Alpha Blockers for Benign Prostatic Hyperplasia (BPH)

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Policy
BCBSKC will provide coverage for brand name Alpha Blockers for BPH when the following criteria are met. The brand name medications affected are:

- Cardura® (doxazosin mesylate tablets – Pfizer, generics)
- Cardura® XL (doxazosin mesylate extended-release tablets – Pfizer)
- Flomax® (tamsulosin capsules – Boehringer Ingelheim, generics)
- Hytrin® (terazosin tablets, capsules – Abbott, generics [capsules only])
- Rapaflo™ (silodosin capsules – Watson)
- UroXatral® (alfuzosin extended-release tablets – Sanofi-Aventis, generics)

When Policy Topic is covered:
The most recent guidelines from the American Urological Association (AUA) for BPH were published in 2010. These guidelines do not prefer one alpha₁-blocker or 5 alpha-reductase inhibitor over another. The guideline state that all second and third generation alpha₁-blockers (alfuzosin, doxazosin, tamsulosin, terazosin, and Rapaflo) are appropriate and effective treatment alternatives for patients with bothersome, moderate to severe LUTS secondary to BPH. The relevant, published articles for Rapaflo were unavailable prior to publishing the guideline. Although there are slight differences in the AE profiles of these agents, all appear to have equal clinical effectiveness. The combination of an alpha₁-blocker and a 5 alpha-reductase inhibitor is an appropriate and effective treatment for patients with LUTS associated with demonstrable prostatic enlargement. The guideline recommends that men with LUTS secondary to BPH for whom alpha₁-blocker therapy is offered should be asked about planned cataract surgery.

A step therapy program has been developed to encourage use of a generic alpha₁-blocker for BPH prior to a brand name alpha₁-blocker. If the step therapy rule is not met at the point of service, coverage will be determined by prior authorization criteria.

Step 1: alfuzosin extended-release tablets, doxazosin tablets, tamsulosin capsules, terazosin capsules

Step 2: Cardura tablets, Cardura XL extended-release tablets, Flomax capsules, Hytrin tablets, Rapaflo capsules, UroXatral extended-release tablets

CRITERIA
Exceptions for a Step 2 agent can be made for patients who meet the following conditions/situations:

1. If the patient has tried a Step 1 agent, then authorization for a Step 2 agent may be given.

2. No other exceptions are recommended.

When Policy Topic is not covered:
The use of Alpha Blockers for BPH is considered investigational for all other indications.
Considerations

Alpha Blockers for BPH require prior authorization through the Clinical Pharmacy Department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

The alpha1-blockers act by blocking the alpha1-adrenergic receptors that cause smooth muscle contraction within the prostate and bladder neck; therefore, alpha1-blockers affect the dynamic component of benign prostatic hyperplasia (BPH). These agents reduce urethral pressure and inhibit smooth muscle tone in the prostate and lower urinary tract by interrupting the motor sympathetic adrenergic nerve supply to the prostate. This reduces the pressure, and improves the lower urinary tract symptoms (LUTS) and urinary function in patients with BPH. The alpha1A receptor subtype is predominantly found within the prostate while the alpha1B and alpha1D receptor subtypes primarily regulate contraction of vascular smooth muscle. Alpha1-blockers are classified as first-, second-, or third-generation agents based on their specificity for the prostate. The first-generation alpha1-blockers are not indicated for the treatment of BPH. Hytrin, doxazosin prazosin are second-generation alpha1-blockers. Terazosin, doxazosin, and prazosin are considered non-uroselective and have affinity for all three alpha1 receptor subtypes. Doxazosin (immediate-release) and terazosin are indicated for the symptomatic treatment of BPH and for hypertension. Prazosin is only indicated for hypertension. Cardura XL is only indicated for the treatment of BPH.

Rationale

Efficacy/Comparative Efficacy

Large, double-blind, comparative clinical trials of alpha1-blockers at approved doses for the treatment of BPH are lacking. Direct comparative studies have shown doxazosin immediate-release (dose titrated up to 8 mg/daily as tolerated) and Cardura XL (dose 4 mg up to 8 mg daily based on response) to have similar therapeutic efficacy. According to data derived from indirect comparisons (e.g., meta-analyses and review articles), the alpha1-blockers used in the treatment of BPH have all demonstrated comparable therapeutic efficacy in terms of symptom relief and urodynamic improvements when used at equivalent doses.

Adverse Events (AEs)

Cardiovascular (CV) Effects

Labeling for all alpha1-blockers contain a warning for syncope and orthostatic (postural) hypotension. Second-generation alpha1-blockers (indicated to treat BPH and hypertension [doxazosin, terazosin]) are associated with a higher incidence of CV-related AEs (i.e., dizziness, orthostatic hypotension) than the third generation alpha1-blockers (indicated only for BPH [tamsulosin, Rapaflo, alfuzosin extended-release]).
Intraoperative Floppy Iris Syndrome (IFIS)

IFIS is listed as a precaution in the product labeling for alpha blockers. This syndrome appears to be associated with alpha1A-blockers based on alpha1-receptor subtype selectivity. Tamsulosin and Rapaflo are the only alpha1-blockers that are specific to the alpha1A receptor subtype.

The association of IFIS with Rapaflo could be similar to that seen with tamsulosin due to similar receptor specificity; however, based on the current evidence and limited data with Rapaflo, this remains to be determined.

References:


Billing Coding/Physician Documentation Information

N/A The Alpha Blockers for BPH are considered a pharmacy benefit.

Additional Policy Key Words

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Related Topics

N/A

Policy Implementation/Update Information

07/2014 New Policy titled ADHD Stimulant Step Therapy Program

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