SELEXIPAG

Generic	Brand	HICL	GCN	Exception/Other
SELEXIPAG	UPTRAVI	42922		

***********Customer Service/PAC Alert************
(For Internal Use Only)

THIS IS A HIGH-IMPACT MEDICATION. DO NOT OVERRIDE OR APPROVE WITHOUT SUBMITTING FOR PHARMACIST REVIEW.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1) and meets **ALL** of the following criteria?
   - The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
   - Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
     - Pulmonary capillary wedge pressure (PCWP) of ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) of > 3 Wood units
   - Patient has NYHA-WHO Functional Class II-IV symptoms

   If yes, **approve for 12 months by GPID for the requested strength with the following quantity limits:**
   - **Uptravi 200mcg tablets (GPID: 40355): #8 tablets per day**
   - **Uptravi 400mcg tablet (GPID: 40356): #2 tablets per day**
   - **Uptravi 600mcg tablet (GPID: 40357): #2 tablets per day**
   - **Uptravi 800mcg tablet (GPID: 40358): #2 tablets per day**
   - **Uptravi 1,000mcg tablet (GPID: 40359): #2 tablets per day**
   - **Uptravi 1,200mcg tablet (GPID: 40374): #2 tablets per day**
   - **Uptravi 1,400mcg tablet (GPID: 40375): #2 tablets per day**
   - **Uptravi 1,600mcg tablet (GPID: 40376): #2 tablets per day**
   - **Uptravi 200-800 Titration pack (GPID: 40378): #1 pack per 12 months**

   If no, do not approve.
   DENIAL TEXT: The guideline for **SELEXIPAG (Uptravi)** requires a diagnosis of pulmonary arterial hypertension. The following criteria must also be met:
   (Denial text continued on next page)

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INITIAL CRITERIA (CONTINUED)

- The requested medication is prescribed by or given in consultation with a cardiologist or pulmonologist
- Documented confirmatory PAH diagnosis based on right heart catheterization with the following parameters:
  - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg
  - Pulmonary capillary wedge pressure (PCWP) of ≤ 15 mmHg
  - Pulmonary vascular resistance (PVR) of > 3 Wood units
- The patient has NYHA-WHO Functional Class II-IV symptoms

RENEWAL CRITERIA

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) (WHO Group 1)?

   If yes, continue to #2.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

2. Has the patient shown improvement from baseline in the 6-minute walk distance test?

   If yes, **approve for 12 months by GPID for the requested strength with the following quantity limits:**
   - **Uptravi 200mcg tablets (GPID: 40355): #8 tablets per day**
   - **Uptravi 400mcg tablet (GPID: 40356): #2 tablets per day**
   - **Uptravi 600mcg tablet (GPID: 40357): #2 tablets per day**
   - **Uptravi 800mcg tablet (GPID: 40358): #2 tablets per day**
   - **Uptravi 1,000mcg tablet (GPID: 40359): #2 tablets per day**
   - **Uptravi 1,200mcg tablet (GPID: 40374): #2 tablets per day**
   - **Uptravi 1,400mcg tablet (GPID: 40375): #2 tablets per day**
   - **Uptravi 1,600mcg tablet (GPID: 40376): #2 tablets per day**

   If no, continue to #3.

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RENEWAL CRITERIA (CONTINUED)

3. Has the patient remained stable from baseline in the 6-minute walk distance test?

   If yes, continue to #4.
   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

4. Has the patients WHO functional class remained stable or has improved?

   If yes, **approve for 12 months by GPID for the requested strength with the following quantity limits:**
   - **Uptravi 200mcg tablets (GPID: 40355): #8 tablets per day**
   - **Uptravi 400mcg tablet (GPID: 40356): #2 tablets per day**
   - **Uptravi 600mcg tablet (GPID: 40357): #2 tablets per day**
   - **Uptravi 800mcg tablet (GPID: 40358): #2 tablets per day**
   - **Uptravi 1,000mcg tablet (GPID: 40359): #2 tablets per day**
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   - **Uptravi 1,400mcg tablet (GPID: 40375): #2 tablets per day**
   - **Uptravi 1,600mcg tablet (GPID: 40376): #2 tablets per day**

   If no, do not approve.
   DENIAL TEXT: See the renewal denial text at the end of the guideline.

RENEWAL DENIAL TEXT: The guideline for **SELEXIPAG (Uptravi)** requires a diagnosis of pulmonary arterial hypertension for renewal. The following criteria must also be met:
- The patient has shown improvement from baseline in the 6-minute walk distance test **OR**
- The patient has a stable 6-minute walk distance test with a stable or improved WHO functional class

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RATIONALE
Promote appropriate utilization of **SELEXIPAG** based on FDA approved indication.

Pulmonary arterial hypertension (PAH) is a chronic, progressive, and debilitating rare lung disease that can lead to death or the need for lung transplantation. The currently available therapeutic options to treat patients with PAH include endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE-5i), soluble guanylate cyclase stimulators, and prostacyclin receptor agonists. Uptravi will be the second oral prostacyclin agent for PAH, joining Orenitram (treprostinil), although unlike the other prostacyclin agents it is selective for the IP receptor. Inhaled, subcutaneous and intravenously administered forms of prostacyclins are often reserved for more severe/progressive PAH patients.

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RATIONALE (CONTINUED)

Guidelines recommend a confirmatory diagnosis of PAH based on right heart catheterization. Optimal therapy for a PAH patient is a highly individualized clinical decision considering several factors such as severity of illness, route of administration, side effects, comorbidities, treatment goals. Baseline severity should be determined prior to initiation of therapy and this is done using the World Health Organization functional classifications (WHO-FC), which categorizes patients into four classes (I-IV) based on symptoms and tolerance of physical activity. The overall treatment goals are to address underlying etiology, improve symptoms/exercise capacity (achieve a low risk status [FC I or II]), prevent progression of disease, and improve survival and quality of life. The currently available oral therapeutic options to treat patients with PAH include endothelin receptor antagonists (ERAs), phosphodiesterase-5 inhibitors (PDE-5i), soluble guanylate cyclase stimulators, and prostacyclin receptor agonists (Orenitram). Monotherapy with an oral drug is recommended for initial treatment of PAH and this can include an ERA or PDE-5i, which are typically first line, or a soluble guanylate cyclase stimulator. For those patients with advanced disease (WHO-FC III- IV), an inhaled, subcutaneous or intravenous prostacyclin may also be considered. Current US guidelines recommend treatment with two or more classes of PAH drugs only when the response is inadequate or the patient deteriorates on monotherapy, but recently published European guidelines include recommendations for initial combination therapy. Although there is limited data available on the effectiveness of combination therapy for initial treatment of PAH, the combination therapy of agents with different mechanisms of action may become preferred over monotherapy due to recent data demonstrating a benefit in morbidity/mortality.

The efficacy of Uptravi was demonstrated in the Phase III GRIPHON trial that showed Uptravi significantly reduced the risk of morbidity/mortality events versus placebo by 40% (HR 0.60; 99% CI: 0.46,0.78, p<0.001) primarily attributable to a reduction in hospitalization and a reduction in other disease progression events (worsening FC, decrease in 6MWD, or need for other PAH therapy). The treatment effect was consistent across baseline functional class, background PAH therapy subgroups, and regardless of dose achieved.

DOSAGE

The starting dose of Uptravi is 200mcg by mouth twice daily and increased in increments of 200 mcg twice daily, usually at weekly intervals, to the highest tolerated dose up to 1600mcg twice daily. The target dose will be individualized based on patient tolerability and tolerability may be improved with food. In addition, a dose reduction should be made in patients that reach a dose that cannot be tolerated.

For patients with moderate hepatic impairment (Child-Pugh class B), the starting dose of Uptravi is 200 mcg once daily. Increase in increments of 200 mcg once daily at weekly intervals, as tolerated.

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FDA APPROVED INDICATION

Uptravi is a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

AVAILABLE STRENGTHS

- 200 microgram tablet
- 400 microgram tablet
- 600 microgram tablet
- 800 microgram tablet
- Titration pack: 140 count bottle of 200 microgram tablets and a 60 count bottle of 800 microgram tablets
- 1000 microgram tablet
- 1200 microgram tablet
- 1400 microgram tablet
- 1600 microgram tablet

REFERENCES

- Uptravi [Prescribing Information]; San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2017.
- FDA Press Release [Online Press Release]: FDA approves new orphan drug to treat pulmonary arterial hypertension. Access here: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm478599.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery
- PAH Info. How common is PAH (2013). Actelion Pharmaceuticals. Access here: http://www.pah-info.com/How_common_is_PAH
- Taichman DB, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults: CHEST guideline and expert panel report. CHEST 2014 Aug; 146(2):449-75.
- Galie N, et al. Updated treatment algorithm of pulmonary arterial hypertension. J Am Coll Cardiol. 2013 Dec 24; 62(25 Suppl): D60-72.
- Galie N, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS). Eur Respir J. 2015 Dec; 46(6):1855-6.

Library	Commercial	NSA
Yes	Yes	No

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