UPTRAVI® (selexipag) IV
INSTRUCTIONS FOR USE

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 pages 10 and 11, and see full Prescribing Information.

Uptravi® (selexipag) for injection

Table of Contents

Storage and Handling[1]

UPTRAVI® IV vials are single doses, for single administration. All remaining reconstituted product must be discarded.

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.

The UPTRAVI® infusion solution must be infused within 4 hours from the first puncture of the vial stopper (including infusion time).

IV=intravenous.

UPTRAVI® IV is for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) in FC II-III patients who are temporarily unable to take oral therapy.

Administer UPTRAVI® IV twice daily by intravenous infusion at a dose that corresponds to the patient's current dose of UPTRAVI® Tablets (see table below or Table 1 in the full Prescribing Information). Patients should return to UPTRAVI® Tablets once they are able to resume oral therapy. Re-titration can be bypassed when transitioning between UPTRAVI® IV and UPTRAVI® Tablets.

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

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 on pages 10 and 11, and see full Prescribing Information.

FC=Functional Class; WHO=World Health Organization.

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

Uptravi® (selexipag) for injection

Reconstitution[1]

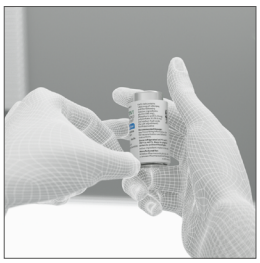
Reconstitute and further dilute UPTRAVI® IV prior to intravenous infusion following aseptic procedures.

1

Remove the carton of UPTRAVI® IV from the refrigerator

- Allow the vial to stand for approximately **30 to 60 minutes** to reach **room temperature (20 °C to 25 °C [68 °F to 77 °F])**

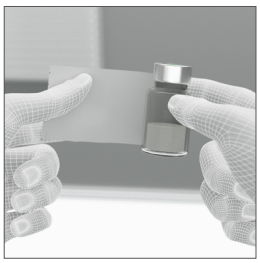
2



The vial needs to be protected from light at all times

- Ensure the protective wraparound label is covering the entire vial

3



Peel back the light protective wrap on the vial to inspect its contents

- UPTRAVI® IV should appear to be a white to almost white, broken cake or powdered material
- **Immediately close the light protective wrap** on the vial

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on pages 10 and 11, and see full Prescribing Information.

4

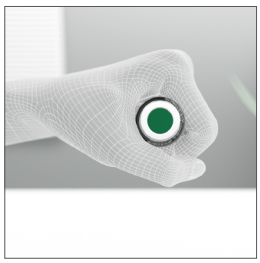
Reconstitute UPTRAVI® IV using a polypropylene syringe with 8.6 mL of 0.9% Sodium Chloride Injection, USP and slowly inject the syringe into the UPTRAVI® IV vial with the stream directed toward the inside wall of the vial to obtain a concentration of 225 mcg/mL of selexipag

5

Document the date and time of the first puncture

- Complete the infusion **within 4 hours of the first puncture**

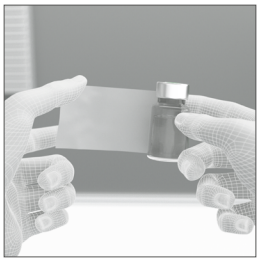
6



Gently invert the vial and repeat until the powder is completely dissolved

⚠ DO NOT SHAKE

7



After gently mixing, inspect the vial by peeling back the light protective wraparound label and check for discoloration

- The reconstituted solution should appear **clear, colorless, and free from foreign material**
- Do not use if the reconstituted solution is discolored, cloudy, or contains visible particles

Uptravi® (selexipag) for injection

Dilution[1]

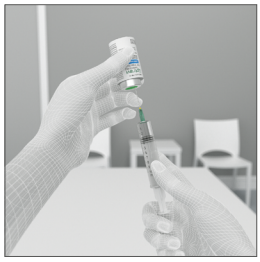
8

UPTRAVI® IV must be diluted in glass containers only

9

Withdraw 100 mL of 0.9% Sodium Chloride Injection, USP and transfer the contents of the syringe into an empty, sterile glass container

10



Withdraw the required volume of reconstituted solution from the UPTRAVI® IV vial using a single, appropriately-sized polypropylene syringe

- See table below or Table 1 in the full Prescribing Information for the reconstituted transfer volume

Dosing Table for UPTRAVI® IV Based on Current UPTRAVI® Tablets Dose

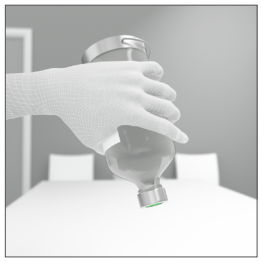
UPTRAVI® Tablets dose (mcg) for twice daily dosing	200	400	600	800	1000	1200	1400	1600
Corresponding UPTRAVI® IV dose (mcg) for twice daily dosing	225	450	675	900	1125	1350	1575	1800
Reconstituted transfer volume (mL) for dilution	1.0	2.0	3.0	4.0	5.0	6.0	7.0	8.0

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on pages 10 and 11, and see full Prescribing Information.

11

Dilute into the glass container containing 100 mL of 0.9% Sodium Chloride Injection, USP to obtain the desired final dose

12



Mix the diluted UPTRAVI® infusion solution by gently inverting the glass container 5 times

DO NOT SHAKE

13

Protect diluted UPTRAVI® infusion solution from light at all times. Assign a 4-hour expiry from the time of first vial puncture

Uptravi® (selexipag) for injection

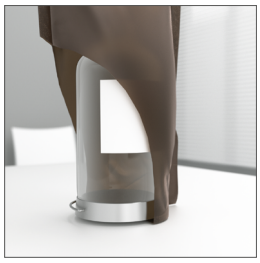
Dilution (continued)[1]

14

Be sure to wrap the container completely with a light protective cover

- The UPTRAVI® infusion solution should 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

15



Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration

- The diluted UPTRAVI® infusion solution should be **clear and colorless**
- Discard if particulate matter is observed
- UPTRAVI® IV vials are single doses, for single administration. All remaining reconstituted product must be discarded

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on pages 10 and 11, and see full Prescribing Information.

Administration

UPTRAVI® IV should be administered twice daily and the dose is determined by the patient's current dose of UPTRAVI® Tablets (see table on page 6 or Table 1 in the full Prescribing Information).

- Administer by intravenous infusion over 80 minutes using an infusion set made of DEHP-free polyvinyl chloride (PVC), natural latex rubber-free microbore tubing protected from light
- **Do not use a filter for administration**
- Once the solution-for-infusion glass container is empty, continue the infusion at the same rate with 0.9% saline to empty the remaining solution for infusion in the IV line. This is to ensure that the entire solution for infusion has been administered

Important Safety Information

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.

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®.

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.

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.

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.

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.

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).

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.

cp-126160v5

Uptravi® (selexipag) for injection

Uptravi® (selexipag) for injection

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

Please see Important Safety Information for UPTRAVI® Tablets and UPTRAVI® IV on pages 10 and 11, and see full Prescribing Information.

Janssen
PHARMACEUTICAL COMPANIES OF
Johnson & Johnson