Drug Coverage Policy

Effective Date..... 11/15/2025
Coverage Policy Number IP0626
Policy Title..... Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors

Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors

- Adcirca® (tadalafil tablets - Eli Lilly/United Therapeutics, generic)
- Alyq™ (tadalafil tablets – Teva, generic)
- LiQrev® (sildenafil oral suspension – CMP)
- Revatio® (sildenafil tablets and suspension – Pfizer, generic)
  Note: Revatio injection is not included in this policy
- Tadliq® (tadalafil oral suspension – CMP)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health

benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW

Adcirca, Alyq, LiQrev, Revatio, and Tadliq are phosphodiesterase type 5 (PDE5) inhibitors indicated for the treatment of **pulmonary arterial hypertension** (PAH).[1-4] Alyq is a generic to Adcirca.[4]

- Adcirca, Alyq, and Tadliq are indicated for the treatment of PAH (World Health Organization [WHO] Group I) to improve exercise ability.[2-4]
- Liqrev and Revatio are indicated for the treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening.[1,16]
- Revatio is also indicated in pediatric patients 1 to 17 years old for the treatment of PAH to improve exercise ability and, in pediatric patients too young to perform standard exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.[1]

Tadalafil and sildenafil have some data in patients with Raynaud's phenomenon at doses provided in strengths used for PAH.[5-8] In many situations, patients also had scleroderma. Benefits were noted, such as decrease frequency and shorter durations of attacks, as well as in selected parameters regarding digital ulceration.

Disease Overview

PAH is a serious but rare condition impacting fewer than 20,000 patients in the US.[9,10] It is classified within Group 1 pulmonary hypertension among the five different groups that are recognized. In this progressive disorder, the small arteries in the lungs become narrowed, restricted, or blocked causing the heart to work harder to pump blood, leading to activity impairment. Although the mean age of diagnosis is between 36 and 50 years, patients of any age may be affected, including pediatric patients. PAH is defined as a mean pulmonary artery pressure (mPAP) > 20 mmHg (at rest) with a pulmonary arterial wedge pressure (PAWP) ≤ 15 mmHg and a pulmonary vascular resistance > 2 Wood units measured by cardiac catheterization.[17] The prognosis in PAH has been described as poor, with the median survival being approximately 3 years. However, primarily due to advances in pharmacological therapies, the long-term prognosis has improved.

Guidelines

Various guidelines address PDE5 inhibitors for the conditions cited above.

- **Pulmonary Arterial Hypertension:** The CHEST guideline and Expert Panel Report regarding therapy for PAH in adults (2019) details many medications. It was noted that PDE5 inhibitors play a vital role and have various benefits in the management of PAH.[10] The European Society of Cardiology and the European Respiratory Society guidelines regarding the treatment of pulmonary hypertension (2022) also recognize PDE5 inhibitors as having a prominent role in the management of this condition, as monotherapy or in use as combination with other agents.[11]
- **Systemic Sclerosis:** In 2017, the European League Against Rheumatism updated recommendations for the treatment of systemic sclerosis.[12] Dihydropyridine calcium channel blockers, usually oral nifedipine, are recommended for first-line therapy of Raynaud phenomenon in patients with systemic sclerosis. PDE5 inhibitors should be considered in such clinical scenarios as well.

Coverage Policy

POLICY STATEMENT

Prior Authorization is required for benefit coverage of Adcirca, Alyq, Liqrev, Revatio (tablets and suspension only), and Tadliq. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Adcirca, Alyq, Liqrev, Revatio (tablets and suspension only), and Tadliq, as well as the monitoring required for adverse events and long-term efficacy, approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for initiation of therapy as noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes and catheterization laboratory reports. All documentation must include patient-specific identifying information. For a patient case in which the documentation requirement of the right heart catheterization upon Prior Authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors Prior Authorization Policy* is considered to be met.

Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors (Adcirca, Alyq, Liqrev, Revatio, Tadliq, and generics) are considered medically necessary when ONE of the following is met (1 or 2):

FDA-Approved Indication

1. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the patient meets all of the following (i, ii, and iii):
     - **i.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has had a right heart catheterization **[documentation required]** (see documentation section above); AND
       - **b)** Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **ii.** The medication is prescribed by or in consultation with a cardiologist or a pulmonologist.
     - **iii.** Preferred product criteria are met for the product(s) as listed in the below table(s)
   - **B)** Patient is Currently Receiving the Requested Phosphodiesterase Type 5 (PDE5) Inhibitor. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient meets the following (a and b):
       - **a)** Patient has had a right heart catheterization; AND
         Note: This refers to prior to starting therapy with a medication for WHO Group 1 PAH.
       - **b)** Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **ii.** The medication is prescribed by or in consultation with a cardiologist or a pulmonologist.

Other Uses with Supportive Evidence

2. **Raynaud's Phenomenon.** Approve for 1 year if the patient meets the following (A or B and C):

A) Patient has tried one calcium channel blocker; OR
Note: Examples of calcium channel blockers include amlodipine, felodipine, and nifedipine.
B) According to the prescriber, use of a calcium channel blocker is contraindicated.
Note: Examples of reasons a patient cannot take calcium channel blocker therapy include right heart failure and decreased cardiac output; AND
C) Preferred product criteria are met for the product(s) as listed in the below table(s)

Employer Plans:

Product	Criteria
Adcirca tablets (tadalafil)	**1.** The patient meets all of the following (A, B, and C): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient has tried Alyq or generic tadalafil 20 mg tablets; AND **C)** Patient cannot continue to use generic tadalafil 20 mg tablets due to a formulation difference in the inactive ingredients(s) [e.g., differences in dyes, fillers, preservatives] between the Brand and the bioequivalent product which, per the prescriber, would result in a significant allergy or serious adverse reaction.
Revatio tablets (sildenafil)	**1.** The patient meets all of the following (A, B, and C): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient has tried generic sildenafil 20 mg tablets; AND **C)** Patient cannot continue to use generic sildenafil 20 mg tablets due to a formulation difference in the inactive ingredients(s) [e.g., differences in dyes, fillers, preservatives] between the Brand and the bioequivalent product which, per the prescriber, would result in a significant allergy or serious adverse reaction.
Revatio suspension (sildenafil) **LiQrev suspension** (sildenafil) **Sildenafil suspension**	**1.** The patient meets both of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets one of the following (i, ii, or iii): **i.** Patient has tried generic sildenafil 20 mg tablets; OR **ii.** Patient cannot swallow or has difficulty swallowing generic sildenafil 20 mg tablets; OR **iii.** Patient requires administration of a dose that cannot be obtained with generic sildenafil 20 mg tablets.
Tadliq suspension (tadalafil)	**1.** The patient meets both of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets one of the following (i, ii, or iii): **i.** Patient has tried Alyq or generic tadalafil 20 mg tablets; OR **ii.** Patient cannot swallow or has difficulty swallowing Alyq, or generic tadalafil 20 mg tablets; OR **iii.** Patient requires administration of a dose that cannot be obtained with generic tadalafil 20 mg tablets.

Individual and Family Plans:

Product	Criteria
Adcirca tablets (tadalafil)	**1.** The patient meets all of the following (A, B, and C): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient has tried Alyq or generic tadalafil 20 mg tablets; AND **C)** Patient cannot continue to use generic tadalafil 20 mg tablets due to a formulation difference in the inactive ingredients(s) [e.g., differences in dyes, fillers, preservatives] between the Brand and the bioequivalent product which, per the prescriber, would result in a significant allergy or serious adverse reaction.
Revatio tablets (sildenafil)	**1.** The patient meets all of the following (A, B, and C): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient has tried generic sildenafil 20 mg tablets; AND **C)** Patient cannot continue to use generic sildenafil 20 mg tablets due to a formulation difference in the inactive ingredients(s) [e.g., differences in dyes, fillers, preservatives] between the Brand and the bioequivalent product which, per the prescriber, would result in a significant allergy or serious adverse reaction.
Revatio suspension (sildenafil) **LiQrev suspension** (sildenafil) **Sildenafil suspension**	**1.** The patient meets both of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets one of the following (i, ii, or iii): **i.** Patient has tried generic sildenafil 20 mg tablets; OR **ii.** Patient cannot swallow or has difficulty swallowing generic sildenafil 20 mg tablets; OR **iii.** Patient requires administration of a dose that cannot be obtained with generic sildenafil 20 mg tablets.
Tadliq suspension (tadalafil)	**1.** The patient meets both of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets one of the following (i, ii, or iii): **i.** Patient has tried Alyq or generic tadalafil 20 mg tablets; OR **ii.** Patient cannot swallow or has difficulty swallowing Alyq, or generic tadalafil 20 mg tablets; OR **iii.** Patient requires administration of a dose that cannot be obtained with generic tadalafil 20 mg tablets.

Conditions Not Covered

Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors (Adcirca, Alyq, Liqrev, Revatio, Tadliq, and generics) for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Use With Guanylate Cyclase Stimulators.** Use of Adcirca, Alyq, Liqrev, Revatio, and/or Tadliq with guanylate cyclase stimulators is contraindicated.[13]
   Note: An example of a guanylate cyclase stimulator is Adempas (riociguat tablets).

2. **Erectile Dysfunction.** Coverage is not recommended. Patients should use other phosphodiesterase type 5 (PDE5) inhibitors indicated for erectile dysfunction (i.e., Viagra [sildenafil tablets], Cialis [tadalafil tablets]).[14,15]

References

1. Revatio® tablets, oral suspension, and intravenous injection [prescribing information]. New York, NY: Pfizer; January 2023.
2. Adcirca® tablets [prescribing information]. Indianapolis, IN: Eli Lilly/United Therapeutics; September 2020.
3. Tadliq® oral suspension [prescribing information]. Farmville, NC: CMP; June 2022.
4. Alyq™ tablets [prescribing information]. North Wales, PA: Teva; September 2021.
5. Roustit M, Blaise S, Allanore Y, et al. Phosphodiesterase-5 inhibitors for the treatment of secondary Raynaud's phenomenon: systematic review and meta-analysis of randomized trials. *Ann Rheum Dis*. 2013; 72:1696-1699.
6. Shenoy PD, Kumar S, Jha LK, et al. Efficacy of tadalafil in secondary Raynaud's phenomenon resistant to vasodilatory therapy: a double-blind, randomized, crossover trial. *Rheumatol*. 2010; 49:2420-2428.
7. Fernandez-Codina A, Canas-Ruano E, Pope JE. Management of Raynaud's phenomenon in systemic sclerosis-a practical approach. *J Scleroderm Relat Disord*. 2019;4(2):102-110.
8. Hinze AM, Wigley FM. Pharmacotherapy options in the management of Raynaud's phenomenon. *Curr Treat Opt Rheumatol*. 2018;4(3):235-254.
9. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. *JAMA*. 2022;327(14):1379-1391.
10. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults. Update of the CHEST guideline and Expert Panel Report. *CHEST*. 2019;155(3):565-586.
11. Humbert M, Kovacs G, Hoeper MM, et al, for the ESC/ERS Scientific Document Group. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731.
12. Kowal-Bielecka O, Fransen J, Avouac J, et al, with the EUSTAR coauthors. Update of EULAR recommendations for the treatment of systemic sclerosis. *Ann Rheum Dis*. 2017;76(8):1327-1339.
13. Adempas tablets® [prescribing information]. Whippany, NJ: Bayer; September 2021.
14. Viagra® tablets [prescribing information]. New York, NY: Pfizer; December 2017.
15. Cialis® tablets [prescribing information]. Indianapolis, IN: Eli Lilly; April 2023.
16. Liqrev® suspension [prescribing information]. Farmville, NC: CMP; April 2023.
17. Maron BA. Revised Definition of Pulmonary Hypertension and Approach to Management: A Clinical Primer. *J Am Heart Assoc*. 2023 Apr 18;12(8): e029024. [Epub].

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	4/4/2024	06/01/2024
Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1]: For a patient currently receiving the requested PDE5 inhibitor, added a *note* to indicate that requirement of a right heart catheterization (RHC) refers to a RHC prior to starting therapy with a medication for WHO Group 1 PAH.	11/7/2024	01/15/2025

Added a policy statement and a documentation statement. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Initial Therapy **Added** documentation to the right heart catheterization requirement. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Patients Currently Receiving the Requested Phosphodiesterase Type 5 (PDE5) Inhibitor **Removed** the preferred product requirement. **Updated** the Conditions Not Covered statement.	10/2/2025	11/15/2025

The policy effective date is in force until updated or retired.