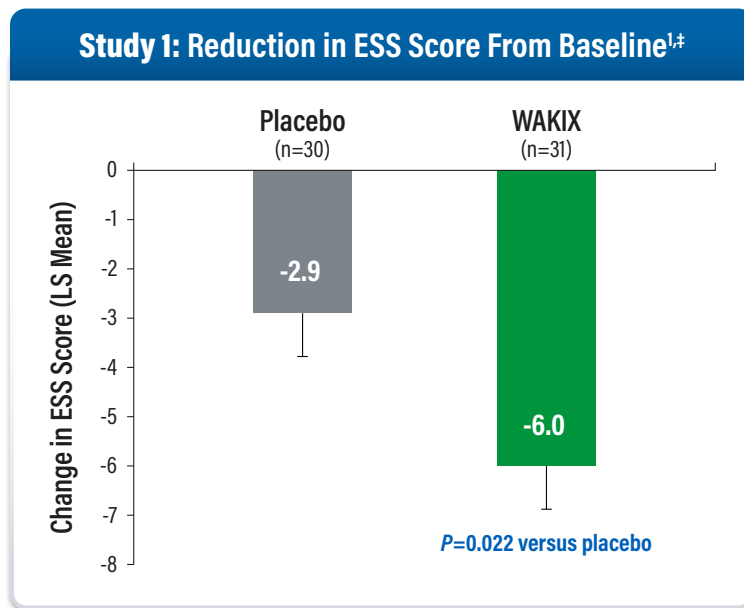


# WAKIX Significantly Reduced EDS Versus Placebo in Two Clinical Studies

Study 1: 35.6 mg once daily maximum potential dosage

- Primary endpoint: the final mean ESS score\* with WAKIX was 12.4 versus 15.5 with placebo (3.1-point difference,  $P=0.022$ )<sup>1,†</sup>
- WAKIX demonstrated a 6-point mean reduction in ESS score from baseline versus 2.9 points with placebo<sup>1,‡</sup>



## Patient population

- ICSD-2 diagnosis of narcolepsy including almost daily EDS for  $\geq 3$  months<sup>1</sup>
- Mean ESS scores at baseline reflected severe EDS<sup>2,§</sup>
  - WAKIX: 17.8
  - Placebo: 18.9
- 61% of all patients taking WAKIX reached a stable dosage of 35.6 mg once daily
- ~80% of patients had a history of cataplexy

**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.

\*Primary endpoint: LS mean final ESS score compared with placebo. Final values shown as LS mean of the final 2 weeks (Week 7 and Week 8).<sup>1</sup> Lower ESS score represents improvement; scores range from 0 (no symptoms) to 24 (worst symptoms).

<sup>†</sup>Placebo-subtracted difference (95% CI -5.73, -0.46).

<sup>‡</sup>LS mean change in ESS score from baseline to the mean of final 2 weeks (Week 7 and Week 8); adjusted mean ESS score at baseline was 18.4.<sup>1</sup>

<sup>§</sup>Baseline values shown as raw mean values.

EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; ICSD-2, *International Classification of Sleep Disorders*, Second Edition; LS, least square.

## 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.

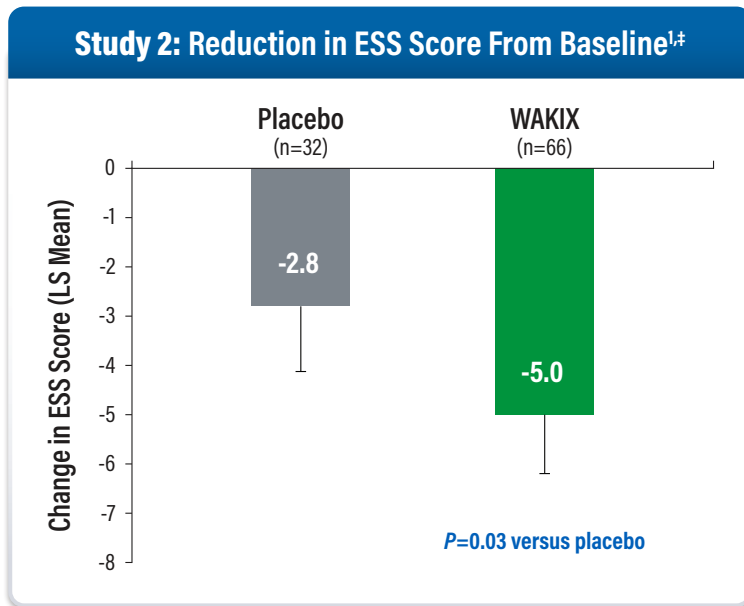
### Warnings and Precautions

- 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 Significantly Reduced EDS Versus Placebo in Two Clinical Studies

Study 2: 17.8 mg once daily maximum potential dosage

- Primary endpoint: the final mean ESS score\* with WAKIX was 13.3 versus 15.5 with placebo (2.2-point difference,  $P=0.03$ )<sup>1,†</sup>
- WAKIX demonstrated a 5-point mean reduction in ESS score from baseline versus 2.8 points with placebo<sup>1‡</sup>



## Patient population

- ICSD-2 diagnosis of narcolepsy including almost daily EDS for  $\geq 3$  months<sup>1</sup>
- Mean ESS scores at baseline reflected severe EDS<sup>2,§</sup>
  - WAKIX: 18.3
  - Placebo: 18.2
- 76% of all patients taking WAKIX reached a stable dosage of 17.8 mg once daily
- 75% of patients had a history of cataplexy

**Study 2:** 8-week, multicenter, randomized, double-blind, placebo-controlled study in 98 adults with narcolepsy with or without cataplexy (based on ICSD-2 criteria). WAKIX was initiated at 4.45 mg once daily and could be increased at weekly intervals to 8.9 mg or 17.8 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, or 17.8 mg once daily for an additional 5 weeks.

\*Primary endpoint: LS mean final ESS score compared with placebo. Final values shown as LS mean at Week 8. Lower ESS score represents improvement; scores range from 0 (no symptoms) to 24 (worst symptoms).

<sup>†</sup>Placebo-subtracted difference (95% CI -4.17, -0.22).

<sup>‡</sup>LS mean change in ESS score from baseline to Week 8; adjusted mean ESS score at baseline was 18.3.<sup>1</sup>

<sup>§</sup>Baseline values shown as raw mean values.

EDS, excessive daytime sleepiness; ESS, Epworth Sleepiness Scale; ICSD-2, *International Classification of Sleep Disorders*, Second Edition; LS, least square.

## 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).
- H<sub>1</sub> receptor antagonists that cross the blood-brain barrier may reduce the effectiveness of WAKIX. Patients should avoid centrally acting H<sub>1</sub> 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 <sup>†</sup>	18%	15%
Insomnia <sup>†</sup>	6%	2%
Nausea	6%	3%
Upper respiratory tract infection <sup>†</sup>	5%	3%
Musculoskeletal pain <sup>†</sup>	5%	3%
Anxiety <sup>†</sup>	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,<sup>†</sup> hallucinations,<sup>†</sup> irritability, abdominal pain,<sup>†</sup> sleep disturbance,<sup>†</sup> decreased appetite, cataplexy, dry mouth, and rash<sup>†</sup>

\*In three placebo-controlled clinical studies conducted in patients with narcolepsy with or without cataplexy.  
<sup>†</sup>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](http://www.fda.gov/medwatch).

Connect with your local WAKIX representative at [WAKIXhcp.com](http://WAKIXhcp.com)

References: 1. Data on file. Harmony Biosciences. 2. Johns M. About the ESS. The Epworth Sleepiness Scale. <https://epworthsleepinessscale.com/about-the-ess>. Accessed March 15, 2021.



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