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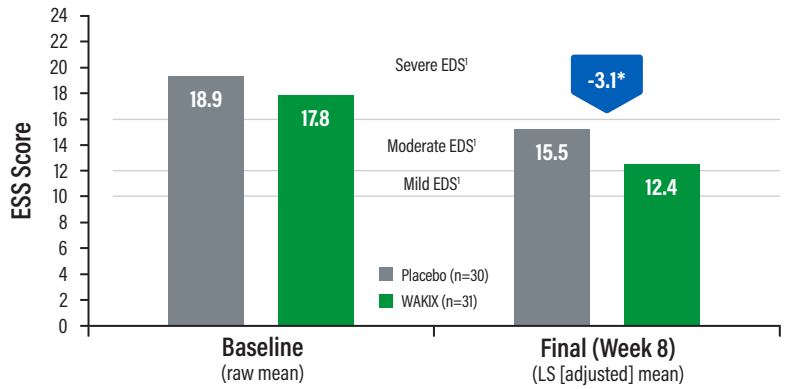
WAKIX® (pitolisant) Demonstrated Statistically Significant Improvement in EDS Versus Placebo in Two Clinical Studies

In Study 1, WAKIX demonstrated a 3.1-point* greater reduction in ESS score† versus placebo

Study 1: Baseline and Final (Week 8) Mean ESS Scores†



Patient population

- All patients had an Epworth Sleepiness Scale (ESS) score ≥14 at baseline
- 61% of patients reached a stable dosage of 35.6 mg once daily
- ~80% of patients had a history of cataplexy

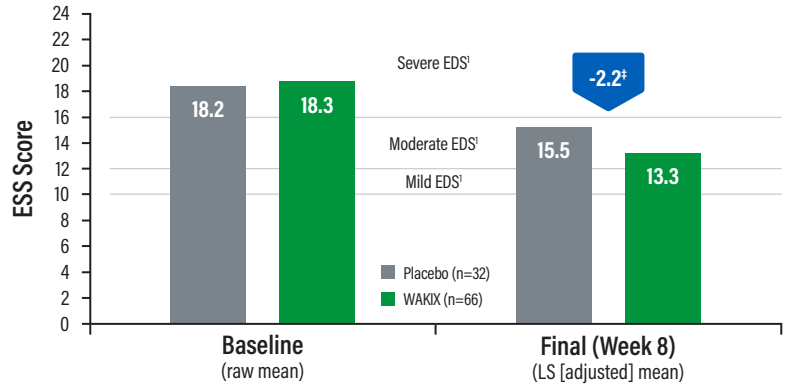
Study 1: 8-week, multicenter, randomized, double-blind, placebo-controlled study in 61 adults with narcolepsy (based on *International Classification of Sleep Disorders*, Second Edition [ICSD-2] criteria). WAKIX was initiated at 8.9 mg once daily and could be increased at weekly intervals to 17.8 mg or 35.6 mg once daily based on efficacy response and tolerability. Between Weeks 3 and 8, patients were maintained on a stable dosage of 8.9 mg, 17.8 mg, or 35.6 mg once daily.

*Placebo-subtracted difference (95% CI -5.73, -0.46); results were statistically significant.

†Lower ESS score represents improvement; scores range from 0 (no symptoms) to 24 (worst symptoms). Baseline values shown as raw mean values; final values shown as least square (LS) mean (e.g., adjusted for baseline).

In Study 2, WAKIX demonstrated a 2.2-point‡ greater reduction in ESS score§ versus placebo

Study 2: Baseline and Final (Week 8) Mean ESS Scores§



Patient population

- All patients had an ESS score ≥14 at baseline
- 76% of patients 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 (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 efficacy response and tolerability. Between Weeks 3 and 8, patients were maintained on a stable dosage of 4.45 mg, 8.9 mg, or 17.8 mg once daily.

‡Placebo-subtracted difference (95% CI -4.17, -0.22); results were statistically significant.

§Lower ESS score represents improvement; scores range from 0 (no symptoms) to 24 (worst symptoms). Baseline values shown as raw mean values; final values shown as least square (LS) mean (e.g., adjusted for baseline).

Indications and Usage

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

Important Safety Information

Contraindications

- WAKIX is 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).

Please see Important Safety Information continued on next page and accompanying Full Prescribing Information.

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Established Safety and Tolerability Profile in Clinical Studies

- In the clinical studies for narcolepsy, 172 patients were treated with WAKIX® (pitolisant) in placebo-controlled studies for up to 8 weeks and in open-label extension studies for up to 5 years
- In the placebo-controlled clinical studies conducted in patients with narcolepsy with or without cataplexy, the most common adverse reactions (occurring in ≥5% of patients and at twice the rate of placebo) with the use of WAKIX were insomnia (6%), nausea (6%), and anxiety (5%)

Adverse Reactions That Occurred in ≥2% of WAKIX-Treated Patients (n=152) and More Frequently Than in Placebo-Treated Patients* (n=114)

Headache†	18% vs 15%	Irritability	3% vs 2%
Insomnia†	6% vs 2%	Abdominal pain†	3% vs 1%
Nausea	6% vs 3%	Sleep disturbance†	3% vs 2%
Upper respiratory tract infection†	5% vs 3%	Decreased appetite	3% vs 0%
Musculoskeletal pain†	5% vs 3%	Cataplexy	2% vs 1%
Anxiety†	5% vs 1%	Dry mouth	2% vs 1%
Heart rate increased†	3% vs 0%	Rash†	2% vs 1%
Hallucinations†	3% vs 0%		

*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 (continued)

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.

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_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. 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.

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

Please see accompanying Full Prescribing Information.

Get your patients started on **WAKIX**. Visit **WAKIXHCP.com/oncedaily**.

Reference

1. Johns M. About the ESS. https://epworthsleepinessscale.com/about-the-ess/. Accessed August 11, 2019.

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