tadalafil (Adcirca, Alyq, Chewtadzy, 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
- Chewable Tablets:
    - Chewtadzy: 5 mg, 10 mg, 20 mg

Summary

Tadalafil 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.
    - Chewable tablets (Chewtadzy) in strengths of 5 mg, 10 mg, and 20 mg are indicated for ED and/or BPH.
    - 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 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.

"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.

"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.

Clinical Indications

For the treatment of Erectile Dysfunction (*if a covered benefit for the member*):

Medical Necessity Criteria for Initial Authorization

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*
3. Clinical chart document is provided showing ALL of the following:
    a. a thorough medical history and physical examination has been undertaken to:
        i. support the diagnosis of erectile dysfunction; *and*
        ii. determine potential underlying causes; *and*
        iii. exclude potentially 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*
    b. a review of the member's current drug regimens has been conducted to detect possible drug-induced ED (e.g., antidepressant, antipsychotic, certain blood pressure medications); *AND*
4. The member will not be taking tadalafil concomitantly with ANY of the following:
    a. Guanylate Cyclase Stimulators (such as Adempas (riociguat)); *or*
    b. Nitrates and nitrites (e.g., nitroglycerin, isosorbide dinitrate); *AND*
5. For chewable tablet formulation (Chewtadzy) requests, ONE of the following:
    a. Documentation of difficulty swallowing solid oral dosage forms; *or*
    b. Clinical rationale for requiring a chewable formulation; *or*
    c. Treatment failure with or intolerance to standard tablet formulation.

If the above prior authorization criteria are met, tadalafil will be approved for 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if BOTH of the following 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.

For the treatment of Benign Prostatic Hyperplasia (BPH):

Medical Necessity Criteria for Initial Authorization

The Plan considers tadalafil 2.5 mg and 5 mg tablets and chewable 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 has tried and failed, or is unable to use an alpha blocker (i.e. alfuzosin, doxazosin, tamsulosin, terazosin); *AND*
4. The member is unable to use, or has tried and failed a 5-alpha reductase inhibitor (i.e. dutasteride, finasteride); *AND*
5. For chewable tablet formulation (Chewtadzy) requests, ONE of the following:
    a. Documentation of difficulty swallowing solid oral dosage forms; *or*
    b. Clinical rationale for requiring a chewable formulation; *or*
    c. Treatment failure with or intolerance to standard tablet formulation; *AND*
6. 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 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if BOTH of the following 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.

For the treatment of Pulmonary Arterial Hypertension (PAH):

Medical Necessity Criteria for Initial Authorization

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

1. The member has a diagnosis of WHO Group 1 pulmonary arterial hypertension (PAH); *AND*
2. The diagnosis of PAH has been confirmed by ONE 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 m^2 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*
3. For chewable tablet formulation (Chewtadzy) requests, ONE of the following:

a. Documentation of difficulty swallowing solid oral dosage forms; *or*
b. Clinical rationale for requiring a chewable formulation; *or*
c. Treatment failure with or intolerance to standard tablet formulation; *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 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if BOTH of the following 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 of the following:
    a. clinical improvement in symptoms since starting the requested medication; *or*
    b. disease stability since starting the requested medication.

For the treatment of Raynaud phenomenon:

Medical Necessity Criteria for Initial Authorization

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

1. The medication is being requested for the treatment of Raynaud phenomenon (also called idiopathic Raynaud phenomenon, primary Raynaud syndrome, or Raynaud disease); *AND*
2. The member has documented history of ONE 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*
3. The member is unable to use, or has tried and failed BOTH of the following:
    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*
4. For chewable tablet formulation (Chewtadzy) requests, ONE of the following:
    a. Documentation of difficulty swallowing solid oral dosage forms; *or*
    b. Clinical rationale for requiring a chewable formulation; *or*
    c. Treatment failure with or intolerance to standard tablet formulation; *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 12 months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if BOTH of the following 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.

For the prevention and treatment of high-altitude pulmonary edema

Medical Necessity Criteria for Authorization

The Plan considers tadalafil 10 mg tablets and chewable 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; *AND*
3. The member is unable to use, or has tried and failed nifedipine; *AND*
4. For chewable tablet formulation (Chewtadzy) requests, ONE of the following:
    a. Documentation of difficulty swallowing solid oral dosage forms; *or*
    b. Clinical rationale for requiring a chewable formulation; *or*
    c. Treatment failure with or intolerance to standard tablet formulation; *AND*
5. The requested dose and duration follow standard dosing guidelines:
    a. For prevention: 10 mg every 12 hours starting 1 day before ascent and continuing for 5-7 days after reaching target altitude; *or*
    b. For treatment: 10 mg every 12 hours until descent is complete, signs/symptoms resolve, and oxygen saturation normalizes for altitude; *AND*
6. 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.

Experimental or Investigational / Not Medically Necessary

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

Appendix

Table 1: Clinical Classification of Pulmonary Hypertension

Group 1: PAH 1.1 Idiopathic 1.1.1 Long-term responders to calcium channel blockers 1.2 Heritable# 1.3 Associated with drugs and toxins# 1.4 Associated with: 1.4.1 connective tissue disease 1.4.2 HIV infection 1.4.3 portal hypertension 1.4.4 congenital heart disease 1.4.5 schistosomiasis 1.5 PAH with features of venous/capillary (PVOD/PCH) involvement 1.6 Persistent PH of the newborn
Group 2: PH associated with left heart disease 2.1 Heart failure: 2.1.1 with preserved ejection fraction 2.1.2 with reduced or mildly reduced ejection fraction 2.1.3 cardiomyopathies with specific aetiologies¶ 2.2 Valvular heart disease: 2.2.1 aortic valve disease 2.2.2 mitral valve disease 2.2.3 mixed valvular disease 2.3 Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3: PH associated with lung diseases and/or hypoxia 3.1 COPD and/or emphysema 3.2 Interstitial lung disease 3.3 Combined pulmonary fibrosis and emphysema 3.4 Other parenchymal lung diseases+ 3.5 Nonparenchymal restrictive diseases: 3.5.1 hypoventilation syndromes 3.5.2 pneumonectomy 3.6 Hypoxia without lung disease (e.g. high altitude) 3.7 Developmental lung diseases
Group 4: PH associated with pulmonary artery obstructions 4.1 Chronic thromboembolic PH 4.2 Other pulmonary artery obstructions§
Group 5: PH with unclear and/or multifactorial mechanisms 5.1 Haematological disorders*ƒ* 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

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; ƒ: including inherited and acquired chronic haemolytic anaemia and chronic myeloproliferative disorders; ##: including glycogen storage diseases and Gaucher disease.

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