Alpha Blockers for Benign Prostatic Hyperplasia (BPH)

Policy Number: 5.01.583  Last Review: 7/2019
Origination: 07/2014  Next Review: 7/2020

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) 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)
- Terazosin capsules – Apotex, generics
- Rapaflo™ (silodosin capsules – Watson)
- UroXatral® (alfuzosin extended-release tablets – Sanofi-Aventis, generics)

When Policy Topic is covered
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 for a Step 2 agent at the point of service, coverage will be determined by the step therapy criteria below. All approvals are provided for 1 year in duration.

Automation: Patients with a history of one Step 1 drug within the 130-day look-back period are excluded from step therapy.

Step 1: alfuzosin extended-release tablets, doxazosin tablets, tamsulosin capsules, terazosin capsules
Step 2: Cardura tablets, Cardura XL extended-release tablets, Flomax capsules, 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: 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 alpha-1-blockers act by blocking the alpha-1-adrenergic receptors that cause smooth muscle contraction within the prostate and bladder neck; therefore, alpha-1-blockers affect the dynamic component of benign prostatic hyperplasia (BPH).\(^1\) 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.\(^2\) Alpha-1-blockers are classified as first-, second-, or third-generation agents based on their specificity for the prostate.\(^3\) The first-generation alpha-1-blockers are not indicated for BPH. Terazosin, doxazosin, and prazosin are second-generation alpha-1-blockers.\(^3\)\(^4\) They are considered non-uroselective and have affinity for all three alpha\(_1\) receptor subtypes. Doxazosin (immediate-release) and terazosin are indicated for the symptomatic treatment of BPH and for hypertension.\(^5\)\(^6\) Prazosin is only indicated for hypertension.\(^7\) Cardura XL is only indicated for the treatment of signs and symptoms of BPH.\(^8\) Tamsulosin, alfuzosin, and Rapaflo are third-generation alpha-1-blockers because they exhibit selectivity for alpha\(_{1A}\)-receptors in the prostate.\(^9\)\(^10\) Alfuzosin is considered functionally and clinically uroselective.\(^3\) Alfuzosin is not selective for a specific alpha\(_1\) receptor subtype, but instead exhibits selectivity for alpha\(_1\)-adrenergic receptors in the lower urinary tract.\(^11\) Blockade of these receptors can result in relaxation of the smooth muscle in the bladder neck and prostate, leading to improved urine flow and reduced BPH symptoms. The clinical significance of selectivity for the alpha\(_{1A}\)-receptor continues to be debated. Theoretically, agents with high selectivity for the alpha\(_{1A}\)-receptor should have less effect on blood pressure compared to other non-selective alpha-1-blockers.

**Rationale**

**Efficacy/Comparative Efficacy**

Large, double-blind, comparative clinical trials of alpha-1-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.\(^8\) According to data derived from indirect comparisons (e.g., meta-analyses and review articles), the alpha-1-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.\(^8\)\(^12\)-\(^15\)

**Guidelines**

The most recent guidelines from the American Urological Association (AUA) for BPH were published in 2010.\(^11\) These guidelines do not prefer one alpha-1-blocker or 5 alpha-reductase inhibitor over another. The guideline state that all second and third generation alpha-1-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.

**References**


Billing Coding/Physician Documentation Information

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

Additional Policy Key Words

Policy Number: 5.01.583

Policy Implementation/Update Information

<table>
<thead>
<tr>
<th>Date</th>
<th>Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>07/2014</td>
<td>New Policy titled Alpha Blockers for Benign Prostatic Hyperplasia (BPH) Step Therapy Program</td>
</tr>
<tr>
<td>07/2015</td>
<td>Annual Review- no changes made</td>
</tr>
<tr>
<td>07/2016</td>
<td>Annual Review- no changes made to policy statement</td>
</tr>
<tr>
<td>07/2017</td>
<td>Annual Review- no changes made to policy statement</td>
</tr>
<tr>
<td>07/2018</td>
<td>Annual review – no changes made</td>
</tr>
<tr>
<td>07/2019</td>
<td>Annual review – no changes made</td>
</tr>
</tbody>
</table>

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.