SCHEDULING STATUS

S4

1. NAME OF MEDICINE:

INNOPECIA 1 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

INNOPECIA 1 mg: Each film-coated tablet contains finasteride

Contains: Sugar (Lactose 87.8 mg).

For full list of excipients, **see section 6.1**

3. PHARMACEUTICAL FORM:

INNOPECIA 1 mg film-coated tablets: Brown colour, round film coated tablets, debossed with ‘H’ on one side and ‘36’ on the other side.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications

INNOPECIA temporarily delays further hair loss and increases the density of hair in the vertex and anterior mid-scalp area in males (between 18 and 41 years) displaying early signs of androgenetic alopecia. **INNOPECIA** is not effective in postmenopausal women with androgenetic alopecia.

4.2 Posology and method of administration

Posology

Adults:

The recommended dose is one 1 mg tablet daily with or without food.

In general, daily use for at least 3 months is necessary before increased hair growth and/or prevention of further hair loss is noticeable. Continued use is recommended for maximum benefit. Effects may be reversed within 12 months after withdrawal of treatment.

INNOPECIA 1mg is not indicated for use in women or children (see section 4.3).

Method of administration

For oral use only, swallow film-coated tablet as a whole with full glass of water.

4.3 Contraindications

Hypersensitivity to **INNOPECIA** or any of the excipients listed in section 6.1.

INNOPECIA is contraindicated in women, including during pregnancy (see section 4.4 and 4.6).

- **INNOPECIA** is not indicated for paediatric use.
- **INNOPECIA** should not be taken by men who are already taking other medicines containing finasteride or any other 5α-reductase inhibitor such a dutasteride for benign prostatic hyperplasia or any other condition.

4.4 Special warnings and precautions for use

Paediatric population

INNOPECIA should not be used in children. There is no data demonstrating efficacy and safety of finasteride in children under the age of 18. (see section 4.3)

Effects on Prostate Specific Antigen (PSA)

In clinical studies the serum prostatic-specific antigen (S-PSA) levels decrease in patients treated with **INNOPECIA**. When **INNOPECIA** 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.

Effects on fertility

Male infertility and/or poor seminal quality have occurred. See also section 4.6.

Exposure to INNOPECIA (by pregnant women) – risk to male foetus:

INNOPECIA tablets are coated and will prevent contamination with finasteride during normal handling, provided that the tablets have not been crushed or broken. Pregnant women should not handle crushed or broken **INNOPECIA** tablets because of the possibility of absorption of **INNOPECIA** and subsequent potential risk to a male foetus (see section 4.6). In addition, since **INNOPECIA** is present in semen, male patients should wear a condom or otherwise avoid exposure of female sexual partners at risk of becoming pregnant.

Breast cancer

Breast cancer has been reported in men taking **INNOPECIA** during the post-marketing period. Healthcare providers should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

Mood alterations and depression

Mood alterations including depressed mood, depression and, less frequently, suicidal ideation have been reported in patients treated with **INNOPECIA**. Patients should be monitored for psychiatric symptoms and if these occur, treatment with **INNOPECIA** should be discontinued and the patient advised to seek medical advice.

Liver disease

Risk of non-alcoholic fatty liver disease (NAFLD) and associated with liver diseases .

Lactose intolerance

INNOPECIA contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interactions with other medicines and other forms of interaction

No interactions of significant clinical importance have been established.

INNOPECIA is metabolised primarily via, but does not appear to significantly affect the cytochrome P450-linked drug metabolising enzyme system. Although the risk for finasteride to affect 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 finasteride. However, based on established safety margins, any increase due to concomitant use of such inhibitors is unlikely to be of clinical significance.

Interaction studies have only been performed in adults.

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

Other Concomitant Therapy:

INNOPECIA has been used concomitantly with ACE-inhibitors, paracetamol, acetylsalicylic acid, alpha-blockers, beta-blockers, calcium-channel blockers, cardiac nitrates, diuretics, H2-antagonists, HMG-CoA reductase inhibitors, non-steroidal anti-inflammatory drugs (NSAID's), quinolones and benzodiazepines without any evidence of clinically significant interactions.

4.6 Fertility, pregnancy, and lactation

Pregnancy

INNOPECIA is contraindicated in women due to risk of pregnancy. Because of the ability of Type II 5-alpha-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these medicines, including **INNOPECIA** may cause abnormalities of the external male foetus genitalia when administered to a woman during pregnancy. See also the boxed warning in section 4.4: "Exposure to **INNOPECIA** (by pregnant women) – risk to male foetus".

Lactation

INNOPECIA is contraindicated for use in women. It is not known if finasteride is excreted in human milk.

Fertility

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Male infertility and/or poor seminal quality have occurred.

INNOPECIA is contraindicated in women who are or may potentially be pregnant as it may cause abnormalities of the external male foetus genitalia when administered during pregnancy.

4.7 Effects on ability to drive and use machines

INNOPECIA has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The adverse reactions during clinical trials and/or postmarketing use are listed in the table below.

System Organ Class	**Frequency**	**Side effects**
Immune system disorders	*Frequency unknown*	Hypersensitivity reactions, including rash, pruritus, urticaria and angioedema (swelling of the lips, tongue, throat and face).
Psychiatric disorders	*Less frequent*	Decreased libido, depression.

	Frequency unknown	Anxiety.
Cardiac disorders	*Frequency unknown*	Palpitation.
Hepatobiliary disorders	*Frequency unknown*	Increased hepatic enzymes and risk of non-alcoholic fatty liver disease (NAFLD) and associated with liver disease
Reproductive system and breast disorders	*Less frequent*	Decrease in volume of ejaculate and ejaculation disorders, impotence and decreased libido.
	Frequency unknown	Breast tenderness, breast enlargement and testicular pain, haematospermia, infertility, poor seminal quality*.

* Normalisation or improvement of seminal quality has been reported after discontinuation of finasteride.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

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 is recommended for overdosage with **INNOPECIA**. Treatment is symptomatic and supportive.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: 5α-reductase inhibitor. ATC code: D11AX10.

Category and class: A.21.12 Hormone Inhibitors

Mechanism of action

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.

5.2 Pharmacokinetic properties

Absorption

Following an oral dose of 14C-finasteride in humans, the bioavailability is approximately 80 % (relative to an intravenous reference dose) and not affected by food. Maximum finasteride plasma concentrations are reached about 2 hours after oral dosing and absorption is complete after 6 to 8 hours.

Distribution

The volume of distribution is 76 litres, protein binding about 93 %.

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; $AUC_{(0-24\ hr)}$ 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 medicine.

Metabolism

Finasteride is metabolised primarily via the cytochrome P450 3A4 enzyme subfamily. Following an oral dose of ^{14}C-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 ^{14}C-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 renal impairment patients

In patients with chronic renal impairment whose creatinine clearance ranged from 9 to 55 ml/min the disposition of a single dose of 14C-finasteride was not different from that in healthy volunteers. Protein binding also did not differ in patients with renal impairment. A portion of the metabolites that are normally excreted renally are excreted in the faeces.

It therefore appears that faecal excretion increases commensurate to the decrease in urinary excretion of metabolites. No adjustment in dosage is necessary in nondialysed patients with renal impairment.

6. Pharmaceutical particulars

6.1 List of excipients

Cellulose microcrystalline, docusate sodium, lactose monohydrate, magnesium stearate, opadry brown, starch pregelatinised, sodium starch glycolate.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25˚C

Protect from moisture and sunlight

6.5 Nature and contents of container

INNOPECIA 1 mg Film-coated Tablets: Aluminium/Aluminium blister strips of 10 tablets per strip packed in a mono-carton containing 30 tablets.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Holder of certificate of registration

Innovata Pharmaceuticals

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South Africa

8. Registration numbers

A 50/21.12/0579

9. Date of first authorization/Renewal of the authorization

21 June 2022

10. Date of revision of the text

30 October 2023

REFERENCES:

1. Reference 1: PROPECIA®, MSD (Pty) Ltd: 20 March 2018.
2. Reference 2: Finasteride 1 mg tablets. SmPC

   Date of first authorization/Date of renewal of the authorization:

   First authorization: 18 February 2014.

   Renewal of authorization: 18 February 2014

31/01/2024

Date of revision of the text: 15 June 2020

Name of registration holder: Milpharm Limited

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