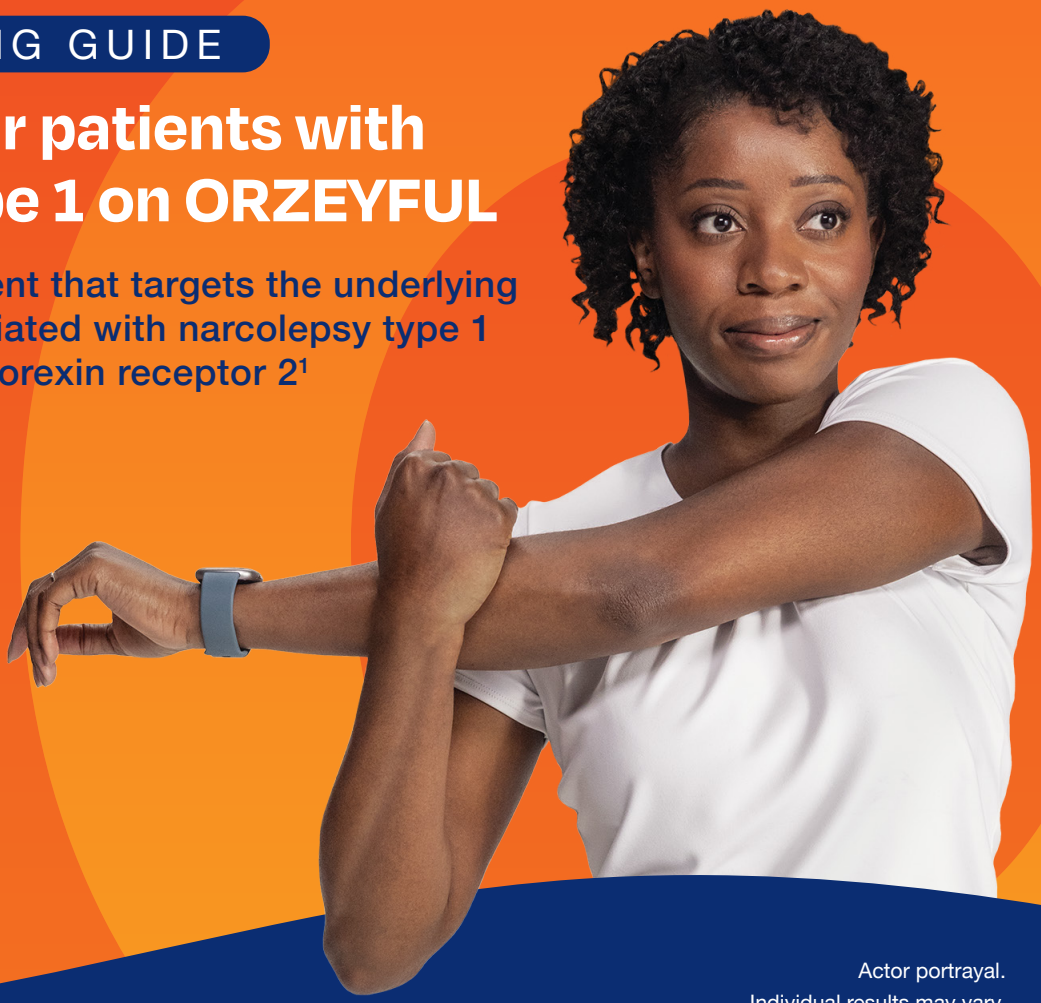
Orzeyful™
oveporexton tablets CIV

DOSING GUIDE

Starting your patients with narcolepsy type 1 on ORZEYFUL

The first and only treatment that targets the underlying orexin deficiency associated with narcolepsy type 1 by activating orexin receptor 2[1]



Actor portrayal.
Individual results may vary.
Medication may not be appropriate for all patients.

INDICATION

ORZEYFUL is indicated for the treatment of narcolepsy type 1 (narcolepsy with cataplexy) in adult patients.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ORZEYFUL is contraindicated in patients taking strong CYP3A inhibitors.

WARNINGS AND PRECAUTIONS

Insomnia: In pooled phase 3 studies in patients with NT1, 60%, 55%, and 1% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed insomnia. Prior to ORZEYFUL treatment initiation, inform patients about the risk of insomnia at initiation of treatment. If insomnia persists beyond 7 days and significantly impacts daytime functioning or quality of life, consider ORZEYFUL dosage reduction or discontinuation.

Please see additional Important Safety Information throughout this brochure, and click for full Prescribing Information.

ORZEYFUL dosing instructions for your patients with narcolepsy type 1 (NT1)[1]



Bottles contain 60 tablets. Drug tablet and bottle images are for illustrative purposes only and are not shown to actual size.

The recommended dosage of ORZEYFUL is 1 mg or 2 mg twice daily[1]

Daytime dosing—no nighttime administration required[1]

One oral tablet
Twice daily

WITH OR WITHOUT FOOD

FIRST TABLET: after awakening

SECOND TABLET: 3 to 5 hours later

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Urinary Frequency and Urgency: ORZEYFUL may cause or worsen urinary frequency and urgency. In pooled phase 3 studies in patients with NT1:

- 58%, 53%, and 5% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed urinary frequency.
- 16%, 15%, and 1% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed urinary urgency.

These lower urinary tract symptoms are consistent with ORZEYFUL's mechanism of action through agonism of the orexin receptor 2 (OX2R) on central micturition pathways. Prior to initiation of ORZEYFUL treatment, inform patients about the risk of urinary frequency and urgency and screen for lower urinary tract symptoms. Monitor ORZEYFUL-treated patients with a history of overactive bladder for worsening urinary tract symptoms.

Please see additional Important Safety Information throughout this brochure, and click for full Prescribing Information.

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Important dosing information to share with your patients[1]

- **Take ORZEYFUL tablets whole with water**
- **Do not split, crush, or chew ORZEYFUL tablets**
- **Do not exceed the ORZEYFUL maximum recommended dosage of 4 mg daily**
- **Take ORZEYFUL tablets at approximately the same time each day**

Guidance for patients who miss a dose[1]

- If a dose is missed, skip the missed dose and take the next dose at the regular time
- Do not take 2 doses at the same time

Dose modifications for patients taking CYP3A inhibitors[1]

- ORZEYFUL is contraindicated with strong CYP3A inhibitors
- If ORZEYFUL is used concomitantly with moderate CYP3A inhibitors, reduce ORZEYFUL dosage to 0.5 mg twice daily
  - Maximum recommended total dosage is 1 mg per day



ORZEYFUL should be stored at 68 °F to 77 °F (20 °C to 25 °C); excursions permitted from 59 °F to 86 °F (15 °C to 30 °C)[1]

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Creatine Phosphokinase Elevations: In pooled phase 3 studies in patients with NT1, asymptomatic creatine phosphokinase elevations >5x ULN were observed in 11% (21/196) of ORZEYFUL-treated patients and 5% (4/76) of placebo-treated patients. Two of these cases were characterized by markedly elevated CPK and transaminase levels; both patients discontinued treatment. None of the cases were associated with myoglobinuria or renal impairment. Advise patients to report unexplained muscle pain, weakness, or dark urine, particularly when engaging in vigorous physical activity or taking concomitant drugs associated with myotoxicity.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥5% and greater than placebo) reported in phase 3 studies with ORZEYFUL were insomnia, pollakiuria, micturition urgency, and salivary hypersecretion.

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Statistically significant improvement in wakefulness compared with placebo at both 1 mg and 2 mg doses at 12 weeks (*P*<0.001)[1,2]

As measured by Maintenance of Wakefulness Test (MWT)[1]

- ORZEYFUL was evaluated in two phase 3 randomized, multicenter, double-blind, placebo-controlled, 12-week, parallel-group studies[1]

Primary efficacy outcomes at 1 mg and 2 mg doses vs placebo[1,*†]

Change from baseline vs placebo at week 12[1]

	Treatment arm (n)	Baseline mean (SD)	LS mean difference from placebo (95% CI)
FirstLight Study	1 mg*† (61)	5.5 (7.7) minutes	**13.8 (10.2, 17.4)**
	2 mg*† (66)	4.4 (5.5) minutes	**17.2 (13.7, 20.7)**
	Placebo* (41)	5.1 (6.8) minutes	
RadiantLight Study	2 mg*† (70)	4.8 (4.9) minutes	**20.1 (16.6, 23.6)**
	Placebo* (35)	4.1 (4.9) minutes	

- MWT is a 40-minute test that measures an individual's ability to remain awake during the daytime in a darkened, quiet environment[1]

* Twice daily, at least 3 to 5 hours apart.
† Statistically significantly superior to placebo after adjusting for multiplicity.
LS=least squares; SD=standard deviation.

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS

- Concomitant use with strong or moderate CYP3A inhibitors increases oveporexton exposures, which may increase the risk of ORZEYFUL-associated adverse reactions
- Concomitant use of strong and moderate CYP3A inducers can increase oveporexton metabolism and decrease plasma levels of oveporexton, which may decrease the effectiveness of ORZEYFUL

USE IN SPECIFIC POPULATIONS

Pregnancy: There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to ORZEYFUL during pregnancy. Patients should be encouraged to enroll in the ORZEYFUL pregnancy registry if they become pregnant. To enroll or obtain information from the registry, patients can call 1-877-371-0309. Available data from clinical trials with ORZEYFUL use during pregnancy are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.

Lactation: There are no data available on the presence of oveporexton in human milk, the effects on the breastfed infant, or the effects on milk production. Animal studies indicate that oveporexton was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

Please see additional Important Safety Information throughout this brochure, and click for full Prescribing Information.

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Safety profile of ORZEYFUL across pivotal studies

Adverse reactions reported in ≥2% of patients treated with ORZEYFUL and greater than placebo in two phase 3 NT1 studies[1]

Adverse Reaction	Placebo (n=76) %	ORZEYFUL 1 mg* twice daily (n=60) %	ORZEYFUL 2 mg* twice daily (n=136) %
Insomnia†	1	55	60
Urinary frequency (pollakiuria)	5	53	58
Urinary urgency (micturition urgency)	1	15	16
Salivary hypersecretion	0	8	7
Influenza	1	5	3
Abdominal pain	0	3	1
Oropharyngeal pain	0	3	1
Paresthesia	0	2	2
Rash	0	0	3
Sinusitis	1	5	2

*The two ORZEYFUL doses were taken at least 3 hours apart with the second dose taken no later than 1 PM.
†Includes insomnia, middle insomnia, and initial insomnia.

For additional data,
scan the QR code or visit
orzeyfulhcp.com

IMPORTANT SAFETY INFORMATION (cont'd)

USE IN SPECIFIC POPULATIONS (cont'd)

Hepatic Impairment: Avoid use of ORZEYFUL in patients with severe hepatic impairment (Child-Pugh C), as it has not been studied in this population.

Renal Impairment: Avoid use of ORZEYFUL in patients with severe renal impairment on dialysis (eGFR <15 mL/minute), as it has not been studied in this population.

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CONSIDER STARTING YOUR APPROPRIATE PATIENTS

with NT1 on ORZEYFUL today

In two phase 3 studies, the primary and secondary endpoints showed statistically significant improvement at week 12 with both 1 mg (FirstLight Study) and 2 mg (both studies) doses compared with placebo ($P<0.001$)[1,2]



Start a patient

Visit orzeyfulhcp.com or scan the QR code

Actor portrayal.
Individual results may vary.
Medication may not be appropriate for all patients.

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG ABUSE AND DEPENDENCE

ORZEYFUL contains oveporexton, a Schedule IV controlled substance.

ORZEYFUL has potential for abuse and misuse. Carefully evaluate patients for a recent history of drug abuse, especially those with a history of CNS stimulant, and follow such patients closely, observing them for signs of misuse or abuse of ORZEYFUL.

Please see additional Important Safety Information throughout this brochure, and click for full Prescribing Information.

DOSAGE FORM AND STRENGTHS

- ORZEYFUL tablets: 0.5 mg, 1 mg, and 2 mg.

References: 1. ORZEYFUL (oveporexton tablets) prescribing information. Takeda Pharmaceuticals. **2.** Data on File. Takeda Pharmaceuticals.

Takeda

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