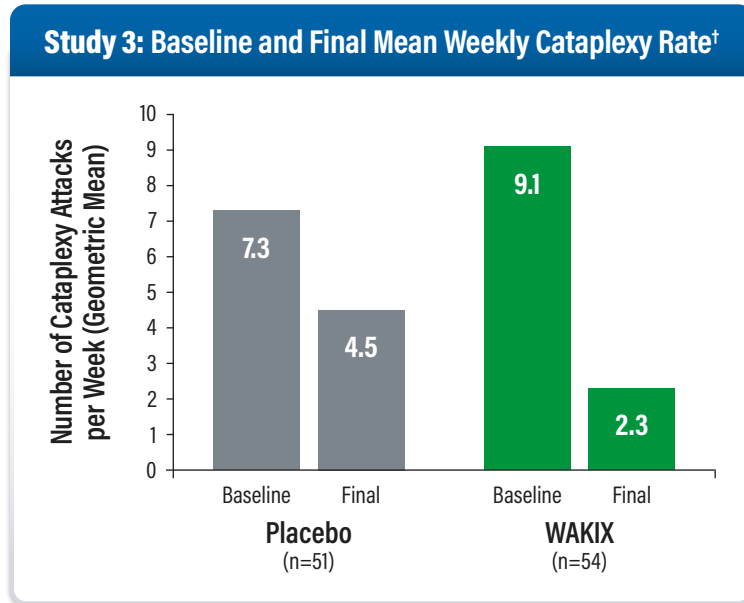


WAKIX Resulted in Significantly Fewer Cataplexy Attacks Versus Placebo in Two Clinical Studies

Study 3: 35.6 mg once daily maximum potential dosage

- WAKIX resulted in approximately half the number of mean weekly cataplexy attacks during the 4-week stable dosing period compared with placebo*
- WAKIX reduced the number of weekly cataplexy attacks



Patient population

- All patients had ongoing cataplexy at baseline (≥ 3 cataplexy attacks per week)
- 65% of all patients taking WAKIX reached a stable dosage of 35.6 mg once daily

Study 3: 7-week, multicenter, randomized, double-blind, placebo-controlled study in 105 adults with narcolepsy with cataplexy (based on ICSD-2 criteria). WAKIX was initiated at 4.45 mg once daily for the first week, increased to 8.9 mg once daily for the second week, and could remain the same or be decreased or increased at the next two weekly intervals to a maximum of 35.6 mg once daily based on clinical response and tolerability. After the 3-week titration period, patients were maintained on a stable dosage of 4.45 mg, 8.9 mg, 17.8 mg, or 35.6 mg once daily for an additional 4 weeks.

*Primary endpoint: Final mean weekly rate of cataplexy over the 4-week stable dosing period compared with placebo (adjusted for baseline differences). Rate ratio 0.51 (95% CI 0.44, 0.60); results were statistically significant.¹

†Statistical comparison of geometric mean values was not conducted.

ICSD-2, *International Classification of Sleep Disorders*, Second Edition.

Indications and Usage

- WAKIX is indicated for the treatment of excessive daytime sleepiness (EDS) or cataplexy in adult patients 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.

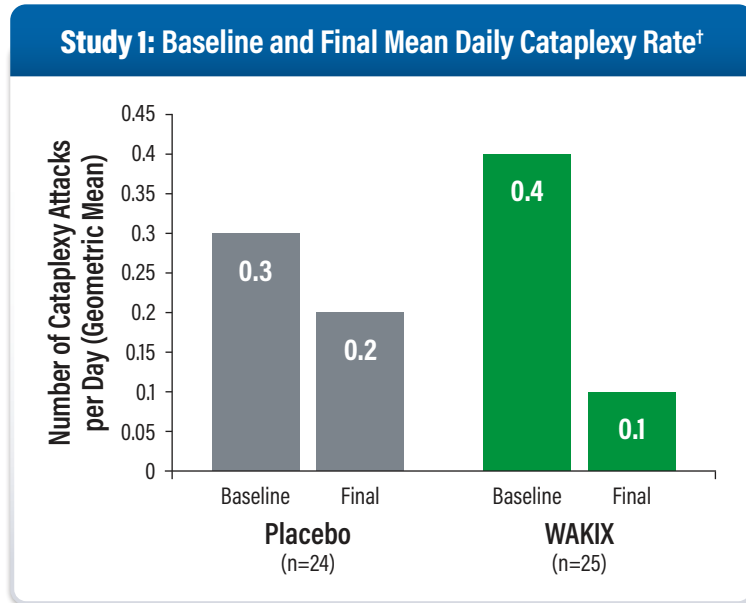
Warnings and Precautions

- 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 (see full prescribing information). WAKIX is not recommended in patients with end-stage renal disease (ESRD).

WAKIX Resulted in Significantly Fewer Cataplexy Attacks Versus Placebo in Two Clinical Studies

Study 1: 35.6 mg once daily maximum potential dosage

- In a supportive study, WAKIX resulted in significantly fewer mean daily cataplexy attacks at Week 8 compared with placebo^{1,*}
- WAKIX reduced the number of daily cataplexy attacks



Patient population

- Subset of 49 patients had a history of cataplexy
- 61% of all patients with or without cataplexy taking WAKIX reached a stable dosage of 35.6 mg once daily

Study 1: 8-week, multicenter, randomized, double-blind, placebo-controlled study in 61 adults with narcolepsy with or without cataplexy (based on ICSD-2 criteria). WAKIX was initiated at 8.9 mg once daily and could be increased at weekly intervals to 17.8 mg or 35.6 mg once daily based on clinical response and tolerability. After the 3-week titration period, patients were maintained on a stable dosage of 8.9 mg, 17.8 mg, or 35.6 mg once daily for an additional 5 weeks.

[†]Secondary endpoint: Final mean daily rate of cataplexy at Week 8 compared with placebo (adjusted for baseline differences).¹ Evaluated in a subset of 49 patients with a history of cataplexy. Rate ratio 0.07 (95% CI 0.01, 0.36); results were statistically significant.¹

¹Statistical comparison of geometric mean values was not conducted.

ICSD-2, *International Classification of Sleep Disorders, Second Edition*.

Important Safety Information

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 (see full prescribing information).
- H₁ receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H₁ receptor antagonists.
- WAKIX is a borderline/weak inducer of CYP3A4. Therefore, reduced effectiveness of sensitive CYP3A4 substrates may occur when used concomitantly with WAKIX. The effectiveness of hormonal contraceptives may be reduced when used with WAKIX and effectiveness may be reduced for 21 days after discontinuation of therapy.

Established Safety and Tolerability Profile in Clinical Studies



- In the placebo-controlled clinical studies conducted in patients with narcolepsy with or without cataplexy, the most common adverse reactions (occurring in $\geq 5\%$ of patients and at least twice the rate of placebo) with the use of WAKIX were insomnia (6%), nausea (6%), and anxiety (5%)

Adverse Reactions That Occurred in $\geq 5\%$ of WAKIX-Treated Patients and More Frequently Than in Placebo-Treated Patients*		
Adverse Reaction	WAKIX (n=152)	Placebo (n=114)
Headache [†]	18%	15%
Insomnia [†]	6%	2%
Nausea	6%	3%
Upper respiratory tract infection [†]	5%	3%
Musculoskeletal pain [†]	5%	3%
Anxiety [†]	5%	1%

- Additional adverse reactions occurring in $\geq 2\%$ of WAKIX-treated patients and more frequently than in placebo-treated patients were heart rate increased,[†] hallucinations,[†] irritability, abdominal pain,[†] sleep disturbance,[†] decreased appetite, cataplexy, dry mouth, and rash[†]

*In three placebo-controlled clinical studies conducted in patients with narcolepsy with or without cataplexy.
[†]Denotes adverse reactions for which similar terms were combined.

Important Safety Information

Use in Specific Populations

- WAKIX may reduce the effectiveness of 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.
- 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 in patients less than 18 years of age.
- WAKIX is extensively metabolized by the liver. WAKIX is contraindicated in patients with severe hepatic impairment. Dosage adjustment is required 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 moderate or severe renal impairment.
- 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.

Connect with your local WAKIX representative at WAKIXhcp.com

Reference: 1. Data on file. Harmony Biosciences.



WAKIX is a registered trademark of Bioprojet Europe, Ltd.
 Harmony Biosciences name and logo are registered trademarks.
 © 2021 Harmony Biosciences. All rights reserved.
 US-WAK-2100037/Mar 2021

