PRIOR AUTHORIZATION POLICY

POLICY: Pulmonary Arterial Hypertension – Phosphodiesterase Type 5 Inhibitors Prior Authorization Policy

- 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)

REVIEW DATE: 10/02/2024

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.

POLICY STATEMENT

Prior Authorization is recommended for prescription 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. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Adcirca, Alyq, Liqrev, Revatio, and Tadliq is recommended in those who meet the following criteria:

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 BOTH of the following (i and ii):
     - **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.
   - **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 BOTH of 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 ONE of the following (A or B):
   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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Adcirca, Alyq, Liqrev, Revatio, and Tadliq is not recommended in the following situations:

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]

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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.
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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.
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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].