3 keys to treating with Orenitram®

A guide to starting patients on Orenitram, supporting a TID dosing schedule, and proactive adverse events management

Tablets not shown at actual size.

Dosage forms

5 tablet strengths for dosing flexibility with no labeled maximum dose[1]

Please see complete Important Safety Information on back cover and Full Prescribing Information and Patient Information for Orenitram in pocket.

orenitram®
treprostinil
EXTENDED-RELEASE TABLETS

1 Start low and titrate ~weekly[1]

- **Initiate** Orenitram at 0.125 mg TID[1]
- **Titrate ~weekly** in 0.125 mg TID increments to reach a dose of 3 mg TID by 6 months[1]*
- **Continue to elevate** dose to clinical response and tolerability[1]
  - **If needed, titrate down** or at a slower rate to manage side effects[1]

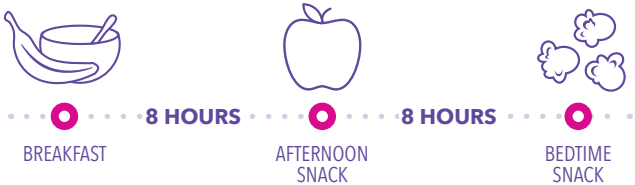
START	MONTH 1	MONTH 3	MONTH 6
0.125 mg TID	0.5 mg TID	1.5 mg TID	3 mg TID

Achieving a target dose of ≥3 mg TID was associated with greater improvement in 6MWD[2]

- Change in 6MWD was not statistically significant at week 24 for the ITT population[3]

2 Support a TID dosing schedule

Orenitram is best tolerated when taken every 8 hours. Provide patients with guidance on how to make Orenitram part of their daily schedule.[1]



A TID regimen (every 8 hours) may reduce peak-to-trough fluctuations[1]

INDICATION

Orenitram is a prostacyclin mimetic indicated for treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and to improve exercise capacity. The studies that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH (66%) or PAH associated with connective tissue disease (26%).

*You can also choose a BID (~12 hours apart) dosing schedule, starting at 0.25 mg BID and titrating in 0.25 mg BID increments as tolerated.[1]

6MWD=6-minute walk distance; BID=2 times daily; ITT=intent-to-treat; TID=3 times daily.

3 Proactively manage adverse events

Reassure patients that adverse events may be managed with adjunctive pharmacologic or nonpharmacologic treatment.[4]

Ensure that patients have prescriptions for adverse event management medications at time of referral.

General strategies for adverse event management[4]

Headache	Nausea	Diarrhea
• Analgesics	• Take with food • Antiemetics	• Add fiber to diet • Antidiarrheal medication

Based on a panel of respondents with expertise using Orenitram (N=11). In this independent analysis, the Delphi process was used to investigate best practices used by panelists for adverse event management in patients treated with Orenitram.[4]

Proactively managing adverse events may help your patients stay compliant with therapy[3,4]

United Therapeutics does not provide medical advice.
Side effect management strategies should be dealt with in accordance with the Orenitram Full Prescribing Information and your clinical judgment.

Advise patients to work with their specialty pharmacy for additional support with taking Orenitram

See more recommendations at **www.orenitram.com/hcp**

IMPORTANT SAFETY INFORMATION

Contraindications

- Avoid use of Orenitram in patients with severe hepatic impairment (Child Pugh Class C) due to increases in systemic exposure.

Please see additional Important Safety Information on back cover and Full Prescribing Information and Patient Information for Orenitram in pocket.

References: 1. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corporation; 2019. **2.** White RJ, Grünig E, Jerjes-Sanchez C, et al. Dose-response relationship of oral treprostinil for secondary endpoints in the FREEDOM-EV study. Poster presented at: European Respiratory Society International Congress; September 28-October 2, 2019; Madrid, Spain. **3.** Data on file. United Therapeutics Corporation. Research Triangle Park, NC. **4.** Rahaghi FF, Feldman JP, Allen RP, et al. Recommendations for the use of oral treprostinil in clinical practice: a Delphi consensus project pulmonary circulation. *Pulm Circ.* 2017;7(1):167-174.

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Warnings and Precautions

- Abrupt discontinuation or sudden large reductions in dosage of Orenitram may result in worsening of PAH symptoms.
- The Orenitram tablet shell does not dissolve. In patients with diverticulosis, Orenitram tablets can lodge in a diverticulum.

Adverse Reactions

- In the 12-week, placebo-controlled, monotherapy study, and an event-driven, placebo-controlled, combination therapy study, adverse reactions that occurred at rates at least 5% higher on Orenitram than on placebo included headache, diarrhea, nausea, vomiting, flushing, pain in jaw, pain in extremity, hypokalemia, abdominal discomfort, and upper abdominal pain.

Drug Interactions

- Co-administration of Orenitram and the CYP2C8 enzyme inhibitor gemfibrozil increases exposure to treprostinil; therefore, Orenitram dosage reduction may be necessary in these patients.

Specific Populations

- Animal reproductive studies with Orenitram have shown an adverse effect on the fetus. There are no adequate and well-controlled studies with Orenitram in pregnant women.
- It is not known whether treprostinil is excreted in human milk or if it affects the breastfed infant or milk production.
- Safety and effectiveness of Orenitram in pediatric patients have not been established.
- Use of Orenitram in patients aged 65 years and over demonstrated slightly higher absolute and relative adverse event rates compared to younger patients. Caution should be used when selecting a dose for geriatric patients.
- There is a marked increase in the systemic exposure to treprostinil in hepatically impaired patients.

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Please see Full Prescribing Information and Patient Information for Orenitram in pocket.

For additional information about Orenitram, visit www.orenitram.com or call 1-877-UNITHER (1-877-864-8437).

United Therapeutics CORPORATION

orenitram® treprostinil EXTENDED-RELEASE TABLETS