PROPOSED AMENDED PACKAGE INSERT FOR

FINCAR 5 TABLETS

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

FINCAR 5 (Tablets)

COMPOSITION:

Each film-coated **FINCAR 5** tablet contains 5 mg finasteride.

Inactive ingredients include colloidal silicon dioxide, docusate sodium benzoate, lactose monohydrate, magnesium stearate, maize starch, opadry blue (containing FD & C blue/indigo carmine aluminium lake, hypromellose, macrogol, titanium dioxide), and sodium starch glycolate.

Contains lactose.

PHARMACOLOGICAL CLASSIFICATION:

A 21.12 Hormone inhibitors.

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Finasteride is a synthetic 4-azasteroid compound. Finasteride is an inhibitor of Type II 5-alpha-reductase, an intracellular enzyme that metabolises testosterone into the more potent androgen dihydrotestosterone (DHT). Finasteride has no affinity for the androgen receptor.

The development of the prostate gland and subsequent benign prostate hyperplasia (BPH) is dependent upon the conversion of testosterone to DHT within the prostate.

Finasteride reduces circulating and intraprostatic DHT. Within 24 hours after oral administration of finasteride, there is a significant reduction in circulating DHT levels as a result of the inhibition of 5-alpha reductase.

Pharmacokinetics:

Absorption:

Following an oral dose of ^{14}C-finasteride in humans, the bioavailability is approximately 80 % (relative to an intravenous reference dose) and is not affected by food.

Maximum finasteride plasma concentrations are reached about 2 hours after dosing and the absorption is complete after 6 – 8 hours.

Distribution:

Protein binding is approximately 93 %, plasma clearance about 165 mℓ/min and the volume of distribution, 76 litres.

Metabolism:

Two metabolites of finasteride have been identified which possess only a small fraction of the 5-alpha reductase inhibitory activity of finasteride.

Elimination:

Finasteride displays a mean plasma elimination half-life of approximately 6 hours (4 – 12 hours) in subjects 46 – 60 years of age and approximately 8 hours in men 70 years of age or older.

36 % of the dose is excreted in the urine in the form of metabolites and 57 % of the total dose is excreted in the faeces.

INDICATIONS:

FINCAR 5 is indicated for the treatment of symptomatic benign prostatic hyperplasia (BPH) in men with enlarged prostate to:

- Improve urinary flow and improve the symptoms associated with BPH by causing regression of the enlarged prostate.
- Decrease the incidence of acute urinary retention.
- Improve the symptoms associated with BPH.
- Decrease the incidence of surgery, including transurethral resection of the prostate (TURP) and prostatectomy.

CONTRAINDICATIONS:

FINCAR 5 is contraindicated in:

- Patients with hypersensitivity to finasteride, or any of the components of **FINCAR 5**.
- Pregnancy (see **"PREGNANCY AND LACTATION: Exposure to FINCAR 5 (by pregnant women) - Risk to male foetus"** and **"Special Precautions"** below).
- Women.
- Paediatric use, as safety and efficacy in children have not been established.

WARNINGS:

FINCAR 5 is contraindicated for use in women when they are or may potentially be pregnant as it may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman (see **"PREGNANCY AND LACTATION: Exposure to FINCAR 5 (by pregnant women) - Risk to male foetus"** below).

It is not known whether **FINCAR 5** is excreted in breast milk.

Serum prostate-specific antigen (S-PSA) levels decrease in patients treated with **FINCAR 5**.

INTERACTIONS:

No interactions of clinical importance have been identified.

FINCAR 5 does not appear to significantly affect the cytochrome P450-linked medicine metabolising enzyme system.

Compounds tested in men included digoxin, propranolol, warfarin, glibenclamide, antipyrine and theophylline and no clinically meaningful interactions were found.

Other concomitant therapy:

FINCAR 5 has been used concomitantly with ACE-inhibitors, paracetamol, acetylsalicylic acid, alpha-blockers, beta-blockers, calcium channel blockers, cardiac nitrates, diuretics, H_2 antagonists, HMG-CoA reductase inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs), quinolones and benzodiazepines without evidence of clinically significant adverse interactions.

Laboratory test interactions:

Prostatic volume is correlated with patient's age, whereas serum prostate-specific antigen (S-PSA) concentration is correlated with patient's age and prostatic volume. When S-PSA laboratory determinations are evaluated, consideration should be given to the fact that S-PSA levels decrease in patients treated with **FINCAR 5** (see **"Special Precautions"**). S-PSA levels decrease rapidly within the first months of therapy, after which time, S-PSA levels stabilise to a new baseline. The post-treatment baseline approximates half of the pre-treatments value. The decrease is predictable over the entire range of S-PSA

values, although it may vary in individual patients. Therefore, in typical patients treated with **FINCAR 5** for six months or more, S-PSA values should be doubled for comparison to normal ranges in untreated men. This adjustment preserves the sensitivity or specificity of the PSA assay and maintains its ability to detect prostate cancer. There is considerable overlap in S-PSA levels among men and without prostate cancer. Therefore, in men with BPH, S-PSA values within the normal reference range, prostate cancer should not be ruled out regardless of **FINCAR 5** treatment. The ability of S-PSA to distinguish between BPH and cancer is not adversely affected by treatment with **FINCAR 5**.

PREGNANCY AND LACTATION:

Use in pregnancy and lactating mothers:

FINCAR 5 is contraindicated in pregnancy (see **"CONTRAINDICATIONS"**).

Because of the ability of Type II 5-alpha reductase inhibitors to inhibit conversion of testosterone to dihydrotesterone, these medicines, including **FINCAR 5**, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

Lactation:

It is not known if **FINCAR 5** is excreted in human milk.

Exposure to FINCAR 5 (by pregnant women) - Risk to male foetus:

FINCAR 5 tablets are coated and will prevent contamination with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

Pregnant women should not handle crushed or broken **FINCAR 5** tablets because of the possibility of absorption of **FINCAR 5** and the subsequent potential risk to a male foetus (see **"Use in pregnancy and lactating mothers"**).

In addition, since **FINCAR 5** is present in semen, male patients should wear a condom or otherwise avoid exposure of female sexual partners at risk of becoming pregnant.

DOSAGE AND DIRECTIONS FOR USE:

The recommended dosage is one 5 mg tablet with or without food.

The tablet should be swallowed whole and must not be divided or crushed.

Although early improvement in symptoms may be seen, a therapeutic trial of 6 – 12 months may be necessary to assess whether a beneficial response has been achieved.

Dosage in renal insufficiency:

Adjustments in dosage are not required in patients with varying degrees of renal insufficiency (creatinine clearance as low as 9 mℓ/min) as there are no changes in the disposition of **FINCAR 5** as compared to healthy subjects.

Dosage in hepatic insufficiency:

There are no data available in patients with hepatic insufficiency (see **"Special Precautions"**).

Dosage in the elderly:

No adjustments in dosage are required even though the elimination of **FINCAR 5** is decreased in patients more than 70 years of age (see **"Pharmacokinetics"**).

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

The most frequent adverse effects are impotence and reduced libido. These effects usually occur at the beginning of the treatment and in the majority, are of a transient nature on continued treatment.

Immune system disorders:

Frequency unknown: Hypersensitivity reactions, including pruritus, urticaria, and swelling of the lips and face.

Nervous system disorders:

Frequent: Decreased libido.

Frequency unknown: Drowsiness.

Cardiac disorders:

Frequency unknown: Palpitations.

Hepatobiliary disorders:

Frequency unknown: Increased hepatic enzymes.

Skin and subcutaneous tissue disorders:

Less frequent: Rash, pruritus, urticaria (see **"Immune system disorders"**).

Reproductive system and breast disorders:

Frequent: Impotence.

Less frequent: Ejaculation disorder, breast tenderness, breast enlargement, breast secretion, breast nodules.

Frequency unknown: Testicular pain.

Investigations:

Frequent: Decreased volume of ejaculate.

Special Precautions:

General:

Consultation of an urologist should be considered in patients treated with **FINCAR 5**.

Obstruction due to trilobular growth pattern of the prostate should be excluded before starting treatment with **FINCAR 5**.

There is no experience in patients with liver insufficiency. Since **FINCAR 5** is metabolised in the liver, caution is advised in patients with decreased hepatic function as plasma levels of finasteride may be increased in such patients.

The beneficial response of **FINCAR 5** may not be manifested immediately and thus patients with large residual urine volumes and/or severely diminished urinary flow should be monitored carefully for obstructive uropathy.

Effects on PSA and prostate cancer detection:

Since serum markers of prostate cancer may be reduced in patients taking **FINCAR 5**, such malignancies should be excluded before treatment of benign prostatic hyperplasia is initiated.

No clinical benefit has been demonstrated in patients with prostate cancer treated with **FINCAR 5**.

Digital rectal examinations as well as other evaluations for prostate cancer are recommended prior to initiating therapy with **FINCAR 5** and periodically thereafter. Serum prostate-specific antigen (S-PSA) is also used for prostate cancer detection. Generally a baseline S-PSA greater than 10 ng/mℓ (Hybritech) prompts further evaluation and consideration of biopsy; for S-PSA levels between 4 to 10 ng/mℓ, further evaluation is advisable. The medical practitioner should be aware that the baseline S-PSA < 4 ng/mℓ does not exclude prostate cancer.

FINCAR 5 causes a decrease in serum S-PSA concentrations by approximately 50 % even in the presence of prostate cancer (see "INTERACTIONS"). The reduction of levels in patients with BPH treated with FINCAR 5 should be considered when evaluating S-PSA data and does not rule out concomitant prostate cancer.

Patients treated with **FINCAR 5** who have a sustained increase in S-PSA levels should be carefully evaluated, including consideration of non-compliance to **FINCAR 5** therapy.

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

Breast cancer in men:

Breast cancer has been reported in men taking finasteride 5 mg, as in **FINCAR 5**. Medical practitioners should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

Laboratory test findings:

Consideration should be given to the fact that S-PSA levels are decreased in patients treated with **FINCAR 5** (see **"INTERACTIONS"**) when S-PSA laboratory test determinations are evaluated.

Lactose:

FINCAR 5 contains lactose. It should not be administered to patients with galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption syndrome.

Effect on the ability to drive and use machines:

There is no available information indicating that **FINCAR 5** would have an influence on the ability to drive or use machines.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

No specific treatment of overdosage with **FINCAR 5** is recommended.

Treatment is symptomatic and supportive.

IDENTIFICATION:

Light blue circular, biconvex, film-coated tablets plain on both sides.

PRESENTATION:

PVC/PVDC aluminium foil blister strips of 10 tablets, packed in 30's.

STORAGE INSTRUCTIONS:

Store at or below 25 ºC. Protect from light.

Keep blisters in the outer carton until required for use.

KEEP THIS MEDICINE OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

41/21.12/0422

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

CIPLA MEDPRO (PTY) LTD

Rosen Heights

Pasita Street

Rosen Park

Bellville

FINCAR 5 CIPLA MEDPRO (PTY) LTD

7530

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