



Drug Quantity Management – Per Rx Medications for Erectile Dysfunction Dispensing Limit

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Product Identifier(s)

31072, 31112, 36934

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National Formulary Medical Necessity

Drugs Affected

- sildenafil citrate tablets (Viagra®, generics)
- tadalafil tablets (Cialis®, generics)
- vardenafil tablets (Levitra®, generics)
- vardenafil orally disintegrating tablets (Staxyn, generics)

Viagra (sildenafil) 25, 50, and 100 mg tablets

Maximum quantity per Rx = 8 or 6 tablets
(based on choice of client plan design)

Viagra is available in 25 mg, 50 mg, and 100 mg tablets. For most individuals the recommended dose for treatment of erectile dysfunction is 50 mg taken from 4 to 0.5 hours before sexual activity (“on demand”); the dose may be increased to 100 mg or decreased to 25 mg based on effectiveness.¹ The maximum recommended dosing frequency is once per day. Eight tablets will supply enough drug for 8 doses. Likewise, six tablets will supply enough drug for 6 doses. If additional medication is needed for erectile/sexual dysfunction, the participant will need to pay an additional co-pay.

Criteria

Cigna covers quantities as medically necessary when the following criteria are met:

All approvals are provided for 12 months in duration unless otherwise noted below.

1. **Erectile dysfunction or sexual dysfunction:** No overrides recommended.
2. **Prophylaxis after radical prostatectomy (early penile rehabilitation).** Approve 30 tablets per dispensing.
 - o Authorization for more than 30 tablets per 30 days is not recommended.
 - o Authorization for additional doses for “on demand” use are not recommended.

Sildenafil 25, 50, or 100 mg given on a daily basis has been used to improve the return of normal spontaneous erectile function, improve tissue oxygenation and prevent penile fibrosis after nerve-sparing radical prostatectomy.³⁰⁻³⁴ This has included using daily sildenafil in combination with alprostadil (injection, suppository) given 2 to 3 times weekly.³³ Very limited published information from well-designed controlled trials in a sufficient number of individuals and with adequate follow-up is available.

According to a recent review article, pharmacological therapy is currently the most attractive option for individuals with ED post radical prostatectomy due to the favorable safety profile and ease of use.⁵⁸

3. **Pulmonary arterial hypertension (PAH) [men or women]:** Approve the quantity requested, not to exceed 150 tablets of Viagra per dispensing.

Revatio® contains sildenafil citrate, the same active ingredient as Viagra, and is FDA-approved for the treatment of PAH.¹⁵ Viagra is available in 25, 50, and 100 mg tablets, and Revatio is available as 20 mg tablets. Sildenafil (Viagra) has been used for PAH based on case reports and placebo-controlled, double-blind studies. Doses of sildenafil that were used in these reports ranged from 25 mg twice daily to 100 mg five times daily.¹⁶⁻²³ Note: PAH can be due to a variety of causes and is associated with many different conditions (e.g., Eisenmenger syndrome).²³⁻²⁷

4. **Raynaud’s phenomenon (men or women):** Approve the quantity requested, not to exceed 90 tablets per dispensing.

Doses ranging from 12.5 mg to 300 mg daily have been used.⁹⁻¹⁴ Typical doses and regimens that have been shown to decrease frequency and duration of Raynaud’s symptoms (i.e., decrease the number of digital ulcers and speed healing time) are sildenafil 50 mg twice daily to 50 mg three times daily.

5. **Benign prostatic hyperplasia (BPH) with or without erectile dysfunction:** Approve 30 tablets per dispensing.

Daily sildenafil has been effective in men with LUTS due to BPH plus erectile dysfunction.²⁸⁻²⁹ In a 12-week, double-blind multicenter study, individuals were randomized to Viagra (50 mg nightly or 30 to 60 minutes before sexual activity for 2 weeks and then increased to 100 mg nightly for 10 weeks) or placebo.²⁸ Individuals were not on 5 α -reductase inhibitors or α_1 -blockers during the study. After 12 weeks, the individuals on Viagra had significant ($P < 0.0001$) improvements in erectile function and in LUTS from baseline. There was no significant difference in urinary flow between the groups.

6. **High-altitude pulmonary edema (HAPE), treatment or prevention:** Approve one time for the quantity requested, not to exceed 90 tablets per dispensing of Viagra 50 mg. Authorization for additional quantities of Viagra 25 mg or 100 mg is not recommended.

Published guidelines for the prevention of HAPE recommend nifedipine as the preferred pharmacologic treatment option in individuals who have a history of HAPE.³⁵ Other pharmacologic therapies mentioned in the guidelines for the prevention and/or treatment of HAPE include salmeterol inhalation powder, sildenafil, tadalafil, dexamethasone, or acetazolamide. For sildenafil, published guidelines recommend a dose of 50 mg every eight hours for the prevention of HAPE. In a randomized, double-blind, placebo-controlled

crossover study sildenafil 50 mg was shown to significantly improve cardiac output and exercise capability and reduce systolic pulmonary artery pressure at rest and during exercise over placebo in healthy individuals who ascended to a high altitude (5400 m).³⁶ But in another double-blind, randomized, placebo-controlled study (n = 62), daily administration of Viagra had no significant effect on pulmonary artery systolic pressure (PASP), which is a prerequisite for the development of HAPE, following a period of acclimatization at 3650 meters.⁵⁷

Cialis 2.5 mg

Maximum quantity per Rx = 30 tablets

Cialis 5 mg, 10 mg, 20 mg tablets

Maximum quantity per Rx = 8 or 6 tablets
(based on choice of client plan design)

Cialis is available in 2.5 mg, 5 mg, 10 mg, and 20 mg tablets.

Cialis for Use as Needed

The recommended starting dose for treatment of erectile dysfunction is 10 mg taken prior to anticipated sexual activity (on demand); the dose may be increased to a maximum of 20 mg or decreased to 5 mg based on efficacy and tolerability.⁷ A starting dose of 5 mg is recommended in individuals with moderate renal impairment and the maximum dose should not exceed 10 mg every 48 hours. The maximum dose in individuals with severe renal impairment on hemodialysis is 5 mg every 72 hours. The maximum dose in individuals with mild or moderate hepatic impairment is 10 mg daily. Eight of the 5 mg, 10 mg or 20 mg tablets will supply enough drug for 8 doses. Likewise, six of the 5 mg, 10 mg or 20 mg tablets will supply enough drug for 6 doses. If additional medication is needed for erectile/sexual dysfunction, the participant will need to pay an additional co-pay.

Cialis for Once Daily Use

The 2.5 mg and 5 mg tablets are indicated for once daily use. For once daily use for ED, the recommended starting dose is 2.5 mg taken at about the same time each day without regard to timing of sexual activity.⁷ The dose for once daily use may be increased to 5 mg based on efficacy and tolerability. For once daily use for benign prostatic hyperplasia (BPH) or BPH and ED, the recommended dose is 5 mg once daily. For individuals with BPH or BPH/ED and a creatinine clearance 30 to 50 ml/min, the recommended starting dose is 2.5 mg, which may be increased to 5 mg based on individual response. Cialis for once daily use is not recommended for use in individuals with a creatinine clearance less than 30 ml/min or individuals on hemodialysis. Therefore, 30 of the 2.5 mg tablets supplies enough drug for daily use in ED at the recommended starting dose. A coverage review is available for individuals who have BPH or are increasing the dose in ED.

Cigna covers quantities as medically necessary when the following criteria are met:

All approvals are provided for 12 months in duration unless otherwise noted below.

Cialis 2.5 mg

No overrides recommended.

Cialis 5 mg

1. **Benign prostatic hyperplasia (BPH) with or without erectile dysfunction.** Approve 60 of the 5 mg tablets per dispensing.

Tadalafil (Cialis) is FDA-approved for the treatment of signs and symptoms of BPH, including men with ED/BPH.⁷ Cialis has been effective in individuals with LUTS secondary to BPH and with or without erectile dysfunction.⁴⁴⁻⁴⁸

2. **For erectile dysfunction and once daily use, without regard to timing of sexual activity.** Approve 30 of the 5 mg tablets per dispensing in men who have tried the 2.5 mg daily dose and are increasing the dose to 5 mg once daily.
 - Authorization for more than 30 tablets per 30 days is not recommended.
 - Authorization for additional doses for “on demand” use are not recommended.

3. **Prophylaxis after radical prostatectomy (early penile rehabilitation).** Approve 30 of the 5 mg tablets for a 30 day supply.
 - Authorization for more than 30 tablets per 30 days is not recommended.
 - Authorization for additional doses for “on demand” use are not recommended.

Phosphodiesterase-5 (PDE5) inhibitors (sildenafil, vardenafil, and tadalafil) have been used to improve the return of normal spontaneous erectile function, improve tissue oxygenation and prevent penile fibrosis after nerve-sparing radical prostatectomy. Very limited published information from well-designed controlled trials in a sufficient number of individuals and with adequate follow-up is available. According to a recent review article, pharmacological therapy is currently the most attractive option for individuals with ED post radical prostatectomy due to the favorable safety profile and ease of use.⁵⁸ Cialis 5 mg has been studied on a dosing schedule where individuals took the drug three days per week.⁵⁹⁻⁶¹

4. **Raynaud’s phenomenon (men or women).** Approve 60 of the 5 mg tablets per dispensing.

Limited information regarding standard dosing is available for the use of Cialis in Raynaud disease.⁴¹⁻⁴³ In a study published as an abstract (study design not described), Cialis 20 mg taken two to three times weekly for 4 weeks was compared to pentoxifylline 600 mg twice daily (BID) for 4 weeks in men with severe Raynaud phenomenon associated with autoimmune diseases.⁴¹ Results for Raynaud’s Condition Score and attack frequency were more favorable with Cialis than with pentoxifylline. In a double-blind, randomized crossover trial involving 24 individuals who were refractory to vasodilators, Cialis 20 mg administered every other day improved symptoms, healed and prevented new digital ulcers, and improved quality of life, compared to placebo.⁴³ In an open-label study, 20 men with systemic sclerosis and Raynaud phenomenon received conventional therapy for Raynaud phenomenon for 12 weeks and then Cialis 10 mg daily for 12 weeks.⁴² Cialis decreased the mean number of Raynaud attacks by more than 68% (from 158 ± 50 to 108 ± 34.3) and improved the Raynaud Condition Score by more than 70% (from 2.8 ± 0.6 to 2.15 ± 0.6).

5. **High-altitude pulmonary edema (HAPE), treatment or prevention:** Approve one time up to 120 tablets of Cialis 5 mg per dispensing.

Published guidelines for the prevention of HAPE recommend nifedipine as the preferred pharmacologic treatment option in individuals who have a history of HAPE.³⁵ Other pharmacologic therapies mentioned in the guidelines for the prevention and/or treatment of HAPE include salmeterol, sildenafil, tadalafil, dexamethasone, or acetazolamide. For tadalafil, published guidelines recommend a dose of 10 mg twice daily for prevention of HAPE.

6. **Pulmonary arterial hypertension (PAH) [men or women].** Approve up to 60 of the 5 mg tablets per dispensing.

Adcirca contains tadalafil, the same active ingredient as Cialis. It comes in 20 mg and 40 mg tablets and is FDA approved at a dose of 40 mg once daily for the treatment of PAH to improve exercise ability.⁴⁹ Tadalafil in doses of 10 mg every 36 hours and 10 mg daily have been used for PAH based on case reports, case series, and a placebo-controlled, double-blind study.⁵⁰⁻⁵⁴ Individuals using 20 mg or 40 mg of Cialis for PAH should use Adcirca.

Cialis 10 mg and 20 mg

7. **Benign prostatic hyperplasia (BPH) with or without erectile dysfunction.** Approve 30 of the 10 mg or 20 mg tablets per dispensing.

While the 2.5 mg and 5 mg strengths of Cialis are FDA-approved for daily use in treating BPH, several studies have demonstrated the effects of daily tadalafil 2.5 mg, 5 mg, 10 mg or 20 mg on lower urinary tract symptoms (LUTS) due to BPH.⁴⁴⁻⁴⁸

8. **Raynaud’s phenomenon (men or women).** Approve 30 of the 10 mg tablets or 15 of the 20 mg tablets per dispensing.

Limited information regarding standard dosing is available for the use of Cialis in Raynaud disease.⁴¹⁻⁴³ In a study published as an abstract (study design not described), Cialis 20 mg taken two to three times weekly for 4 weeks was compared to pentoxifylline 600 mg twice daily (BID) for 4 weeks in men with severe Raynaud phenomenon associated with autoimmune diseases.⁴¹ Results for Raynaud's Condition Score and attack frequency were more favorable with Cialis than with pentoxifylline. In a double-blind, randomized crossover trial involving 24 individuals who were refractory to vasodilators, Cialis 20 mg administered every other day improved symptoms, healed and prevented new digital ulcers, and improved quality of life, compared to placebo.⁴³ In an open-label study, 20 men with systemic sclerosis and Raynaud phenomenon received conventional therapy for Raynaud phenomenon for 12 weeks and then Cialis 10 mg daily for 12 weeks.⁴² Cialis decreased the mean number of Raynaud attacks by more than 68% (from 158 ± 50 to 108 ± 34.3) and improved the Raynaud Condition Score by more than 70% (from 2.8 ± 0.6 to 2.15 ± 0.6).

9. **Prophylaxis after radical prostatectomy (early penile rehabilitation).** Approve 13 of the 10 mg or 20 mg tablets per dispensing.
- Authorization for more than 13 tablets per dispensing is not recommended.
 - Authorization for additional doses for “on demand” use are not recommended.

Phosphodiesterase-5 (PDE5) inhibitors (sildenafil, vardenafil, and tadalafil) have been used to improve the return of normal spontaneous erectile function, improve tissue oxygenation and prevent penile fibrosis after nerve-sparing radical prostatectomy. Very limited published information from well-designed controlled trials in a sufficient number of individuals and with adequate follow-up is available. According to a recent review article, pharmacological therapy is currently the most attractive option for individuals with ED post radical prostatectomy due to the favorable safety profile and ease of use.⁵⁸ Cialis 10 mg and 20 mg have been studied on a dosing schedule where individuals took the drug three days per week.^{40,59-61}

10. **High-altitude pulmonary edema (HAPE), treatment or prevention:** Approve one time up to 60 tablets of Cialis 10 mg or 30 tablets of Cialis 20 mg per dispensing.

Published guidelines for the prevention of HAPE recommend nifedipine as the preferred pharmacologic treatment option in individuals who have a history of HAPE.³⁵ Other pharmacologic therapies mentioned in the guidelines for the prevention and/or treatment of HAPE include salmeterol, sildenafil, tadalafil, dexamethasone, or acetazolamide. For tadalafil, published guidelines recommend a dose of 10 mg twice daily for prevention of HAPE.

11. **Pulmonary arterial hypertension (PAH) [men or women].** Approve up to 30 of the 10 mg tablets per dispensing. Authorization for additional quantities of Cialis 20 mg is not recommended.

Adcirca contains tadalafil, the same active ingredient as Cialis. It comes in 20 mg and 40 mg tablets and is FDA approved at a dose of 40 mg once daily for the treatment of PAH to improve exercise ability.⁴⁹ Tadalafil in doses of 10 mg every 36 hours and 10 mg daily have been used for PAH based on case reports, case series, and a placebo-controlled, double-blind study.⁵⁰⁻⁵⁴ Individuals using 20 mg or 40 mg of Cialis for PAH should use Adcirca.

Levitra 10 mg tablets Maximum quantity per Rx = 8 or 6 tablets (based on choice of client plan design)

Staxyn 10 mg tablets Maximum quantity per Rx = 8 or 6 tablets (based on choice of client plan design)

Levitra and Staxyn both contain the same active ingredient: vardenafil. Levitra is available in 2.5 mg, 5 mg, 10 mg, and 20 mg film-coated tablets. The recommended starting dose for treatment of erectile dysfunction is 10 mg taken approximately 1 hour before sexual activity (“on demand”).² The dose may be increased to a maximum of 20 mg or decreased to 5 mg based on efficacy and tolerability. A starting dose of 5 mg is recommended in individuals ≥ 65 years of age and in individuals with moderate hepatic impairment. The maximum dose in individuals with moderate hepatic impairment is 10 mg. The dosage may need to be adjusted in individuals taking certain other medications (e.g., 2.5 mg every 72 hours when taken with ritonavir; 2.5 mg or 5 mg every 24 hours maximum when taken with itraconazole or ketoconazole depending on the dosage of the antifungal). The maximum dosing frequency is once per day for erectile dysfunction.

Staxyn is available as a 10 mg orally disintegrating tablets (ODT). The recommended dose for the treatment of erectile dysfunction is 10 mg taken orally, as needed, approximately 60 minutes before sexual activity.⁸ The maximum dosing frequency is one tablet per day for erectile dysfunction. Staxyn is not recommended for use in individuals with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment and individuals on renal dialysis. Staxyn is also not recommended in individuals also taking potent or moderate CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, ritonavir, clarithromycin). The package labeling notes Staxyn is not interchangeable with vardenafil 10 mg film-coated tablets because Staxyn provides higher systemic exposure compared to vardenafil 10 mg film-coated tablets. When comparing vardenafil film-coated tablets and the ODT formulation maximum concentrations in plasma after a single dose (C_{max}) are comparable, while time to maximum plasma concentration (T_{max}) is slightly longer with the ODT formulation. However, it is thought that this is unlikely to result in clinically relevant differences in drug absorption. For individuals that require a lower or higher dose of vardenafil, it is recommended that they use vardenafil film-coated tablets.²

Eight tablets of either Levitra or Staxyn will supply enough drug for eight doses. Likewise, six tablets will supply enough drug for six doses. Staxyn is supplied in foil blisterpacks and supplied as a four tablet unit, so dispensing six tablets will require that part of a blisterpack will be dispensed. If additional medication is needed for erectile/sexual dysfunction, the participant will need to pay an additional co-pay.

Cigna covers quantities as medically necessary when the following criteria are met:

All approvals are provided for 12 months in duration unless otherwise noted below.

Levitra 2.5 mg, 5 mg, 20 mg

1. **Prophylaxis after radical prostatectomy (early penile rehabilitation).** Approve 30 tablets per dispensing.
 - Authorization for more than 30 tablets per 30 days is not recommended.
 - Authorization for additional doses for “on demand” use are not recommended.

Phosphodiesterase-5 (PDE5) inhibitors (sildenafil, vardenafil, and tadalafil) have been used to improve the return of normal spontaneous erectile function, improve tissue oxygenation and prevent penile fibrosis after nerve-sparing radical prostatectomy. Very limited published information from well-designed controlled trials in a sufficient number of individuals and with adequate follow-up is available. According to a recent review article, pharmacological therapy is currently the most attractive option for individuals with ED post radical prostatectomy due to the favorable safety profile and ease of use.⁵⁸ Levitra has been studied on a dosing schedule where individuals took the drug once daily.^{39, 57}

2. No other overrides recommended.

Levitra 10 mg and Staxyn 10 mg

1. **Raynaud’s phenomenon (men or women).** Approve the requested quantity, not to exceed 60 of the 10 mg tablets per dispensing.

At a dose of vardenafil 10 mg twice daily, individuals with primary and secondary Raynaud Phenomenon reported a reduction in the number duration of Raynaud attacks per day as well as improvements in digital blood flow and Raynaud Condition Score (RCS).^{37,41,62}

2. **Benign prostatic hyperplasia (BPH) with or without erectile dysfunction.** Approve the requested quantity, not to exceed 60 of the 10 mg tablets per dispensing.

In a phase 2b, multicenter, parallel group, double-blind trial, 222 men with lower urinary tract symptoms (LUTS) secondary to BPH with or without concomitant erectile dysfunction were randomized to vardenafil 10 mg or placebo twice daily for 8 weeks.³⁸ There was an initial 4-week run-in period where no study drug or placebo was given. Other medications for BPH and erectile dysfunction were stopped before and during the study. Individuals had an International Prostate Symptom Score (IPSS) ≥ 12 (mean baseline scores 16.8). The primary efficacy parameters were the IPSS total score and the maximum urinary flow rate (Q_{max}) with 2.2 points difference in IPSS and 2 mL/sec in Q_{max} being significant. After 8 weeks there was a significant improvement in the IPSS total score for vardenafil vs. placebo (-5.9 and -3.6, respectively; difference = 2.3; $P = 0.0013$). This improvement is comparable to those reported with α -blockers. Q_{max} did not change

significantly with therapy, but baseline values were already close to normal. Vardenafil therapy was associated with a nominally statistically significant improvement in erectile function compared to placebo.

3. **Prophylaxis after radical prostatectomy (early penile rehabilitation).** Approve 30 of the 10 mg tablets per dispensing.
 - Authorization for more than 30 tablets per 30 days is not recommended.
 - Authorization for additional doses for “on demand” use are not recommended.

Phosphodiesterase-5 (PDE5) inhibitors (sildenafil, vardenafil, and tadalafil) have been used to improve the return of normal spontaneous erectile function, improve tissue oxygenation and prevent penile fibrosis after nerve-sparing radical prostatectomy. Very limited published information from well-designed controlled trials in a sufficient number of individuals and with adequate follow-up is available. According to a recent review article, pharmacological therapy is currently the most attractive option for individuals with ED post radical prostatectomy due to the favorable safety profile and ease of use.⁵⁸ Levitra has been studied on a dosing schedule where individuals took the drug once daily.^{39, 57}

NOTE: Stendra, alprostadil injection (Caverject, Edex), and urethral suppository (Muse) are subject to Per Rx quantity limits, but do not have exceptions and are not included in this policy.

Conditions Not Covered

Any other exception is considered not medically necessary.

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Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	Reviewed by Clinical Specialists. No changes to criteria.	02/28/2021

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