PROPOSED AMENDED PACKAGE INSERT FOR

FINPECIA TABLETS

SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

FINPECIA (Tablets)

COMPOSITION:

Each film-coated **FINPECIA** tablet contains 1 mg of finasteride.

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

Contains lactose.

PHARMACOLOGICAL CLASSIFICATION:

A21.12 Hormone inhibitors.

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Finasteride is a synthetic 4-azasteriod 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 and has no androgenic, anti-androgenic, oestrogenic, anti-oestrogenic, or progestational effects.

Finasteride decreases scalp and serum DHT concentrations and inhibits the process responsible for miniaturisation of the scalp hair follicles in men with male pattern hair loss.

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 to 8 hours.

Distribution:

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

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

Metabolism:

Finasteride is metabolised primarily via the cytochrome P450 3A4 enzyme subfamily. Two metabolites of finasteride have been identified which possess only a small fraction of the 5-alpha-reductase inhibitory activity of finasteride.

Elimination:

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.

Special populations:

The elderly:

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.

Renal impairment:

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

Hepatic impairment:

The effect of hepatic insufficiency on the pharmacokinetics of finasteride has not been studied.

INDICATIONS:

FINPECIA temporarily delays further hair loss and increases hair density in the vertex and anterior mid scalp area in men (between 18 and 41 years) with early signs of androgenetic alopecia (male pattern hair loss).

CONTRAINDICATIONS:

FINPECIA is contraindicated in:

- Hypersensitivity to finasteride or any of the components of **FINPECIA**.
- Pregnancy and lactation (see **"WARNINGS"** and **"PREGNANCY AND LACTATION"**).
- Women.
- Paediatric use, as safety and efficacy in children and adolescents under the age of 18 have not been established.
- Combination with finasteride 5 mg, or any other 5α-reductase inhibitors for benign prostatic hyperplasia (BPH) or any other condition.

WARNINGS:

FINPECIA 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"**).

It is not known whether **FINPECIA** is excreted in breast milk (see **"PREGNANCY AND LACTATION"**).

Serum prostate-specific antigen (S-PSA) levels decrease in patients treated with

FINPECIA (see **"Special Precautions"**).

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

FINPECIA 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 **FINPECIA** tablets because of the possibility of absorption of **FINPECIA** and the subsequent potential risk to a male foetus (see **"PREGNANCY AND LACTATION"**).

A small amount of finasteride, less than 0,001 % of the 1 mg dose per ejaculation, has been detected in the seminal fluid of men taking **FINPECIA**. This amount is unlikely to constitute a risk to the developing male foetus. However, since **FINPECIA** is present in semen, male patients should wear a condom or otherwise avoid exposure of female sexual partners at risk of becoming pregnant.

INTERACTIONS:

No interactions of clinical importance have been identified.

FINPECIA is metabolised primarily via, but does not appear to significantly affect, the cytochrome P450-linked medicine metabolising enzyme system. Compounds tested in men included digoxin, propranolol, warfarin, glibenclamide and theophylline and no clinically meaningful interactions were found.

Other concomitant therapy:

FINPECIA 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.

Although the risk of **FINPECIA** affecting the pharmacokinetics of other medicines is estimated to be small, it is probable that inhibitors and inducers of cytochrome P450 3A4 will affect the plasma concentration of **FINPECIA**. However, based on established safety margins, any increase due to concomitant use of such inhibitors is unlikely to be of clinical significance.

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

PREGNANCY AND LACTATION:

Use in pregnancy and lactating mothers:

FINPECIA is contraindicated in pregnancy (see **"CONTRAINDICATIONS"** and **"WARNINGS"**). Because of the ability of Type II 5-alpha-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these medicines, including **FINPECIA**, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.

Lactation:

It is not known if **FINPECIA** is excreted in human milk. **FINPECIA** is contraindicated for use in lactation (see **"CONTRAINDICATIONS"**).

DOSAGE AND DIRECTIONS FOR USE:

The recommended dose is one 1 mg tablet daily 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 medical practitioner. In general, daily use for 3 to 6 months is necessary before increased hair growth and/or prevention of further hair loss is observed. Continued use is recommended to obtain maximum benefit. Withdrawal of treatment leads to reversibility of effect by 6 months and return to baseline by 9 to 12 months.

Dosage in renal insufficiency:

Adjustments in dosage are not required in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 mℓ/min) as there are no changes in the disposition of a single dose of **FINPECIA** as compared to healthy subjects (see **"Pharmacokinetics: Special populations"**).

Dosage in the elderly:

No adjustments in dosage are required even though the elimination of **FINPECIA** is decreased in patients more than 70 years of age (see

"Pharmacokinetics: Special populations").

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

Side-Effects:

Immune system disorders:

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

Nervous system disorders:

Less frequent: Decreased libido.

Cardiac disorders:

Frequency unknown: Palpitations.

Hepatobiliary disorders:

Frequency unknown: Increased hepatic enzymes.

Skin and subcutaneous tissue disorders:

Frequency unknown: Rash, pruritus, urticaria (see **"Immune system disorders"**).

Reproductive system and breast disorders:

Frequent: Impotence.

Less frequent: Decrease in volume of ejaculate and ejaculation

	disorder, erectile dysfunction (see **"Special Precautions"**).
Frequency unknown:	Breast tenderness, breast enlargement, testicular pain, infertility (see **"Special Precautions"**).

Special Precautions:

When **FINPECIA** is used for treatment of male pattern hair loss in older men who also have benign prostatic hyperplasia (BPH), consideration should be given to the fact that, in older men with BPH, PSA levels are decreased by approximately 50 % (see **"WARNINGS"**). Doubling the PSA level in men taking **FINPECIA** should be considered before evaluating this test result.

Resolution of decreased libido, erectile dysfunction and decreased volume of ejaculate occurred in men who discontinued therapy with **FINPECIA**, and in many who continued therapy. Persistence of erectile dysfunction after discontinuation of treatment has been reported during post-marketing use.

Breast cancer has been reported in men taking finasteride 1 mg, as contained in **FINPECIA**, during the post-marketing period. Medical practitioners should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge (see **"Side-Effects"**).

Long-term data on fertility in humans are lacking and specific studies in subfertile men have not been conducted. Although animal studies did not show relevant negative effects on fertility, spontaneous reports of infertility and/or poor

seminal quality were received (see **"Side-Effects"**). In some of these reports, patients had other risk factors that may have contributed to infertility. Normalisation or improvement of seminal quality has been reported after discontinuation of **FINPECIA**.

Lactose:

FINPECIA 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 are no data to suggest that **FINPECIA** affects the ability to drive or use machines.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

No specific treatment of overdosage with **FINPECIA** is recommended. Treatment is symptomatic and supportive.

IDENTIFICATION:

Reddish brown coloured, circular, biconvex, film-coated tablets plain on both sides.

PRESENTATION:

FINPECIA tablets are packed as 30's in white coloured, opaque HDPE 60 cc bottles with 38 mm screw caps and in blister packs of 30 tablets.

STORAGE INSTRUCTIONS:

KEEP OUT OF REACH OF CHILDREN.

Store at or below 25 °C. Protect from light and moisture.

REGISTRATION NUMBER:

41/21.12/0221

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

CIPLA MEDPRO (PTY) LTD

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R.S.A.

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