Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Finasteride 1mg film-coated tablets

(finasteride)

PL 50640/0002

Careforsons Limited

LAY SUMMARY

Finasteride 1mg film-coated tablets

(finasteride)

This is a summary of the Public Assessment Report (PAR) for Finasteride 1mg film-coated tablets. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Finasteride film-coated tablets in this lay summary for ease of reading.

For practical information about using Finasteride film-coated tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Finasteride film-coated tablets and what are they used for?
This application is for a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised in the European Union (EU) called Propecia 1mg film-coated tablets.

Finasteride film-coated tablets are used in the treatment of male pattern hair loss (also known as androgenetic hair loss).

Male pattern hair loss is a common condition thought to be caused by a combination of genetic factors and a particular hormone called dihydrotestosterone (DHT). DHT contributes to shortening of the growth phase of the hair and thinning of the hair.

How do Finasteride film-coated tablets work?
In the scalp, the active substance, finasteride, specifically lowers the levels of DHT by blocking an enzyme (Type II 5-alpha reductase) that converts testosterone to DHT. Only men with mild to moderate, but not complete hair loss can expect to benefit from the use of Finasteride film-coated tablets. Finasteride increases hair growth on the scalp and prevents further hair loss in men.

How are Finasteride film-coated tablets used?
The pharmaceutical form of this medicine is a film-coated tablet and the route of administration is oral (taken by mouth).

The usual dose is one tablet each day. The tablets can be taken with or without food

Finasteride film-coated tablets will not work better if the patient takes more than once a day.

The patient's doctor will help them determine if Finasteride film-coated tablets are working for them. It is important that the patient takes Finasteride film-coated tablets for as long as their doctor prescribes it. Finasteride 1 mg tablets can only work over the long term if the patient continues taking them.

For further information on how Finasteride film-coated tablets, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Finasteride film-coated tablets have been shown in studies?
Because Finasteride film-coated tablets are a generic medicine, studies in healthy volunteers have been limited to tests to determine that it is bioequivalent to the reference medicine. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Finasteride film-coated tablets?
Because Finasteride film-coated tablets are a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

For the full list of all side effects reported with this medicine, see Section 4 of the package leaflet or the Summary of Product Characteristics (SmPC) available on the MHRA website.

Why were Finasteride film-coated tablets approved?
It was concluded that, in accordance with EU requirements, Finasteride film-coated tablets have been shown to be comparable to and to be bioequivalent to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Finasteride film-coated tablets?
A Risk Management Plan (RMP) has been developed to ensure that Finasteride film-coated tablets are used as safely as possible. Based on this plan, safety information has been included in the SmPC and the package leaflet, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Finasteride film-coated tablets
A Marketing Authorisation for Finasteride 1 mg film-coated tablets was granted in the UK on 25 June 2020.

The full PAR for Finasteride film-coated tablets follows this summary.

This summary was last updated in August 2020.

TABLE OF CONTENTS

Contents

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Finasteride 1mg film-coated tablets (PL 50640/0002) could be approved.

The product is approved for the following indication:

- the treatment of men with male pattern hair loss (androgenetic alopecia) to increase hair growth and prevent further hair loss.

Finasteride 1mg film-coated tablets are not indicated for use in women or children and adolescents.

Finasteride is a competitive and specific inhibitor of Type II 5 alpha-reductase (Type II 5α-reductase). Inhibition of this enzyme blocks the peripheral conversion of testosterone to the androgen DHT. 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. Finasteride inhibits a process responsible for miniaturisation of the scalp hair follicles, which can lead to reversal of the balding process.

This application was submitted under Article 10(1) of Directive 2001/83/EC, as amended, as a generic medicine of a suitable originator medicinal product, Propecia 1mg film-coated tablets, that has been licensed within the EU for a suitable time, in line with the legal requirements.

No new non-clinical studies were conducted, which is acceptable given that the application is based on being a generic medicinal product of a reference product that has been licensed for over 10 years.

With the exception of the bioequivalence study, no new clinical studies were conducted, which is acceptable given that the application is based on being a generic medicinal product of a reference product that has been in clinical use for over 10 years. The bioequivalence study was conducted in line with current Good Clinical Practice (GCP).

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A Marketing authorisation was granted for this product on 25 June 2020.

II QUALITY ASPECTS

II.1 Introduction

This product contains 1mg of finasteride in each tablet.

In addition to finasteride, this product also contains the excipients lactose monohydrate, pregelatinised maize starch, docusate sodium, iron oxide yellow (E172, sodium starch glycolate (type A), microcrystalline cellulose, colloidal anhydrous silica, magnesium stearate and purified water in the tablet core, and hydroxypropyl cellulose, hypromellose, talc, titanium dioxide (E171), iron oxide red (E172) and iron oxide yellow (E172) in the tablet coating.

The finished product is packaged in white polyvinyl chloride/polyethylene/polyvinylidene chloride/aluminium and aluminium/aluminium blisters, packed in boxes in pack sizes of 14, 20, 28, 30, 50, 60 or 100 film-coated tablets. Not all pack sizes may be marketed.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

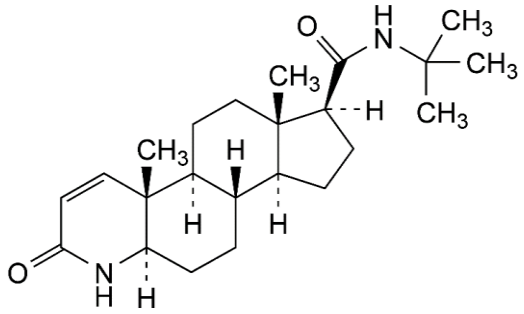
II.2 ACTIVE SUBSTANCE

rINN: Finasteride

Chemical Name: N-(1,1-Dimethylethyl)-3-oxo-4-aza-5α-androst-1-ene-17β-carboxamide

Molecular Formula: $C_{23}H_{36}N_2O_2$

Chemical Structure:



Molecular Weight: 372.6 g/mol

Appearance: White or almost white, crystalline powder

Solubility: Practically insoluble in water, freely soluble in ethanol and in methylene chloride

Finasteride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the final products.

With the exception of lactose monohydrate, no excipients of animal or human origin are used in the final products. The supplier of lactose monohydrate has confirmed that it is sourced from healthy animals under the same conditions as milk for human consumption.

Confirmation has been given that the magnesium stearate used in the tablets is of vegetable origin.

This product does not contain or consist of genetically modified organisms (GMO).

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

A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specification
The finished product specification is satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of two years, with the no special storage conditions, is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of finasteride are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for this application.

III.4 Toxicology
No new toxicology data were provided and none were required for this application

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is for generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the Marketing Authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The pharmacology, efficacy and safety of finasteride are well-known. With the exception of data from one bioequivalence study, no new clinical data are provided or are required for this type of application. An overview based on a literature review and a review of this study is, thus, satisfactory.

IV. 2 Pharmacokinetics

In support of the application, the applicant submitted the following bioequivalence study.

This study was an open label, randomised, two treatment, two-period, two sequence, single-dose, crossover bioequivalence study comparing the test product Finasteride 5 mg tablets versus the reference product PROSCAR 5 mg film-coated tablets in normal, healthy, adult, male human subjects under fasted conditions.

Subjects were administered a single dose (5mg; 1 tablet) of the test or reference product with 240 ml of water, following an overnight fast of at least 10 hours.

Blood samples were taken pre-dose and up to 24 hours post dose, with a washout period of 8 days between the treatment periods.
A summary of the pharmacokinetic results is presented below:

Table 1: Pharmacokinetic parameters (non-transformed values; arithmetic mean ± SD)

Treatment	AUC_{0-t} ng/ml/h	$AUC_{0-\infty}$ ng/ml/h	C_{max} ng/ml
Test	342.24 ± 99.38	375.67 ± 125.97	44.83 ± 9.24
Reference	352.49 ± 105.14	387.15 ± 129.24	46.31 ± 9.76
***Ratio (90% CI)**	97.12 **(93.58 – 100.80)**	96.85 **(92.97 – 100.90)**	96.82 **(91.85 – 102.05)**

AUC_{0-t}: Area under the plasma concentration curve from administration to last observed concentration at time t
$AUC_{0-\infty}$: Area under the plasma concentration curve extrapolated to infinite time
C_{max}: Maximum plasma concentration
*ln-transformed values

In line with the Guideline on the Investigation of Bioequivalence (CPMP/EWP/QWP/1401/98 Rev 1/Corr**), the Test/Reference ratios and their 90% confidence intervals were within the specified limits to show bioequivalence between the test product and the reference product.

As the 1 mg strength of the product meets the biowaiver criteria specified in the current bioequivalence guideline, the results and conclusions from the bioequivalence study on the 5 mg strength tablet can be extrapolated to the 1 mg strength tablet.

IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for this application and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety

With the exception of the safety data submitted with the bioequivalence study, no new safety data were submitted with this application.

The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from the bioequivalence study.

IV.6 Risk Management Plan (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Directive 2001/83/EC, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of a marketing authorisation is recommended for this application.

V USER CONSULTATION

The Patient Information Leaflet (PIL) has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

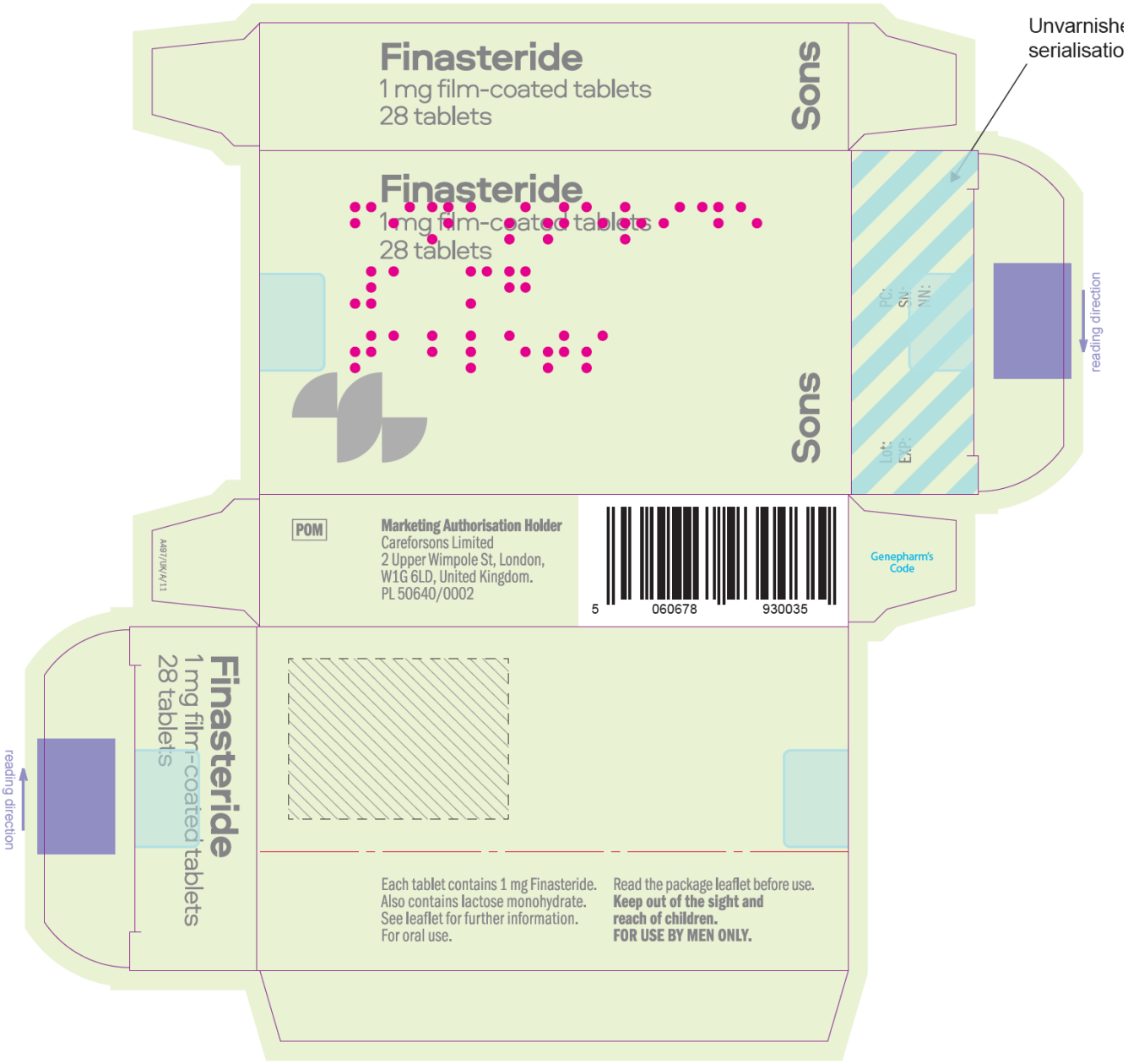
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with finasteride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below.


Finasteride
1 mg film-coated tablets
28 tablets
Sons
Finasteride
1 mg film-coated tablets
28 tablets
Sons
Unvarnish
serialisatio
reading direction
POM
Marketing Authorisation Holder
Careforsons Limited
2 Upper Wimpole St, London,
W1G 6LD, United Kingdom.
PL 50640/0002
5 060678 930035
Genepharm's Code
A497/UK/V/11
Finasteride
1 mg film-coated tablets
28 tablets
reading direction
Each tablet contains 1 mg Finasteride.
Also contains lactose monohydrate.
See leaflet for further information.
For oral use.
Read the package leaflet before use.
Keep out of the sight and reach of children.
FOR USE BY MEN ONLY.


Careforsons Limited. Careforsons Limited. Careforsons Limited.
Finasteride 1 mg film-coated tablets
Careforsons Limited. Careforsons Limited. Careforsons Limited.
Finasteride 1 mg film-coated tablets
Careforsons Limited. Careforsons Limited. Careforsons Limited.
Finasteride 1 mg film-coated tablets
Careforsons Limited. Careforsons Limited. Careforsons Limited.
Finasteride 1 mg film-coated tablets
Careforsons Limited. Careforsons Limited. Careforsons Limited.
Finasteride 1 mg film-coated tablets
Careforsons Limited. Careforsons Limited. Careforsons Limited.
Lot:
EXP:
A495/UK/V/07

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**