

New Zealand Datasheet

1 PRODUCT NAME

Ricit

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Finasteride 5mg film coated tablets

3 PHARMACEUTICAL FORM

Ricit 5mg film coated tablets are light blue, circular, biconvex, and plain on both sides.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Ricit 5mg film coated tablets are indicated for the treatment and control of benign prostatic hyperplasia (BPH) and for the prevention of urologic events to;

- Reduce the risk of acute urinary retention
- Reduce the risk of surgery including transurethral resection of the prostate (TURP) and prostatectomy

Ricit 5mg film coated tablets cause regression of the enlarged prostate, improved urinary flow and improves the symptoms associated with BPH.

Patients with enlarged prostate are the appropriate candidates for therapy with Ricit 5mg film coated tablets.

4.2 Dose and method of administration

The recommended dosage is one Ricit 5mg film coated tablet daily with or without food.

Dosage in Renal Insufficiency

No adjustment in dosage is required in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 ml/min) as pharmacokinetic studies did not indicate any change in the disposition of finasteride.

Dosage in the Elderly

No adjustment in dosage is required although pharmacokinetic studies indicated the elimination of finasteride is somewhat decreased in patients more than 70 years of age.

4.3 Contraindications

Ricit 5mg film coated tablets are not indicated for use in women or children.

Ricit 5mg film coated tablets are contraindicated in the following:

- Hypersensitivity to any component of this product.
- Pregnancy - Women who are or may potentially be pregnant (see Warnings and Precautions: Pregnancy and Exposure to Finasteride - Risk to Male Foetus)

4.4 Special warnings and precautions for use

Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy.

Effects on PSA and Prostate Cancer Detection

No clinical benefit has yet been demonstrated in patients with prostate cancer treated with finasteride. Patients with BPH and elevated prostate-specific antigen (PSA) were monitored in controlled clinical studies with serial PSAs and prostate biopsies. In these BPH studies, finasteride did not appear to alter the rate of prostate cancer detection and the overall incidence of prostate cancer was not significantly different in patients treated with finasteride tablets or placebo.

Digital rectal examinations as well as other evaluations for prostate cancer are recommended prior to initiating therapy with finasteride 5mg film coated tablets and periodically thereafter. Serum PSA is also used for prostate cancer detection. Generally a baseline PSA > 10 ng/ml (Hybritech) prompts further evaluation and consideration of biopsy; for PSA levels between 4 and 10 ng/ml, further evaluation is advisable. 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. A baseline PSA < 4 ng/ml does not exclude prostate cancer.

Ricit 5mg film coated tablets cause 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 5mg film coated tablets 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. Analysis of PSA data from over 3000 patients in the 4-year, double blind, placebo controlled finasteride long-term efficacy and safety study confirmed that in typical 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 and specificity of the PSA assay and maintains its ability to detect prostate cancer.

Any sustained increase in PSA levels of patients treated with Ricit 5mg film coated tablets should be carefully evaluated, including consideration of non-compliance to therapy with finasteride 5mg film coated tablets.

Medicine/Laboratory Test Interactions

Effect on Levels of PSA

Serum PSA concentration is correlated with patient age and prostatic volume, and prostatic volume is correlated with patient age. When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels decrease in patients treated with finasteride 5mg tablets. In most 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 5mg tablets for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men. For clinical interpretation, see Warnings and Precautions, Effects on PSA and Prostate Cancer Detection.

Percent free PSA (free to total PSA ratio) is not significantly decreased by finasteride. The ratio of free to total PSA 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 to its value is necessary.

Paediatric Use

Ricit 5mg film coated tablets are not indicated for use in children.

Safety and effectiveness in children have not been established.

Breast Cancer in Men

Breast cancer has been reported in men taking finasteride during clinical trials and in the post-marketing period. Physicians should instruct their patients to promptly report any changes in their breast tissue such as lumps, pain, gynaecomastia or nipple discharge.

Lactose

The tablet contains lactose monohydrate. Patients with any of the following genetic deficiencies should not take this drug: galactose intolerance, total lactase deficiency or glucose-galactose malabsorption.

4.5 Interaction with other medicines and other forms of interaction

No medicine interactions of clinical importance have been identified. Finasteride 5mg tablets do not appear to significantly affect the cytochrome P450-linked medicine metabolising enzyme system. Compounds which have been tested in man have included propranolol, digoxin, glyburide, warfarin, theophylline, and antipyrine and no clinically meaningful interactions were found.

Other Concomitant Therapy

Although specific interaction studies were not performed, in clinical studies finasteride 5mg tablets were used concomitantly with ACE-inhibitors, acetaminophen, acetylsalicylic acid, alpha-blockers, beta-blockers, calcium channel blockers, cardiac nitrates, diuretics, H₂ antagonists, HMG-CoA reductase inhibitors, nonsteroidal anti-inflammatory medicines (NSAIDs), quinolones, and benzodiazepines without evidence of clinically significant adverse interactions.

4.6 Fertility, pregnancy and lactation

Ricit 5mg film coated tablets are contraindicated in women who are or may potentially be pregnant (See Contraindications).

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

Exposure to Finasteride - Risk to Male Foetus

Women should not handle crushed or broken finasteride tablets when they are or may potentially be pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus (see Pregnancy). Ricit 5mg tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

Similarly, small amounts of finasteride have been recovered from the semen in subjects receiving finasteride 5mg/day. The amount of finasteride measured in ejaculate was 50 - to 100-fold less than the dose of finasteride (5 micrograms) that had no effect on circulating DHT levels in adult males. It is not known whether a male foetus may be adversely affected if his mother is exposed to the semen of a patient being treated with finasteride. Therefore, when the patient's sexual partner is or may potentially be pregnant, the patient should either avoid exposure of his partner to semen or discontinue finasteride 5mg film coated tablets (See Contraindications and Pregnancy).

Use in Lactation

Ricit 5mg film coated tablets are not indicated for use in women.

It is not known whether finasteride is excreted in human milk.

4.7 Effects on ability to drive and use machines

There are no data to suggest that finasteride affects the ability to drive or use machines.

4.8 Undesirable effects

Finasteride tablets are well tolerated.

The most frequent adverse reactions are impotence and decreased libido. These adverse reactions occur early in the course of therapy and resolve with continued treatment in the majority of patients.

The adverse reactions reported during clinical trials and/or post-marketing use are listed in the table below.

Frequency of adverse reactions is determined as follows:

Very common ($\geq 1/10$), Common ($\geq 1/100$ to $< 1/10$), Uncommon ($\geq 1/1,000$ to $< 1/100$), Rare ($\geq 1/10,000$ to $< 1/1,000$), Very rare ($< 1/10,000$), not known (cannot be estimated from the available data). The frequency of adverse reactions reported during post-marketing use cannot be determined as they are derived from spontaneous reports.

System Organ Class	Frequency: adverse reaction
Immune system disorders	<i>Unknown:</i> hypersensitivity reactions including swelling of the lips, tongue, throat and face
Psychiatric disorders	<i>Common:</i> decreased libido <i>Unknown:</i> decreased libido that may continue after discontinuation of therapy, depression
Cardiac disorders	<i>Unknown:</i> palpitation
Hepatobiliary disorders	<i>Unknown:</i> increased hepatic enzymes
Skin and subcutaneous tissue disorders	<i>Uncommon:</i> rash <i>Unknown:</i> pruritus, urticaria
Reproductive system and breast disorders	<i>Common:</i> impotence <i>Uncommon:</i> ejaculation disorder, breast tenderness, breast enlargement. <i>Unknown:</i> testicular pain, sexual dysfunction (erectile dysfunction and ejaculation disorder) which may continue after discontinuation of treatment; male infertility and/or poor seminal quality. Normalization or improvement of seminal quality has been reported after discontinuation of finasteride.
Investigations	<i>Common:</i> decreased volume of ejaculate

In addition, the following has been reported in clinical trials and post-marketing use: male breast cancer (see below).

Other 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%) men receiving finasteride 5mg film coated tablets and 1147 (24.4%) men receiving placebo. In the finasteride group, 280 (6.4%) men had prostate cancer with Gleason scores of 7-10 detected on needle biopsy vs 237 (5.1%) men in the placebo group. Additional analyses suggest that the increase in the prevalence of high-grade prostate cancer observed in the finasteride group may be explained by a detection bias due to the effect of finasteride 5mg film coated tablets on prostate volume. Of the total cases of prostate cancer diagnosed in this study, approximately 98% were classified as intracapsular (clinical stage T1 or T2) at diagnosis. The clinical significance of the Gleason 7-10 data is unknown.

Breast Cancer

During the 4 to 6-year placebo and comparator-controlled MTOPS study that enrolled 3047 men, there were 4 cases of breast cancer in men treated with finasteride but no cases in men not treated with finasteride. During the 4-year, placebo-controlled PLESS study that enrolled 3040 men, there were 2 cases of breast cancer in placebo-treated men but no cases in men treated with finasteride. During the 7-year placebo-controlled Prostate Cancer Prevention Trial (PCPT) that enrolled 18,882 men, there was 1 case of breast cancer in men treated with finasteride, and 1 case of breast cancer in men treated with placebo. There have been post-marketing reports of male breast cancer with the

use of finasteride. The relationship between long-term use of finasteride and male breast neoplasia is currently unknown.

Laboratory Test Findings

When PSA laboratory determinations are evaluated, consideration should be given to the fact that PSA levels are decreased in patients treated with finasteride 5mg film coated tablets (See Warnings and Precautions).

No other difference in standard laboratory parameters was observed between patients treated with placebo or finasteride 5mg tablets.

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. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

Patients have received single doses of finasteride up to 400 mg and multiple doses of finasteride up to 80 mg/day for three months without adverse effects.

No specific treatment of overdosage with finasteride is recommended.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: G04CB - Testosterone-5-alpha reductase inhibitors

Finasteride, a synthetic 4-azasteroid compound, is a specific inhibitor of type II 5 α -reductase, an intracellular enzyme which metabolises testosterone into the more potent androgen dihydrotestosterone (DHT). In benign prostatic hyperplasia (BPH), enlargement of the prostate gland is dependant upon the conversion of testosterone to DHT within the prostate, finasteride is highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor.

In the finasteride long-term clinical efficacy and safety study, the effect of therapy with finasteride 5mg tablets on BPH-related urologic events (surgical intervention [e.g. transurethral resection of the prostate and prostatectomy] or acute urinary retention requiring catheterisation) was assessed over a four year period in 3016 patients with moderate or severe symptoms of BPH. In this double blind, randomised, placebo-controlled, multicentre study, treatment with finasteride 5mg tablets decreased the risk of total urological events by 51% and was also associated with a marked and sustained regression in prostate volume, and a sustained increase in maximum urinary flow rate and improvement in symptoms.

5.2 Pharmacokinetic properties

Following an oral dose of ¹⁴C-finasteride in man, 39% of the dose was excreted in the urine in the form of metabolites (virtually no unchanged medicine was excreted in the

urine) and 57% of total dose was excreted in the faeces. In this study, two metabolites of finasteride were identified which possess only a small fraction of the 5 α -reductase inhibitory activity of finasteride.

Relative to an intravenous reference dose, the oral bioavailability of finasteride is approximately 80%. The bioavailability is not affected by food. Maximum finasteride plasma concentrations are reached approximately two hours after dosing and the absorption is complete after six to eight hours. Finasteride displays a mean plasma elimination half-life of six hours. Protein binding is approximately 93%. Plasma clearance and the volume of distribution of finasteride are approximately 165 ml/min and 76 l, respectively.

A multiple dose study demonstrated a slow accumulation of small amounts of finasteride over time. After daily dosing of 5 mg/day, steady-state trough plasma concentrations of finasteride are estimated to be 8-10 ng/ml and remained stable over time.

The elimination rate of finasteride is somewhat decreased in the elderly. As subjects advance in age, half-life is prolonged from a mean half-life of approximately 6 hours in men 18-60 years of age to 8 hours in men more than 70 years of age. This finding is of no clinical significance and hence, a reduction in dosage is not warranted.

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

Finasteride has been recovered in the cerebrospinal fluid (CSF) of patients treated with a 7-10 day course of finasteride, but the medicine does not appear to concentrate preferentially to the CSF. Finasteride has also been recovered in the seminal fluid of subjects receiving 5 mg/day finasteride. The amount of finasteride in the seminal fluid was 50 to 100 fold less than the dose of finasteride (5 mcg) that had no effect on circulating DHT levels in adult males.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of repeated dose toxicity, genotoxicity, and carcinogenic potential. 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. Intravenous administration of finasteride to pregnant rhesus monkeys at doses up to 800 ng/day during the entire period of embryonic and foetal development resulted in no abnormalities in male foetuses. This dose is about 60-120 times higher than the estimated amount in semen of a man who have taken 5 mg finasteride, and to which a woman could be exposed via

semen. In confirmation of the relevance of the Rhesus model for human foetal development, oral administration of finasteride 2 mg/kg/day (the systemic exposure (AUC) of monkeys was slightly higher (3x) than that of men who have taken 5 mg finasteride, or approximately 1-2 million times the estimated amount of finasteride in semen) to pregnant monkeys resulted in external genital abnormalities in male foetuses. No other abnormalities were observed in male foetuses and no finasteride-related abnormalities were observed in female foetuses at any dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose, sodium starch glycolate, maize starch, colloidal silicon dioxide, docusate sodium, benzoate, magnesium stearate, Opadry 04F50702 blue, purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf life is 36 months (3 years) from manufacture.

6.4 Special precautions for storage

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

6.5 Nature and contents of container

Ricit 5mg film coated tablets are available in cartons containing blisters of 30 or 100 tablets.

6.6 Special precautions for disposal

Women should not handle crushed or broken Ricit 5 mg film coated tablets when they are or may potentially be pregnant (see Contraindications, Pregnancy and lactation, Exposure to finasteride - risk to male foetus).

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

15 April 2010

10 DATE OF REVISION OF THE TEXT

5 May 2017

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
4.4	Inclusion of lactose warning
4.8	Inclusion of adverse effect incidence
5.3	Updated from UK SPC