



Medication Policy Manual

Policy No: dru184

Topic: tadalafil-containing medications: Adcirca® 20 mg, Cialis® 2.5, 5, 10, and 20 mg

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June 2009 (Adcirca)

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IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Administration of Contract

Tadalafil for impotence is generally a benefit not covered by member contracts regardless of medical necessity.

If tadalafil for impotence is a covered benefit, contract language will be applied to determine coverage (See Appendix VI). Generally, contract language specifies one of the following types of coverage to determine when this medication policy is applicable.

Table 1: Contract Language for Impotence Medications

Coverage Type	Maximum Quantity Already defined by Contract Language	Coverage is based on Medical Necessity	Medication Policy Applies
1.	Yes	No	No
2.	Yes	Yes	Yes
3.*	No	Yes	Yes

* This applies, but is not limited to benefit plans where contracts are silent on coverage of impotence treatments and/or impotence medications.

Note: For groups who fall under OAR 836-053-1405, this mandate takes precedence over any contract limitations.

Description

Tadalafil is an oral medication used in the treatment of pulmonary arterial hypertension (PAH) to improve exercise capacity. Tadalafil is also used in the treatment of erectile dysfunction (ED), and to treat signs and symptoms of benign prostatic hyperplasia (BPH) in men with or without concurrent ED.

Policy/Criteria

- I. Most contracts require prior authorization approval of tadalafil for coverage. Tadalafil may be considered medically necessary for when the following criteria A, B or C below are met:
- A. **Erectile dysfunction (ED)** in men, when the following criteria 1 and 2 have been met:
1. There is a diagnosis of organic impotence.
- AND
2. There is clinical documentation that includes an evaluation of reversible causes of impotence.
- OR
- B. **Pulmonary arterial hypertension (PAH)** when the following criteria 1 and 2 have been met:
1. There is a diagnosis of WHO Group 1 pulmonary arterial hypertension (PAH) (See Appendix I).
- AND
2. Sildenafil has been ineffective, not tolerated, or contraindicated.
- OR
- C. **Benign Prostatic Hyperplasia (BPH)** when the following criteria 1 and 2 have been met:
1. At least one preferred alpha-1 adrenergic blocker has been ineffective, not tolerated, or contraindicated. (See Appendix III)
- AND
2. At least one preferred 5-alpha reductase inhibitor has been ineffective, not tolerated, or contraindicated. (See Appendix III)
- II. **FOR GROUP MEMBERS IN OREGON WHO FALL UNDER OAR 836-053-1405:** Tadalafil may also be considered medically necessary for erectile dysfunction in men when a licensed mental health practitioner has diagnosed sexual dysfunction as defined by the DSM-5 criteria (see Appendix VII).
- III. Administration, Quantity Limitations, and Authorization Period
- A. OmedaRx considers tadalafil to be a self-administered medication.
- B. When prior authorization is approved, tadalafil may be authorized in quantities as follows:
1. **Organic impotence:** Up to six tablets per month (or the maximum quantity specified in the contract).
 2. **Pulmonary arterial hypertension (PAH):** Up to sixty tablets per month.
 3. **Benign prostatic hyperplasia (BPH):** Up to thirty 2.5 mg or thirty 5 mg tablets per month.

- C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.
- IV. Tadalafil is considered not medically necessary when used for the following conditions:
- A. In combination with riociguat (Adempas) or treprostinil oral (Orenitram)
 - B. Psychogenic impotence.
 - C. Impotence resulting from medication use.
- V. Tadalafil is considered investigational when used for all other conditions, including, but not limited to:
- A. Achalasia.
 - B. Chronic obstructive pulmonary disease (COPD), with or without pulmonary hypertension
 - C. Doses exceeding 5 mg daily for the treatment of BPH.
 - D. Enhancing exercise performance.
 - E. Female arousal disorders.
 - F. Heart failure.
 - G. Males with a functioning penile prosthesis or post removal of prosthesis.
 - H. Pulmonary hypertension (PH) WHO Groups 2-5 (see Appendix II), including PH associated with:
 1. Left heart disease, including congestive heart failure (CHF)
 2. Lung diseases, including COPD and idiopathic pulmonary fibrosis (IPF)
 3. Chronic thrombotic and/or embolic disease
 4. Sarcoidosis
 - I. Preservation of penile function after radical prostatectomy.
 - J. Raynaud's phenomenon.

Position Statement

Summary

ERECTILE DYSFUNCTION (ED)

- The type 5 phosphodiesterase (PDE-5) inhibitors [sildenafil, tadalafil, vardenafil (Levitra®), vardenafil ODT (Staxyn®) and avanafil] are used to treat erectile dysfunction (ED). [1-5]
- All PDE-5 inhibitors are effective for treatment of ED. There is no conclusive evidence of any difference in efficacy among the PDE-5 inhibitors in improving the quality or duration of erection in men with erectile dysfunction due to organic, psychogenic, or mixed causes, including diabetes mellitus. [6]

- Sildenafil has gained the most clinical data to support efficacy in many different patient subgroups, such as erectile dysfunction associated with angina, parkinsonism, spina bifida, spinal cord injury, ischemic heart disease, multiple sclerosis, kidney transplant recipients or chronic dialysis. [6] Tadalafil and vardenafil have also been studied in different subpopulations. [6]
- Daily dosing of PDE-5 inhibitors has not been shown to be superior to as needed dosing in the treatment of erectile dysfunction. [6]
- Several studies demonstrate the efficacy of PDE-5 inhibitors in drug-induced (antidepressant and antipsychotic) erectile dysfunction. [6] This use is considered not medically necessary, as treatment of the underlying cause of erectile dysfunction is the first-line of treatment (reversible cause).
- PDE-5 inhibitors are considered investigational when used for conditions for which there is poor to no available evidence of efficacy.

PULMONARY ARTERIAL HYPERTENSION (PAH)

- The World Health Organization (WHO) classifies pulmonary hypertension (PH) in five groups, based on underlying etiology of PH.[7]
 - * Patients diagnosed with Group 1 pulmonary arterial hypertension (PAH) have generally irreversible disease and may require treatment with PAH-specific therapies.
 - * For patients with Groups 2-5, PH may be reversible. Therapy should be directed at treating the underlying cause.[7,8]
- Pharmacologic treatment of PAH includes oral anticoagulants, diuretics, oxygen, inotropic agents (digoxin and dobutamine), calcium channel blockers, prostacyclin and prostacyclin analogs (PGEs) (epoprostenol, treprostinil, and iloprost), endothelin-receptor antagonists (ETAs) (ambrisentan, bosentan, macitentan), PDE-5 inhibitors (sildenafil, tadalafil), and riociguat, a soluble guanylate cyclase (sGC) stimulator.
- The place in therapy of individual agents for PAH is not well defined and is typically symptom driven. Generally, a step-wise approach is used to manage patients. In early disease or with less severe symptoms, oral therapies may be used. As symptoms progress, inhaled or injectable therapies, such as epoprostenol injectable, iloprost inhaled and treprostinil injectable/inhaled become necessary. [7]
- Tadalafil 40 mg is used in the treatment of patients with PAH. It has been shown to improve exercise tolerance in this patient population. [9]
- There are currently no trials of adequate design or of sufficient duration that demonstrate improved survival with tadalafil in patients with PAH.
- Both sildenafil and tadalafil have been studied individually in the treatment of PAH. [9,10] To date, there is no evidence that either one of these products is clearly superior to the other. Generic sildenafil is the lowest-cost oral medication for PAH and a treatment option for most treatment-naïve PAH patients.

- There are currently no trials of sildenafil or tadalafil in patients with Groups 2-5 PH that found improvement in exercise capacity or overall functional status. Choosing Wisely®, an evidence-based initiative to promote wise use of medical resources, states that medications for PAH (e.g. PGEs, PDE5s, and ETAs) should not be used in patients with pulmonary hypertension due left heart disease or hypoxemic lung diseases (Groups 2 and 3), due to a lack of established benefit. In addition, medications for PAH may be harmful in some situations and raises the overall cost of care. [11]

BENIGN PROSTATIC HYPERPLASIA (BPH)

- Tadalafil is the only PDE-5 inhibitor approved for the treatment of BPH. It can be used in men with or without concurrent erectile dysfunction. [1]
- Tadalafil is intended to treat the signs and symptoms of BPH, and has not been shown to reduce the risk of urinary retention or the need for surgery. The 5-alpha reductase inhibitors (e.g. finasteride, dutasteride) have been shown to reduce these risks. [12]
- Although tadalafil 2.5 mg daily and tadalafil 5 mg daily were both studied for the treatment of BPH, 5 mg daily is the only approved dosing regimen. [1]
- There are no studies directly comparing the efficacy of tadalafil to any other treatment for signs and symptoms associated with BPH.

Clinical Efficacy

ERECTILE DYSFUNCTION (ED)

- Efficacy of PDE-5 inhibitors was based on ability to achieve and maintain erection sufficient for sexual activity. [1-5]
- Assessments were made by patients from 4 weeks to 3 months. [1-5]
- Overall, success rates with PDE-5 inhibitors were better than those achieved with placebo. [1-5]
- Better results were generally achieved in patients with less impairment at baseline. [12]
- There are no well-done studies that support the use of Adcirca (tadalafil) 40mg doses to increase the quality and duration of erection in men with erectile dysfunction.

PULMONARY ARTERIAL HYPERTENSION (PAH)

- Sildenafil and tadalafil are used for the treatment pulmonary arterial hypertension (PAH) to improve exercise ability. [9,10] Both were found to improve performance on the 6-minute walk test relative to placebo. The six-minute walk test is a measure of exercise tolerance and measures the distance that is covered in a 6-minute timeframe. Improvements in this test have been correlated to improve survival in PAH patients.
- In a single unreliable pivotal trial in 405 patients with PAH: [9,13]
 - * Tadalafil 40 mg once daily improved exercise capacity at 16-weeks compared to placebo, based on a six-minute walking distance test.

- * Patients using tadalafil 40 mg once daily were less likely to show clinical worsening than those taking placebo or patients treated with lower doses of tadalafil. Clinical worsening was defined as death, lung transplantation, atrial septostomy, hospitalization for worsening PAH, new PAH therapy, or worsening WHO functional class.
- * Results of this trial may not be reliable due to flaws that included a dropout rate of approximately 15%. Also, approximately half of the subjects were allowed to take bosentan. Use of bosentan may have contributed to the differences that were observed between groups.
- There is no reliable evidence that doses of tadalafil exceeding 40 mg daily provide any additional clinical benefit when used in the treatment of PAH.
- There are no trials with tadalafil in patients with PAH that are adequately designed or of sufficient duration to determine the long-term safety or survival benefit with treatment.
- There are no well-designed trials that demonstrate additional clinical benefit with tadalafil when used in combination with other PDE5s, riociguat, any prostacyclins, bosentan, or ambrisentan. ^[14-16] A recent trial (AMBITION) evaluated the use of tadalafil, ambrisentan, or the combination of tadalafil with ambrisentan as first-line therapy in patients with PAH, with an endpoint of time to clinical worsening (TTCW). However, the trial is unpublished and there are insufficient details available on the study conduct and study results to fully evaluate the clinical significance of the findings. ^[17]
- * TTCW was measured as a composite of PAH symptoms (e.g. hospitalization, disease progression, 6MWD), morbidity events, and mortality, and was improved in patients receiving combination therapy.
- * However, the trial had a significant loss of intent-to-treat population. Therefore, it is uncertain if groups remained adequately randomized. Additionally, there was a post-randomization protocol amendment that may confound both safety and efficacy results, and subjects were able to cross over to other therapies, which confounds interpretation of any mortality data.
- * The trial was not powered for reduction of mortality. The majority of patients met the TTCW endpoint with hospitalization for worsening of PAH, which is driven by symptoms and potentially 6MWD, and considered a surrogate marker of PAH and prone to assessment bias.
- The use of ETAs, or PDE5s, including tadalafil, in combination with treprostinil oral is considered investigational. Treprostinil oral has not been proven effective as add-on therapy to other PAH-specific medications, including PDE5s or ETAs. In two Phase 3 trials, addition of treprostinil oral did not significantly increase 6MWD in patients on a PDE5, ETA, or both (10 to 11 meters more than placebo). ^[18,19] A third combination therapy study protocol was withdrawn, prior to trial enrollment. ^[20]

- ACCP guidelines for treatment of pulmonary arterial hypertension recommend the use of an ETA, PDE-5, or riociguat for treatment naïve PAH patients with WHO functional class (FC) II/III symptoms. The guidelines do not differentiate between medication options within each class. Guidelines also recommend consideration of initial therapy with an injectable prostacyclin analog in WHO FC IV patients and select WHO FC III patients with rapid disease progression or poor prognostic markers. [21] ACCF/AHA guidelines recommend the use of tadalafil in WHO Group 1 PAH (see Appendix I), based on systematic review of the literature. [7]

BENIGN PROSTATIC HYPERPLASIA (BPH)

- The efficacy of tadalafil for daily use in the treatment of BPH was evaluated in three randomized, double-blind, placebo-controlled trials. Two trials studied men with BPH [1,22], while the third trial studied men with concurrent BPH and erectile dysfunction (ED). [23]
 - * The primary endpoint evaluated for the effect of tadalafil on lower urinary tract symptoms (LUTS) of BPH was the International Prostate Symptom Score (IPSS). The IPSS is a subjective, 7-item recall questionnaire with a maximum total score of 35 points. Higher scores represent more severe symptoms of BPH.
 - * In the two clinical trials of men with BPH-LUTS without concurrent ED, tadalafil improved total IPSS from baseline to 12 weeks by 2 to 3 points more than placebo. Although these improvements were considered statistically significant, the clinical significance of a 2 to 3 point improvement on the 35-point IPSS is unknown. [1,22]
 - * In the clinical trial of men with concurrent BPH-LUTS and ED, both erectile function, as measured by the International Index of Erectile Function, and total IPSS were statistically significantly improved with tadalafil relative to placebo. Tadalafil improved IPSS from baseline to week 12 by 6.1 points, whereas placebo improved IPSS by 3.8 points. [23] The clinical relevance of a 2.3 point improvement on the 35-point IPSS is unknown.
- There is no reliable evidence that doses of tadalafil beyond 5 mg daily provide any additional benefit for improving signs and symptoms of BPH.
- Trials of both vardenafil [24] and sildenafil [25] in men with BPH with or without erectile dysfunction showed improvement in total IPSS from baseline by 1.7 to 4 points more than placebo, however clinical relevance of this improvement is unknown.
- The efficacy of tadalafil, nor any PDE-5 inhibitor, relative to other treatments for BPH, such as alpha-1 adrenergic blockers (e.g. doxazosin, tamsulosin) and 5-alpha reductase inhibitors (e.g. finasteride, dutasteride, is unknown. [12]

OTHER CONDITIONS

- PDE-5 inhibitors are considered investigational when used in conditions for which there is poor or no available evidence of efficacy:
 - * There is no evidence to support the use of tadalafil in any other conditions, including, but not limited to, achalasia, female arousal disorders, heart failure, or for exercise performance.

- * Several studies support the efficacy of PDE-5 inhibitors in men with erectile dysfunction after undergoing bilateral nerve sparing radical retropubic prostatectomy. [26-37] Although some patients were able to achieve an erection with these agents, there is no reliable evidence that these agents preserve penile erectile function after prostate resection.
 - Evidence was not reliable due to flaws that included: retrospective or open-label design; lack of randomization, control groups, blinding, and/or intent-to-treat analysis; small numbers of patients, and short duration of study.
- * PDE-5 inhibitors have been used in a small number of patients with Raynaud's phenomenon to improve peripheral blood flow. Evidence is preliminary. Larger, well-controlled trials are necessary to establish the efficacy and safety of these medications in this disease. [38-40]
 - Two small placebo-controlled, cross-over studies evaluated sildenafil (n=18) and tadalafil (n=50) inpatients with Raynaud's phenomenon that was resistant to conventional vasodilatory treatment. [39,40] Frequency and duration of attacks was significantly lower in both the sildenafil and tadalafil treated groups. There was also improvement in digital ulcerations in several of the sildenafil-treated patients and ulcer healing reported in all of the tadalafil-treated patients with digital ulcers at baseline.
 - One small Phase 2, placebo-controlled, cross-over study (n = 50) evaluated vardenafil in patients with primary or secondary Raynaud's phenomenon, resistant to conventional vasodilatory treatment. Despite a significantly greater decrease in frequency, duration and severity of Raynaud's symptoms in the vardenafil group, there was no significant difference in digital blood flow. Clinical outcomes, such as digital ulceration or amputation, were not reported. [41]
 - Larger, well-controlled trials are needed to establish the safety and effectiveness of PDE-5 inhibitors in the treatment of Raynaud's.
- There is insufficient evidence to establish tadalafil is safe or effective for use in patients with pulmonary hypertension Groups 2-5.
 - * One small (n=10) Phase 2, placebo-controlled, cross-over trial of sildenafil found no beneficial effect on exercise capacity in COPD patients without pulmonary hypertension. Sildenafil significantly worsened oxygenation (gas-exchange), symptoms, and quality of life. Similarly, a larger trial (n=120) double-blind, placebo-controlled trial of tadalafil found no beneficial effect on exercise capacity or quality of life in COPD patients. [42,43]
 - * Guidelines do not support the use of tadalafil for treatment of pulmonary hypertension (PH) in WHO Groups 2-5, including PH related to chronic left heart disease (WHO Group 2) or chronic hypoxic states (WHO Group 3). Instead, these patients require optimization of therapies targeting their underlying disease state. [7]

- * Choosing Wisely®, an evidence-based initiative to promote wise use of medical resources, states that medications for PAH (e.g. PGEs, PDE5s, and ETAs) to should not be used in patients with pulmonary hypertension due left heart disease or hypoxemic lung diseases (Groups 2 and 3). There is no consistent evidence that due to a lack of established benefit. In addition, medications for PAH may be harmful in some situations and raises the overall cost of care. [11]
- No randomized, controlled trials have been published evaluating the use of tadalafil in patients with sarcoidosis.

Safety

- All PDE-5 products carry similar product safety labeling that includes the contraindication for use in patients on nitrates and warnings about their use in patients on nitrates and alpha-adrenergic inhibitors. [1-5,9,10]
- Headache, dyspepsia and back pain are the predominant adverse effects reported among all PDE-5 inhibitors. [1-5,9,10]
- Co-administration of PDE5s with nitrates in any form is contraindicated. [1-5,10,11]
- Use of tadalafil with alcohol, alpha-blockers (e.g. terazosin, doxazosin), or other PDE-5 inhibitors (e.g. sildenafil, vardenafil) should be avoided. [1,9] Tadalafil should not be used in combination with alpha-blockers for the treatment of BPH.
- Use of tadalafil with potent CYP3A4 inhibitors or inducers may substantially alter serum levels of tadalafil and is not recommended. [1,9]
- Use of riociguat with any phosphodiesterase inhibitor (e.g. sildenafil, tadalafil, dipyridamole, or theophylline) is contraindicated due to excessive hypotension in combination. [1-5,10,11]
- Safety data for tadalafil 40 mg is limited to adverse events described in the 16-week pivotal trial and an open-label, non-comparator extension trial of up to one year. [9].

Dosing and administration

ERECTILE DYSFUNCTION (ED)

- Avanafil, sildenafil and vardenafil doses need to be given between 0.4-4 hours prior to sexual intercourse to be effective. [2-5]
- Tadalafil has a longer half-life and in clinical trials has shown to improve erectile dysfunction compared to placebo up to 36 hours following dosing, allowing a longer window (36 hours) opportunity or "full day" coverage for intercourse to occur. [1]

PULMONARY ARTERIAL HYPERTENSION (PAH)

- The recommended dose of tadalafil for the treatment of PAH is 40 mg once daily. It is not recommended that this dose be divided up over the course of the day. [9]

BENIGN PROSTATIC HYPERPLASIA (BPH)

- The recommended dose of tadalafil for the treatment of BPH is 5 mg once daily. For men with concurrent erectile dysfunction, the dose of tadalafil is 5 mg once daily without regard to timing of sexual activity. [1]
- For creatinine clearance 30 to 50 ml/min, a starting dose of 2.5 mg daily is recommended. An increase to 5 mg daily may be considered based on individual response. [1]

Cross References
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bosentan-containing medications, Tracleer®, Medication Policy Manual dru218
Letairis®, ambrisentan, Medication Policy Manual dru219
Opsumit®, macitentan, Medication Policy Manual dru324
Orenitram®, tadalafil oral tablets, Medication Policy Manual dru337
Remodulin®, treprostinil injectable, Medication Policy Manual dru222
Viagra®, Medication Policy Manual dru461
Tyvaso®, treprostinil inhalation, Medication Policy Manual dru221
Uptravi®, selexipag, Medication Policy Manual, dru446
ildenafil-containing medications, Levitra®, Staxyn®, Medication Policy Manual dru096
Ventavis®, iloprost inhalation, Medication Policy Manual dru220

Codes	Number	Description
ICD-10	N52.9	Impotence of organic origin.
ICD-10	N40.0	Hyperplasia (benign) of the prostate.

Appendix I: Revised WHO Classification of Pulmonary Hypertension – Group 1 ^[7]

Group 1. Pulmonary arterial hypertension (PAH)

- Idiopathic (IPAH)
- Familial (FPAH)
- Associated with (APAH):*
 - Connective tissue disorder (e.g. rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), scleroderma, systemic sclerosis (formerly known as CREST syndrome))
 - Congenital systemic-to-pulmonary shunts (e.g. congenital heart disease (CHD), including atrial or ventricular septal defect, patent ductus arteriosus (PDA), patent foramen ovale (PFO), truncus arteriosus, Eisenmenger syndrome, tetralogy of Fallot, transposition of the great vessels)
 - Portal hypertension
 - HIV infection
 - Drugs and toxins (e.g. anorexic agents, cocaine, methamphetamine, L-tryptophan)
 - Other (thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies (e.g. sickle cell anemia, thalassemia), chronic myeloproliferative disorders, splenectomy)
- Associated with significant venous or capillary involvement
 - Pulmonary veno-occlusive disease (PVOD)
 - Pulmonary capillary hemangiomatosis (PCH)
- Persistent pulmonary hypertension of the newborn

* Diagnoses, include, but are not limited to these common diagnoses.

Appendix II: Investigational Indications for Tadalafil - Revised WHO Classification of PH – Groups 2-5 ^[7]

Group 2. Pulmonary hypertension with left heart disease

- Left-sided atrial or ventricular heart disease (systolic dysfunction, diastolic dysfunction)
- Left-sided valvular heart disease

Group 3. Pulmonary hypertension associated with lung diseases and/or hypoxemia

- Chronic obstructive pulmonary disease (COPD)
- Interstitial lung disease (e.g. idiopathic pulmonary fibrosis)
- Sleep disordered breathing (e.g. obstructive sleep apnea (OSA))
- Alveolar hypoventilation disorders
- Chronic exposure to high altitude
- Developmental abnormalities

Group 4. Pulmonary hypertension due to chronic thrombotic and/or embolic disease (CTEPH)

- Thromboembolic obstruction of proximal pulmonary arteries
- Thromboembolic obstruction of distal pulmonary arteries
- Nonthrombotic pulmonary embolism (tumor, parasites, foreign material)

Group 5. Miscellaneous

- Sarcoidosis, histiocytosis X, lymphangiomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis)

Appendix III: Preferred Alternative Treatment Options for BPH

Alpha-1 Adrenergic Blockers	alfuzosin (generic) doxazosin (generic) prazosin (generic; off-label use) tamsulosin (generic) terazosin (generic)
5-alpha Reductase Inhibitors	finasteride (generic) dutasteride (Avodart®)

Appendix IV: Functional Status with Heart Failure

World Health Organization (WHO) functional assessment classification: ^[44]

- Class I: Patients with pulmonary hypertension (PH) 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 PH resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
- Class III: Patients with PH resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
- Class IV: Patients with PH with inability to carry out any physical activity without symptoms. These patients manifest signs of right-heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by physical activity.

New York Heart Association (NYHA) Heart Failure Classification: ^[45]

- Class I: Patients with no limitation of activities; they suffer no symptoms from ordinary activities.
- Class II: Patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion.
- Class III: Patients with marked limitation of activity; they are comfortable only at rest.
- Class IV: Patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest.

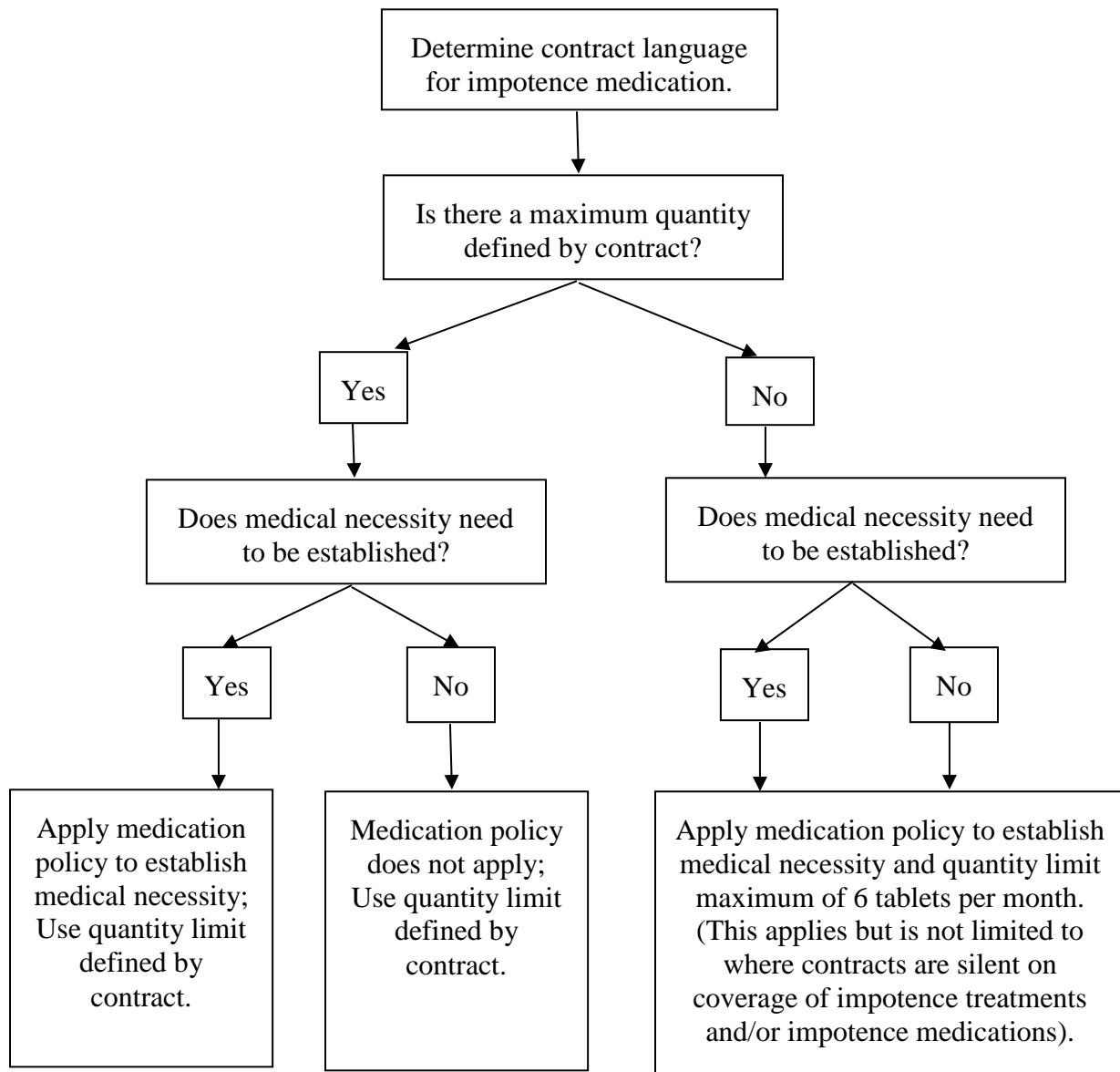
Appendix V. Vasoactive alternatives for treatment of Raynaud's phenomenon and digital ulcers ^[46]

Calcium channel blockers (i.e. amlodipine, diltiazem, nifedipine)

Renin-angiotensin inhibitors [angiotensin-converting enzyme inhibitors (i.e. enalapril, lisinopril) or angiotensin II receptor blockers (ARBs) (i.e. losartan, olmesartan (Benicar®), telmisartan (Micardis®)]

Appendix VI

Impotence Medications - Administration of Contract Language and Medication Policy



Note: For fully insured members in Oregon, OAR 836-053-1405 takes precedence over any contract limitations.

Appendix VII: DSM-5 Recognized Sexual Dysfunctions

Codes	Number	Description
ICD-10	F52.32	Delayed Ejaculation
ICD-10	F52.21	Erectile Disorder
ICD-10	F52.0	Male Hypoactive Sexual Desire Disorder
ICD-10	F52.8	Other Specified Sexual Dysfunction
ICD-10	F52.9	Unspecified Sexual Dysfunction

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Revision History

Revision Date	Revision Summary
6/9/2017	No changes to coverage criteria with this annual update.
6/10/2016	No changes