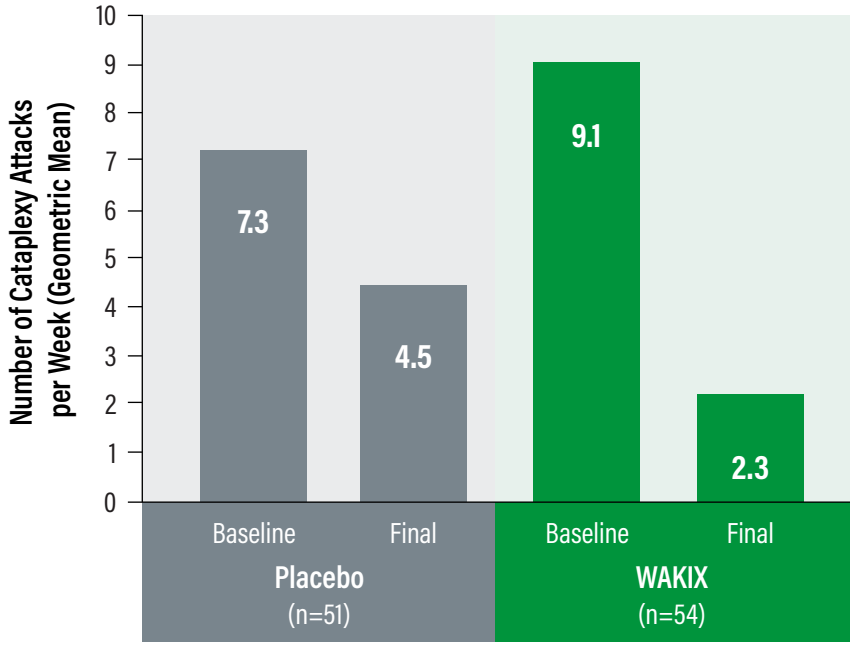
Wakix pitolisant tablets

WAKIX Resulted in Significantly Fewer Weekly Cataplexy Attacks Versus Placebo in Study 3

- 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

Study 3: Baseline and Final Mean Weekly Cataplexy Rate†



Patient population

- All patients had ≥3 cataplexy attacks per week at baseline
- 65% of all WAKIX-treated patients 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).[1] Rate ratio 0.51 (95% CI: 0.44, 0.60); results were statistically significant.[1] †Statistical comparison of geometric mean values was not conducted.

CI, confidence interval; ICSD-2, *International Classification of Sleep Disorders,* 2nd edition.

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

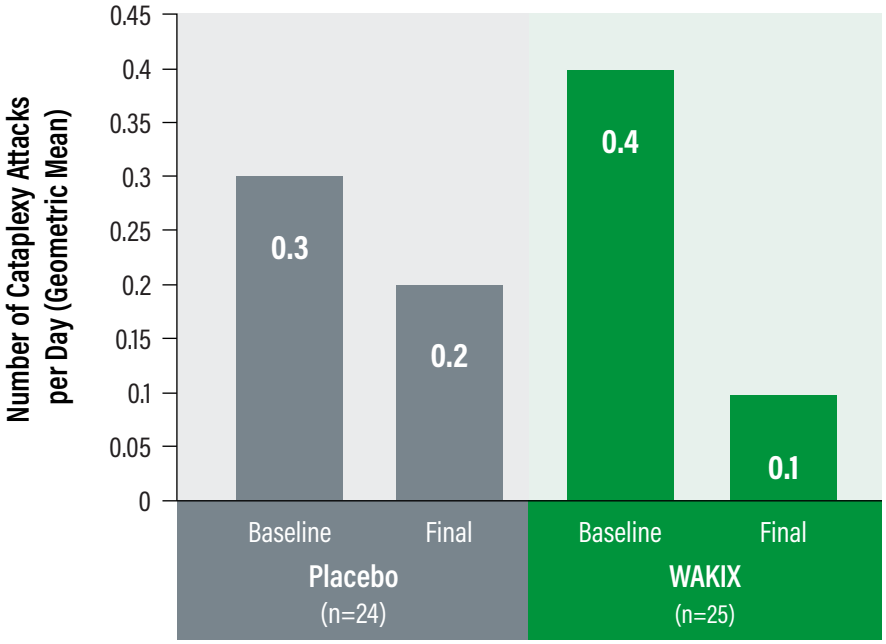
- WAKIX prolongs the QT interval. Avoid use of WAKIX in patients with known QT prolongation or in combination with other drugs known to prolong the QT interval. Avoid use in patients with a history of cardiac arrhythmias, as well as other circumstances that may increase the risk of the occurrence of torsade de pointes or sudden death, including symptomatic bradycardia, hypokalemia or hypomagnesemia, and the presence of congenital prolongation of the QT interval.

Wakix pitolisant tablets

WAKIX Resulted in Significantly Fewer Daily Cataplexy Attacks Versus Placebo in Study 1[1]

- 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

Study 1: Baseline and Final Mean Daily Cataplexy Rate[†]



Patient population

- Subset of 49 patients with a history of cataplexy
- 61% of all WAKIX-treated patients with or without cataplexy 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] †Statistical comparison of geometric mean values was not conducted.

CI, confidence interval; ICSD-2, *International Classification of Sleep Disorders,* 2nd edition.

Listen to Dr. Abhinav Singh, a sleep specialist, discuss the clinical study results for cataplexy in adult patients with narcolepsy

Important Safety Information

Warnings and Precautions

- 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

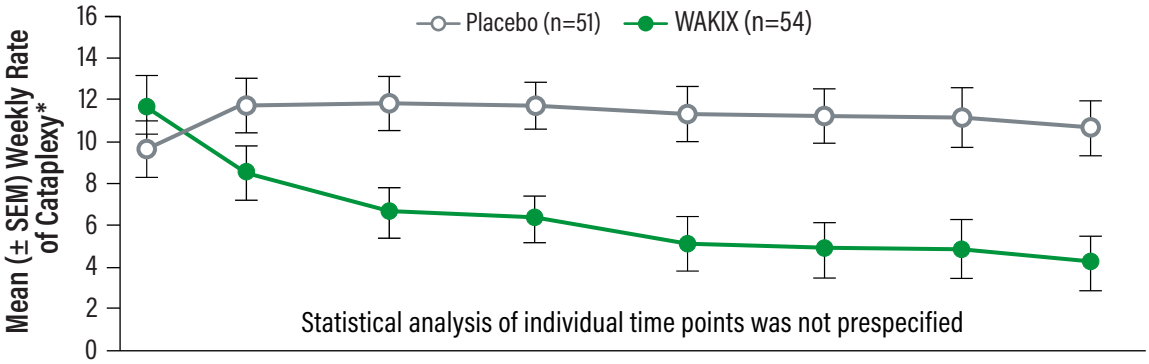
- Concomitant administration of WAKIX with strong CYP2D6 inhibitors increases pitolisant exposure by 2.2-fold. Reduce the dose of WAKIX by half.
- Concomitant use of WAKIX with strong CYP3A4 inducers decreases exposure of pitolisant by 50%. Dosage adjustments may be required.
- H_1 receptor antagonists 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.

Wakix pitolisant tablets

Post Hoc Analysis: Study 3

Reduction in Weekly Cataplexy Rate During the Study Period[2]

Study 3: Weekly Rate of Cataplexy From Baseline to Week 7[2]



	BL	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7
WAKIX Once-Daily Dose (%)	—	4.45 mg (100%)	8.9 mg (100%)	4.45 mg (1.9%) 8.9 mg (9.3%) 17.8 mg (88.9%)	8.9 mg (13%) 17.8 mg (16.7%) 35.6 mg (64.8%)			

Post hoc analysis of Study 3. Please see study design on front cover.

*Data are shown as mean at baseline and LS mean at other time points.[2]

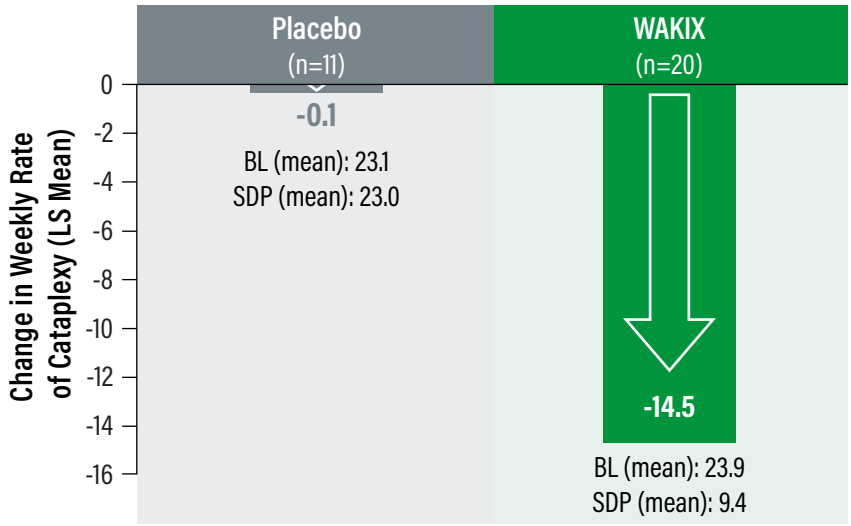
Adapted by permission from Springer Nature Customer Service Centre GmbH: Springer Nature *CNS Drugs.* Time to onset of response to pitolisant for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy: an analysis of randomized, placebo-controlled trials. Watson NF et al, 2021

BL, baseline; LS, least squares; SEM, standard error of the mean.

Post Hoc Analysis: Studies 1 & 3

Reduction in Weekly Cataplexy Rate in Patients With Severe Cataplexy at Baseline[3]

Mean Change in Weekly Cataplexy Rate† in Patients With ≥15 Cataplexy Attacks per Week at Baseline[3]



- Post hoc analysis of patients pooled from Studies 1 and 3. Statistical comparison of the treatment groups was not prespecified, and the sample size was small

Please see Study 1 study design on page 2 and Study 3 study design on front cover.

†LS mean change from baseline to stable dosing period.

BL, baseline; LS, least squares; SDP, stable dosing period.

Important Safety Information

Use in Specific Populations

- 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 eGFR <60 mL/minute/1.73 m2.
- Dosage reduction is recommended in patients known to be poor CYP2D6 metabolizers; these patients have higher concentrations of WAKIX than normal CYP2D6 metabolizers.

Wakix pitolisant tablets

Safety and Tolerability Profile in Narcolepsy Clinical Studies in Adult Patients

Clinical studies in adult patients with narcolepsy

- In the placebo-controlled clinical studies conducted in adult patients with narcolepsy with or without cataplexy, the most common adverse reactions (occurring in ≥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 Reaction	WAKIX (n=152)	Placebo (n=114)
Adverse Reactions That Occurred in ≥5% of WAKIX-Treated Patients and More Frequently Than in Placebo-Treated Patients*	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 ≥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 narcolepsy clinical studies in which WAKIX was directly compared with placebo, the incidence of patients who discontinued because of an adverse reaction was similar between the WAKIX and placebo groups (3.9% [n=6/152] vs 3.5% [n=4/114], respectively)

*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

- 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.

Visit WAKIXhcp.com for resources, real patient cases, and to download the WAKIX Prescription Referral Form

Adverse Reactions

- In the placebo-controlled phase of the clinical trial conducted in pediatric patients 6 years and older with narcolepsy with or without cataplexy, the most common adverse reactions (≥5% and greater than placebo) for WAKIX were headache (19%) and insomnia (7%). The overall adverse reaction profile of WAKIX in the pediatric clinical trial was similar to that seen in the adult clinical trial program.

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.

References
1. Data on file. Harmony Biosciences. **2.** Watson NF et al. *CNS Drugs.* 2021;35(12):1303-1315. **3.** Davis CW et al. *Sleep Med.* 2021;81:210-217.

HARMONY BIOSCIENCES