Erectile Dysfunction Agents
Prior Authorization Criteria

NOTE: This prior authorization (PA) criteria contains a quantity limit of 8 tablets total for any combination of the 3 oral products (sildenafil, tadalafil, or vardenafil) or a quantity limit of 8 units total for any combination of the 3 non-oral alprostadil products (Caverject injection, Edex injection, Muse urethral suppository).

<table>
<thead>
<tr>
<th>Brand</th>
<th>generic</th>
<th>Dosage Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caverject®</td>
<td>alprostadil</td>
<td>injection</td>
</tr>
<tr>
<td>Cialis®</td>
<td>tadalafil</td>
<td>oral tablet</td>
</tr>
<tr>
<td>Edex®</td>
<td>alprostadil</td>
<td>injection</td>
</tr>
<tr>
<td>Levitra®</td>
<td>vardenafil</td>
<td>oral tablet</td>
</tr>
<tr>
<td>Muse®</td>
<td>alprostadil</td>
<td>urethral suppository</td>
</tr>
<tr>
<td>Viagra®</td>
<td>sildenafil</td>
<td>oral tablet</td>
</tr>
</tbody>
</table>

FDA APPROVED INDICATIONS1-6

The following information is taken from individual drug prescribing information and is provided here as background information only. Not all FDA-approved indications may be considered medically necessary. All criteria are found in the section “Prior Authorization Criteria for Approval.”

Cialis2, Levitra4, Viagra6
Cialis (tadalafil), Levitra (vardenafil), and Viagra (sildenafil) are indicated for the treatment of erectile dysfunction.

Caverject1
Caverject (alprostadil) is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology. Intracavernosal Caverject is also indicated as an adjunct to other diagnostic tests in the diagnosis of erectile dysfunction.

Edex3
Edex (alprostadil) is indicated for the treatment of erectile dysfunction due to neurogenic, vasculogenic, psychogenic, or mixed etiology.

Muse5
Muse (alprostadil) is indicated for the treatment of erectile dysfunction. Studies that established benefit demonstrated improvements in success rates for sexual intercourse compared with similarly administered placebo.
SUMMARY OF PRIOR AUTHORIZATION

The intent of the Erectile Dysfunction Prior Authorization (PA) Criteria is to appropriately select patients for therapy according to product labeling and/or guidelines and/or clinical studies. Patients meeting the selection requirements of the PA criteria will be approved for up to 8 units of the requested erectile dysfunction (ED) agent per month for twelve months. For the oral phosphodiesterase type 5 (PDE5) inhibitors (sildenafil, tadalafil, or vardenafil) the PA criteria will approve a quantity of 8 tablets total for any combination of these 3 oral products. Similarly, for the non-oral alprostadil products (Caverject injection, Edex injection, Muse urethral suppository) the PA criteria will approve a quantity of 8 units total for any combination of these 3 products.

The claims adjudication system will reject ED agent claims when the agents are not a covered benefit or for patients who are designated as female or less than eighteen years of age. These claims will be directed to the health plans for determination of coverage.

Male patients eighteen years of age and older may be approved for up to eight units of an ED agent if the following requirements are met:

- The primary diagnosis is erectile dysfunction or impotence (not a primary diagnosis of another sexual disorder) AND
- The diagnosis is erectile dysfunction or impotence secondary to an organic etiology (e.g., diabetes, prostate cancer, vascular insufficiency) that has persisted for a minimum of six months. (NOTE: ED agents are not covered when impotency is an adverse effect of prescription or recreational drug use or lifestyle enhancement) AND
- The patient has not been diagnosed with a bleeding disorder, an active peptic ulcer, or retinitis pigmentosa AND
- The patient does not have genital anatomical deformities that impair erection (e.g. angulation, cavernosal fibrosis, Peyronie’s disease) AND
- The patient is not concurrently prescribed an androgen (patients with hypogonadism may be prescribed testosterone and PDE5 agent concomitantly) AND
- Sildenafil, vardenafil, or tadalafil is not concurrently prescribed with a nitrate or nitric oxide AND
- The patient will not be receiving two ED agents concurrently

CLINICAL RATIONALE FOR PRIOR AUTHORIZATION

The Erectile Dysfunction PA criteria considers therapy with an ED agent appropriate when the patient has been diagnosed with primary erectile dysfunction or impotence and if the erectile dysfunction is secondary to an organic comorbidity such as hypertension, atherosclerosis or other vascular insufficiency, hyperlipidemia, diabetes mellitus, or prostate cancer.

Once ED has been diagnosed and the underlying causes have been treated, the American Urological Association (AUA) in a 2006 guideline recommends treatment with an oral phosphodiesterase type 5 (PDE5) inhibitor (sildenafil, tadalafil, or vardenafil) as first-line therapy, unless contraindicated. Other options include intra-urethral alprostadil, intracavernous vasoactive drug injection, vacuum constriction devices, and penile prosthesis implantation. Use of an ED agent for treatment of ED secondary to prescription or recreational drug use or for lifestyle enhancement will not be considered approvable by this criteria.

The PDE5 inhibitors also have an inhibitory effect on PDE6, located in the rod and cone photoreceptors of the eye. Studies in mice indicate that sildenafil has a significant impact on retinal function and may have an impact on human carriers of retinosa pigmentosa. There is no controlled clinical data evaluating the safety and efficacy of the PDE5 agents in patients with retinitis pigmentosa. This group of patients has been excluded from PDE5 efficacy and safety trials. Use in patients with known hereditary degenerative retinal disorders, including retinitis pigmentosa, is not recommended.
The PDE5 agents have not been evaluated in patients with bleeding disorders or significant active peptic ulcers. Although these agents have not been shown to increase bleeding times in healthy people, use in patients with bleeding disorders or significant peptic ulceration should be based upon careful risk-benefit assessment and used with caution.2

The oral PDE5 ED medications are contraindicated in patients who are taking organic nitrates or nitric oxide due to potentiation of hypotensive effects.2,4,6 Patients prescribed these agents are not candidates for ED agent approval.

All three of the oral PDE5 agents interact with alpha blocking agents to some degree and treatment with an alpha antagonist and all doses of vardenafil and tadalafil as well as 50 mg and 100 mg doses of sildenafil should be administered with caution.7 Prescribing information for PDE5 agents do not list concomitant alpha-blocker use as a contraindication but do recommend that for patients on alpha-blockers, the PDE5 agents should be started only when the patients are stable on alpha-blocker therapy and that they should be started on the lowest PDE5 dose. In those patients already taking an optimized dose of a PDE5 inhibitor, alpha-blocker therapy should be initiated at the lowest dose. Safety of combined use of PDE5 inhibitors and alpha-blockers may be affected by other variables, including intravascular volume depletion and other anti-hypertensive drugs.2,4,6

Current AUA guidelines do not recommend the use of testosterone or other androgens for the treatment of erectile dysfunction in patients with normal testosterone levels. However, men with hypogonadism have a reduced response to PDE5 inhibitors and treatment with testosterone has been shown to improve the response to sildenafil in men with erectile dysfunction with initially low serum testosterone levels.9-10 The PA criteria will allow concomitant use of testosterone and an ED agent when there is evidence if hypogonadism.

The use of alprostadil is contraindicated in patients with anatomical deformation of the penis, such as angulation, cavernosal fibrosis, or Peyronie’s disease.1-6 Alprostadil is contraindicated for patients with penile implants also.1,5,6 Use of alprostadil urethral suppositories has not been evaluated in patients with implants.5 If used, the PDE5 inhibitors should be used with caution in patients with anatomical deformation of the penis.2,4,6

The safety and efficacy of erectile dysfunction agent combinations has not been extensively studied.1-6,12,13 Small studies evaluating alprostadil combined with a PDE5 agent report response rates of ninety-two to one hundred percent in patients who did not respond to oral sildenafil alone.11 Double blind randomized controlled clinical trials are needed to establish benefits, optimal dosage, and possible adverse effects before combination therapy can be recommended.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Erectile Dysfunction Agents

Initial and Renewal Evaluation

1. Is the patient at least 18 years of age and male, and the requested agent is covered under their benefit plan?
   If yes to all requirements, continue to 2.
   If no to any requirement, forward to plan for benefit determination.

2. Does the patient have a diagnosis of primary erectile dysfunction or impotence (not another sexual disorder)?
   If yes, continue to 4. If no, continue to 3.

3. Does the patient have a diagnosis of erectile dysfunction or impotence secondary to an organic (not medication) etiology (e.g., diabetes, prostate cancer, vascular insufficiency) that has persisted for a minimum of 6 month?
   If yes, continue to 4. If no, deny.
4. Does the patient have a genital anatomical deformity (e.g., angulation, cavernosal fibrosis, Peyronie’s disease) that significantly impairs erection or does the patient have a penile implant?  
   If yes, deny. If no, continue to 5.

5. Is the patient prescribed sildenafil, vardenafil, or tadalafil and also being treated with an androgen agent?  
   If yes, continue to 6. If no, continue to 7.

6. Is the androgen agent being prescribed to treat a patient diagnosed with hypogonadism?  
   If yes, continue to 7. If no, deny.

7. Is the patient prescribed sildenafil, vardenafil, or tadalafil and also being treated with a nitrate or nitric oxide?  
   If yes, deny. If no, continue to 8.

8. Has the patient been diagnosed with one of the following:  
   a) bleeding disorder  
   b) active peptic ulcer  
   c) retinitis pigmentosa  
   If yes, deny. If no, continue to 9.

9. Is the patient currently receiving another ED agent?  
   If yes, discontinue previous ED agent and approve for a quantity of 8 units per month for 12 months.  
   If no, approve for a quantity of 8 units per month for 12 months.

NOTE: The PA criteria will approve a quantity of 8 tablets total for any combination of the 3 oral products (sildenafil, tadalafil, or vardenafil) or a quantity of 8 units total for any combination of the 3 non-oral alprostadil products (Caverject injection, Edex injection, Muse urethral suppository).

SUMMARY
The use of an ED agent is appropriate when the patient has been diagnosed with primary erectile dysfunction or impotence and if the erectile dysfunction is secondary to an organic comorbidity such as hypertension, atherosclerosis or other vascular insufficiency, hyperlipidemia, diabetes mellitus, or prostate cancer. Use of an ED agent for treatment of ED secondary to prescription or recreational drug use or for lifestyle enhancement will not be considered approvable by these criteria. The PA criteria for Cialis, Levitra, Viagra, Caverject, Edex, and Muse provide an approval mechanism for patients for whom ED agents are appropriate. Patients meeting the selection requirements of the PA criteria will be approved for up to 8 units of the requested ED agent per month for twelve months. When ED agents are not a covered benefit, when members are designated as female, or when members are less than eighteen years of age, requests will be directed to the health plans for determination of coverage.

REFERENCES


