Safeguarding public health

MHRA

Public Assessment Report

Decentralised Procedure

Finamed 5mg Film-coated Tablets

UK/H/901/01/DC

PL 27867/0001

Dermapharm AG

Medicines and Healthcare products Regulatory Agency

Lay summary

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Dermapharm AG a Marketing Authorisation (licence) for the medicinal product Finamed 5mg Film-coated Tablets (Product Licence number: 27867/0001). This medicine is available on prescription only.

With advancing age some men suffer from enlargement of the prostate gland, giving them problems 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.

The data submitted in support of the application for Finamed 5mg 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 a Marketing Authorisation has been granted.

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Module 1

INFORMATION ABOUT DECENTRALISED PROCEDURE

Name of the product in the Reference Member State	Finamed 5mg Film-coated Tablets
Type of application (Eudratrack details)	Level 1 Abridged Level 2 Initial Level 3 10.1 Level 4 Chemical substance Level 5 Prescription only
Name of the active substance (INN)	Finasteride
Pharmacotherapeutic classification (ATC code)	Alpha-adrenoceptor-antagonist (G04CB01)
Pharmaceutical form and strength	Film-coated tablet, 5mg
Reference numbers for the Mutual Recognition Procedure	UK/H/901/001/DC
Reference Member State	United Kingdom
Member States concerned	DE
Date of start of the procedure	25 July 2006
End date of decentralised procedure	28 November 2007
Marketing Authorisation Number	PL 27867/0001
Name and address of the authorisation holder	Dermapharm AG Luise-Ullrich-Straße 5 82031 Grünwald, Germany

Module 2

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Finamed 5mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One film-coated tablet contains 5mg finasteride.
Excipient: One film-coated tablet contains 75mg of lactose monohydrate.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
White, round biconvex film-coated tablet marked “F” on one side and “5” on the other side. The diameter is 7 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Finamed is indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with an enlarged prostate (prostate volume above ca. 40 ml) 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

Oral use.
The recommended dosage is one 5mg tablet daily with or without food. The tablet should be swallowed whole and must not be divided or crushed (see section 6.6). Even if improvement can be seen within a short time, treatment for at least 6 months may be necessary in order to determine objectively whether a satisfactory response to treatment has been achieved. Thereafter, treatment should be continued long term.
Dosage in hepatic insufficiency
There are no data available in patients with hepatic insufficiency (see section 4.4).
Dosage in renal insufficiency
Dosage adjustments are not necessary in patients with varying degrees of renal insufficiency (with creatinine clearance down to as low as 9 ml/min) as in pharmacokinetic studies renal insufficiency was not found to affect the elimination of finasteride. Finasteride has not been studied in patients on haemodialysis.

Dosage in the elderly
Dosage adjustments are not necessary although pharmacokinetic studies have shown that the elimination rate of finasteride is slightly decreased in patients above 70 years of age.
Peadiatric Population
Finamed is contra-indicated in children.

4.3 Contraindications
Finamed tablets are contraindicated in women and children.
Hypersensitivity to finasteride or to any of the excipients.

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
- Consultation with a urologist should be considered in patients treated with finasteride
- Obstruction due to trilobular growth pattern of the prostate should be excluded before starting treatment with finasteride
- There is no experience in patients with hepatic insufficiency. Caution is advised in patients with impaired hepatic function as the plasma levels of finasteride may be increased in such patients (see section 4.2)
- Since finasteride inhibits the conversion of testosterone to dihydrotestosterone, it can inhibit the development of the external genitalia of the foetus if it is given to a woman carrying a male foetus (see sections 5.3 and 6.6)
- Finamed tablets contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption 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.
Digital rectal examination, and, if necessary, determination of prostate-specific-antigen (PSA) in serum should be carried out on patients prior to initiating therapy with finasteride and periodically during treatment to rule out prostate cancer. 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.
Finasteride causes 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 should be considered when evaluating PSA data and does not rule out concomitant prostate cancer. This decrease is predictable over the entire range of PSA values, although it may vary in individual patients. In patients treated with finasteride for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. This adjustment preserves the sensitivity or 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 finasteride therapy.
Percent free PSA (free to total PSA ratio) is not significantly decreased by finasteride and remains constant even under the influence of finasteride.
When percent 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 significant interactions with other medicinal products have been identified. Finasteride does not appear to affect the cytochrome P450 enzyme system significantly. The following medicinal products have been investigated in humans and no clinically significant interactions have been identified: propranolol, digoxin, glibenclamide, warfarin, theophylline and phenazone.

4.6 Pregnancy and lactation

Pregnancy

Finamed is contraindicated in women (see section 4.3 Contraindications).
As with other 5α-reductase-inhibitors finasteride inhibits the conversion of testosterone to dihydrotestosterone, and might cause abnormalities of the external genitals of a male foetus when administered to a pregnant woman (see sections 4.3, 4.4, 5.3 and 6.6).
Pregnant women and women who may become pregnant should not handle crushed or broken tablets, due to the risk of absorption of finasteride through the skin and the consequent potential risk to a male foetus. Finamed tablets have a film-coating which will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.
Small amounts of finasteride have been recovered from the semen in subjects receiving 'Finasteride 5mg/day', see also sections 5.2 and 5.3.

Lactation

Finamed 5mg Film-coated Tablets are only indicated for use in men**.** It is not known whether finasteride is excreted in breast milk.

4.7 Effects on ability to drive and use machines

Finamed has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The most common adverse reactions are impotence and reduced libido. These effects usually occur at the beginning of the treatment and in the majority of patients they are of a transient nature on continued treatment.
The frequencies are defined as:
Very common (> 1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000) including isolated reports.
<u>Skin and subcutaneous tissue disorders</u>
Uncommon:
Skin rash
Rare:
Pruritus, urticaria

Reproductive system and breast disorders
Very common:
Impotence
Common:
Reduced libido, reduced volume of ejaculate
Breast tenderness/breast enlargement, ejaculation disorder
Rare:
Testicular pain
Very rare:
Breast secretion, breast nodules that were surgically removed in single patients
General disorders and administration site conditions
Rare:
Hypersensitivity reactions such as swelling of the face and lips.
There was no evidence of increased adverse experiences with increased duration of treatment with finasteride and the incidence of new drug-related sexual adverse experiences decreased with duration of treatment.
Laboratory tests:
When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels generally decrease in patients treated with finasteride. In a majority of the 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 for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men. For details and clinical interpretation see section 4.4 (paragraph Effects on prostate-specific antigen (PSA) and prostate cancer detection).
No other difference was observed in patients treated with placebo or finasteride in standard laboratory tests.
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%) of men receiving finasteride and in 1147 (24.4%) of 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 versus 237 (5.1%) in the 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 and tumours with Gleason scores of 7-10 is unknown.
Medical therapy of prostatic symptoms (MTOPS)
The MTOPS study compared finasteride 5mg/day (n=768), doxazosin 4 or 8mg/day (n=756), combination therapy of finasteride 5mg/day and doxazosin 4 or 8mg/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%.

4.9 Overdose

Single doses of finasteride up to 400mg and multiple doses of up to 80mg daily for 3 months did not produce any dose related undesirable effects. No specific treatment in connection with overdosing of finasteride can be recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Testosterone-5α-reductase-inhibitors
ATC CODE: G04CB01

Finasteride is a synthetic 4-azasteroid, a specific competitive inhibitor of the intracellular enzyme Type-II-5α-reductase. The enzyme converts testosterone into the more potent androgen dihydrotestosterone (DHT). The prostate gland and, consequently, also the hyperplasic prostate tissue are dependent on the conversion of testosterone to DHT for their normal function and growth. Finasteride has no affinity for the androgen receptor.

Clinical studies show a rapid reduction of the serum DHT levels of 70%, which leads to a reduction of prostate volume. After 3 months, a reduction of approx. 20% in the volume of the gland occurs, and the shrinking continues and reaches approx. 27% after 3 years. Marked reduction takes place in the periurethral zone immediately surrounding the urethra. Urodynamic measurements have also confirmed a significant reduction of detrusor pressure as a result of the reduced obstruction.

Significant improvements in maximum urinary flow rate and symptoms have been obtained after a couple of weeks, compared with the start of treatment. Differences from placebo have been documented at 4 and 7 months, respectively.

All efficacy parameters have been maintained over a 3 year follow-up period.

Effects of four years treatment with finasteride on incidence of acute urine retention, need for surgery, symptom score and prostate volume:

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 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 (range0-34), 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 5mg/day, doxazosin 4 or 8mg/day*, the combination of finasteride 5mg/day and doxazosin 4 or 8mg/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 1mg to 4 or 8mg as tolerated over a 3-week period

5.2 Pharmacokinetic properties

Absorption

The bioavailability of finasteride is approx. 80%. Peak plasma concentrations are reached approx. 2 hours after intake, and absorption is complete after 6-8 hours.

Distribution

Binding to plasma proteins is approx. 93%.

Clearance and volume of distribution are approx. 165 ml/min (70-279 ml/min) and 76 l (44-96 l), respectively. Accumulation of small amounts of finasteride is seen on repeated administration. After a daily dose of 5mg the lowest steady-state concentration of finasteride has been calculated to be 8-10 ng/ml, which remains stable over time.

Biotransformation

Finasteride is metabolised in the liver. Finasteride does not significantly affect the cytochrome P 450 enzyme system. Two metabolites with low 5α-reductase-inhibiting effects have been identified.

Elimination

The plasma half life is a mean of 6 hours (4-12 hours) (in men > 70 years: 8 hours, range 6 – 15 hours).

Following administration of radioactively labelled finasteride, approx. 39% (32 – 46%) of the dose was excreted in the urine in the form of metabolites. Virtually no unchanged finasteride was recovered in the urine. Approx. 57% (51 – 64%) of the total dose was excreted in the faeces.

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 renal impairment (creatinine clearance above 9 ml/min), no changes in the elimination of finasteride have been seen (see section 4.2). 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

Reproduction toxicology studies in male rats have demonstrated reduced prostate and seminal vesicular weights, reduced secretion from accessory genital glands and reduced fertility index (caused by the primary pharmacological effect of finasteride). The clinical relevance of these findings is unclear.

As with other 5-alpha-reductase inhibitors, femininisation of male rat foetuses has been seen with administration of finasteride in the gestation period. When finasteride was administered to primates during gestation no femininisation of male foetuses was seen at a blood exposure level well above the expected levels in human semen. It is not likely that exposure of male foetuses to finasteride from semen will cause negative effects.

In animal developmental studies, dose-dependent hypospadias were observed in the male offspring of pregnant rats given finasteride at doses ranging from 100 μg/kg/day to 100mg/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 Type II 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 Type II 5 alpha-reductase.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Microcrystalline cellulose
Pregelatinised starch
Sodium starch glycolate (type A)
Sodium laurilsulfate
Magnesium stearate
Tablet coating:
Microcrystalline cellulose
Hypromellose
Macrogol (8) stearate (Type I)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage
Store in the original container.

6.5 Nature and contents of container
Blister packs PVC/PVDC/Al: 30, 50 or 100 tablets.
HDPE bottles with PP caps: 30 or 100 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Women who are pregnant or may become pregnant should not handle crushed or broken Finamed tablets because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see section 4.6).

7 MARKETING AUTHORISATION HOLDER

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Fax: +498964186130
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8 MARKETING AUTHORISATION NUMBER(S)

PL 27867/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/11/2007

10 DATE OF REVISION OF THE TEXT

28/11/2007

Module 3

PRODUCT INFORMATION LEAFLET

Dermapharm AG

PACKAGE LEAFLET: INFORMATION FOR THE USER

Finamed 5mg Film-coated Tablets

Finasteride

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 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 gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT FINAMED 5MG FILM-COATED TABLETS ARE AND WHAT THEY ARE USED FOR

Finamed 5mg Film-coated Tablets belong to a group of medicines called 5-alpha reductase inhibitors. They act by reducing the size of the prostate gland.
Finamed Tablets are used in the treatment and control of benign enlargement of the prostate.

2. BEFORE YOU TAKE FINAMED 5MG FILM-COATED TABLETS

Do not take Finamed 5mg Film-coated Tablets

- if you are allergic (hypersensitive) to finasteride or any of the other ingredients of Finamed Tablets.
- if you are a woman.
- if you are a child.

Take special care with Finamed 5mg Film-coated Tablets

- if you have reduced liver function
- if you have difficulty emptying your bladder completely or a greatly reduced flow of urine, you should be examined by your doctor before you start taking Finamed Tablets to exclude other obstructions in the urinary tract.
- if you need to have a blood test called PSA. Finamed 5mg Film-coated Tablets may alter the results of this test. If you are to have this test please make sure you tell your doctor or nurse that you are taking Finamed Tablets.

Taking other medicines

Finamed 5mg Film-coated Tablets can normally be taken with other medicines, however, please ask your doctor before you take other medicines at the same time.
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Taking Finamed 5mg Film-coated Tablets with food and drink

Finamed 5mg Film-coated Tablets can be taken with or without food.

Important information about some of the ingredients of Finamed 5mg Film-coated Tablets

Finamed 5mg Film-coated Tablets contain lactose monohydrate.
If you do not tolerate some types of sugar you should contact your doctor before you take this medicine.

Pregnancy

Finamed 5mg Film-coated Tablets are only intended for men (see "Do not take Finamed 5mg Film-coated Tablets").
WARNING: Please inform all women in your household who are pregnant or may become pregnant not to handle broken or crushed Finamed 5mg Film-coated Tablets.
Women who are pregnant or may become pregnant should not handle broken or crushed Finamed Tablets. If finasteride is absorbed through the skin or taken by mouth by a woman pregnant with a male foetus, the child may be born with malformed genital organs. The tablets are film-coated, which prevents contact with finasteride provided the tablets are not broken or crushed.

Breast Feeding

Finamed 5mg Film-coated Tablets are only intended for men (see "Do not take Finamed 5mg Film-coated Tablets"). It is not known if finasteride is excreted in breast milk.

Driving and using machines

Finamed 5mg Film-coated Tablets have no influence on the ability to drive and use machines.

3. HOW TO TAKE FINAMED 5MG FILM-COATED TABLETS

Always take Finamed 5mg Film-coated Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
The usual dose is 1 tablet daily. It may be taken with or without food.
The tablet should be swallowed whole and should not be broken or crushed. (see section 2, under "Pregnancy").

If you take more Finamed 5mg Film-coated Tablets than you should

If you take too much medicine, or if children have been taken medicine by accident, always contact a doctor or the hospital for advice and evaluation of risk.

If you forget to take Finamed 5mg Film-coated Tablets
Do not take a double dose to make up for a forgotten tablet. Just take the next one when it is due.

If you stop taking Finamed 5mg Film-coated Tablets
Although an improvement is often noticed after a short time, it may be necessary to continue the treatment for at least 6 months. Do not alter the dose or stop treatment without asking your doctor.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Finamed 5mg Film-coated Tablets can cause side effects, although not everybody gets them.
The most frequent side effects are impotence (inability to obtain an erection) and decreased sex drive. These effects usually occur at the beginning of the treatment and in most patients they are short-term.
Other side effects that may occur have been listed by body systems and frequency.
The frequencies are defined as:
Very common (occur in more than 1 in 10 patients), common (occur in less than 1 in 10 but more than 1 in 100 patients), uncommon (occur in less than 1 in 100 but more than 1 in 1,000 patients)
rare (occur in less than 1 in 1,000 but more than 1 in 10,000 patients), very rare (occur in less than 1 in 10,000 patients, including isolated reports).
Skin disorders
Uncommon:
Skin rash
Rare:
Pruritus (itching), urticaria (hives)
Reproductive system and breast disorders
Very common:
Impotence (inability to obtain an erection)
Common:
Reduced libido (decreased sex drive), reduced volume of ejaculate
Uncommon:
Breast tenderness/breast enlargement, ejaculation disorder
Rare:
Testicular pain
Very rare:
Breast secretion, breast nodules that were surgically removed in a few patients
General disorders
Rare:
Hypersensitivity (allergic) reactions such as swelling of the face and lips
Stop taking Finamed 5mg Film-coated Tablets and contact your doctor immediately if you develop any of the following symptoms: swelling of the face, tongue or face, difficulty swallowing or urticaria and difficulty breathing.
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. If possible note what you experienced and when it started and how long it lasted.

5. HOW TO STORE FINAMED 5MG FILM-COATED TABLETS
Keep out of the reach and sight of children.
Use before the expiry date which is stated on the package after Expiry date:. The expiry date refers to the last day of that month.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.
Keep your tablets in the original container.

6. FURTHER INFORMATION
What Finamed 5mg Film-coated Tablets contain
- The active substance is finasteride 5mg
- The other ingredients are lactose monohydrate, microcrystalline cellulose, pregelatinised starch, sodium starch glycolate (Type A), sodium laurilsulfate, magnesium stearate, hypromellose, macrogol (8) stearate (type I).

What Finamed 5mg Film-coated Tablets look like and contents of the pack
Finamed 5mg Film-coated Tablets are white, round, biconvex, film-coated tablets marked "F" on one side and "5" on the other side. The diameter is 7 mm.
Blister packs containing, 30, 50 or 100 tablets.
Bottles containing 30 or 100 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
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Manufacturer:
Kern Pharma, S.L., Venus 72, 08228 Terrassa, Barcelona, Spain
and
Orion Corporation Pharma, Turku plant, Tengströminkatu 6-8, 20360 Turku, Finland.

This medicinal product is authorised in the Member States of the EEA under the following names:
UK: Finamed 5mg Film-coated Tablets
DE: Finamed 5 mg Filmtabletten

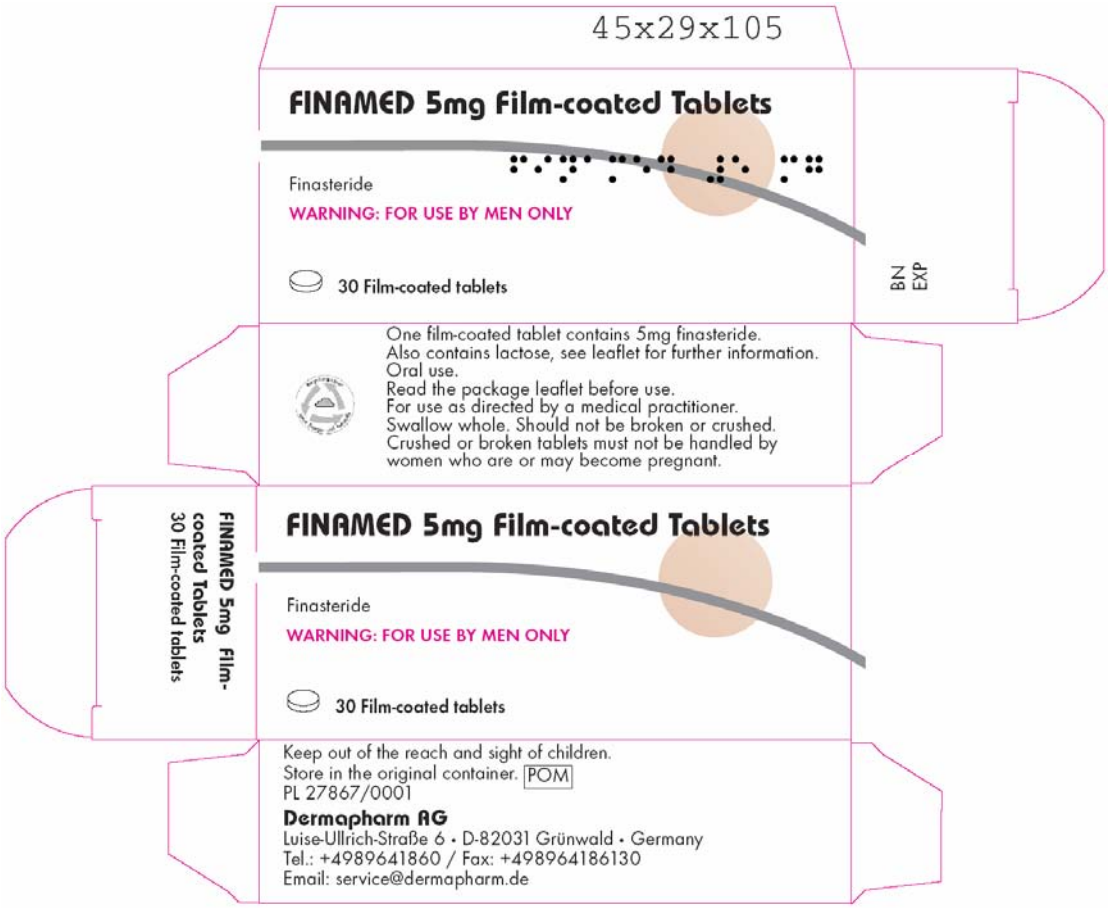
This leaflet was last approved in 05/2007
Detailed information on this medicine is available on the web site of: UK/Medicines and Healthcare products Regulatory Agency (MHRA)

Module 4

Labelling

Label:

Carton (30 tablet pack):



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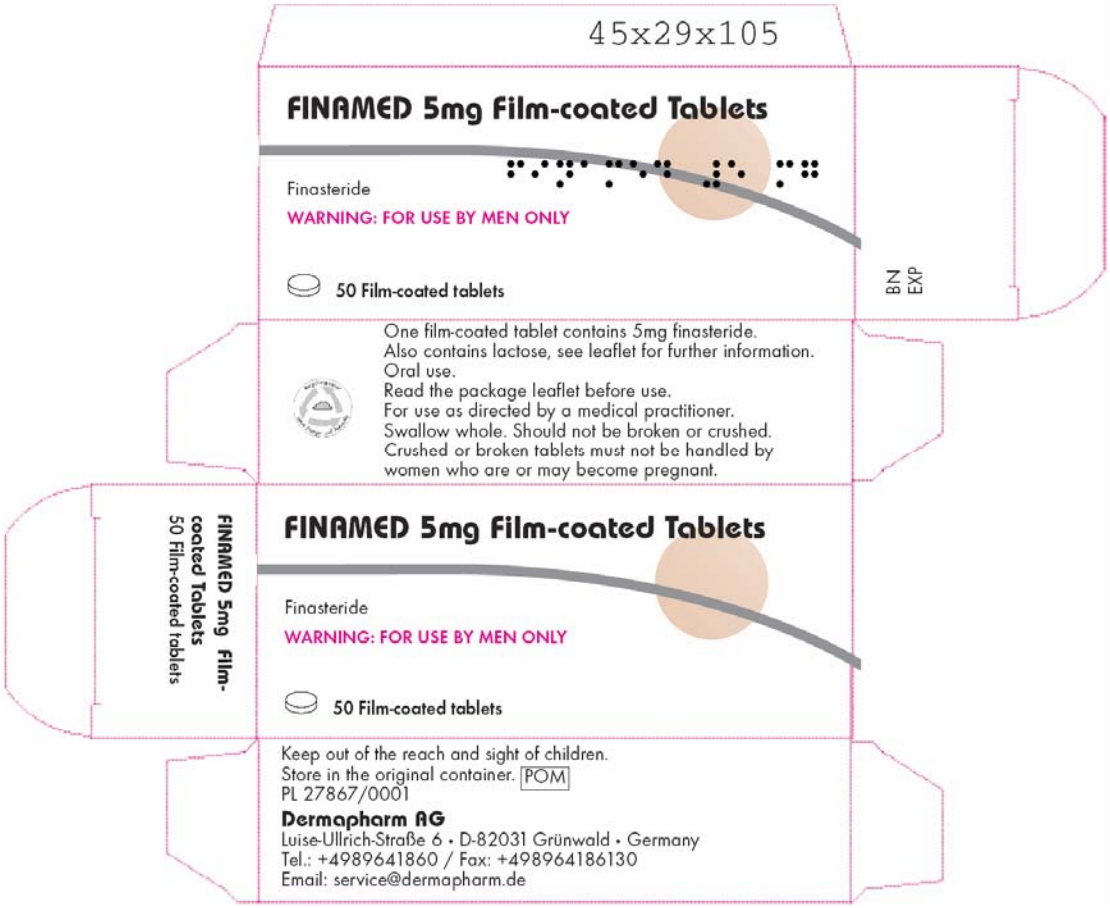
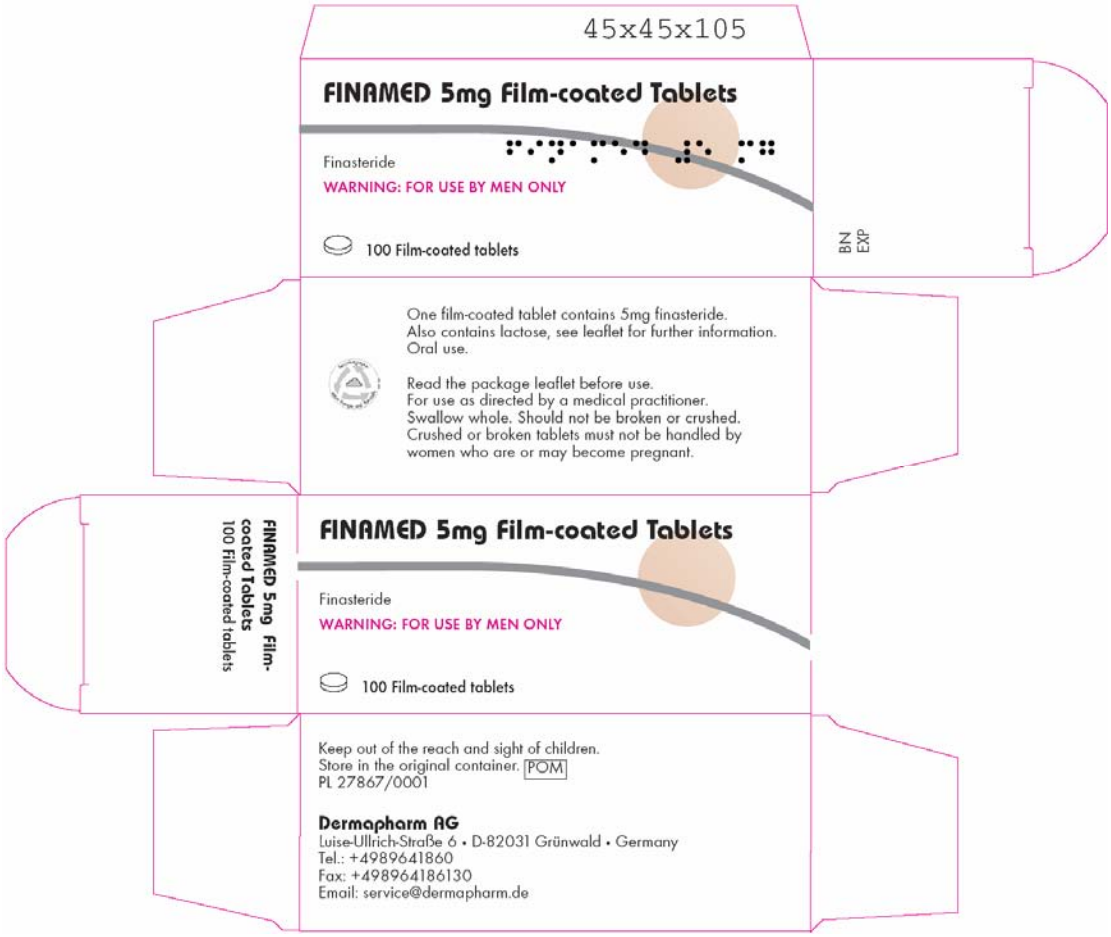


Carton (100 tablet pack):



Module 5

Scientific discussion during initial procedure

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the RMS considers that the application for Finamed 5mg Film-coated Tablets to be used in the treatment of benign prostatic hyperplasia can be approved.

EXECUTIVE SUMMARY

Problem statement

This application for marketing authorisation (MAA), via the decentralised procedure with the UK as Reference Member State (RMS), concerns a generic version of finasteride, going under the trade name Finamed 5mg Film-coated Tablets.

The application is submitted under article 10.1 of Council Directive 2001/83/EC, as amended, claiming that the proposed product is generic to the reference medicinal product Proscar®, marketed by Merck Sharp Dohme, Netherlands. Proscar® 5 mg Tabletten has been licensed in The Netherlands since July 1992.

About the product

The active compound in this product is finasteride, a competitive and specific inhibitor of the enzyme steroid type II 5α-reductase, which catalyses the 5α-reduction of testosterone to the more potent androgen dihydro-testosterone (DHT). Finasteride is chemically similar to testosterone but does not affect the binding of testosterone or DHT to the androgen receptor, nor does it possess any steroid hormone-related properties.

Therefore, the major effect of finasteride is to decrease prostatic and circulating DHT levels.

The finasteride product submitted with this application is considered to be a generic of the reference medicinal product Proscar® as it satisfies the criteria of having the same qualitative and quantitative composition in terms of active ingredients, the same pharmaceutical form and is considered bioequivalent to the reference medicinal product.

General comments on the submitted dossier

For this application reference is made to the Dutch product Proscar®, marketed by Merck Sharp Dohme, Netherlands. The Dutch reference product has been licensed in The Netherlands since July 1992.

To support the application the applicant has submitted one study to prove bioequivalence, comparing the test product Finamed 5mg Film-coated Tablets and the reference products Proscar® Germany and Proscar® U.S.A.

The submitted dossier is adequate and sufficient.

General comments on compliance with GMP, GLP, GCP and agreed ethical principles

The study was conducted in accordance with Good Clinical Practices, Good Laboratory Practices, other applicable regulations and implemented internal standard operation procedures

Suitable details have been provided to confirm GMP compliance.

SCIENTIFIC OVERVIEW AND DISCUSSION

Quality aspects

The product is formulated as immediate release, film-coated tablets. The tablets are packaged in blister packs or HDPE containers. The information provided in the dossier is satisfactory.

Drug substance

The drug substance, finasteride, is the subject of a European Pharmacopoeia monograph and is procured from two sources. A CEP has been submitted by one manufacturer and an EDMF has been submitted in support of the other. The stability data presented support a retest period of three years.

The drug substance specifications of the active substance manufacturers are based on the Ph Eur monograph. The analytical methods have been validated in accordance with current guidelines.

Suitable details are provided on the specification employed by the finished product manufacturer upon receipt of the active substance. The retest period adopted by the finished product manufacturer is consistent with that of the active ingredient manufacturers.

Drug product

The drug product is a film-coated tablet, which is manufactured from conventional pharmaceutical excipients using a standard, direct compression method. Comparative studies show the proposed product to be generic to the reference product in terms of dissolution and impurity profiles. The manufacturing method has been satisfactorily validated using production scale batches. The finished product specification is based on relevant development and stability studies. Appropriate validation data has been provided for the analytical methods. Batch analyses data support the proposed finished product specification. Stability studies have been carried out in accordance with ICH guidelines. Updated stability data support the proposed three year shelf-life.

Non clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of finasteride are well known. As finasteride is a widely used, well-known active substance, no further studies are required. An overview based on a literature review is, thus, appropriate.

Critical evaluation of the Non-Clinical Overview and Summary
There are no objections to approval of Finasteride 5mg tablets from a non-clinical point of view.

Clinical aspects
Pharmacokinetics

To support the application, the applicant has submitted a study to prove bioequivalence between Finasteride 5mg Tablets and Proscar Filmtabletten (Merck Sharp Dohme, Germany). The study is a randomised, single-dose, 3-way crossover study. The primary parameters on which bioequivalence is based are AUC_{0-t} and $C_{max.}$

After a single-dose administration of the finasteride oral test formulation and the reference formulations in healthy male subjects the pharmacokinetic parameters were similar between both treatments. In the fasted state, the 90% CIs of the pharmacokinetic parameters AUC_{0-t} (88.94 – 100.98 using Proscar® USA and 94.41 – 107.19 using Proscar® Germany) and $C_{max.}$ (87.26 – 96.17 using Proscar® USA and 91.75 – 101.12 using Proscar® Germany) were within the bioequivalence acceptance range of 80% -125%. Therefore, the results obtained in this study demonstrate that the test formulation is bioequivalent to the reference formulations in fasted state.

The application contains an adequate review of published clinical data and bioequivalence, with respect to extent and rate of absorption of Finasteride 5mg Tablets, has been shown.

Pharmacodynamics
Not applicable.

Clinical efficacy
Not applicable.

Clinical safety
A total of 24 adverse events (AEs) occurred during the study (9 AEs following administration of test product, 4 AEs following administration of Proscar® USA and 11 AEs following administration of Proscar® Germany)

The most commonly reported AEs were hot flushes and scratching.

Of the 24 post-dose AEs, 20 were graded as mild and 4 as moderate, the relationship to the study medication was judged as “remote” in 9 cases and “unrelated” in 15 cases. There were no deaths or serious adverse events.

The safety results do not elicit new safety concerns with regard to the test product. In addition, there is vast clinical experience with other finasteride containing medicinal products indicating a good tolerability and safety of the active substance finasteride.

BENEFIT RISK ASSESSMENT
The quality dossier confirms that a product of consistently good quality meeting all

requirements is produced.

There are no objections to approval of a Marketing Authorisation for Finamed 5mg Film-coated Tablets from a non-clinical point of view.

The application contains an adequate review of the published clinical data. Based on the submitted bioequivalence study, Finamed 5mg Film-coated Tablets is considered bioequivalent to 5mg Proscar® Germany and Proscar® USA.

CONCLUSION

A marketing authorisation may be granted for this product.

Overall conclusion

QUALITY

The important quality characteristics of Finamed 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 preclinical data are needed for this application.

No new or unexpected safety concerns arise from these applications.

EFFICACY

Clinical studies have demonstrated the efficacy of Finamed 5mg Film-coated Tablets in the treatment of enlarged prostate.

The SPC, PIL and labelling are satisfactory and consistent with that for the innovator product.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified.