UPTRAVI® (selexipag) IV FREQUENTLY ASKED QUESTIONS

LEARN MORE ABOUT UPTRAVI® IV

For additional information, visit **UptraviHCP.com/iv** or **scan the QR code** to the left

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on page 11, and see full Prescribing Information.

Uptravi® (selexipag) for injection

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IV=intravenous.

When should UPTRAVI® IV be used in patients with PAH?

- UPTRAVI® IV is for the treatment of PAH (WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy[1]
- UPTRAVI® IV helps avoid treatment disruption by temporarily transitioning patients from UPTRAVI® Tablets to IV treatment and returning patients to UPTRAVI® Tablets when possible[1,2]
- UPTRAVI® IV is the intravenous formulation of selexipag[1]
- UPTRAVI® IV is not intended for treatment escalation, long-term use, self-administration, or for patients who are naïve to UPTRAVI® Tablets. Patients should return to UPTRAVI® Tablets once they are able to resume oral therapy[1,2]

For patients who are naïve to UPTRAVI® Tablets, can I initiate UPTRAVI® IV in the hospital?

- The study evaluating the pharmacokinetics and safety of UPTRAVI® IV did not include patients who were naïve to UPTRAVI®[2]
- UPTRAVI® IV was evaluated in a phase 3, prospective, multicenter, open-label, single-sequence crossover study with 20 patients, who switched from stable doses of UPTRAVI® Tablets to corresponding doses of UPTRAVI® IV[2]
- UPTRAVI® IV is for the treatment of PAH (WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy[1]
- Administer UPTRAVI® IV twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets.[1] Refer to Table 1 in the full Prescribing Information for more details

INDICATION

UPTRAVI® (selexipag) is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness of UPTRAVI® Tablets was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms.

Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), and PAH associated with congenital heart disease with repaired shunts (10%).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Concomitant use of strong inhibitors of CYP2C8 (eg, gemfibrozil) with UPTRAVI® is contraindicated.

Hypersensitivity to the active substance or to any of the excipients is contraindicated.

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV throughout and on page 11, and see full Prescribing Information.

FC=Functional Class; WHO=World Health Organization.

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Can I titrate with UPTRAVI® IV?

- The study evaluating the pharmacokinetics and safety of UPTRAVI® IV did not examine patients who were titrated with UPTRAVI® IV[2]
- UPTRAVI® IV was evaluated in a phase 3, prospective, multicenter, open-label, single-sequence crossover study with 20 patients, who switched from stable doses of UPTRAVI® Tablets to corresponding doses of UPTRAVI® IV[2]
- UPTRAVI® IV is for the treatment of PAH (WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy[1]
- Administer UPTRAVI® IV twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets.[1] Refer to Table 1 in the full Prescribing Information for more details

What is the difference between UPTRAVI® IV and VELETRI® (epoprostenol)?

- VELETRI® is indicated for the treatment of PAH (WHO Group I) to improve exercise capacity Studies establishing effectiveness included predominantly patients with FC III-IV symptoms[3]
- VELETRI® is administered by continuous intravenous infusion via a central venous catheter using an ambulatory infusion pump[3]
- As a reminder, UPTRAVI® is indicated for the treatment of PAH (WHO Group I, FC II-III) to delay disease progression and reduce the risk of hospitalization for PAH[1]
- UPTRAVI® IV is for the treatment of PAH (WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy[1]
- Patients can avoid treatment disruptions by temporarily transitioning from their current UPTRAVI® Tablets dose to UPTRAVI® IV treatment when unable to take oral therapy[1]

WARNINGS AND PRECAUTIONS

Pulmonary Edema with Pulmonary Veno-Occlusive Disease (PVOD)
Should signs of pulmonary edema occur, consider the possibility of associated PVOD. If confirmed, discontinue UPTRAVI®.

How should UPTRAVI® IV be stored prior to infusion?

- The original carton containing the UPTRAVI® IV glass vial should be stored in a refrigerator at 2 °C to 8 °C (36 °F to 46 °F) until use in order to protect from light[1]
- The UPTRAVI® infusion solution should be kept at room temperature (20 °C to 25 °C [68 °F to 77 °F])[1]

How long can UPTRAVI® IV be kept at room temperature?

- Before reconstitution and dilution, UPTRAVI® IV should be removed from the refrigerator and allowed to stand for approximately 30 to 60 minutes to reach room temperature (20 °C to 25 °C [68 °F to 77 °F])[1]
- After reconstitution and dilution, the UPTRAVI® infusion solution should also be kept at room temperature (20 °C to 25 °C [68 °F to 77 °F]). The solution must be infused within 4 hours from the first puncture of the vial stopper, including infusion time[1]

Can unused, reconstituted UPTRAVI® IV be saved for future use and/or infusion?

- UPTRAVI® IV vials are single doses, for single administration[1]
- All remaining reconstituted product must be discarded[1]

ADVERSE REACTIONS

Adverse reactions more frequent compared to placebo (≥3%) seen with UPTRAVI® Tablets are headache (65% vs 32%), diarrhea (42% vs 18%), jaw pain (26% vs 6%), nausea (33% vs 18%), myalgia (16% vs 6%), vomiting (18% vs 9%), pain in extremity (17% vs 8%), flushing (12% vs 5%), arthralgia (11% vs 8%), anemia (8% vs 5%), decreased appetite (6% vs 3%), and rash (11% vs 8%).

These adverse reactions are more frequent during the dose titration phase.

Hyperthyroidism was observed in 1% (n=8) of patients on UPTRAVI® Tablets and in none of the patients on placebo.

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV throughout and on page 11, and see full Prescribing Information.

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Dosing and Administration

What dose of UPTRAVI® IV should my patient receive?

- Administer UPTRAVI® IV twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets[1]
- Refer to table below or Table 1 in the full Prescribing Information to determine the corresponding UPTRAVI® IV dose

UPTRAVI® Tablets (twice daily)*	200 mcg	400 mcg	600 mcg	800 mcg	1000 mcg	1200 mcg	1400 mcg	1600 mcg
UPTRAVI® IV (twice daily infusions)	225 mcg	450 mcg	675 mcg	900 mcg	1125 mcg	1350 mcg	1575 mcg	1800 mcg

- Please see complete UPTRAVI® IV dosing, reconstitution, and dilution instructions as listed in the full Prescribing Information

How is UPTRAVI® IV administered?

- Administer UPTRAVI® IV twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets[1]
- For complete instructions on how to prepare, reconstitute, and dilute UPTRAVI® IV before administration, please refer to the UPTRAVI® full Prescribing Information or the UPTRAVI® IV Instructions For Use at UptraviHCP.com/iv

DRUG INTERACTIONS

CYP2C8 Inhibitors

Concomitant administration with gemfibrozil, a strong inhibitor of CYP2C8, doubled exposure to selexipag and increased exposure to the active metabolite by approximately 11-fold. Concomitant use of UPTRAVI® with strong inhibitors of CYP2C8 is contraindicated.

Concomitant administration of UPTRAVI® with clopidogrel, a moderate inhibitor of CYP2C8, had no relevant effect on the exposure to selexipag and increased the exposure to the active metabolite by approximately 2.7–fold. Reduce the dosing of UPTRAVI® to once daily in patients on a moderate CYP2C8 inhibitor.

*Once daily for patients with moderate hepatic impairment and co-administration with moderate CYP2C8 inhibitors.[1]

How long can patients stay on UPTRAVI® IV?

- UPTRAVI® IV is for the treatment of PAH (WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy[1]
- Patients should return to UPTRAVI® Tablets once they are able to resume oral therapy[2]

How do patients transition back to UPTRAVI® Tablets?

- Patients can return to their UPTRAVI® Tablets dose once they are able to take oral therapy, without the need to re-titrate[1,2]
- Refer to table below or Table 1 in the full Prescribing Information to determine the corresponding UPTRAVI® IV dose

UPTRAVI® Tablets (twice daily)*	200 mcg	400 mcg	600 mcg	800 mcg	1000 mcg	1200 mcg	1400 mcg	1600 mcg
UPTRAVI® IV (twice daily infusions)	225 mcg	450 mcg	675 mcg	900 mcg	1125 mcg	1350 mcg	1575 mcg	1800 mcg

DRUG INTERACTIONS (continued)

CYP2C8 Inducers

Concomitant administration with an inducer of CYP2C8 and UGT 1A3 and 2B7 enzymes (rifampin) halved exposure to the active metabolite. Increase UPTRAVI® dose, up to twice, when co-administered with rifampin. Reduce UPTRAVI® when rifampin is stopped.

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV throughout and on page 11, and see full Prescribing Information.

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Pharmacokinetics and Safety

Can my patients expect to receive the same efficacy as UPTRAVI® Tablets with the intravenous formulation?

- There was a phase 3, prospective, multicenter, open-label, single-sequence crossover study evaluating the pharmacokinetics and safety of UPTRAVI® IV[2]
- In this study, 20 patients with PAH in FC I-III receiving stable doses of UPTRAVI® Tablets for at least 28 days switched to corresponding doses of UPTRAVI® IV[2]
  – Note that in the study, 1 patient (5%) was in FC I
- These patients were monitored to assess the safety, tolerability, and pharmacokinetics (including exposure to the active metabolite) of switching from a stable dose of UPTRAVI® Tablets to a corresponding dose of UPTRAVI® IV and back to UPTRAVI® Tablets[2]
- Results demonstrated a comparable exposure to the active metabolite following UPTRAVI® Tablets and UPTRAVI® IV administration. Time to maximum concentration of the active metabolite was comparable as well[2]
- It is assumed that achieving similar exposure to the active metabolite following either UPTRAVI® IV or UPTRAVI® Tablets use will result in comparable efficacy[2]
- Similar maintenance of UPTRAVI® efficacy and safety can be expected, with the exception of infusion-site reactions, when temporarily using UPTRAVI® IV in the hospital[1,2]
- As a reminder, UPTRAVI® is indicated for the treatment of PAH (WHO Group I, FC II-III) to delay disease progression and reduce the risk of hospitalization for PAH[1]
- Patient tolerability was similar between UPTRAVI® IV and Tablets, with the exception of infusion-site reactions[1,2]
- Infusion-site reactions (infusion-site erythema/redness, pain, and swelling) were reported with UPTRAVI® IV[1]

DOSAGE AND ADMINISTRATION

Recommended Dosage

Recommended starting dose is 200 mcg twice daily for UPTRAVI® Tablets. Tolerability may be improved when taken with food. Increase by 200 mcg twice daily, usually at weekly intervals, to the highest tolerated dose up to 1600 mcg twice daily. If dose is not tolerated, reduce to the previous tolerated dose.

Are my patients getting the same dose of selexipag on UPTRAVI® IV?

- There was a phase 3, prospective, multicenter, open-label, single-sequence crossover study evaluating the pharmacokinetics and safety of UPTRAVI® IV[2]
- In this study, the dosing regimen for UPTRAVI® IV was selected to help patients achieve similar exposure to the active metabolite when compared with UPTRAVI® Tablets[2]
- Based on the pharmacokinetic assessments conducted, IV doses that were 12.5% higher than the corresponding oral doses provided comparable exposure to the active metabolite following UPTRAVI® Tablets and UPTRAVI® IV administration[2]
- Refer to Table 1 in the full Prescribing Information to learn more about corresponding UPTRAVI® IV and UPTRAVI® Tablets dosing
- For additional information about the study, please visit UptraviHCP.com/iv

How is UPTRAVI® IV tolerated in patients with PAH?

- The transition from UPTRAVI® Tablets to UPTRAVI® IV and back was well tolerated[2]
- Patient tolerability was similar between UPTRAVI® IV and Tablets, with the exception of infusion-site reactions[1,2]
- 10% of patients reported infusion-site reactions during UPTRAVI® IV administration, including infusion-site erythema/redness, pain, and swelling[1,2]

DOSAGE AND ADMINISTRATION (continued)

Patients With Hepatic Impairment

For patients with moderate hepatic impairment (Child-Pugh class B), the starting dose of UPTRAVI® Tablets is 200 mcg once daily. Increase by 200 mcg once daily at weekly intervals, as tolerated. Avoid use of UPTRAVI® in patients with severe hepatic impairment (Child-Pugh class C).

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV throughout and on page 11, and see full Prescribing Information.

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Pricing

What is the price of UPTRAVI® IV?

- Please contact CuraScript SD for pricing information
  - **Phone:** (877) 900-9223
  - www.curascriptsd.com

Medical Information

If you require immediate assistance or wish to report a side effect or product complaint, Janssen Medical Information can be reached by phone at 1-800-JANSSEN (1-800-526-7736) Monday-Friday, 9 AM - 8 PM ET.

PHONE

Please call: 1-800-JANSSEN (1-800-526-7736)
Monday-Friday, 9 AM - 8 PM ET.

MAIL

Janssen Scientific Affairs Medical Information Center
PO Box 200
Titusville, NJ 08560

Important Safety Information (continued)

DOSAGE AND ADMINISTRATION (continued)

Co-administration With Moderate CYP2C8 Inhibitors
When co-administered with moderate CYP2C8 inhibitors (eg, clopidogrel, deferasirox and teriflunomide), reduce the dosing of UPTRAVI® to once daily.

Dosage Strengths
UPTRAVI® tablet strengths:
200, 400, 600, 800, 1000, 1200, 1400, and 1600 mcg.

Additional Important Safety Information for UPTRAVI® IV

Use UPTRAVI® for injection in patients who are temporarily unable to take oral therapy.

Administer UPTRAVI® for injection twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets (see Table 1 in full Prescribing Information). Administer UPTRAVI® for injection as an 80-minute intravenous infusion.

Adverse Reactions: Infusion-site reactions (infusion-site erythema/redness, pain and swelling) were reported with UPTRAVI® for injection.

Please see full Prescribing Information.

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LEARN MORE ABOUT UPTRAVI® IV

For additional information, visit **UptraviHCP.com/iv** or **scan the QR code** to the left

References: 1. UPTRAVI® (selexipag) full Prescribing Information. Actelion Pharmaceuticals US, Inc. **2.** Klose H, Chin KM, Ewert R, et al. Temporarily switching from oral to intravenous selexipag in patients with pulmonary arterial hypertension: safety, tolerability, and pharmacokinetic results from an open-label, phase III study. *Respir Res*. 2021;22(1):34. doi:10.1186/s12931-020-01594-8 **3.** VELETRI® (epoprostenol) for Injection full Prescribing Information. Actelion Pharmaceuticals US, Inc.

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on page 11, and see full Prescribing Information.

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