BlueCross BlueShield of Alabama

Phosphodiesterase Type 5 Quantity Limit Program Summary

This program applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

Self-funded groups may exclude this class of medications from coverage or have varying age and/or quantity limitations. Group specific policies will supersede this general policy when applicable. Refer to member's benefit plan for further details regarding erectile dysfunction medications (may be referred to as Impotence Drugs).

OBJECTIVE

The intent of the Phosphodiesterase Type 5 (PDE5) Inhibitors Quantity Limit (QL) program is to recommend the monthly quantity of thirty tablets, cumulative, for Cialis 2.5 mg and 5 mg tablets and the monthly quantity limit of eight tablets, cumulative for any combination of the other products and Cialis 10 mg and 20 mg tablets, based on Food and Drug Administration (FDA) approved indications and dosing schedule and/or clinical studies of erectile dysfunction. The program will review for increased quantities for the accepted off-label uses for the preservation of erectile function following retropubic prostatectomy. These criteria may not apply if these agents are excluded from coverage under the member's pharmacy benefit plan.

QUANTITY LIMIT TARGET AGENTS - RECOMMENDED LIMITS

Brand (generic)	GPI	Quantity per month
Cialis® (tadalafil)		
2.5 mg tablets	40304080000302	30
5 mg tablets	40304080000305	
10 mg tablets	40304080000310	8*
20 mg tablets	40304080000320	
Levitra® (vardenafil)		
2.5 mg tablets	40304090100310	
5 mg tablets	40304090100320	
10 mg tablets	40304090100330	
20 mg tablets	40304090100340	
Staxyn® (vardenafil)		
10 mg orally disintegrating tablets	40304090107230	
Stendra® (avanafil)		
50 mg tablets	40304015000320	
100 mg tablets	40304015000330	
200 mg tablets	40304015000340	
Viagra® (sildenafil)		
25 mg tablets[c]	40304070100310	
50 mg tablets[c]	40304070100320	
100 mg tablets[c]	40304070100330	

* Some groups cover less than or more than 8 tablets per month. Group specific policies will supersede this policy when applicable. Please refer to member's benefit plan. Only 1 oral agent will be covered per month.

c – Generic available

CRITERIA FOR APPROVAL

Increased quantities of **Phosphodiesterase Type 5 Inhibitors** will be approved when BOTH of the following are met:

1. The phosphodiesterase type 5 inhibitor has been prescribed for preservation of erectile function following a radical retropubic prostatectomy
   AND
2. The quantity requested is equal to or less than 30 tablets per month

Length of Approval:

Preservation of erectile function following a radical retropubic prostatectomy – 30 tablets per month for 12 months

FDA APPROVED INDICATIONS AND DOSAGE[1-4,23]

Agent	FDA Approved Indication	Dosage and Administration
Cialis (tadalafil)	Erectile Dysfunction (ED)	**ED; As needed:** Initially, 10 mg taken prior to anticipated sexual activity. Increase to 20 mg or decrease to 5 mg based upon efficacy and tolerability. Maximum recommended dosing frequency is once per day. Improves erectile function vs placebo up to 36 hours post dose. **ED; Once daily:** 2.5 mg taken once daily, without regard to timing of sexual activity. May increase to 5 mg based upon efficacy and tolerability.
	Benign Prostatic Hyperplasia (BPH)	**BPH:** 5 mg taken once daily; a starting dose of 2.5 mg daily is recommended if creatinine clearance is 30 to 50 mL/min. **BPH & ED:** 5 mg taken once daily, without regard to timing of sexual activity; a starting dose of 2.5 mg daily is recommended if creatinine clearance is 30 to 50 mL/min.
Levitra (vardenafil)	Erectile Dysfunction	For most patients, the starting dose is 10 mg, approximately 60 minutes before sexual activity. May be increased to a maximum dose of 20 mg or decreased to 5 mg based on efficacy and side effects. Maximum frequency is once per day.
Staxyn (vardenafil)	Erectile Dysfunction	The dose is 10 mg, approximately 60 minutes before sexual activity; The maximum dose is one tablet per day. Patients who require a lower or higher dose need to receive vardenafil film-coated tablets. Staxyn provides higher systemic exposure and is not interchangeable with vardenafil film-coated 10 mg tablets (Levitra).
Stendra (avanafil)	Erectile Dysfunction	For most patients, the recommended starting dose is 100 mg, approximately 30 minutes before sexual activity on an as needed basis; may be increased to maximum dose 200 mg or decreased to 50 mg based on efficacy and/or tolerability. Maximum frequency is once per day.
Viagra[a] (sildenafil)	Erectile Dysfunction	For most patients, 50 mg as needed, approximately 1 hour before sexual activity. May be taken from 4 hours to 0.5 hour before sexual activity. Based on effectiveness and toleration, may be increased to a maximum dose of 100 mg or decreased to 25 mg. Maximum frequency is once per day.

a – generic available

Limitations of Use:
The listed phosphodiesterase 5 inhibitors are not indicated for use in pediatrics.[1-4,19] If tadalafil is used with finasteride to initiate BPH treatment, such use is recommended for up to 26 weeks because the incremental benefit of tadalafil decreases from 4 weeks until 26 weeks, and the incremental benefit of tadalafil beyond 26 weeks is unknown.[1]

CLINICAL RATIONALE

Efficacy – Erectile Dysfunction (ED)

American Urological Association (AUA) guidelines state that oral phosphodiesterase type 5 (PDE5) inhibitors, unless contraindicated, should be offered as a first-line therapy for ED. At this time, there is insufficient evidence to support the superiority of one agent over the others. Currently, there are not sufficient data to counsel patients on the likelihood of success with a different PDE5 inhibitor if they failed an "adequate" trial with one drug. Once an adequate trial has been completed with one drug and all modifiable risk factors have been addressed, the patient may be treated with a different PDE5 inhibitor or proceed with other, more invasive therapies for ED.[5,22]

Sexual behavior studies indicate that commonly prescribed PDE5 inhibitor quantities range from 3 to 6 tablets per patient per month.[6]

Efficacy – Benign Prostatic Hyperplasia (BPH)

Tadalafil is FDA approved for benign prostatic hyperplasia (BPH) and for patients with ED and BPH.[1] Alpha-1-adrenergic antagonists are initial treatment option for the treatment of BPH.[23,24] Tadalafil is a reasonable option for patients who have erectile dysfunction and mild to moderate symptoms of BPH.[23]

Preservation of Erectile Function following Prostatectomy

Penile sensation and the ability to have an orgasm are preserved even if the erectile nerves are removed during radical prostatectomy, leaving several options for treatment of erectile dysfunction. These include the use of oral phosphodiesterase-5 inhibitors, vacuum-assisted erection devices, penile self-injection (prostaglandin E1, papaverine, phentolamine), and intraurethral alprostadil. Phosphodiesterase inhibitors are most helpful in men who have undergone a nerve-sparing procedure.[27] In one study of 91 men presenting with erectile dysfunction following radical prostatectomy, the response rates to sildenafil in men who had undergone bilateral nerve-sparing, unilateral nerve-sparing, and a non-nerve sparing approach were 72, 50, and 15 percent, respectively.[29] A study of 174 men showed a response rate to sildenafil in men who had undergone bilateral nerve-sparing, unilateral nverve-sparing, and non-nerve-sparing were 76%, 53.5%, and 14.2% respectively.[34]

The response to sildenafil increases with time following radical prostatectomy.[27] The recovery of erectile function can require as long as 18 to 24 months. Initial failures of therapy might be followed by successful rechallenge at 18 to 24 months postoperatively.[28] In a study in which 95 percent of men had undergone nerve-sparing procedures, 60 percent reported benefit from sildenafil at 18 to 24 months after surgery, significantly higher than the 29 percent who reported benefit in the first six months after surgery.[27]

Safety

Cialis is contraindicated in the following:[1]

- Administration of Cialis to patients using any form of organic nitrate is contraindicated. Cialis was shown to potentiate the hypotensive effect of nitrates
- History of known serious hypersensitivity reaction to Cialis or Adcirca
- Administration with guanylate cyclase (GC) stimulators, such as riociguat

Levitra is contraindicated in the following:[2]

- Administration with nitrates and nitric oxide donors
- Administration with guanylate cyclase (GC) stimulators, such as riociguat

Viagra is contraindicated in the following:[3]

- Administration of Viagra to patients using nitric oxide donors, such as organic nitrates or organic nitrites in any form. Viagra was shown to potentiate the hypotensive effect of nitrates
- Known hypersensitivity to sildenafil or any component of tablet
- Administration with guanylate cyclase (GC) stimulators, such as riociguat

Staxyn is contraindicated in the following:[4]
- Administration with nitrates and nitric oxide donors
- Administration with guanylate cyclase (GC) stimulators, such as riociguat

Stendra is contraindicated in the following:[19]
- Administration of Stendra to patients using any form of organic nitrate is contraindicated
- Hypersensitivity to any component of the Stendra tablet
- Administration with guanylate cyclase (GC) stimulators, such as riociguat

For additional clinical information see Prime Therapeutics Formulary Chapter 5.10C: Impotence Agents.

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