FINASTERIDE 5MG FILM-COATED TABLETS

PL 04569/0721

UKPAR

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FINASTERIDE 5MG FILM-COATED TABLETS

PL 04569/0721

LAY SUMMARY

The MHRA granted Generics (UK) Limited a Marketing Authorisation (licence) for the medicinal product Finasteride 5mg Film-Coated Tablets (PL 04569/0721). This medicine is available by prescription only.

With advancing age some men suffer from enlargement of the prostate gland, causing them problems with passing urine. Finasteride works by reducing levels of the chemical that causes prostate enlargement, thus reducing the size of the enlarged prostate and relieving urinary symptoms.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Finasteride 5mg Film-Coated Tablets outweigh the risks, hence Marketing Authorisation has been granted.

FINASTERIDE 5MG FILM-COATED TABLETS

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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisation for the medicinal product Finasteride 5mg Film-Coated Tablets (PL 04569/0721) to Generics UK Limited on 12th April 2007. This is a prescription-only medicine (POM).

This is a national application for Finasteride 5mg Film-Coated Tablets submitted under Article 10.1 of Directive 2001/83, claiming to be a generic medicinal product of Proscar 5mg tablets (PL 00025/0279) licensed to Merck, Sharp and Dohme in May 1992.

Finasteride is a competitive inhibitor of 5 α-reductase, a chemical that metabolises the conversion of testosterone into the more potent dihydrotestosterone. Enlargement of the prostate gland is dependent upon the conversion of testosterone to dihydotestosterone within the prostate. Finasteride thus inhibits prostatic enlargement by reducing circulating and intraprostatic dihydrotestosterone.

PHARMACEUTICAL ASSESSMENT

DRUG SUBSTANCE

This is subject to DMF. A letter of access has been provided

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

An appropriate specification based on the European Pharmacopoeia has been provided.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Active finasteride is stored in appropriate packaging. The specifications and typical analytical test reports are provided and are satisfactory.

Batch analysis data are provided and comply with the proposed specification.

Satisfactory certificates of analysis have been provided for working standards used by the active substance manufacturer and finished product manufacturer during validation studies.

Appropriate stability data has been provided.

DRUG PRODUCT

Other ingredients

Other ingredients consist of pharmaceutical excipients, namely cellulose, microcrystalline, docusate sodium, lactose monohydrate, magnesium stearate, pregelatinised maize starch, sodium starch glycolate, povidone, Indigo carmine (E132), titanium dioxide (E171), hypromellose, hydroxypropylcellulose, and purified talc. All excipients used comply with their respective European Pharmacopoeia monograph with the exception of Indigo carmine (E132) and purified talc. Satisfactory certificates of analysis have been provided for all excipients.

The only excipients used that contain material of animal or human origin are lactose monohydrate and magnesium stearate. The applicant has provided a declaration that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption. Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

Pharmaceutical development

The objective of the pharmaceutical development programme was to produce a product containing Finasteride 5mg Film-Coated Tablets that are tolerable and which could be considered as generic products to the originator product Proscar 5mg Tablets.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

Dissolution and impurity profiles
Dissolution and impurity profiles for the drug product were found to be similar to that for the reference product.

Manufacture
A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation has been carried out on batches. The results are satisfactory.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and appropriate in-process controls are applied.

Finished product specification
The finished product specification is satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container Closure System
Product is packaged in to PVC/Aluminium blisters. Specifications and Certificates of Analysis for all packaging types used have been provided. These are satisfactory. All primary product packaging complies with EU legislation regarding contact with food.

Stability
Finished product stability studies have been conducted in accordance with current guidelines. Based on the results, a shelf-life of 3 years has been set. This is acceptable.

Bioequivalence/bioavailability
Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence study. Bio-analytical methods used have been satisfactorily validated. Satisfactory bioequivalence is seen between the test and reference product.

SPC, PIL, Labels
The SPC, PIL and labels are pharmaceutically acceptable.

The PIL is in compliance with current guidelines. The marketing authorisation holder has provided a commitment to update the marketing authorisation with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

Conclusion

The proposed product has been shown to be a generic product of the reference product and has met the requirements with respect to qualitative and quantitative content of the active substance. Similar dissolution profiles have been demonstrated for the proposed and reference products. It is recommended that Marketing Authorisation should be granted for this application.

PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required for an application of this type.

CLINICAL ASSESSMENT

1. INTRODUCTION

Finasteride is a competitive inhibitor of 5 α-reductase that metabolises the conversion of testosterone into the more potent dihydrotestosterone. Enlargement of the prostate gland is dependent upon the conversion of testosterone to dihydotestosterone within the prostate. Finasteride thus inhibits prostatic enlargement by reducing circulating and intraprostatic dihydrotestosterone.
This application is claiming to be a generic medicinal product of Proscar manufactured by Merck Sharpe and Dohme Limited.

2. BACKGROUND

Merck Sharpe and Dohme Limited was granted a product licence (00025/0279) in the UK for their Proscar 5 mg tablets on 4 April 2002. Proscar was first licensed in the EEA in France in 1992, the applicant has supplied proof of this; thus the 10 year rule has been fulfilled.

3. INDICATIONS

The applicant has submitted the following:

Finasteride 5 mg film coated tablets are indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with an enlarged prostate to :

-cause regression of the enlarged prostate, improve urinary flow and improve the symptoms associated with BPH

-reduce the incidence of acute urinary retention and the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.

4. DOSE & DOSE SCHEDULE

See the SPC for full details. The recommended dosages and dose schedules are consistent with those for Proscar 5 mg tablets.

5. TOXICOLOGY

No formal data are provided under this heading and none are required for this application.

6. CLINICAL PHARMACOLOGY

A bioequivalence study comparing one 5 mg finasteride film coated tablet to one 5 mg Proscar tablet was undertaken. The Applicant confirms that it was performed according to the standards of GCP.
Healthy volunteers were initially starved overnight then received either one 5 mg finasteride film coated tablet or one 5 mg Proscar Tablet, after a washout period of 10 days they received the alternative therapy. Blood samples were taken for measuring plasma levels of finasteride pre-dose and at regular intervals up to 30 hours post-dose. Statistical analysis of the pharmacokinetic parameters was undertaken according to the study protocol using analysis of variance on the results of the first 24 patients who completed the study. Point estimates and 90% confidence intervals for the "test/reference" mean rations of those variables were calculated. The 90% confidence intervals for the results can be seen in the table below.

Pharmacokinetics of Finasteride 5 mg Film coated tablets and Proscar 5 mg tablets				
Variable	Finasteride Film coated tablets	Proscar Tablets	Mean Ratio	Confidence Interval (%)
Cmax (nanog/ml)	39.90	40.89	97.13	92.77-101.69
AUC 0-t (nanog.h/ml)	325.78	320.92	101.075	96.27-106.12
AUC 0-α (nanog.h/ml)	340.18	332.58	101.81	96.93-106.92

Assessor's Comment
The bioequivalence study was of an appropriate design and sufficient quality. From the results it can be concluded that the test and reference product are bioequivalent according to CPMP guidelines.

7. EFFICACY
No new data are submitted and none are required for this type of application.

8. SAFETY
No formal safety data are presented. The adverse events that can be expected are listed in the SPC and are consistent with those for the reference product.

9. CLINICAL OVERVIEW
A clinical expert report has been written by clinical consultant to the pharmaceutical industry. The report is satisfactory.

10. SUMMARY OF PRODUCT CHARACTERISTICS
The SPC is consistent with that for the innovator product and is acceptable.

11. PATIENT INFORMATION LEAFLET
This is satisfactory.

12. LABELLING
These are satisfactory.

13. MARKETING AUTHORISATION
This is satisfactory

14. DISCUSSION
The data presented has shown that Finasteride 5 mg Film-Coated Tablets are a generic medicinal product of Proscar 5 mg Tablets.

15. RECOMMENDATIONS
The efficacy and safety of the product are satisfactory for the grant of a product licence.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Finasteride 5mg Film-Coated Tablets are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Based on the submitted bioequivalence study Finasteride 5mg Film-Coated Tablets are considered bioequivalent with Proscar 5mg Tablets.

No new or unexpected safety concerns arise from this application.

The SPC, PIL and labelling are satisfactory..

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's product and the innovator product are interchangeable. Extensive clinical experience with Finasteride 5mg Film-Coated Tablets is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

FINASTERIDE 5MG FILM-COATED TABLETS

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STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 20th January 2005
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 3rd February 2005
3	Following assessment of the applications the MHRA requested further information relating to the clinical dossiers on 25th November 2005 and on the quality dossier on 12th October 2005, 26th May 2006, 20th June 2006
4	The applicant responded to the MHRA's requests, providing further information to the clinical section on 26th May 2006 and on the quality section on 20th June 2006, 15th December 2006
5	The applications were determined on 12th April 2007

FINASTERIDE 5MG FILM-COATED TABLETS

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Finasteride 5 mg film coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg of finasteride.

Excipients:

Each tablet contains 1.667 mg docusate sodium.
Each tablet contains 97.583 mg lactose monohydrate.
For a full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
Light blue, biconvex film-coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Finasteride 5 mg film coated tablets are indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with an enlarged prostate to:
-cause regression of the enlarged prostate, improve urinary flow and improve the symptoms associated with BPH
-reduce the incidence of acute urinary retention and the need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.

4.2 Posology and method of administration

In adults
The recommended adult dose is one 5 mg tablet daily, with or without food.
Finasteride 5 mg film coated tablets can be administered alone or in combination with the alpha-blocker doxazosin (see section 5.1 'Pharmacodynamic properties').

Although early improvement in symptoms may be seen, treatment for at least six months may be necessary to assess whether a beneficial response has been achieved. Thereafter, treatment should be continued long term.

In the elderly
No dosage adjustment is required in the elderly.
In patients with renal insufficiency
No dosage adjustment is required in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 ml/min).

In patients with hepatic insufficiency
There are no data available in patients with hepatic insufficiency.

In children
Finasteride 5 mg film coated tablets are contra-indicated in children.

4.3 Contraindications

Hypersensitivity to any component of this product
Women who are or may potentially be pregnant
Children.

4.4 Special warnings and precautions for use

General

Patients with large residual urine volume and / or severely diminished urinary flow should be carefully monitored for obstructive uropathy.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltae insufficiency should not take this medicine.

Effects on prostate - specific antigen (PSA) and prostate cancer detection

No clinical benefit has yet been demonstrated in patients with prostate cancer treated with Finasteride 5 mg film coated tablets.

Digital rectal examination, as well as other evaluations for prostate cancer, should be carried out on patients with BPH prior to initiating therapy with Finasteride 5 mg film coated tablets and periodically thereafter. Generally, when PSA assays are performed, a baseline PSA >10ng/ml (Hybritech) prompts further evaluation and consideration of biopsy; for PSA levels between 4 and 10ng/ml, further evaluation is advisable. There is considerable overlap in PSA levels among men with and without prostate cancer. Therefore, in men with BPH, PSA values within the normal reference range do not rule out prostate cancer regardless of treatment with Finasteride 5 mg film coated tablets. A baseline PSA <4ng/ml does not exclude prostate cancer.

Finasteride 5 mg film coated tablets cause a decrease in serum PSA concentrations by approximately 50% in patients with BPH even in the presence of prostate cancer. This decrease in serum PSA levels in patients with BPH treated with Finasteride 5 mg film coated tablets should be considered when evaluating PSA data and does not rule out concomitant prostate cancer. This decrease is predictable over the entire range of the PSA values, although it may vary in individual patients. In patients treated with Finasteride 5 mg film coated tablets for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. This adjustment preserves the sensitivity and specificity of the PSA assay and maintains its ability to detect prostate cancer.

Any sustained increase in PSA levels of patients treated with finasteride should be carefully evaluated, including consideration of non-compliance to therapy with Finasteride 5 mg film coated tablets.

Free PSA percentage (free to total PSA ratio) is not significantly decreased by Finasteride 5 mg film coated tablets and remains constant even under the influence of Finasteride 5 mg film coated tablets. When percentage free PSA is used as an aid in the detection of prostate cancer, no adjustment is necessary.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically important drug interactions have been identified. Finasteride 5 mg film coated tablets do not appear to significantly affect the cytochrome P450-linked drug metabolising enzyme system. Compounds which have been tested in man include propranolol, digoxin, glibenclamide, warfarin, theophylline, and antipyrine.

Other Concomitant therapy:

Although specific interaction studies were not performed in clinical studies, Finasteride 5 mg film coated tablets were used concomitantly with ACE inhibitors, alpha-blockers, beta-blockers, calcium channel blockers, cardiac nitrates, diuretics, H_2 antagonists, HMG-CoA reductase inhibitors, non-steroidal anti-inflammatory drugs (NSAID's), quinolones and benzodiazepines without evidence of clinically significant adverse interactions.

4.6 Pregnancy and lactation

Pregnancy

Finasteride 5 mg film coated tablets are contra-indicated in women who are or may potentially be pregnant.

Because of the ability of 5 alpha-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including finasteride, may cause abnormalities of the external genitalia of a male fetus when administered to a pregnant woman.
In animal developmental studies, hypospadias were observed in the male offspring of pregnant rats given finasteride at doses ranging from 100 µg/kg/day to 100 mg/kg/day, at an incidence of 3.6% to 100%. Additionally, pregnant rats produced male offspring with decreased prostatic and seminal vesicular weights, delayed preputial separation, transient nipple development and decreased anogenital distance, when given finasteride at doses below the recommended human dose. The critical period during which these effects can be induced has been defined in rats as days 16-17 of gestation.
The changes described above are expected pharmacological effects of 5 alpha-reductase inhibitors. Many of the changes, such as hypospadias, observed in male rats exposed *in utero* to finasteride are similar to those reported in male infants with a genetic deficiency of 5 alpha reductase. It is for these reasons that Finasteride 5 mg film coated tablets are contra-indicated in women who are or may potentially be pregnant.
No effects were seen in female offspring exposed *in utero* to any dose of finasteride.

Exposure to finasteride - risk to male fetus

Crushed or broken Finasteride 5 mg film coated tablet tablets should not be handled by women who are or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male fetus.
Similarly, small amounts of finasteride have been recovered from the semen in subjects receiving Finasteride 5 mg film coated tablets/day. It is not known whether a male fetus may be adversely affected if his mother is exposed to the semen of a patient being treated with finasteride. Therefore, when the sexual partner of a patient is or may potentially be pregnant, the patient should either avoid exposure of his partner to semen (e.g. by use of a condom) or discontinue Finasteride 5 mg film coated tablets.

Lactation
Finasteride 5 mg film coated tablets are not indicated for use in women. It is not known whether finasteride is excreted in human milk.

4.7 Effects on ability to drive and use machines
None reported.

4.8 Undesirable effects
Finasteride 5 mg film coated tablets are well tolerated. In controlled clinical studies where patients received 5 mg of finasteride over periods of up to four years, the following adverse reactions were considered possibly, probably or definitely drug-related and occurred with a frequency greater than placebo and greater than or equal to 1%: impotence, decreased libido, ejaculation disorder, decreased volume of ejaculate; breast enlargement, breast tenderness and rash. There was no evidence of increased adverse experiences with increased duration of treatment with Finasteride 5 mg film coated tablets and the incidence of new drug-related sexual adverse experiences decreased with duration of treatment.

Medical therapy of prostatic symptoms (MTOPS)

The MTOPS study compared finasteride 5 mg/day (n=768), doxazosin 4 or 8 mg/day (n=756), combination therapy of finasteride 5 mg/day and doxazosin 4 or 8 mg/day (n=786), and placebo (n=737). In this study, the safety and tolerability profile of the combination therapy was generally consistent with the profiles of the individual components. The incidence of ejaculation disorder events without regard to drug relationship were: finasteride 8.3%, doxazosin 5.3%, combination 15.0%, placebo 3.9%.

Other long-term data
In a 7 year placebo-controlled trial that enrolled 18,882 healthy men, of whom 9060 had prostate needle biopsy data available for analysis, prostate cancer was detected in 803 (18.4%) men receiving finasteride and 1147 (24.4%) men receiving placebo. In the finasteride group,

280 (6.4%) of men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy vs 237 (5.1%). Of the total cases of prostate cancer diagnosed in this study, approximately 98% were classified as intracapsular (stage T1 or T2). The relationship between long-term use of finasteride and tumours with Gleason scores of 7-10 is unknown.

Post Marketing Experience

The following additional adverse experiences have been reported in post-marketing experience:

- hypersensitivity reactions, including pruritus, urticaria and swelling of the lips and face
- testicular pain.

Laboratory test findings
Serum PSA concentration is correlated with patient age and prostatic volume, and prostatic volume is correlated with patient age. When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels generally decrease in patients treated with Finasteride 5 mg film coated tablets. In most patients, a rapid decrease in PSA is seen within the first months of therapy, after which time PSA levels stabilise to a new baseline. The post-treatment baseline approximates half of the pre-treatment value. Therefore, in typical patients treated with Finasteride 5 mg film coated tablets for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men.

For clinical interpretation see 'Special warnings and precautions for use', *Effects on prostate-specific antigen (PSA) and prostate cancer detection.*

No other difference was observed in patients treated with placebo or Finasteride 5 mg film coated tablets in standard laboratory tests.

4.9 Overdose

No specific treatment of overdosage with Finasteride 5 mg film coated tablets are recommended. Patients have received single doses of Finasteride 5 mg film coated tablets up to 400 mg and multiple doses of Finasteride 5 mg film coated tablets up to 80 mg/day for up to three months without any adverse effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Finasteride is a competitive inhibitor of human Type II 5 α-reductase, an intracellular enzyme which metabolises 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 5 mg film coated tablets are highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor.

In clinical studies of patients with moderate to severe symptoms of BPH, an enlarged prostate on digital rectal examination and low residual urinary volumes, Finasteride 5 mg film coated tablets reduced the incidence of acute retention of urine from 7/100 to 3/100 over four years and the need for surgery (TURP or prostatectomy) from 10/100 to 5/100. These reductions were associated with a 2-point improvement in QUASI-AUA symptom score (range 0-34), a sustained regression in prostate volume of approximately 20% and a sustained increase in urinary flow rate.

Medical therapy of prostatic symptoms
The Medical Therapy of Prostatic Symptoms (MTOPS) Trial was a 4- to 6-year study in 3047 men with symptomatic BPH who were randomised to receive finasteride 5 mg/day, doxazosin 4 or 8 mg/day*, the combination of finasteride 5 mg/day and doxazosin 4 or 8 mg/day*, or placebo. The primary endpoint was time to clinical progression of BPH, defined as a ≥4 point confirmed increase from baseline in symptom score, acute urinary retention, BPH-related

renal insufficiency, recurrent urinary tract infections or urosepsis, or incontinence. Compared to placebo, treatment with finasteride, doxazosin, or combination therapy resulted in a significant reduction in the risk of clinical progression of BPH by 34(p=0.002), 39 (p<0.001), and 67% (p<0.001), respectively. The majority of the events (274 out of 351) that constituted BPH progression were confirmed ≥4 point increases in symptom score; the risk of symptom score progression was reduced by 30 (95% CI 6 to 48%), 46 (95% CI 25 to 60%), and 64% (95% CI 48 to 75%) in the finasteride, doxazosin, and combination groups, respectively, compared to placebo. Acute urinary retention accounted for 41 of the 351 events of BPH progression; the risk of developing acute urinary retention was reduced by 67(p=0.011), 31 (p=0.296), and 79% (p=0.001) in the finasteride, doxazosin, and combination groups, respectively, compared to placebo. Only the finasteride and combination therapy groups were significantly different from placebo

* Titrated from 1 mg to 4 or 8 mg as tolerated over a 3-week period

5.2 Pharmacokinetic properties

After an oral dose of ^{14}C-finasteride in man, 39% of the dose was excreted in the urine in the form of metabolites (virtually no unchanged drug was excreted in the urine), and 57% of total dose was excreted in the faeces. Two metabolites have been identified which possess only a small fraction of the 5 alpha-reductase activity of finasteride.

The oral bioavailability of finasteride is approximately 80%, relative to an intravenous reference dose, and is unaffected by food. Maximum plasma concentrations are reached approximately two hours after dosing and the absorption is complete within 6-8 hours. Protein binding is approximately 93%. Plasma clearance and the volume of distribution are approximately 165 ml/min and 76 1, respectively.

In the elderly, the elimination rate of finasteride is somewhat decreased. Half-life is prolonged from a mean half-life of approximately 6 hours in men aged 18-60 years to 8 hours in men aged more than 70 years. This is of no clinical significance and does not warrant a reduction in dosage.

In patients with chronic renal impairment, whose creatinine clearance ranged from 9-55 ml/min, the disposition of a single dose of ^{14}C-finasteride was not different from that in healthy volunteers. Protein binding also did not differ in patients with renal impairment. A portion of the metabolites which normally is excreted renally was excreted in the faeces. It therefore appears that faecal excretion increases commensurate to the decrease in urinary excretion of metabolites. Dosage adjustment in non-dialysed patients with renal impairment is not necessary.

There are no data available in patients with hepatic insufficiency.

Finasteride has been found to cross the blood-brain barrier. Small amounts of finasteride have been recovered in the seminal fluid of treated patients.

5.3 Preclinical safety data

No further information provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core

Cellulose, Microcrystalline
Docusate sodium
Lactose monohydrate
Magnesium stearate
Pregelatinised maize starch
Sodium starch glycolate
Povidone

Coating
Indigo carmine (E132)
Titanium dioxide (E171)
Hypromellose
Hydroxypropylcellulose
Purified talc

6.2 Incompatibilities
None reported.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container
PVC/Aluminium blisters packs of 10, 14, 15, 20, 28, 30, 50, 56, 98, 100, 300 tablets
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Women should not handle crushed or broken Finasteride 5 mg film coated tablets when they are or may potentially be pregnant (see 'Contraindications', 'Pregnancy and Lactation', *Exposure to finasteride - risk to male foetus*).

7 MARKETING AUTHORISATION HOLDER
Generics [UK] Ltd.
Station Close,
Potters Bar,
Herts.
EN6 1TL
U.K.

8 MARKETING AUTHORISATION NUMBER(S)
PL 04569/0721

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
12/04/2007

10 DATE OF REVISION OF THE TEXT
12/04/2007

PATIENT INFORMATION LEAFLET

FINASTERIDE 5 mg FILM-COATED TABLETS

Read all of this leaflet carefully before you start taking this medicine.
• Keep this leaflet. You may need to read it again • If you have further questions, ask your doctor or pharmacist • This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours • If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

The name of your medicine is Finasteride 5 mg Film-Coated Tablets (we call them Finasteride Tablets throughout this leaflet).

1. WHAT FINASTERIDE TABLETS ARE AND WHAT THEY ARE USED FOR

Finasteride belongs to a group of medicines called "5-alpha reductase inhibitors".
It can be used to treat men with benign prostatic hyperplasia (BPH). In this condition, your prostate is enlarged and this can make it difficult to pass urine. Your prostate is a gland near the bladder. It produces a fluid which carries sperm. Finasteride works by shrinking the prostate gland. This allows urine to pass more easily. It also helps lower the risk of you suddenly being unable to pass urine. This is called "acute urinary retention" and may need surgery. Although BPH is not cancer and does not cause cancer, the two conditions can be present at the same time. Only a doctor can assess the symptoms and their possible causes.

2. BEFORE YOU TAKE FINASTERIDE TABLETS

Do not take Finasteride Tablets:
• if you have taken Finasteride or any of the tablet ingredients before, and suffered an allergic or unusual reaction.

Finasteride is only for men.
• It must not be given to women or children.

Take special care with Finasteride Tablets and talk to your doctor before taking:
• if you need a blood test for something called "PSA" which stands for 'prostate-specific antigen'. This is because Finasteride can lower PSA levels and affect the results of this test. PSA is released into a man's blood by his prostate gland. The amount of PSA in the blood normally increases as a man's prostrate enlarges
• if your sexual partner is pregnant, as you will need to use a condom (see 'Pregnancy and Breast-feeding' section below).

Taking other medicines - Finasteride does not usually interfere with other medicines. However, please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Finasteride Tablets with food and drink - Finasteride Tablets can be taken with or without food.

Pregnancy and breastfeeding - Finasteride must not be given to women, including pregnant women. It can affect the normal development of a male baby's sex organs.
• Crushed or broken tablets should not be handled by a pregnant woman because of the risk of Finasteride being absorbed through the skin.
• If your sexual partner is pregnant, you must use a condom. This is because Finasteride has been found in the semen of men taking Finasteride.
If you have any questions, ask your doctor.

Driving and using machines - Finasteride Tablets should not affect your ability to drive or use machines.

Important information about some of the ingredients of Finasteride Tablets -
Finasteride Tablets contain lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

3. HOW TO TAKE FINASTERIDE TABLETS

Always take Finasteride exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Adults (including the elderly):
• Swallow one tablet each day. You can take it with or without food.
• In some cases, your doctor may also give you other medicine to take (such as Doxazosin).
Finasteride works best when it is taken long-term. It may take at least six months before some patients notice an improvement.

Children: Finasteride must not be given to children.

If you forget to take Finasteride, take it as soon as you remember, unless it is almost time for your next dose. **Do not** take a double dose to make up for a forgotten dose. **If you take more Finasteride than you should**, tell your doctor immediately or go to your nearest casualty department.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Finasteride can cause side effects, although not everybody gets them. **Stop taking Finasteride and tell your doctor straight away or go to your nearest casualty department if you have:**
• swelling of the lips, tongue or face
• difficulty breathing or swallowing
• a skin rash.
You may be allergic to this medicine

Other side effects which are common (more than 1 out of 100) include:
• impotence or less desire to have sex
• ejaculation problems and less fluid produced than normal (this does not appear to affect normal sexual function)
• sore or enlarged breasts
• rash
• pain in the testicles.
If any of the side effects becomes serious, or if you notice any side effects not listed in this leaflet, please tell your pharmacist or doctor.

5. HOW TO STORE THIS MEDICINE

• Keep out of the reach and sight of children • This medicinal product does not require any special storage conditions • Do not take this medicine after the expiry date which is shown on the pack.

6. FURTHER INFORMATION

What Finasteride Tablets contain: Each tablet contains 5 mg of the active ingredient Finasteride. It also contains docusate sodium, magnesium stearate, microcrystalline cellulose, lactose monohydrate, pregelatinised maize starch, sodium starch glycolate and povidone. The tablet coating contains indigo carmine (E132), titanium dioxide (E171), hypromellose, hydroxypropylcellulose and purified talc.

What Finasteride Tablets look like and contents of the pack: Your medicine comes as a 'film-coated' tablet. The tablets are light blue. Finasteride Tablets are available in blister packs of 28 tablets.

Marketing Authorisation Holder and manufacturer: Generics [UK] Limited, Station Close, Potters Bar, Hertfordshire, EN6 1TL.

Date of leaflet preparation: April 2007

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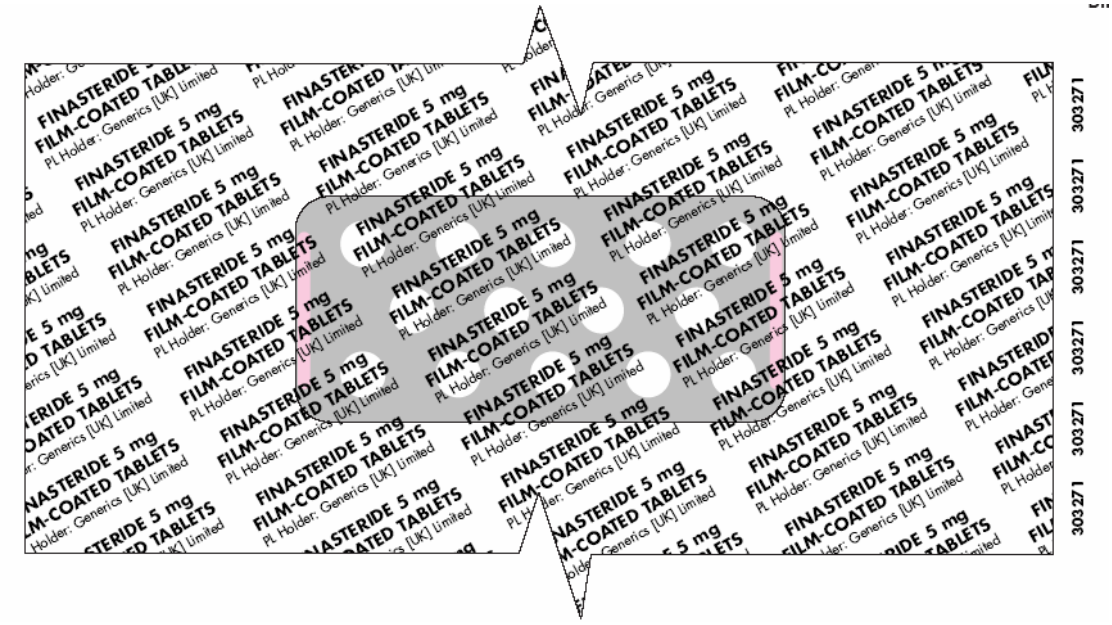
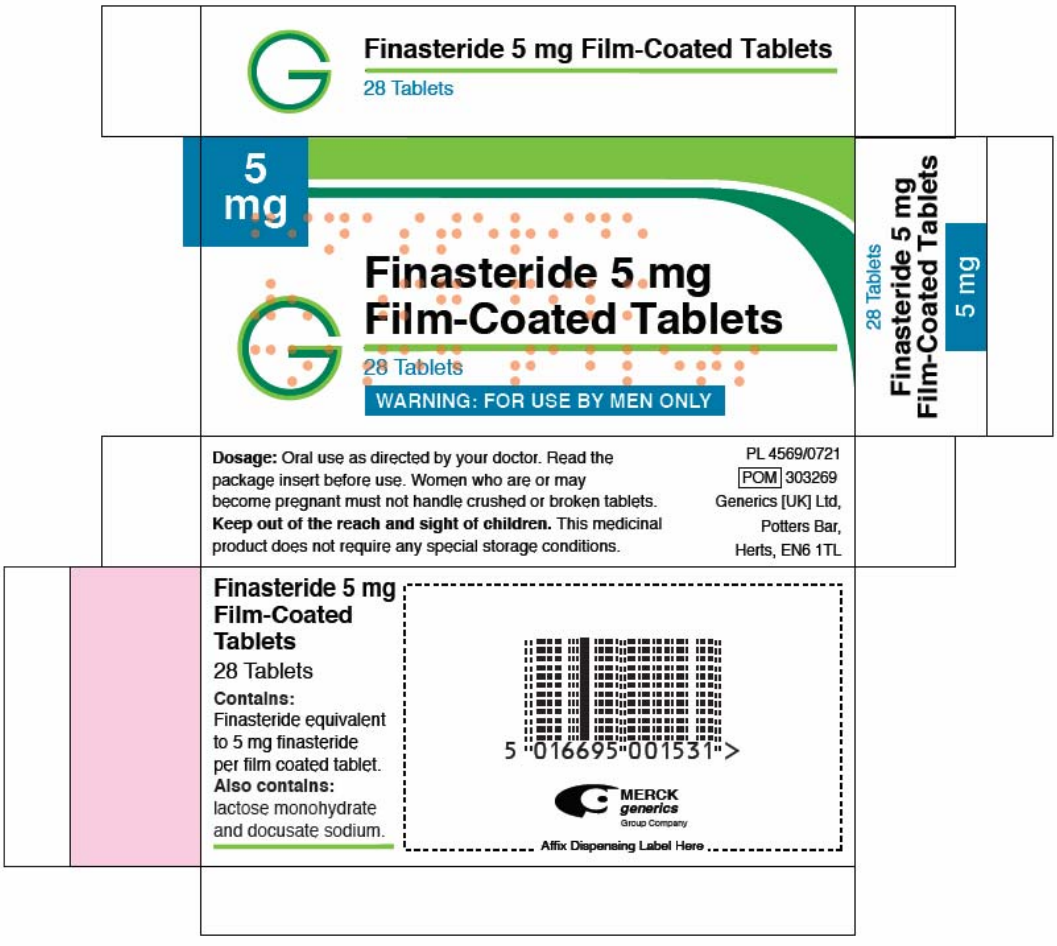
LABELLING


FINASTERIDE 5 mg FILM-COATED TABLETS
PL Holder: Generics [UK] Limited
303271


Finasteride 5 mg Film-Coated Tablets
28 Tablets
5 mg
Finasteride 5 mg Film-Coated Tablets
28 Tablets
WARNING: FOR USE BY MEN ONLY
28 Tablets
Finasteride 5 mg Film-Coated Tablets
5 mg
Dosage: Oral use as directed by your doctor. Read the package insert before use. Women who are or may become pregnant must not handle crushed or broken tablets. Keep out of the reach and sight of children. This medicinal product does not require any special storage conditions.
PL 4569/0721
POM 303269
Generics [UK] Ltd,
Potters Bar,
Herts, EN6 1TL
Finasteride 5 mg Film-Coated Tablets
28 Tablets
Contains:
Finasteride equivalent to 5 mg finasteride per film coated tablet.
Also contains:
lactose monohydrate and docusate sodium.
5 "016695"001531">
MERCK generics
Group Company
Affix Dispensing Label Here