0
  - WAKIX: 20.2

Study Design: 8-week, multicenter, randomized, double-blind, placebo-controlled study in 110 pediatric patients 6 to 17 years of age with narcolepsy with or without cataplexy (based on ICSD-3 criteria). WAKIX was initiated at 4.45 mg once daily and could be increased at weekly intervals to 17.8 mg (patients weighing <40 kg) or 35.6 mg (patients weighing ≥40 kg) once daily based on clinical response and tolerability. After the 4-week titration period, patients were treated with a stable dosage for an additional 4 weeks. No dosage adjustments were permitted during the stable dose phase.

*Placebo-subtracted difference (95% CI: -5.52, -1.31). †LS mean change in PDSS total score from baseline to mean of the final 2 weeks (Week 7 and Week 8).[1] ‡Baseline values shown as raw mean values.[1]

CI, confidence interval; EDS, excessive daytime sleepiness; ICSD-3, *International Classification of Sleep Disorders*, 3rd edition; LS, least squares; PDSS, Pediatric Daytime Sleepiness Scale.

Indications and Usage

- WAKIX is indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients with narcolepsy and for the treatment of excessive daytime sleepiness (EDS) in pediatric patients 6 years of age and older with narcolepsy.

Important Safety Information

Contraindications

- WAKIX is contraindicated in patients with known hypersensitivity to pitolisant or any component of the formulation. Anaphylaxis has been reported. WAKIX is also contraindicated in patients with severe hepatic impairment.

Warnings and Precautions

- WAKIX prolongs the QT interval. Avoid use of WAKIX in patients with known QT prolongation or in combination with other drugs known to prolong the QT interval. Avoid use in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval.
- The risk of QT prolongation may be greater in patients with hepatic or renal impairment due to higher concentrations of pitolisant; monitor these patients for increased QTc. Dosage modification is recommended in patients with moderate hepatic impairment and moderate or severe renal impairment. WAKIX is contraindicated in patients with severe hepatic impairment and not recommended in patients with end-stage renal disease (ESRD).

Drug Interactions

- Concomitant administration of WAKIX with strong CYP2D6 inhibitors increases pitolisant exposure by 2.2-fold. Reduce the dose of WAKIX by half.
- Concomitant use of WAKIX with strong CYP3A4 inducers decreases exposure of pitolisant by 50%. Dosage adjustments may be required.
- H_1 receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H_1 receptor antagonists.
- WAKIX is a borderline/weak inducer of CYP3A4. WAKIX may reduce the effectiveness of sensitive CYP3A4 substrates, including hormonal contraceptives. Patients using hormonal contraception should be advised to use an alternative non-hormonal contraceptive method during treatment with WAKIX and for at least 21 days after discontinuing treatment.

Established Safety and Tolerability in Clinical Trials

Clinical study in pediatric patients (6 years and older) with narcolepsy

- In the placebo-controlled phase of the study, the most common adverse reactions (occurring in ≥5% of patients and greater than the rate of placebo) with the use of WAKIX were headache (19%) and insomnia (7%)

Adverse Reactions That Occurred in ≥5% of WAKIX-Treated Pediatric Patients and More Frequently Than in Placebo-Treated Patients*

Adverse Reaction	WAKIX (n=73)
Headache	19%
Insomnia	7%

*Reported in patients treated with WAKIX (n=73) and placebo (n=37) in the placebo-controlled phase of the clinical trial conducted in patients 6 to 17 years of age with narcolepsy with or without cataplexy.

- The overall adverse reaction profile of WAKIX in the pediatric clinical trial was similar to that seen in the adult clinical trial program

Clinical studies in adult patients with narcolepsy

- In the placebo-controlled clinical trials conducted in adult patients with narcolepsy with or without cataplexy,† adverse reactions for WAKIX that occurred at ≥5% and more frequently than in patients treated with placebo included headache‡ (18% vs 15%), insomnia‡ (6% vs 2%), nausea (6% vs 3%), upper respiratory tract infection‡ (5% vs 3%), musculoskeletal pain‡ (5% vs 3%), and anxiety‡ (5% vs 1%)
- Other adverse reactions† that occurred at ≥2% and more frequently than in patients treated with placebo included heart rate increased,‡ hallucinations,‡ irritability, abdominal pain,‡ sleep disturbance,‡ decreased appetite, cataplexy, dry mouth, and rash‡

†Reported in patients treated with WAKIX (n=152) and placebo (n=114) in 3 placebo-controlled narcolepsy studies in which WAKIX was directly compared to placebo.

‡Denotes adverse reactions for which similar terms were combined.

Download the WAKIX Prescription Referral Form

Important Safety Information

Use in Specific Populations

- There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to WAKIX during pregnancy. Patients should be encouraged to enroll in the WAKIX pregnancy registry if they become pregnant. To enroll or obtain information from the registry, patients can call 1-800-833-7460.
- The safety and effectiveness of WAKIX have not been established for the treatment of excessive daytime sleepiness in pediatric patients less than 6 years of age with narcolepsy. The safety and effectiveness of WAKIX have not been established for the treatment of cataplexy in pediatric patients with narcolepsy.
- WAKIX is extensively metabolized by the liver. WAKIX is contraindicated in patients with severe hepatic impairment. Dosage adjustment is recommended in patients with moderate hepatic impairment.
- WAKIX is not recommended in patients with end-stage renal disease. Dosage adjustment of WAKIX is recommended in patients with eGFR <60 mL/minute/1.73 m^2.
- Dosage reduction is recommended in patients known to be poor CYP2D6 metabolizers; these patients have higher concentrations of WAKIX than normal CYP2D6 metabolizers.

To report suspected adverse reactions, contact Harmony Biosciences at 1-800-833-7460 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Reference

1. Dauvilliers Y, Lecendreux M, Lammers GJ, et al. Safety and efficacy of pitolisant in children aged 6 years or older with narcolepsy with or without cataplexy: a double-blind, randomised, placebo-controlled trial. [published correction appears in *Lancet Neurol.* 2023;22(5):e7] [published correction appears in *Lancet Neurol.* 2023;22(10):e11]. *Lancet Neurol.* 2023;22(4):303-311.