MEDICAL MUTUAL®

# Drug Policy

| Policy: | Phosphodiesterase Type 5 Inhibitors<br>• Adcirca® (tadalafil tablets – Eli Lilly/United Therapeutics, generic)<br>• Alyq™ (tadalafil tablets – Teva, generic)<br>• Tadliq® (tadalafil oral suspension – CMP)<br>• Revatio® (sildenafil tablets and suspension – Pfizer, generic)<br>• Liqrev® (sildenafil oral suspension – CMP)<br>Note: Revatio injection is not included in this policy | **Annual Review Date:**<br>**03/21/2024**<br>**Last Revised Date:**<br>**03/21/2024** |
|---|---|---|

## 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] 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.

## POLICY STATEMENT

This policy involves the use of Adcirca, Alyq, Liqrev, Revatio, and Tadliq. Prior authorization is recommended for pharmacy benefit coverage of Adcirca, Alyq, Liqrev, Revatio, and Tadliq. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Adcirca, Alyq, Liqrev, Revatio, and Tadliq as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Adcirca, Alyq, Liqrev, Revatio, and Tadliq be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

MEDICAL MUTUAL®

# Drug Policy

**Automation:** When available, claim history for amlodipine, felodipine, nicardipine, or nifedipine AND the ICD-10 codes for Raynaud's Phenomenon (ICD-10: I73.0*) will be used for automation to allow approval of tadalafil (generic to Adcirca) and sildenafil (generic to Revatio).

## RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Pulmonary Arterial Hypertension (World Health Organization [WHO] Group 1), Initial Therapy- Revatio tablets, sildenafil tablets, Liqrev suspension, Revatio suspension, sildenafil suspension, Adcirca tablets, Alyq tablets, and tadalafil tablets**
   **Criteria.** *Patient must meet the following criteria (A, B, C, D, E, and either F, G, H, or I):*
   - **A.** The patient has a diagnosis of PAH (WHO Group 1); AND
   - **B.** The patient has had a right heart catheterization to confirm the diagnosis of PAH (WHO Group 1) [documentation required] ; AND
   - **C.** The requested agent is prescribed by or in consultation with a cardiologist or pulmonologist; AND
   - **D.** If brand Revatio tablets are prescribed, the patient must meet the following criteria (a and b):
     - **a.** The patient has previously failed or is intolerant to generic 20 mg sildenafil tablets [documentation required or verification of prescription claims history required; AND
     - **b.** Brand Revatio tablets are being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required].
   - **E.** If generic sildenafil suspension, Revatio suspension, or Liqrev suspension is prescribed, the patient must meet the following criteria (a, b, or c):
     - **a.** The patient has previously failed or is intolerant to generic 20 mg sildenafil tablets; OR
     - **b.** Patient cannot swallow or has difficulty swallowing generic sildenafil 20 mg tablets; OR
     - **c.** Patient requires administration of a dose that cannot be obtained with generic sildenafil 20 mg tablets.
   - **F.** If brand Adcirca is prescribed, the patient must meet the following criteria (a and b):
     - **a.** The patient has previously failed or is intolerant to generic tadalafil 20 mg tablets [documentation required or verification of prescription claims history required]; AND
     - **b.** Brand Adcirca is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required].
   - **G.** If brand Tadliq is prescribed, the patient must meet the following criteria (a, b, or c):
     - **a.** The patient has previously failed or is intolerant to Alyq or generic tadalafil 20 mg tablets; OR
     - **b.** Patient cannot swallow or has difficulty swallowing Alyq or generic tadalafil 20 mg tablets; OR
     - **c.** Patient requires administration of a dose that cannot be obtained with generic tadalafil 20 mg tablets.

2. **Pulmonary Arterial Hypertension (World Health Organization [WHO] Group 1), Patients Currently Receiving the Requested PDE5 Inhibitor- Revatio tablets, sildenafil tablets, Liqrev suspension, Revatio suspension, sildenafil suspension, Adcirca tablets, Alyq tablets, and tadalafil tablets**
**Criteria.** *Patient must meet the following criteria (A, B, C, D, E, F, and either G, H, I, or J):*
   - **A.** The patient has a diagnosis of PAH (WHO Group 1); AND
   - **B.** The patient has had a right heart catheterization to confirm the diagnosis of PAH (WHO Group 1) [documentation required]; AND
   - **C.** The patient is experiencing a beneficial response to therapy with the PDE5 as determined by the physician (e.g. improvement in functional class or quality of life, or in other hemodynamic or clinical parameters); AND
   - **D.** The requested agent is prescribed by or in consultation with a cardiologist or pulmonologist; AND
   - **E.** If brand Revatio tablets are prescribed, the patient must meet the following criteria (a and b):
     - **a.** The patient has previously failed or is intolerant to generic 20 mg sildenafil tablets [documentation required or verification of prescription claims history required; AND
     - **b.** Brand Revatio tablets are being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required].
   - **F.** If generic sildenafil suspension or Liqrev is prescribed, the patient must meet the following criteria (a, b, or c):
     - **a.** The patient has previously failed or is intolerant to generic 20 mg sildenafil tablets; OR
     - **b.** Patient cannot swallow or has difficulty swallowing generic sildenafil 20 mg tablets; OR
     - **c.** Patient requires administration of a dose that cannot be obtained with generic sildenafil 20 mg tablets.
   - **G.** If brand Adcirca is prescribed, the patient must meet the following criteria (a and b):
     - **a.** The patient has previously failed or is intolerant to generic tadalafil 20 mg tablets [documentation required or verification of prescription claims history required; AND
     - **b.** Brand Adcirca is being requested due to a formulation difference in the inactive ingredient(s) [e.g., preservatives] between the brand and the bioequivalent generic product which, per the prescribing physician, has or would result in a significant allergy or serious adverse reaction. [documentation required].
   - **H.** If brand Tadliq is prescribed, the patient must meet the following criteria (a, b, or c):
     - **a.** The patient has previously failed or is intolerant to Alyq or generic tadalafil 20 mg tablets; OR
     - **b.** Patient cannot swallow or has difficulty swallowing Alyq or generic tadalafil 20 mg tablets; OR
     - **c.** Patient requires administration of a dose that cannot be obtained with generic tadalafil 20 mg tablets.

**Other Uses with Supportive Evidence**

1. **Raynaud's Phenomenon – tadalafil tablets (generic to Adcirca) and sildenafil tablets (generic to Revatio)**
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 or decreased cardiac output.

**Initial Approval/ Extended Approval.**
**A)** *Initial Approval:* 1 year
**B)** *Extended Approval:* 1 year

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Adcirca, Alyq, Liqrev, Revatio, and Tadliq have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concurrent Use With Guanylate Cyclase Stimulators.** Use of Liqrev, Revatio, Adcirca, Alyq, and/or Tadliq with guanylate cyclase stimulators is contraindicated.[1-6]
   Note: An example of a guanylate cyclase stimulator is Adempas (riociguat tablets).

2. **Concurrent Use With Organic Nitrates, either regularly or intermittently.** Use of Liqrev, Revatio, Adcirca, Alyq, and/or Tadliq with organic nitrates is contraindicated.[1-6]
   Note: An example of an organic nitrate is Nitrostat (nitroglycerin sublingual tablets).

3. **Erectile Dysfunction.** Coverage of Adcirca or Revatio is not recommended. Patients should use other PDE5 inhibitors indicated for erectile dysfunction. (i.e., Viagra [sildenafil tablets], Cialis [tadalafil tablets])

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

**Documentation Requirements:**

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

## REFERENCES

1. Revatio® tablets, oral suspension, and injection [prescribing information]. New York, NY: Pfizer; January 2023.
2. Adcirca® tablets [prescribing information]. Indianapolis, IN: Eli Lilly (marketed by lung Biotechnology, a subsidiary of United Therapeutics Corporation); September 2020.

3. Viagra® tablets [prescribing information]. New York, NY: Pfizer Labs; December 2017.
4. Cialis® tablets [prescribing information]. Indianapolis, IN: Eli Lilly; February 2018.
5. Tadliq® suspension [prescribing information]. Farmville, NC: CMP; June 2022.
6. Liqrev® suspension [prescribing information]. Farmville, NC: CMP; April 2023.
7. McGoon M, Gutterman D, Steen V, et al. Screening, early detection, and diagnosis of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *CHEST*. 2004;126:14-34.
8. McLaughlin VV, Archer SL, Badesch DB, et al; Writing committee members. ACCF/AHA 2009 Expert consensus document on pulmonary hypertension: A report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association: Developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *Circulation*. 2009;119:2250-2294.
9. Badesch, Abman SH, Simonneau G, et al. Medical therapy for pulmonary arterial hypertension. Updated ACCP Evidence-based clinical practice guidelines. *CHEST*. 2007;131:1917-1928.
10. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol*. 2013;62(25 Suppl):D34-D41.