



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Finasteride (Proscar®)**

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## Hyperlink to Related Coverage Policies

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

## Coverage Policy

**CIGNA covers finasteride (Proscar®) as medically necessary for the treatment of symptomatic benign prostatic hyperplasia (BPH)**

### FDA Approved Indications

Proscar is indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to - improve symptoms, reduce the risk of acute urinary retention, reduce the risk of the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy. Proscar administered in combination with the alpha-blocker doxazosin is indicated to reduce the risk of symptomatic progression of BPH (a confirmed ε4 point increase in AUA symptom score).

### FDA Recommended Dosing

The recommended dose is 5 mg orally once a day. Proscar can be administered alone or in combination with the alpha-blocker doxazosin. Proscar may be administered with or without meals. No dosage adjustment is necessary for patients with renal impairment or for the elderly.

### Drug Availability

Proscar tablets 5 mg are blue, modified apple-shaped, film-coated tablets, with the code MSD 72 on one side and PROSCAR on the other. They are supplied as follows in bottles of 30 or bottles of 100.

## General Background

### Pharmacology

Finasteride, a synthetic 4-azasteroid compound, is an inhibitor of Type II 5 alpha-reductase, an intracellular enzyme which metabolizes testosterone into the more potent androgen dihydrotestosterone (DHT). In benign prostatic hyperplasia (BPH), enlargement of the prostate gland is dependent upon the conversion of testosterone to DHT within the prostate. Finasteride is highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor and has no androgenic, antiandrogenic, estrogenic, antiestrogenic, or progestational effects.

Approximately 90% of circulating finasteride is bound to plasma proteins. Finasteride has been found to cross the blood-brain barrier. The elimination rate of finasteride is decreased in the elderly, but no dosage adjustment is necessary. No dosage adjustment is necessary in patients with renal insufficiency. After a single dose of <sup>14</sup>C-finasteride, all values including area under the curve (AUC), maximum plasma concentration, half-life, and protein binding in patients with chronic renal impairment with creatinine clearances ranging from 0.15 to 0.92 mL/s (9.0 to 55 mL/min) were similar to those values obtained in healthy volunteers.

### Clinical Efficacy

Finasteride at 5 mg/day was initially evaluated in patients with symptoms of BPH and enlarged prostates by digital rectal examination in two one-year, placebo-controlled, randomized, double-blind, Phase III studies and their five-year open extensions. Of 536 patients originally randomized to receive finasteride 5 mg/day, 234 completed an additional five years of therapy and were available for analysis. The efficacy parameters were symptom score, maximum urinary flow rate, and prostate volume. Mean total symptom scores decreased from baseline as early as week two. Mean prostate volume at baseline ranged between 40–50 cc. In both studies, prostate volume was significantly reduced compared to baseline and placebo at first evaluation (three months). Compared with placebo, a significant improvement in symptoms was observed by months seven and ten in these studies. Although an early improvement in urinary symptoms was seen in some patients, a therapeutic trial of at least six months was generally necessary to assess whether a beneficial response in symptom relief had been achieved. In addition, the maximum urinary flow rate was significantly increased compared to baseline by week two. Compared with placebo, a significant increase in maximum urinary flow rate was observed by months four and seven in these studies. These effects were maintained through the first year and throughout an additional five years of extension studies.

Finasteride was further evaluated in the Proscar Long-Term Efficacy and Safety Study (PLESS), a double-blind, randomized, placebo-controlled, four-year multicenter study. This study assessed the effect of therapy with finasteride 5 mg/day on symptoms of BPH and BPH-related urologic events (surgical intervention [e.g., transurethral resection of the prostate and prostatectomy] or acute urinary retention requiring catheterization). A total of 3040 patients between the ages of 45 and 78, with moderate to severe symptoms of BPH and an enlarged prostate, were randomized into the study (1524 to finasteride, 1516 to placebo) and 3016 patients were evaluable for efficacy. A total of 1883 patients completed the four-year study (1000 in the finasteride group, 883 in the placebo group). In this study, surgery or acute urinary retention requiring catheterization occurred in 13.2% of the patients taking placebo compared with 6.6% of the patients taking finasteride, representing a 51% reduction in risk for surgery or acute urinary retention over four years. Finasteride reduced the risk of surgery by 55% (10.1% for placebo vs. 4.6% for finasteride,  $p < 0.001$ ) and reduced the risk of acute urinary retention by 57% (6.6% for placebo vs. 2.8% for finasteride,  $p < 0.001$ ). The reduction in risk was evident between treatment groups at first evaluation (four months) and was maintained throughout the four-year study. In the patients who remained on therapy for the duration of the four-year study, finasteride improved the symptom score by 3.3 points compared with 1.3 points in the placebo group ( $p < 0.001$ ). An improvement in symptom score was evident at one year in patients treated with finasteride, and this improvement continued through the fourth year. Symptom scores improved in patients treated with placebo in the first year but worsened thereafter. Patients with moderate to severe symptoms at baseline tended to have the greatest improvement in symptom score. There was a clear separation between treatment groups in maximum urinary flow rate in favor of finasteride by the fourth month, which was maintained throughout the study. Mean maximum urinary flow rate at baseline was approximately 11 mL/sec in both treatment groups. In the patients who remained on therapy for the duration of the study and had evaluable urinary flow data, finasteride increased maximum urinary flow rate by 1.9 mL/sec compared with 0.2 mL/sec in the placebo group. Prostate volume was assessed yearly by magnetic resonance imaging (MRI) in a subset of patients ( $n = 284$ ). In patients treated with finasteride, prostate volume was reduced compared to both baseline and placebo throughout the four-year

study. Of the patients in the MRI subset who remained on therapy for the duration of the study, finasteride decreased prostate volume by 17.9% (from 55.9 mL at baseline to 45.8 mL at four years) compared with an increase of 14.1% (from 51.3 mL to 58.5 mL) in the placebo group ( $p < 0.001$ ). The drug-related adverse experiences seen in this study were consistent with those seen in previous studies. Although the clinical significance is unclear, a higher incidence of cataracts (4.2%, finasteride vs. 2.5%, placebo) and diabetes (2.8%, finasteride vs. 1.7%, placebo) was observed in patients receiving finasteride. None of these cases was considered drug related by the investigator.

The Medical Therapy of Prostatic Symptoms (MTOPS) Trial was a double-blind, randomized, placebo-controlled, multicenter, four- to six-year study (average five years) in 3047 men with symptomatic BPH, who were randomized to receive finasteride 5 mg/day ( $n=768$ ), doxazosin 4 or 8 mg/day ( $n=756$ ), the combination of finasteride 5 mg/day and doxazosin 4 or 8 mg/day ( $n=786$ ), or placebo ( $n=737$ ). The mean patient age at randomization was 62.6 years ( $\pm 7.3$  years). The mean duration of BPH symptoms was 4.7 years ( $\pm 4.6$  years). The primary endpoint was a composite measure of the first occurrence of any of the following five outcomes: a  $\geq 4$  point confirmed increase from baseline in symptom score, acute urinary retention, BPH related renal insufficiency (i.e., creatinine rise), recurrent urinary tract infections or urosepsis, or incontinence. Compared to placebo, treatment with finasteride, doxazosin, or combination therapy resulted in a reduction in the risk of experiencing one of these five outcome events by 34% ( $p=0.002$ ), 39% ( $p < 0.001$ ), and 67% ( $p < 0.001$ ), respectively. Combination therapy resulted in a significant reduction in the risk of the primary endpoint compared to treatment with finasteride alone (49%;  $p \leq 0.001$ ) or doxazosin alone (46%;  $p \leq 0.001$ ). Combination therapy reduced the risk of clinical progression of BPH to a significantly greater extent than either finasteride or doxazosin alone, which were not significantly different from each other. The majority of the events (274 out of 351) that constituted BPH progression were confirmed  $\geq 4$  point increases in symptom score; the risk of symptom score progression was reduced by 30% ( $p=0.016$ ), 46% ( $p < 0.001$ ), and 64% ( $p < 0.001$ ) in the finasteride, doxazosin, and combination groups, respectively, compared to placebo (9.6% for finasteride, 7.8% for doxazosin, 5.2% for the combination and 13.6% for the placebo). Treatment with finasteride, doxazosin or the combination reduced the mean symptom score from the baseline at year four. In MTOPS, the risk of developing acute urinary retention was reduced by 67% and 79% in the finasteride and combination groups, respectively, compared to the placebo group (0.8% for finasteride, 0.5% for combination and 2.4% for placebo). Also, the risk of requiring BPH-related invasive therapy was reduced by 64% and 67% in the finasteride and combination groups, respectively, compared to the placebo group (2% for finasteride, 1.8% for the combination and 5.4% for placebo).

The results of MTOPS confirm the findings of the four-year placebo-controlled study PLESS that treatment with finasteride reduces the risk of acute urinary retention and the need for BPH-related surgery. The results of MTOPS further demonstrate that the combination of finasteride and doxazosin reduces the risk of BPH progression to a significantly greater extent than either therapy administered alone.

### **Adverse Reactions/Contraindications**

Finasteride is contraindicated for use in women when they are or may potentially be pregnant. Because of the ability of Type II 5 alpha-reductase inhibitors such as finasteride to inhibit conversion of testosterone to dihydrotestosterone, finasteride may cause abnormalities of the external genitalia of a male fetus when administered to a pregnant woman. It is not known whether finasteride is excreted in human milk. The most common adverse event reported is impotence, and less common side effects include breast enlargement and tenderness, skin rash, and swelling of lips.

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## **Coding/Billing Information**

**Note:** This section is not in use.

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