Finasteride 1 mg Film-coated Tablets

PL 00289/0825

UKPAR

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FINASTERIDE 1 MG FILM-COATED TABLETS

PL 00289/0825

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted a Marketing Authorisation (licence) for the medicinal product Finasteride 1 mg Film-coated Tablets (product licence number: PL 00289/0825). This medicine is only available on prescription.

Finasteride 1 mg Film-coated Tablets belong to a group of medicines called testosterone 5-alpha reductase inhibitors. Finasteride is used in the treatment of men with male pattern hair loss (androgenetic alopecia), to increase hair growth and prevent hair loss.

Finasteride 1 mg Film-coated Tablets raised no clinically significant safety concerns and it was, therefore, judged that the benefits of using this product outweigh the risks; hence this Marketing Authorisation has been granted.
FINASTERIDE 1 MG FILM-COATED TABLETS

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK granted a Marketing Authorisation for the medicinal product Finasteride 1 mg Film-coated Tablets on 10 August 2009.

This is a national, abridged application for Finasteride 1mg Film-coated Tablets, submitted under article 10.1. The applicant claims that the proposed product is a generic version of Chimbro-Proscar 5mg tablets, authorised to MSD, France in 1992. The equivalent UK brand leader product is Proscar 5mg Tablets (PL 00025/0279), licensed on 27 May 1992 and marketed by MSD. However, the UK reference product is Propecia 1mg tablets (PL 00025/0351), which was licensed on 20 September 1999 to MSD, UK. The UK brand leader, Proscar 5mg tablets, is used in the bioequivalence study.

Finasteride is a competitive inhibitor of human 5-alpha-reductase, an intracellular enzyme which metabolises testosterone into the more potent androgen, dihydrotestosterone (DHT). The tablets are indicated for the treatment of men with male pattern hair loss (adrogenetic alopecia) to increase hair growth and prevent further hair loss. The recommended adult dose is one tablet daily, with or without food.
**PHARMACEUTICAL ASSESSMENT**

**DRUG SUBSTANCE**
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 have been generated supporting a retest period of 18 months, with no specific storage instructions.

**DRUG PRODUCT**

**Other ingredients**
Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate (200 mesh), pregelatinised starch, sodium laurilsulfate, sodium starch glycolate (Type A), povidone (K30), microcrystalline cellulose, magnesium stearate, hypromellose 6 cP (E464), titanium dioxide (E171), macrogol 6000, macrogol 400, iron oxide red (E172) and iron oxide yellow (E172). Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeia monographs, with the exception of iron oxide red (E172) and iron oxide yellow (E172), which are controlled through an in-house reference standard (in the absence of a European Pharmacopoeia monograph, this is acceptable). Satisfactory certificates of analysis have been provided for all excipients.

No excipients used contain any material of human origin. The only excipient used that contains material of animal origin is lactose monohydrate. The supplier of lactose monohydrate has confirmed that the lactose used is sourced from healthy animals under the same conditions as milk for human consumption.

There were no novel excipients used and no overages.

**Dissolution and impurity profiles**
Dissolution and impurity profiles for the drug product were found to be similar to those 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 product batches. The results are satisfactory.
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
The product is packaged in transparent PVC/PVdC-aluminium blisters packs of 7, 28, 30, 50 (hospital packs), 84, 98 and 100 Film-coated Tablets. 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, which is satisfactory. The precaution for storage is “Store in the original package.”

Conclusion
It is recommended that a Marketing Authorisation is granted for this application.

The requirements for essential similarity of the proposed and reference product have been met with respect to qualitative and quantitative content of the active substance, pharmaceutical form and bioequivalence.
NON-CLINICAL ASSESSMENT

No new non-clinical data have been supplied with this application and none is required for an application of this type.
CLINICAL ASSESSMENT

INDICATIONS
The applicant has submitted the following:

“Finasteride is indicated for the treatment of men with male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss.

Finasteride is not indicated for use in women or children.”

This is consistent with the reference product.

DOSE & DOSE SCHEDULE
The applicant has submitted the following:

“The recommended dosage is one 1 mg tablet daily. Finasteride may be taken with or without food.

There is no evidence that an increase in dosage will result in increased efficacy.

Efficacy and duration of treatment should continuously be assessed by the treating physician. Generally, three to six months of once daily treatment are required before evidence of stabilisation of hair loss can be expected. Continuous use is recommended to sustain benefit. If treatment is stopped, the beneficial effects begin to reverse by six months and return to baseline by 9 to 12 months.

No dosage adjustment is required in patients with renal insufficiency.

No data are available on the concomitant use of Finasteride and topical minoxidil in male pattern hair loss.”

This is consistent with the reference product.

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

CLINICAL PHARMACOLOGY
A bioequivalence study comparing one Finasteride 5 mg Film-coated Tablets to one 5 mg Proscar tablet was undertaken. The study was a randomised, single-dose, cross-over study that was carried out in 26 healthy male volunteers. The volunteers fasted overnight then received either one Finasteride 5 mg Film-coated Tablet or one 5 mg Proscar Tablet. After a washout period of 7 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 ratios of those variables were calculated. The 90% confidence intervals for the results can be seen in the table below. The 90% confidence intervals for AUC and C_{max} fell within the CPMP.
guidelines of 80%-125% and from this study and the two products can be considered bioequivalent.

Results for finasteride are presented below as log-transformed values:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>$C_{\text{max}}$ (ng/ml)</th>
<th>$T_{\text{max}}$ (h)</th>
<th>$T_{1/2}$ (h)</th>
<th>AUC$_{0-\infty}$ (ng/ml/h)</th>
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</thead>
<tbody>
<tr>
<td>Test</td>
<td>32.8</td>
<td>2.0</td>
<td>5.79</td>
<td>259.65</td>
</tr>
<tr>
<td>Reference</td>
<td>32.09</td>
<td>2.26</td>
<td>5.63</td>
<td>257.45</td>
</tr>
<tr>
<td>Ratio (90% CI)</td>
<td>93.40 – 107.99</td>
<td>-</td>
<td>-</td>
<td>90.93 – 104.78</td>
</tr>
</tbody>
</table>

AUC$_{0-\infty}$ area under the plasma concentration-time curve from time zero to infinity
$C_{\text{max}}$ maximum plasma concentration

Finasteride demonstrates linear kinetics in the dose range 1 mg to 38 mg, therefore it is acceptable to extrapolate the results of the bioequivalence study for the 5 mg product to that for the 1 mg product. Further justifications provided by the applicant are:

- The pharmaceutical products are manufactured by the same manufacturer and process
- The strength where the sensitivity is largest to identify differences in the two products has been used to establish bioequivalence.
- The ratio between amounts of active ingredient and the excipients is the same.
- The qualitative composition of the different strengths is the same
- The in vitro dissolution profiles are the same.

Therefore it is accepted that the results for the 5 mg preparation of finasteride are applicable to that for the 1 mg dose strength and, therefore, bioequivalence is accepted.

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

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

**CLINICAL OVERVIEW**
There is a clinical overview from a consultant to the pharmaceutical industry who is appropriately qualified.

**PRODUCT LITERATURE**
All product literature (SmPC, PIL and labelling) are medically satisfactory. The SmPC is consistent in its entirety with that for the reference product.

**DISCUSSION**
The data presented has shown that Finasteride 1 mg Film-coated Tablets are essentially similar to Propecia 1 mg tablets.

**RECOMMENDATIONS**
The efficacy and safety of the product are satisfactory for the grant of this Marketing Authorisation.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The important quality characteristics of Finasteride 1 mg 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.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Finasteride 5 mg Film-coated Tablets and Proscar 5mg Tablets. Given that linear kinetics apply in the dose range 1 mg to 38 mg, it is acceptable to extrapolate the results of the bioequivalence study from the 5 mg product to that for the 1 mg product and a separate bioequivalence study using the other tablet strengths is not considered necessary.

No new or unexpected safety concerns arise from this application.

The SmPC, PIL and labelling are satisfactory and consistent with that for Proscar Tablets.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant’s products and the innovator products are interchangeable. Extensive clinical experience with finasteride is considered to have demonstrated the therapeutic value of the compound. The risk benefit ratio is, therefore, considered to be acceptable.
FINASTERIDE 1 MG FILM-COATED TABLETS

PL 00289/0825

STEPS TAKEN FOR ASSESSMENT

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 15 December 2004</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 4 August 2005</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the application the MHRA requested further information relating to the quality dossier on 16 May 2006</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 19 July 2007</td>
</tr>
<tr>
<td>5</td>
<td>Following assessment of the response the MHRA requested further information relating to the quality dossier on 29 October 2007</td>
</tr>
<tr>
<td>6</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the quality dossier on 12 September 2008</td>
</tr>
<tr>
<td>7</td>
<td>The applications were determined on 10 August 2009</td>
</tr>
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</table>
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Finasteride 1 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 1 mg of finasteride.

Excipients:
Each tablet contains 112 mg of lactose monohydrate (see section 4.4).
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Film-coated Tablets.
Brown, round film-coated tablets, debossed “FNT1” on one side and plain on the other.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Finasteride is indicated for the treatment of men with male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss.

Finasteride is not indicated for use in women or children.

4.2 Posology and method of administration
The recommended dosage is one 1 mg tablet daily. Finasteride may be taken with or without food.

There is no evidence that an increase in dosage will result in increased efficacy.

Efficacy and duration of treatment should continuously be assessed by the treating physician. Generally, three to six months of once daily treatment are required before evidence of stabilisation of hair loss can be expected. Continuous use is recommended to sustain benefit. If treatment is stopped, the beneficial effects begin to reverse by six months and return to baseline by 9 to 12 months.

No dosage adjustment is required in patients with renal insufficiency.

No data are available on the concomitant use of Finasteride and topical minoxidil in male pattern hair loss.

4.3 Contraindications
Finasteride is contra-indicated for use in women due to the risk in pregnancy (see 4.6 ‘Pregnancy and lactation’) and in patients with hypersensitivity to any component of this product.

Finasteride is not indicated for use in women or children.

Finasteride should not be taken by men who are taking finasteride 5 mg or any other 5α-reductase inhibitor for benign prostatic hyperplasia or any other condition.

4.4 Special warnings and precautions for use
In clinical studies with Finasteride in men 18-41 years of age, the mean value of serum prostate-specific antigen (PSA) decreased from 0.7 ng/ml at baseline to 0.5 ng/ml at month 12. This decrease in serum PSA concentrations needs to be considered if, during treatment with Finasteride, a patient requires a PSA assay. In this case, the PSA value should be doubled before making a comparison with the results from untreated men.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction
No drug interactions of clinical importance have been identified. Finasteride does not appear to affect the cytochrome P450-linked drug metabolising enzyme system. Compounds which have been tested in man have included antipyrine, digoxin, glibenclamide, propranolol, theophylline, and warfarin and no interactions were found.
Although specific interaction studies were not performed, in clinical studies finasteride doses of 1 mg or more were used concomitantly with ACE inhibitors, paracetamol, alpha blockers, benzodiazepines, beta blockers, calcium-channel blockers, cardiac nitrates, diuretics, H2 antagonists, HMG-CoA reductase inhibitors, prostaglandin synthetase inhibitors (NSAIDs), and quinolones, without evidence of clinically significant adverse interactions.

4.6 Pregnancy and lactation

Use during pregnancy

Finasteride is contra-indicated for use in women due to the risk in pregnancy.

Because of the ability of type II 5α-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone (DHT) in some tissues, these drugs, including finasteride, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

Exposure to finasteride: risk to male foetus

A small amount of finasteride, less than 0.01% of the 1 mg dose per ejaculation, has been detected in the seminal fluid of men taking Finasteride. Studies in Rhesus monkeys have indicated that this amount is unlikely to constitute a risk to the developing male foetus (see Section 5.3).

During continual collection of adverse experiences, post-marketing reports of exposure to finasteride during pregnancy via semen of men taking Finasteride. Studies in Rhesus monkeys have indicated that this amount is unlikely to constitute a risk to the developing male foetus (see Section 5.3).

During continual collection of adverse experiences, post-marketing reports of exposure to finasteride during pregnancy via semen of men taking Finasteride. Studies in Rhesus monkeys have indicated that this amount is unlikely to constitute a risk to the developing male foetus (see Section 5.3).

Crushed or broken tablets of Finasteride should not be handled by women when they are or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus. Finasteride tablets are coated to prevent contact with the active ingredient during normal handling, provided that the tablets are not broken or crushed.

Use during lactation

Finasteride is contra-indicated for use in lactation.

4.7 Effects on ability to drive and use machines

There are no data to suggest that Finasteride affects the ability to drive or use machines.

4.8 Undesirable effects

Side effects, which usually have been mild, generally have not required discontinuation of therapy.

Finasteride for male pattern hair loss has been evaluated for safety in clinical studies involving more than 3,200 men. In three 12-month, placebo-controlled, double-blind, multicentre studies of comparable design, the overall safety profiles of Finasteride and placebo were similar. Discontinuation of therapy due to any clinical adverse experience occurred in 1.7% of 945 men treated with Finasteride and 2.1% of 934 men treated with placebo.

In these studies, the following drug-related adverse experiences were reported in ≥1% of men treated with Finasteride: decreased libido (Finasteride, 1.8% vs. placebo, 1.3%) and erectile dysfunction (1.3%, 0.7%). In addition, decreased volume of ejaculate was reported in 0.8% of men treated with Finasteride and 0.4% of men treated with placebo. Resolution of these side effects occurred in men who discontinued therapy with Finasteride and in many who continued therapy. The effect of Finasteride on ejaculate volume was measured in a separate study and was not different from that seen with placebo.

By the fifth year of treatment with Finasteride, the proportion of patients reporting each of the above side effects decreased to ≤0.3%.

Finasteride has also been studied for prostate cancer risk reduction at 5 times the dosage recommended for male pattern hair loss. 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
In the finasteride 5 mg group, 280 (6.4%) men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy vs. 237 (5.1%) men in placebo group. 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 5 mg and tumours with Gleason scores of 7-10 is unknown.

The following undesirable effects have been reported in post-marketing use: ejaculation disorder; breast tenderness and enlargement; hypersensitivity reactions including rash, pruritus, urticaria and swelling of the lips and face; and testicular pain.

4.9 Overdose
In clinical studies, single doses of finasteride up to 400 mg and multiple doses of finasteride up to 80 mg/day for three months did not result in side effects.

No specific treatment of overdosage with Finasteride is recommended.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Finasteride is a competitive and specific inhibitor of type II 5α-reductase. Finasteride has no affinity for the androgen receptor and has no androgenic, anti-androgenic, oestrogenic, anti-oestrogenic, or progestational effects. Inhibition of this enzyme blocks the peripheral conversion of testosterone to the androgen DHT, resulting in significant decreases in serum and tissue DHT concentrations. Finasteride produces a rapid reduction in serum DHT concentration, reaching significant suppression within 24 hours of dosing.

Hair follicles contain type II 5α-reductase. In men with male pattern hair loss, the balding scalp contains miniaturised hair follicles and increased amounts of DHT. Administration of finasteride decreases scalp and serum DHT concentrations in these men. Men with a genetic deficiency of type II 5α-reductase do not suffer from male pattern hair loss. Finasteride inhibits a process responsible for miniaturisation of the scalp hair follicles, which can lead to reversal of the balding process.

Studies in men
Clinical studies were conducted in 1879 men aged 18 to 41 with mild to moderate, but not complete, vertex hair loss and/or frontal/mid-area hair loss. In the two studies in men with vertex hair loss (n=1553), 290 men completed 5 years of treatment with Finasteride vs. 16 patients on placebo. In these two studies, efficacy was assessed by the following methods: (i) hair count in a representative 5.1cm² area of scalp, (ii) patient self assessment questionnaire, (iii) investigator assessment using a seven point scale, and (iv) photographic assessment of standardised paired photographs by a blinded expert panel of dermatologists using a seven point scale.

In these 5-year studies men treated with Finasteride improved compared to both baseline and placebo beginning as early as 3 months, as determined by both the patient and investigator assessments of efficacy. With regard to hair count, the primary endpoint in these studies, increases compared to baseline were demonstrated starting at 6 months (the earliest time point assessed) through to the end of the study. In men treated with Finasteride these increases were greatest at 2 years and gradually declined thereafter to the end of 5 years; where as hair loss in the placebo group progressively worsened compared to baseline over the entire 5 year period. In Finasteride treated patients, a mean increase from baseline of 88 hairs [p <0.01; 95% CI (77.9, 97.8); n=433] in the representative 5.1 cm² area was observed at 2 years and an increase from baseline of 38 hairs [p <0.01; 95% CI (20.8, 55.6); n=219] was observed at 5 years, compared with a decrease from baseline of 50 hairs [p <0.01; 95% CI (-80.5, -20.6); n=47] at 2 years and a decrease from baseline of 239 hairs [p <0.01; 95% CI (-304.4, -173.4); n=15] at 5 years in patients who received placebo. Standardised photographic assessment of efficacy demonstrated that 48% of men treated with finasteride for 5 years were rated as improved, and an additional 42% were rated as unchanged. This is in comparison to 25% of men treated with placebo for 5 years who were rated as improved or unchanged. These data demonstrate that treatment with Finasteride for 5 years resulted in a stabilisation of the hair loss that occurred in men treated with placebo.

An additional 48-week, placebo-controlled study designed to assess the effect of Finasteride on the phases of the hair-growth cycle (growing phase [anagen] and resting phase [telogen]) in vertex baldness enrolled 212 men with androgenetic alopecia. At baseline and 48 weeks, total, anagen and telogen hair counts were obtained in a 1-cm² target area of the scalp. Treatment with Finasteride led to
improvements in anagen hair counts, while men in the placebo group lost anagen hair. At 48 weeks, men treated with Finasteride showed net increases in total and anagen hair counts of 17 hairs and 27 hairs, respectively, compared to placebo. This increase in anagen hair count, compared to total hair count, led to a net improvement in the anagen-to-telogen ratio of 47% at 48 weeks for men treated with Finasteride, compared to placebo. These data provide direct evidence that treatment with Finasteride promotes the conversion of hair follicles into the actively growing phase.

Studies in women
Lack of efficacy was demonstrated in post-menopausal women with androgenetic alopecia who were treated with Finasteride in a 12 month, placebo-controlled study (n=137). These women did not show any improvement in hair count, patient self-assessment, investigator assessment, or ratings based on standardised photographs, compared with the placebo group.

5.2 Pharmacokinetic properties

Absorption
Relative to an intravenous reference dose, the oral bioavailability of finasteride is approximately 80%. The bioavailability is not affected by food. Maximum finasteride plasma concentrations are reached approximately two hours after dosing and the absorption is complete after six to eight hours.

Distribution
Protein binding is approximately 93%. The volume of distribution of finasteride is approximately 76 litres.

At steady state following dosing with 1 mg/day, maximum finasteride plasma concentration averaged 9.2 ng/ml and was reached 1 to 2 hours postdose; AUC (0-24 hr) was 53 ng•hr/ml.

Finasteride has been recovered in the cerebrospinal fluid (CSF), but the drug does not appear to concentrate preferentially to the CSF. A small amount of finasteride has also been detected in the seminal fluid of subjects receiving the drug.

Biotransformation
Finasteride is metabolised primarily via the cytochrome P450 3A4 enzyme subfamily. Following an oral dose of 14C-finasteride in man, two metabolites of the drug were identified that possess only a small fraction of the 5α-reductase inhibitory activity of finasteride.

Elimination
Following an oral dose of 14C-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.

Plasma clearance is approximately 165 ml/min.

The elimination rate of finasteride decreases somewhat with age. Mean terminal half-life is approximately 5-6 hours in men 18-60 years of age and 8 hours in men more than 70 years of age. These findings are of no clinical significance and hence, a reduction in dosage in the elderly is not warranted.

Characteristics in Patients
No adjustment in dosage is necessary in non-dialysed patients with renal impairment.

5.3 Preclinical safety data
In general, the findings in laboratory animal studies with oral finasteride were related to the pharmacological effects of 5α-reductase inhibition.

Intravenous administration of finasteride to pregnant rhesus monkeys at doses as high as 800 ng/day during the entire period of embryonic and foetal development resulted in no abnormalities in male foetuses. This represents at least 750 times the highest estimated exposure of pregnant women to finasteride from semen. In confirmation of the relevance of the Rhesus model for human foetal development, oral administration of finasteride 2 mg/kg/day (100 times the recommended human dose or approximately 12 million times the highest estimated exposure to finasteride from semen) to pregnant monkeys resulted in external genital abnormalities in male foetuses. No other abnormalities
were observed in male foetuses and no finasteride-related abnormalities were observed in female foetuses at any dose.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Core
Lactose monohydrate (200 mesh)
Starch, pregelatinised
Sodium laurilsulfate
Sodium starch glycolate (Type A)
Povidone (K30)
Cellulose, microcrystalline
Magnesium stearate

Coating
Hypromellose 6 cP (E464)
Titanium dioxide (E171)
Macrogol 6000
Macrogol 400
Iron oxide red (E172)
Iron oxide yellow (E172)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store in the original package.

6.5 Nature and contents of container
Transparent PVC/PVdC-aluminium blisters.
Blister packs of 7, 28, 30, 50 (Hospital Packs), 84, 98 and 100 Film-coated Tablets
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements

7 MARKETING AUTHORISATION HOLDER
TEVA UK Ltd
Brampton Road, Hampden Park
Eastbourne, BN22 9AG
England

8 MARKETING AUTHORISATION NUMBER(S)
PL 00289/0825

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
10/08/2009

10 DATE OF REVISION OF THE TEXT
10/08/2009
FINASTERIDE 1 mg
FILM-COATED TABLETS

PACKAGE LEAFLET INFORMATION FOR THE USER

Read all of this leaflet carefully before you start using this medicine.
• Keep this leaflet. You may need to read it again.
• If you have any 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 get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

IN THIS LEAFLET
1. What Finasteride 1 mg Film-Coated Tablets is and what it is used for
2. Before you take Finasteride 1 mg Film-Coated Tablets
3. How to take Finasteride 1 mg Film-Coated Tablets
4. Possible side effects
5. How to store Finasteride 1 mg Film-Coated Tablets
6. Further information

WHAT FINASTERIDE 1 mg FILM-COATED TABLETS IS AND WHAT IT IS USED FOR

• Finasteride belongs to a group of medicines called testosterone 5α-reductase inhibitors.
• Finasteride is used in the treatment of men with male pattern hair loss (androgenetic alopecia), to increase hair growth and prevent hair loss.

BEFORE YOU TAKE FINASTERIDE 1 mg FILM-COATED TABLETS

Do not take Finasteride if you:
• are allergic (hypersensitive) to finasteride or any of the other ingredients of this medicine
• are taking Finasteride tablets or any other 5α-reductase inhibitors to treat an enlarged prostate
• are pregnant.

The tablets must not be taken by women or children. The condition for which Finasteride is prescribed only occurs in men.

Take special care with Finasteride
Tell your doctor before you start to take this medicine if you:
• have a blood test called prostate-specific antigen (PSA) tell your doctor that you are taking Finasteride as it may affect the results.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and breastfeeding
• Finasteride is only intended for men.
• If the drug is absorbed by a pregnant woman or a baby, the development of the baby's sex organs may be affected. Therefore women who are pregnant, think they may be pregnant or may become pregnant should:
  • not handle broken or crushed tablets (the whole tablets are film-coated to stop contact with the medicine during normal use).
  • avoid exposure to their partners semen (e.g. by use of a condom), as the drug is present in semen.

• If a pregnant woman does come into contact with Finasteride, a doctor should be consulted.

Driving and using machines
Finasteride is not expected to be known to affect your ability to drive or operate machinery.

Important information about some of the ingredients of Finasteride
Patients who are intolerant to lactose should note that Finasteride tablets contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.
4 POSSIBLE SIDE EFFECTS

Like all medicines, Finasteride can cause side effects, although not everybody gets them.

If you get any side effects, stop taking the tablets and tell your doctor immediately, or go to the casualty department of your nearest hospital:

- an allergic reaction (swelling of the lips, face or neck leading to severe difficulty in breathing; skin rash or itches),

This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.

The following side effects have been reported:

- Impotence (difficulty getting an erection), decreased libido
- Problems with ejaculation (including a decreased amount of semen)
- Breast enlargement and tenderness
- Pain in the testes
- Allergic reactions including itching, nettle rash (hives) and swelling of the lips and face.

Tell your doctor or pharmacist if any of the side effects get serious, or if you notice any side effects not listed in this leaflet.

5 HOW TO STORE FINASTERIDE 1 mg FILM-COATED TABLETS

Keep out of the reach and sight of children.

Store in the original package. Do not use Finasteride after the expiry date that is stated on the outer packaging. The expiry date refers to the last day of that month.

Medicines should not be disposed of via waste water or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6 FURTHER INFORMATION

What Finasteride 1 mg Film-Coated Tablets contain:

- The active ingredient is finasteride.
- The other ingredients are: lactose monohydrate, pregelatinised starch, sodium lauryl sulphate, sodium starch glycolate (type A), povidone, microcrystalline cellulose, magnesium stearate, hypromellose 60 K (E464), titanium dioxide (E171), magnesium stearate 6000, macrogol 6000, iron oxide red (E172) and iron oxide yellow (E172).

What Finasteride 1 mg Film-Coated Tablets look like and the contents of the pack:

- Finasteride 1 mg Film-Coated tablets are brown and round in shape. The tablets are marked with "FIN" on one side and plain on the other.

- The product is available in pack sizes of 7, 28, 30, 50 (hospital packs), 81, 98 and 103 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

TEVA UK Limited, Eastbourne, BN22 9AG,

This leaflet was last revised: March 2009

PL 00289/0825
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