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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Cardiovascular Agents	**Original Policy Date:**	June 9, 2011
Subject:	Adcirca Alyq Tadliq	**Page:**	1 of 8

Last Review Date: March 8, 2024

Adcirca Alyq Tadliq

Description

Adcirca, **Alyq,** Tadliq (**tadalafil**)

Preferred products: Alyq, tadalafil

Background
Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. This condition can progress to cause right-sided heart failure and death. Tadalafil received approval for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1. Adcirca/Alyq/Tadliq is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve the exercise ability. Tadalafil, at different dosages, is currently also marketed as Cialis for the treatment of erectile dysfunction (1-3).

The World Health Organization (WHO) has classified pulmonary hypertension into five different groups: (4)

WHO Group 1: Pulmonary Arterial Hypertension (PAH)
1.1 Idiopathic (IPAH)
1.2 Heritable PAH
- 1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
- 1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
- 1.2.3 Unknown

1.3 Drug-and toxin-induced

1.4 Associated with:
- 1.4.1 Connective tissue diseases
- 1.4.2 HIV infection
- 1.4.3 Portal hypertension
- 1.4.4 Congenital heart diseases (e.g., pulmonary atresia)
- 1.4.5 Schistosomiasis

1'. Pulmonary vena-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)

1". Persistent pulmonary hypertension of the newborn (PPHN)

The diagnosis of WHO Group 1 PAH requires a right heart catheterization to demonstrate an mPAP ≥ 20mmHg at rest and a pulmonary vascular resistance (PVR) ≥ 3 Wood units, mean pulmonary capillary wedge pressure ≤ 15mmHg (to exclude pulmonary hypertension due to left heart disease, i.e., WHO Group 2 pulmonary hypertension) (8-10).

WHO Group 2: Pulmonary Hypertension Owing to Left Heart Disease

2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3: Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia

3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4: Chronic Thromboembolic Pulmonary Hypertension <CTEPHl

WHO Group 5: Pulmonary Hypertension with Unclear Multifactorial Mechanisms

5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher's disease, thyroid disorders

5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

The American College of Chest Physicians (ACCP) has published an updated clinical practice guideline for treating PAH. These guidelines use the New York Heart Association (NYHA) functional classification of physical activity scale to classify PAH patients in classes I-IV based on the severity of their symptoms. The American College of Chest Physicians (ACCP) has published an updated clinical practice guideline for treating PAH. These guidelines use the New York Heart Association (NYHA) functional classification of physical activity scale to classify PAH patients in classes I-IV based on the severity of their symptoms (5). Adcirca/Alyq/Tadliq is indicated for patients with NYHA Functional Class II and III symptoms (1-3).

ADULT NYHA FUNCTIONAL CLASS CHART

Class I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
Class II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. These patients are comfortable at rest, but ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. These patients are comfortable at rest, but less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV	Patients with pulmonary hypertension resulting in inability to perform any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present at rest, and discomfort is increased by any physical activity.

(4)

CHILDRENS NYHA FUNCTIONAL CLASS CHART

Class I	Asymptomatic.
Class II	Mild tachypnea or diaphoresis with feeding in infants Dyspnea on exertion in older children
Class III	Marked tachypnea or diaphoresis with feeding in infants Marked dyspnea on exertion Prolonged feeding times with growth failure
Class IV	Symptoms such as tachypnea, retractions, grunting, or diaphoresis at rest

(5)

These guidelines recommend that oral therapy with a phosphodiesterase inhibitor (sildenafil) be used as first-line therapy for NYHA Class II and III patients (5). Adcirca/Alyq (tadalafil) is the same therapeutic class as Revatio (sildenafil) and has the same indication for PAH (WHO group 1).

Regulatory Status
FDA-approved indication: Adcirca/Alyq/Tadliq is a phosphodiesterase 5 (PDE5) inhibitor 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%) (1-3).

Off-Label Uses:
Adcirca/Alyq/Tadliq may be used off-label for the treatment of pediatric with PAH. PDE5 expression and activity are increased in PAH and specific PDE5 inhibitors such as sildenafil or tadalafil increase smooth muscle cell cGMP levels and promote pulmonary vascular dilation and remodeling in pediatric patients (7).

The use of Adcirca/Alyq/Tadliq is contraindicated in patients who are using any form of organic nitrate, either regularly or intermittently. Adcirca/Alyq/Tadliq potentiates the hypotensive effect of nitrates. This potentiation is thought to result from the combined effects of nitrates and Adcirca/Alyq/Tadliq on the nitric oxide/cGMP pathway. Adcirca/Alyq/Tadliq is also contraindicated in patients on guanylate cyclase (GC) stimulators (1-3).

Appropriate studies have not been performed on the relationship of age to the effects of Adcirca/Alyq/Tadliq in the pediatric population. Safety and efficacy have not been established (1-3).

Related policies
Adempas, Flolan/Veletri, Letairis, Opsumit, Orenitram, PDE5 Inhibitor powders, Remodulin, Revatio, Tracleer, Tyvaso, Uptravi, Ventavis

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Adcirca/Alyq/Tadliq may be considered **medically necessary** if the conditions indicated below are met.

Adcirca/Alyq/Tadliq may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following

1. Pulmonary Arterial Hypertension (PAH) - WHO Group I
    a. NYHA functional classification of physical activity - Class II or III
    b. Prescribed by or recommended by a cardiologist or pulmonologist

AND NONE of the following:

a. Concurrent therapy with any nitrates (in any form)
b. Concurrent therapy with another phosphodiesterase 5 (PDE5) inhibitor
c. Concurrent therapy with guanylate cyclase (GC) stimulators
d. Concurrent therapy with alpha blockers
e. Severe hepatic impairment (Child-Pugh Class C)
f. Severe renal impairment (creatinine clearance <30 mL/min)

AND ALL of the following:

1. Prescriber agrees to counsel and evaluate the patient for sudden loss of vision or hearing associated with this medication
2. **Tadliq only:** Patient is unable to swallow or has difficulty swallowing tadalafil tablets
3. **Brand Adcirca only:** Patient **MUST** have tried **BOTH** of the preferred products (generic Adcirca: tadalafil and Alyq) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have the following

1. Pulmonary Arterial Hypertension (PAH) - WHO Group I

AND NONE of the following:

a. Concurrent therapy with any nitrates (in any form)
b. Concurrent therapy with another phosphodiesterase 5 (PDE5) inhibitor
c. Concurrent therapy with guanylate cyclase (GC) stimulators
d. Concurrent therapy with alpha blockers
e. Severe hepatic impairment (Child-Pugh Class C)

f. Severe renal impairment (creatinine clearance <30 mL/min)

AND ALL of the following:

1. Symptoms have improved or stabilized
2. Prescriber agrees to counsel and evaluate the patient for sudden loss of vision or hearing associated with this medication
3. **Brand Adcirca only:** Patient **MUST** have tried **BOTH** of the preferred products (generic Adcirca: tadalafil and Alyq) unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Pulmonary arterial hypertension is a rare disorder of the pulmonary arteries in which the pulmonary arterial pressure rises above normal levels in the absence of left ventricular failure. Adcirca/Alyq/Tadliq is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve exercise ability (1-3).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Adcirca/Alyq/Tadliq while maintaining optimal therapeutic outcomes.

References

1. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2020.
2. Alyq [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; September 2021.
3. Tadliq [package insert]. Farmville, NC: CMP Pharma, Inc.; October 2023.
4. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll* Cardiol. 2013; 62:034-841.

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9. Rose-Jones LJ and Mclaughlin V. Pulmonary Hypertension: Types and Treatments. Curr Cardiol Rev. 2015 Feb; 11(1): 73–79.
10. Rudolf KF, et al. Usefulness of pulmonary capillary wedge pressure as a correlate of left ventricular filling pressures in pulmonary arterial hypertension. The Journal of Heart and Lung Transplantation, Vol33, No2. February 2014.

Policy History

Date	Action
December 2009	Both PDE5 inhibitors are indicated for the treatment of PAH WHO group 1, NYHA class II, III. Patients taking tadalafil or sildenafil may see an improvement in NYHA class that could prevent them from qualifying for prior approval renewal. Studies show evidence of improvements in functional class (NYHA class), usually one class jump only; such as from class II to class I. Renewal requirements have been modified to allow continuation of therapy for patients who were previously NYHA Class II for tadalafil or sildenafil, but whose condition has improved on therapy to NYHA Class I.
June 2012	Delete NYHA Class IV; add not on nitrate
March 2013	Annual editorial review and reference update
March 2015	Annual editorial review and reference update Addition of no concurrent therapy with phosphodiesterase inhibitors Removal of Nitrate examples
June 2016	Annual editorial review and reference update Addition of age 18, no concurrent therapy with guanylate cyclase (GC) stimulators, change to lifetime approval to match other PAH medications Addition of no severe hepatic impairment (Child-Pugh Class C) and severe renal impairment (creatinine clearance < 30 mL/min) and Prescriber agrees to counsel and evaluate the patient for sudden loss of vision or hearing associated with this medication Policy number change from 5.06.01 to 5.40.14
September 2017	Annual editorial review

November 2017	Change in age of approval from 18 years of age and older to no age restrictions
March 2018	Annual review
August 2019	Changed policy name to Adcirca Alyq (tadalafil). Changed approval duration from lifetime to 2 years
September 2019	Annual review
March 2020	Annual review. Revised background section and added requirement of no concomitant therapy with alpha blockers. Also added initial requirement of prescribed by or recommended by a cardiologist or pulmonologist per SME
December 2020	Annual review and reference update. Added requirement that brand Adcirca has to t/f the preferred products tadalafil and Alyq
March 2021	Annual review
December 2021	Annual editorial review
March 2022	Annual review
September 2022	Annual review
October 2022	Addition of Tadliq to policy and changed policy name to Adcirca Alyq Tadliq (tadalafil)
December 2022	Annual review
March 2023	Annual review and reference update
September 2023	Annual review
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.