

Tadalafil (Adcirca, Alyq, Cialis, Tadliq)

- Oral Suspension - Tadliq 20 mg/5 mL
- Oral Tablet:
 - Cialis: 2.5 mg, 5 mg, 10 mg, 20 mg
 - Generic: Tadalafil Oral 2.5 mg, 5 mg, 10 mg, 20 mg
- Oral Tablet [Pulmonary Hypertension]
 - Adcirca: 20 mg
 - Alyq: 20 mg
 - Generic: Tadalafil 20mg

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

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Summary

Tadalafil (brand names: Adcirca, Alyq, Cialis, Tadliq) is a medication that belongs to a class of drugs called phosphodiesterase-5 (PDE5) inhibitors. It is primarily used to treat several conditions, including pulmonary arterial hypertension (PAH), erectile dysfunction (ED), benign prostatic hyperplasia (BPH), and concurrent ED/BPH. There is also evidence supporting the off-label use of tadalafil for Raynaud phenomenon and for the prevention and treatment of high-altitude pulmonary edema.

Tadalafil is available in different forms and strengths.

- It comes in several oral formulations:
 - Standard tablets in strengths of 2.5 mg, 5 mg, 10 mg, and 20 mg are indicated for ED and/or BPH.
 - Standard tablets with a strength of 20 mg are indicated for PAH.
 - Oral suspension (Tadliq) with a strength of 20 mg/5mL is indicated for PAH.
- The 20 mg tablets and oral suspension labeled for pulmonary arterial hypertension (PAH) are specifically indicated for the treatment of PAH and are labeled accordingly.
- The 2.5 mg and 5 mg tablets are FDA-approved for the treatment of BPH.
- All tablet strengths and formulations can be used to treat ED, although coverage for ED treatment may vary based on the member's specific plan's benefits and coverage.

NOTE: Erectile dysfunction is an excluded benefit for certain Plans. Coverage for medications to treat sexual dysfunction, including erectile dysfunction, varies depending on a member's benefit policy. Please review the member's coverage benefits to determine if erectile dysfunction is a covered benefit.

- Tadalafil formulations indicated for PAH should be used for PAH, while those indicated for ED or BPH should be used for ED or BPH, respectively, unless otherwise noted in the medical necessity criteria.

Definitions

“Benign prostatic hyperplasia (BPH)” is a histologic diagnosis that refers to the proliferation of glandular epithelial tissue, smooth muscle, and connective tissue within the prostate transition zone.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Erectile Dysfunction" is the consistent or recurrent inability to acquire or sustain an erection of sufficient rigidity and duration for sexual intercourse.

"High-altitude pulmonary edema (HAPE)" is a life-threatening condition that can occur in some people who rapidly ascend to high altitudes, usually higher than 2500 m [8202 ft] above sea level.

"Ischemia" refers to a compromise/reduction of blood to an affected area.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the member does not qualify.

"Pulmonary arterial hypertension (PAH)" is a subset of pulmonary hypertension (PH). Pulmonary hypertension is classified into five groups based upon etiology. Patients in the first group are considered to have PAH, whereas patients in the remaining four groups are considered to have PH.

"Raynaud phenomenon (RP)", (also referred to as idiopathic Raynaud phenomenon, primary Raynaud syndrome, or Raynaud disease) is a condition which causes the blood vessels that carry blood to the fingers and toes (sometimes even the ears, lips, nipples, and tip of the nose) to narrow for a time, leading to color changes in the skin, numbness, tingling, and other potential complications.

"Right heart catheterization (RHC)" refers to the gold standard diagnostic test used to definitively diagnose PAH and differentiate it from other types of pulmonary hypertension. RHC directly measures pressures in the right side of the heart and pulmonary arteries. PAH is defined hemodynamically by a mean pulmonary artery pressure (mPAP) ≥ 25 mmHg, pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg, and pulmonary vascular resistance (PVR) > 3 Wood units.

"[s]" indicates state mandates may apply.

"WHO functional class (FC)" is a system to categorize the severity of functional impairment in patients with PAH based on symptom burden and activity limitation. WHO FC ranges from I to IV, with higher classes reflecting more severe symptoms and limitations.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Erectile Dysfunction (if a covered benefit for the member):

The Plan considers tadalafil tablets (all strengths and formulations) medically necessary when ALL the following criteria are met:

1. The member is 18 years of age and older; *AND*
2. The member is a male with erectile dysfunction (ED, impotence); *AND*
 - i. The member has no evidence of ED due to reversible or treatable causes (e.g., hypogonadism with inadequate testosterone replacement, hyperprolactinemia, drug-induced dysfunction, dyslipidemias, alcoholism, other substance abuse, hypertension, thyroid disease, cardiovascular or cerebrovascular disease, neurologic disease, adrenal dysfunction, psychologic dysfunction, marital discord, smoking); *AND*
3. The member meets ALL of the following:
 - a. No evidence of concomitant guanylate cyclase stimulators (such as Adempas (riociguat)); *or*
 - b. No evidence of concomitant nitrates and nitrites (e.g., nitroglycerin, isosorbide dinitrate).

If the above prior authorization criteria are met, tadalafil will be approved for up to 12 months.^[s]

Benign Prostatic Hyperplasia (BPH)

The Plan considers tadalafil 2.5 mg and 5 mg tablets medically necessary when ALL the following criteria are met:

1. The member is 18 years of age and older; *AND*
2. The member has a confirmed diagnosis of BPH; *AND*
3. The member is unable to use or has tried and failed ONE (1) of the following^[s]:
 - a. An alpha blocker (i.e. alfuzosin, doxazosin, tamsulosin, terazosin); *or*
 - b. A 5-alpha reductase inhibitor (i.e. dutasteride, finasteride); *AND*
4. The member meets ALL of the following:
 - a. No evidence of concomitant guanylate cyclase stimulators (such as Adempas (riociguat)); *or*
 - b. No evidence of concomitant nitrates and nitrites (e.g., nitroglycerin, isosorbide dinitrate); *AND*
5. Chart documentation and supporting lab work are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, tadalafil will be approved for up to 12 months.^[s]

Pulmonary Arterial Hypertension (PAH)

The Plan considers tadalafil 20 mg tablets (PAH), and tadalafil 20 mg/5 mL oral suspension medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a cardiologist or pulmonologist with expertise in treating PAH; *AND*
2. The member has a diagnosis of WHO Group 1 pulmonary arterial hypertension (PAH); *AND*
3. The diagnosis of PAH has been confirmed by ONE (1) of the following methods:
 - a. Pre-treatment right heart catheterization with ALL of the following:
 - i. Mean pulmonary artery pressure (mPAP) > 20 mmHg; *and*
 - ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg; *and*
 - iii. Pulmonary vascular resistance (PVR) > 2 Wood units *or* pulmonary vascular resistance index (PVRI) > 3 Wood units x m² also acceptable for pediatric members; *or*
 - b. Doppler echocardiogram if right heart catheterization cannot be performed (e.g., for infants less than one year of age with post cardiac surgery, chronic heart disease, chronic lung disease associated with prematurity, or congenital diaphragmatic hernia); *AND*
4. Chart documentation and supporting lab work are provided for review to substantiate the above-listed requirements.

If the above prior authorization criteria are met, tadalafil will be approved for up to 12 months.^[s]

Raynaud Phenomenon

The Plan considers tadalafil 20 mg tablets medically necessary when ALL of the following criteria are met:

1. Prescribed by or in consultation with a rheumatologist or a provider with expertise in treating Raynaud phenomenon; *AND*
2. The medication is being requested for the treatment of Raynaud phenomenon (also called idiopathic Raynaud phenomenon, primary Raynaud syndrome, or Raynaud disease); *AND*
3. The member has documented history of ONE (1) of the following:
 - a. Signs of critical ischemia at the affected areas (e.g., fingers, toes, ears, lips, nipples, or the tip the nose); *or*
 - b. The quality of life of the member is affected to the degree that activities of normal living are no longer possible; *AND*
4. The member is unable to use, or has tried and failed BOTH of the following^[s]:
 - a. Non-pharmacologic therapies (e.g., relaxation techniques, avoiding stressful situations, avoiding cold exposure, avoiding drugs that may precipitate RP); *and*
 - b. Calcium channel blocker (e.g., amlodipine, nifedipine); *AND*
5. Chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, tadalafil will be approved for up to 12 months.^[s]

Prevention and Treatment of High-Altitude Pulmonary Edema

Medical Necessity Criteria for Authorization

The Plan considers tadalafil 10 mg tablets medically necessary when ALL of the following criteria are met:

1. Tadalafil is being requested for prevention or treatment of high-altitude pulmonary edema **AND**
BOTH of the following:
 - a. The member will be or has been exposed to high altitudes, defined as higher than 2500 m [8202 ft] above sea level; *and*
 - b. The member has a history of high-altitude pulmonary edema **OR** known risk factors that increase susceptibility (e.g. intracardiac shunts, pulmonary hypertension); **AND**
2. The member has tried and failed or has contraindications to first-line therapies such as gradual descent, oxygen therapy/supplementation, and/or portable hyperbaric therapy^[s]; **AND**
3. The member is unable to use, or has tried and failed nifedipine^[s]; **AND**
4. Tadalafil is being prescribed at a dose and frequency that is supported by compendia or evidence-based published dosing guidelines for the requested indication; **AND**
5. Chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, tadalafil will be approved for the member's duration of high altitude exposure or persistence of signs/symptoms.^[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Erectile dysfunction

The Plan considers tadalafil tablets (all strengths and formulations) medically necessary when ALL the following criteria are met:

1. The member still meets the applicable initial criteria; **AND**
2. Chart documentation shows the member has experienced a clinical improvement in symptoms since starting the requested medication.

If the above reauthorization criteria are met, the requested product will be approved for up to 12 months.^[s]

Benign Prostatic Hyperplasia:

The Plan considers tadalafil 2.5 mg and 5 mg tablets medically necessary when ALL the following criteria are met:

1. The member still meets the applicable initial criteria; **AND**

2. Chart documentation shows the member has experienced a clinical improvement in symptoms since starting the requested medication.

If the above reauthorization criteria are met, the requested product will be approved for up to 12 months.^[s]

Pulmonary Arterial Hypertension:

The Plan considers tadalafil 20 mg tablets (PAH), and tadalafil 20 mg/5 mL oral suspension medically necessary when ALL of the following criteria are met:

1. The member still meets the applicable initial criteria; *AND*
2. Recent chart documentation shows the member experiencing therapeutic response to the requested medication as evidenced by ONE (1) of the following:
 - a. Clinical improvement in symptoms since starting the requested medication; *or*
 - b. Disease stability since starting the requested medication.

If the above reauthorization criteria are met, the requested product will be approved for up to 12 months.^[s]

Raynaud phenomenon

The Plan considers tadalafil 20 mg tablets medically necessary when ALL of the following criteria are met:

1. The member still meets the applicable initial criteria; *AND*
2. Chart documentation shows the member has experienced a clinical improvement in symptoms, quality of life, or experienced disease stability since starting the requested medication.

If the above reauthorization criteria are met, the requested product will be approved for up to 12 months.^[s]

Experimental or Investigational / Not Medically Necessary^[s]

Tadalafil for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

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Appendix A

Table 1: Clinical Classification of Pulmonary Hypertension

<p>Group 1: PAH</p> <p>1.1 Idiopathic</p> <p> 1.1.1 Long-term responders to calcium channel blockers</p> <p>1.2 Heritable#</p> <p>1.3 Associated with drugs and toxins#</p> <p>1.4 Associated with:</p> <p> 1.4.1 connective tissue disease</p> <p> 1.4.2 HIV infection</p> <p> 1.4.3 portal hypertension</p> <p> 1.4.4 congenital heart disease</p> <p> 1.4.5 schistosomiasis</p> <p>1.5 PAH with features of venous/capillary (PVOD/PCH) involvement</p> <p>1.6 Persistent PH of the newborn</p>
<p>Group 2: PH associated with left heart disease</p> <p>2.1 Heart failure:</p> <p> 2.1.1 with preserved ejection fraction</p> <p> 2.1.2 with reduced or mildly reduced ejection fraction</p> <p> 2.1.3 cardiomyopathies with specific aetiologies¶</p> <p>2.2 Valvular heart disease:</p> <p> 2.2.1 aortic valve disease</p> <p> 2.2.2 mitral valve disease</p> <p> 2.2.3 mixed valvular disease</p> <p>2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH</p>
<p>Group 3: PH associated with lung diseases and/or hypoxia</p> <p>3.1 COPD and/or emphysema</p> <p>3.2 Interstitial lung disease</p> <p>3.3 Combined pulmonary fibrosis and emphysema</p> <p>3.4 Other parenchymal lung diseases+</p> <p>3.5 Nonparenchymal restrictive diseases:</p>

<p>3.5.1 hypoventilation syndromes 3.5.2 pneumonectomy 3.6 Hypoxia without lung disease (e.g. high altitude) 3.7 Developmental lung diseases</p>
<p>Group 4: PH associated with pulmonary artery obstructions 4.1 Chronic thromboembolic PH 4.2 Other pulmonary artery obstructions§</p>
<p>Group 5: PH with unclear and/or multifactorial mechanisms 5.1 Haematological disorders^f 5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1 5.3 Metabolic disorders## 5.4 Chronic renal failure with or without haemodialysis 5.5 Pulmonary tumour thrombotic microangiopathy 5.6 Fibrosing mediastinitis 5.7 Complex congenital heart disease</p>

COPD: chronic obstructive pulmonary disease; PAH: pulmonary arterial hypertension; PVOD: pulmonary veno-occlusive disease; PCH: pulmonary capillary haemangiomatosis. #: patients with heritable PAH or PAH associated with drugs and toxins might be long-term responders to calcium channel blockers; ¶: hypertrophic, amyloid, Fabry disease and Chagas disease; +: parenchymal lung diseases not included in group 5; §: other causes of pulmonary artery obstructions include sarcomas (high- or intermediate-grade or angiosarcoma), other malignant tumours (e.g. renal carcinoma, uterine carcinoma, germ-cell tumours of the testis), nonmalignant tumours (e.g. uterine leiomyoma), arteritis without connective tissue disease, congenital pulmonary arterial stenoses and hydatidosis; f: including inherited and acquired chronic haemolytic anaemia and chronic myeloproliferative disorders; ##: including glycogen storage diseases and Gaucher disease.

Clinical Guideline Revision / History Information

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