



PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

NEXT REVIEW DATE: 4th QTR 2012

ORIGINAL EFFECTIVE DATE: 3-13-2012
LAST REVIEW DATE: 2-16-2012
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Cialis® (Tadalafil)

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety. The guideline is not a guarantee of coverage.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational & thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available. The guideline in effect on the date of service will determine coverage.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

The release of nitric oxide by nerves and endothelial cells in the penis in response to sexual stimulation results in the formation of cyclic guanosine monophosphate (cGMP). Increased cGMP results in the relaxation of smooth muscles in the corpus cavernosum, leading to an inflow of blood, which can produce an erection. Phosphodiesterase type 5 (PDE5) is the predominant isoenzyme in penile tissue and is responsible for the metabolism of cGMP. Cialis (tadalafil) selectively inhibit PDE5, thereby preventing the breakdown of cGMP and enhancing or restoring the natural erectile response. PDE5 is also found in pulmonary vascular and visceral smooth muscle, skeletal muscle, platelets, kidney, lung, cerebellum, and pancreas.

The mechanism for reducing benign prostatic hyperplasia symptoms has not been established. The effect of PDE5 inhibition on cGMP concentration in the corpus cavernosum and pulmonary arteries is also observed in the smooth muscle of the prostate, the bladder and their vascular supply. Cialis (tadalafil) also inhibits PDE11, an isoenzyme found in human prostate, testes, skeletal muscle, and other tissues. The physiologic role and clinical consequence of PDE11 inhibition in humans have not been defined.

In men, enlargement of the prostate gland from hyperplasia can cause bladder outlet obstruction (BOO) and be a major cause of lower urinary tract symptoms (LUTS). Symptoms include storage and/or voiding disturbances common in aging men and can include daytime frequency and nocturia.



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LUTS may be due to structural or functional abnormalities in one or more parts of the lower urinary tract that includes the bladder, bladder neck, prostate, distal sphincter mechanism, and urethra. LUTS may also result from abnormalities of the peripheral and/or central nervous systems that provide neural control to the lower urinary tract.

The term benign prostatic hyperplasia (BPH) is reserved for the histological pattern it describes. Benign prostatic enlargement is used when there is gland enlargement and is usually a presumptive diagnosis based on the size of the prostate. Benign prostatic obstruction (BPO) is used when obstruction has been proven by pressure flow studies, or is highly suspected from flow rates and if the gland is enlarged. BOO is the generic term for all forms of obstruction to the bladder outlet (e.g., urethral stricture) including BPO.

Erectile dysfunction (ED) is defined as the consistent or recurrent inability to attain or maintain an erection sufficient for satisfactory intercourse or other sexual expression.

Causes of ED can be categorized as organic (vascular and neurogenic origin) or psychological. Several risk factors have been identified for ED including aging, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, conditions associated with endothelial dysfunction, trauma (either localized or spinal cord), medications, and depression.

Precertification:

Precertification* for Cialis is required for members with a Blue Cross Blue Shield of Arizona (BCBSAZ) retail and mail order prescription benefit. Medications requiring precertification are identified on the following list located on the Internet at <http://www.azblue.com/pdfs/medications/pharmacy/QIList.pdf>:

"Prescription Limitations and Precertification Requirements for Retail and Mail Order Prescriptions"

This list may also be requested by calling (602) 864-4273 or (800) 232-2345, ext. 4273.

Please refer to this list for other Cialis prescription claim limitations where applicable.

* Precertification will not be required for certain individuals who are already receiving Cialis. Members having at least one BCBSAZ paid claim for Cialis within the three months preceding the initial effective date of this guideline will not need to obtain precertification.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

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Cialis® (Tadalafil) (cont.)

Criteria:

- FDA-approved dosage of Cialis is considered **medically necessary** in men 18 years of age or older with a documented diagnosis of either of the following conditions below:
 - Erectile dysfunction (ED) **OR**
 - Signs and symptoms of benign prostatic hyperplasia (BPH) **OR**
 - Erectile dysfunction and signs and symptoms of benign prostatic hyperplasia (ED/BPH)

And documentation that:

- The American Urological Association-Symptom Index (AUA-SI) score is less than 8
- Estimated creatinine clearance is > 30 mL/min for once daily use of Cialis
- Individual is not using nitrates regularly or intermittently in any form
- Individual is not concurrently using other Phosphodiesterase type 5 inhibitors such as Viagra, Levitra, Revatio, Staxyn, or Adcirca
- Individual does not have any of the following conditions:
 - Severe hepatic impairment (Child Pugh Class C)
 - High risk for hereditary degenerative retinal disorders, including retinitis pigmentosa
 - Myocardial infarction within the last 90 days
 - Unstable angina or angina during sexual intercourse
 - New York Heart Association Class 2 or greater heart failure within the last 6 months
 - Uncontrolled arrhythmias
 - Hypotension (blood pressure < 90/50)
 - Uncontrolled hypertension (blood pressure > 170/100)
 - Stroke within the last 6 months
 - Clinically significant aortic and mitral valve disease, pericardial constriction, restrictive or congestive cardiomyopathy, significant left ventricular dysfunction, life-threatening arrhythmias, or symptomatic coronary artery disease

Cialis for all other indications not previously listed, is considered experimental or investigational based upon;

1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
2. Insufficient evidence to support improvement of the net health outcome, and
3. Insufficient evidence to support improvement of the net health outcome as much as, or more than established alternatives

History:

Date:

Activity:

Pharmacy and Therapeutics review	2-16-2012	Adopted guideline
Director Pharmacy Mgmt review	2-16-2012	Development



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Criteria Revisions:

Resources:

Cialis package insert reference ID number 3024692 revised by manufacturer on October 2011 reviewed on October 27, 2011.

2010 American Urologic Association Guideline on the Management of Benign Prostatic Hypertrophy

2005 American Urologic Association Guideline on the Management of Erectile Dysfunction: Diagnosis and Treatment Recommendations

FDA Product Approval Information for Cialis:

- FDA approved indications
 - For the treatment of erectile dysfunction (ED);
 - For the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH); and
 - For the treatment of ED and the signs and symptoms of BPH (ED/BPH)

- FDA approved dosage
 - Cialis for Use As Needed for Erectile Dysfunction:
 - The recommended starting dose of Cialis for use as needed in most patients is 10 mg, taken prior to anticipated sexual activity.
 - The dose may be increased to 20 mg or decreased to 5 mg, based on individual efficacy and tolerability. The maximum recommended dosing frequency is once per day.

 - Cialis for Once Daily Use for Erectile Dysfunction:
 - The recommended starting dose of Cialis for once daily use is 2.5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.
 - The Cialis dose for once daily use may be increased to 5 mg, based on individual efficacy and tolerability.

 - Cialis for Once Daily Use for Benign Prostatic Hyperplasia:
 - The recommended dose of Cialis for once daily use is 5 mg, taken at approximately the same time every day.

 - Cialis for Once Daily Use for Erectile Dysfunction and Benign Prostatic Hyperplasia:
 - The recommended dose of Cialis for once daily use is 5 mg, taken at approximately the same time every day, without regard to timing of sexual activity.

- FDA use in specific populations
 - Use in severe hepatic impairment (Child Pugh Class C) is not recommended



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- Once daily use in patients with a creatinine clearance less than 30 ml/min is not recommended
 - Not indicated for use in women
 - Not indicated for use in pediatric patients below the age of 18 years of age
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