HARVARD PILGRIM HEALTH CARE
RECOMMENDED MEDICATION REQUEST GUIDELINES

PULMONARY ARTERIAL HYPERTENSION

Generic	Brand	HICL	GCN	Exception/Other
AMBRISENTAN	LETAIRIS	34849		
BOSENTAN	TRACLEER	22990		
MACITENTAN	OPSUMIT	40677		
RIOCIGUAT	ADEMPAS	40644		
SELEXIPAG	UPTRAVI	42922		
SILDENAFIL	REVATIO SILDENAFIL			STC = A819
TADALAFIL	ADCRICA TADALAFIL			STC = A819
TREPROSTINIL	ORENITRAM ER	40827		

If the caller wishes to initiate a request then a MRF must be completed. This drug requires a written request for prior authorization. All requests for high-impact medications require review by a pharmacist prior to final approval.

NOTE: sildenafil and tadalafil are not high-impact medications and do not require a pharmacist review prior to final approval.

GUIDELINES FOR USE

INITIAL CRITERIA (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

PHOSPHODIESTERASE-5 INHIBITORS: SILDENAFIL (REVATIO), TADALAFIL (ADCIRCA)

1. Does the patient meet **ONE** of the following conditions?
   - Diagnosis of Raynaud's Syndrome or scleroderma **OR**
   - Diagnosis of Pulmonary Arterial Hypertension (PAH) - World Health Organization (WHO) Group 1 diagnosis, and **ALL** of the following:
     - o Prescribed by, or in consultation with, a cardiologist or pulmonologist
     - o Diagnosis confirmed by right heart catheterization with **AT LEAST ONE** of the following parameters:
       - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
       - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
       - Pulmonary vascular resistance (PVR) > 3 wood units

   If yes, **approve open-ended by GPID.** Please use status code #050 and the approval text provided.

   APPROVAL TEXT: Your request for **[drug name]** has been approved as requested.
   If no, do not approve.

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INITIAL CRITERIA (CONTINUED)

DENIAL TEXT: Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for members who meet ONE of the following conditions:

- Diagnosis of Raynaud's Syndrome or Scleroderma OR
- Diagnosis of Pulmonary Arterial Hypertension (PAH) AND all of the following criteria:
  - Prescribed by, or in consultation with, a cardiologist or pulmonologist
  - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with at least one of the following parameters:
    - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
    - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
    - Pulmonary vascular resistance (PVR) > 3 Wood units

Your provider did not submit information that you meet these criteria, specifically **[criteria not met]** and therefore your request was not approved.

ENDOTHELIN RECEPTOR ANTAGONISTS: AMBRISENTAN (LETAIRIS), BOSENTAN (TRACLEER), MACITENTAN (OPSUMIT)

1. Does the patient have a diagnosis of Pulmonary Arterial Hypertension (PAH) and meet **ALL** of the following criteria?
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with **AT LEAST ONE** of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units

   If yes, **approve by HICL for 12 months.** Please use status code #050 and the approval text provided.
   APPROVAL TEXT: Your request for **[drug name]** has been approved for 12 months.
   If no, do not approve.
   DENIAL TEXT: Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for Pulmonary Arterial Hypertension (PAH) who meet **ALL** of the following conditions:
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with at least one of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units

   Your provider did not submit information that you **[criteria not met]** and therefore your request was not approved.

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PULMONARY ARTERIAL HYPERTENSION

INITIAL CRITERIA (CONTINUED)

Riociguat (Adempas)

1. Does the patient have a diagnosis of pulmonary arterial hypertension (PAH) and meets ALL of the following criteria?
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of pulmonary arterial hypertension (PAH) – World Health Organization (WHO) Group 1 diagnosis, confirmed by right heart catheterization with at least one of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 wood units

   If yes, **approve by HICL for 12 months.**
   APPROVAL TEXT: Your request for Adempas (riociguat) has been approved for 12 months.
   If no, continue to #2.

2. Does the patient have a diagnosis of Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) and meets ALL of the following criteria?
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Persistent or recurrent condition following surgery or an inoperable condition
   - Diagnosis is confirmed by right heart catheterization or pulmonary angiography

   If yes, **please approve by HICL for 12 months.**
   APPROVAL TEXT: Your request for Adempas (riociguat) has been approved for 12 months.
   If no, do not approve.
   DENIAL TEXT (PAH): Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for Pulmonary Arterial Hypertension (PAH) who meet **ALL** the following conditions:
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with at least one of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units

   Your provider did not submit information that you **[criteria not met]** and therefore your request was not approved.

(Denial text continued on next page)

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INITIAL CRITERIA (CONTINUED)

DENIAL TEXT (CTEPH): Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for Chronic Thromboembolic Pulmonary Hypertension (CTEPH) who meet **ALL** the following conditions:
- Prescribed by, or in consultation with, a cardiologist or pulmonologist
- Persistent or recurrent condition following surgery or an inoperable condition
- Diagnosis is confirmed by right heart catheterization or pulmonary angiography

Your provider did not submit information that you **[criteria not met]** and therefore your request was not approved.

DENIAL TEXT (Diagnosis not met): Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for members with a diagnosis of Pulmonary Arterial Hypertension (PAH) or Chronic Thromboembolic Pulmonary Hypertension (CTEPH). Your provider did not submit information that you have one of these diagnoses and therefore your request was not approved.

Prostacyclin Vasodilators: selexipag (Uptravi), treprostinil (Orenitram)

1. Does the patient have a diagnosis of Pulmonary Arterial Hypertension (PAH) and meet **ALL** of the following criteria?
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with at least one of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units

   If yes, continue to #2.
   If no, do not approve. Please use status code #238 and the denial text provided.
   DENIAL TEXT: Per your health plan's **PULMONARY ARTERIAL HYERTENSION** guideline, this medication is only covered for members with Pulmonary Arterial Hypertension (PAH) who meet all the following conditions:
   - Prescribed by, or in consultation with, a cardiologist or pulmonologist
   - Diagnosis of PAH-WHO Group 1 confirmed by right heart catheterization with at least one of the following parameters:
     - Mean pulmonary artery pressure (PAP) of ≥ 25 mmHg at rest or > 30 mm Hg with exertion
     - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
     - Pulmonary vascular resistance (PVR) > 3 Wood units

   Your provider did not submit information that you meet these criteria, specifically **[criteria not met]** and therefore your request was not approved.

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PULMONARY ARTERIAL HYPERTENSION

INITIAL CRITERIA (CONTINUED)

2. Is the patient currently taking, tried and failed therapy with, or have a contraindication to a phosphodiesterase-5 inhibitor (PDE5I) [i.e., sildenafil (Revatio) or tadalafil (Adcirca)] or an endothelin receptor antagonist (ERA) [i.e., bosentan (Tracleer), ambrisentan (Letairis), or macitentan (Opsumit)]?

   If yes, continue to #3.
   If no, do not approve. Please use status code #238 and the denial text provided.
   DENIAL TEXT: Per your health plan's **Pulmonary Arterial Hypertension** guideline, this medication is covered for pulmonary arterial hypertension in patients who are currently taking, tried and failed therapy with, or have a contraindication to first line medications such as sildenafil (Revatio), tadalafil (Adcirca), bosentan (Tracleer), ambrisentan (Letairis), or macitentan (Opsumit). Your provider did not indicate that you are on, have tried and failed, or have a contraindication to any of these agents and therefore your request was not approved.

3. **Please approve for 6 months with the following quantity limits:**
   - If the patient is new to therapy, the request is for the lowest dose or the request notes a titrating dosage regimen, please enter proactive prior authorization(s) by GPIDs with the QL(s) as listed in the table to allow for dose titration.
   - If the request is for a member stable on therapy or maintenance dose, please approve by HICL with an MDD = 2.
   - Please use status code #056 and the approval text provided.

   Requests for products on formulary with a restriction:
   APPROVAL TEXT: Your request for **[requested medication]** has been approved for a 6-month period with a quantity limit of **[one pack per 6 months/[X] tablets per day]**.

   Requests for products not on formulary:
   APPROVAL TEXT: Your request for **[requested medication]** has been approved for a 6-month period with a quantity limit of **[one pack per 6 months/ [X] tablets per day]** at your highest cost-share tier.

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INITIAL CRITERIA (CONTINUED)

Uptravi Dose		Approve	Quantity Limits
200-800 Titration pack	(GPID: 40378)	by GPID	1 pack per 6 months
200 mcg tablets	(GPID: 40355)	by GPID	8 tablets per day
400 mcg tablet 600mcg tablet 800 mcg tablet 1,000mcg tablet 1,200 mcg tablet 1,400 mcg tablet 1,600 mcg tablet	(GPID: 40356) (GPID: 40357) (GPID: 40358) (GPID: 40359) (GPID: 40374) (GPID: 40375) (GPID: 40376)	One strength by HICL	2 tablets per day
Orenitram Dose		**Approve**	**Quantity Limits**
0.125 mg ER tablet	(GPID: 35799)	by GPID	3 tablets per day
0.25 mg ER tablet 1 mg ER tablet 2.5 mg ER tablet 5 mg ER tablet	(GPID: 35798) (GPID: 35803) (GPID: 35804) (GPID: 43521)	One strength by HICL	2 tablets per day

RENEWAL CRITERIA

1. Has the requested medication been prescribed by, or in consultation with, a cardiologist or pulmonologist?

   If yes, continue to #2.
   If no, do not approve. Please use status code #238 and the denial text provided.
   DENIAL TEXT: Per your health plan's **Pulmonary Arterial Hypertension** guideline, this medication is only covered when prescribed by or in consultation with a cardiologist or pulmonologist. Your provider did not indicate that he or she specializes in one of these areas or has consulted with a specialist and therefore your request was not approved.

2. Has the patient experienced an improvement while on therapy, i.e., stabilization or improvement in functional class symptoms or stabilization or improvement in 6MWD (6-minute walk distance)?

   If yes, **approve by HICL for 12 months with the following quantity limits:** [**PAC NOTE:** If the request is for a titrating dosing regimen, please enter proactive prior authorization(s) by GPID to allow for dose titration.] Please use status code #056 and the approval text provided.

   Requests for products on formulary with a restriction:
   APPROVAL TEXT: Your request for **[requested medication]** has been approved for a 12-month period with a quantity limit of **[x]** tablets per day.

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PULMONARY ARTERIAL HYPERTENSION

RENEWAL CRITERIA (CONTINUED)

Requests for products not on formulary:
APPROVAL TEXT: Your request for **[requested medication]** has been approved for a 12-month period with a quantity limit of **[X]** tablets per day at your highest cost-share tier.

Uptravi Dose		**Approve**	**Quantity Limits**
200 mcg tablets	(GPID: 40355)	by GPID	8 tablets per day
400 mcg tablet 600mcg tablet 800 mcg tablet 1,000mcg tablet 1,200 mcg tablet 1,400 mcg tablet 1,600 mcg tablet	(GPID: 40356) (GPID: 40357) (GPID: 40358) (GPID: 40359) (GPID: 40374) (GPID: 40375) (GPID: 40376)	One strength by HICL	2 tablets per day
Orenitram Dose		**Approve**	**Quantity Limits**
0.125 mg ER tablet	(GPID: 35799)	by GPID	3 tablets per day
0.25 mg ER tablet 1 mg ER tablet 2.5 mg ER tablet 5 mg ER tablet	(GPID: 35798) (GPID: 35803) (GPID: 35804) (GPID: 43521)	One strength by HICL	2 tablets per day

If no, do not approve. Please use status code #238 and the denial text provided.
DENIAL TEXT: Per your health plan's **Pulmonary Arterial Hypertension - Prostacyclin Vasodilators** guideline, authorization for renewal requires documentation of improvement of symptoms while on therapy with **[requested medication]**. Your provider did not indicate that your symptoms have improved with **[requested medication]** therapy and therefore your request was not approved.

RATIONALE

Ensure appropriate utilization of medications indicated for PAH based on FDA approved indications and appropriate clinical criteria.

FDA APPROVED INDICATIONS

ADEMPAS is indicated for the treatment of adults with:

- Persistent/recurrent Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class.
- Pulmonary Arterial Hypertension (PAH) (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening.

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PULMONARY ARTERIAL HYPERTENSION

FDA APPROVED INDICATIONS (CONTINUED)

LETAIRIS is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):

- To improve exercise ability and delay clinical worsening.
- In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.
- Studies establishing effectiveness included trials predominantly in patients with WHO Functional Class II–III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%).

OPSUMIT is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression.

ORENITRAM is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

Sildenafil (REVATIO) is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) in adults to improve exercise ability and delay clinical worsening. Studies establishing effectiveness were short-term (12 to 16 weeks), and included predominately patients with NYHA Functional Class II–III symptoms. Etiologies
were idiopathic (71%) or associated with connective tissue disease (25%).

- Limitation of Use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.

Tadalafil (ADCIRCA) is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

TRACLEER is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1):

- In adults to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominantly patients with who functional class ii-iv symptoms and etiologies of idiopathic or heritable pah (60%), pah associated with connective tissue diseases (21%), and pah associated with congenital heart disease with left-toright shunts (18%).
- In pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability.

UPTRAVI is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

DOSING

ADEMPAS: Initiate treatment at 1 mg taken three times a day.

- For patients who may not tolerate the hypotensive effect of Adempas, consider a starting dose of 0.5 mg, three times a day.
- Increase dosage by 0.5 mg at intervals of no sooner than 2-weeks as tolerated to a maximum of 2.5 mg three times a day.

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PULMONARY ARTERIAL HYPERTENSION

FDA APPROVED INDICATIONS (CONTINUED)

LETAIRIS: Initiate treatment at 5 mg once daily.

- At 4-week intervals, either the dose of Letairis or tadalafil can be increased, as needed and tolerated, to Letairis 10 mg or tadalafil 40 mg.

OPSUMIT: 10 mg once daily. Doses higher than 10 mg once daily have not been studied in patients with PAH and are not recommended.

ORENITRAM: Starting dose: 0.25 mg BID or 0.125 mg TID.

- Titrate by 0.25 mg or 0.5 mg BID or 0.125 mg TID, not more than every 3 to 4 days as tolerated. Maximum dose is determined by tolerability.

Sildenafil (REVATIO) tablets and oral suspension: 5 mg or 20 mg three times a day, 4–6 hours apart.

Tadalafil (ADCIRCA): 40 mg once daily, with or without food.

TRACLEER: Patients older than 12 years of age: initiate at 62.5 mg orally twice daily; for patients weighing greater than 40 kg, increase to 125 mg orally twice daily after 4 weeks.

- Patients 12 years of age and younger: initial and maintenance dosing is weight-based:
  - ≥ 4-8 kg: 16 mg twice daily
  - > 8-16 kg: 32 mg twice daily
  - > 16-24 kg: 48 mg twice daily
  - > 24-40 kg: 64 mg twice daily

UPTRAVI: Increase by 200 mcg twice daily usually at weekly intervals to the highest tolerated dose. If a dose is not tolerated, reduce dose to previously tolerated dose.

REFERENCES

- Adcirca (tadalafil) [prescribing information]. Indianapolis, IN: Eli Lilly and Company. December 2017.
- Adempas (riociguat) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.: January 2018.
- Letairis (ambrisentan) [prescribing information]. Foster City, CA: Gilead Sciences, Inc. October 2015.
- Opsumit (macitentan) [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; March 2017.
- Uptravi (selexipag) [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; July 2017.
- Orenitram (treprostinil extended-release tablets) [prescribing information]. Research Triangle Park, NC: United Therapeutics Corp; January 2017.
- Revatio (sildenafil) [prescribing information]. New York, NY: Pfizer Labs; February 2018.
- Tracleer (bosentan) [prescribing information]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2017.
- Hopkins W, Rubin LJ. Treatment of pulmonary hypertension in adults. Finlay G, ed. UpToDate Inc. http://www.uptodate.com (Accessed August 15, 2018).

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PULMONARY ARTERIAL HYPERTENSION

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- Galiè N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. J Am Coll Cardiol 2013; 62: D60.
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