Adcirca Alyq

**Description**

Adcirca (tadalafil), 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 (1). Adcirca received approval on May 26, 2009 for treatment of pulmonary arterial hypertension (PAH) which is classified by WHO as Group 1 (1). Adcirca/Alyq is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve the exercise ability (1). Tadalafil, at different dosages, is currently also marketed as Cialis for the treatment of erectile dysfunction (1-2).

The World Health Organization (WHO) has classified pulmonary hypertension into five different groups: (3)

**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:
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 (4). Adcirca/Alyq is indicated for patients with NYHA Functional Class II and III symptoms (1-2).

**ADULT NYHA FUNCTIONAL CLASS CHART**

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>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.</td>
</tr>
<tr>
<td>II</td>
<td>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.</td>
</tr>
<tr>
<td>III</td>
<td>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.</td>
</tr>
<tr>
<td>IV</td>
<td>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.</td>
</tr>
</tbody>
</table>

**CHILDRENS NYHA FUNCTIONAL CLASS CHART**

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Asymptomatic.</td>
</tr>
<tr>
<td>II</td>
<td>Mild tachypnea or diaphoresis with feeding in infants</td>
</tr>
<tr>
<td></td>
<td>Dyspnea on exertion in older children</td>
</tr>
<tr>
<td>III</td>
<td>Marked tachypnea or diaphoresis with feeding in infants</td>
</tr>
<tr>
<td></td>
<td>Marked dyspnea on exertion</td>
</tr>
<tr>
<td></td>
<td>Prolonged feeding times with growth failure</td>
</tr>
<tr>
<td>IV</td>
<td>Symptoms such as tachypnea, retractions, grunting, or diaphoresis at rest</td>
</tr>
</tbody>
</table>

These guidelines recommend that oral therapy with a phosphodiesterase inhibitor (sildenafil) be used as first-line therapy for NYHA Class II and III patients (4). 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 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%) (1-2).

Off Label Uses:
Adcirca/Alyq 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 (6).

The use of Adcirca/Alyq is contraindicated in patients who are using any form of organic nitrate, either regularly or intermittently. Adcirca/Alyq potentiates the hypotensive effect of nitrates. This potentiation is thought to result from the combined effects of nitrates and Adcirca/Alyq on the nitric oxide/cGMP pathway. Adcirca/Alyq is also contraindicated in patients on guanylate cyclase (GC) stimulators (1-2).
Appropriate studies have not been performed on the relationship of age to the effects of Adcirca/Alyq tablet in the pediatric population. Safety and efficacy have not been established (1-2).

Related policies
Adempas, Flolan/Veletri, Letairis, Opsumit, Orenitram, 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 may be considered medically necessary for the treatment of patients with pulmonary arterial hypertension, WHO Group I and if the conditions indicated below are met.

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

Prior-Approval Requirements

Diagnosis

Patient must have BOTH of the following

1. Pulmonary Arterial Hypertension (PAH) - WHO Group I
2. NYHA functional classification of physical activity - **Class II or III**

**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. Severe hepatic impairment (Child-Pugh Class C)
   e. 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

### 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. Severe hepatic impairment (Child-Pugh Class C)
   e. 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

### 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 is used to treat pulmonary arterial hypertension (PAH, high blood pressure in the lungs) to improve exercise ability (1-2).

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

References


Policy History

Date Action
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.

Delete NYHA Class IV; add not on nitrate

Addition of no concurrent therapy with phosphodiesterase inhibitors

Removal of Nitrate examples

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

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.