FINASID®

(finasteride)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains 5 mg of finasteride.

PHARMACEUTICAL FORM
Blue-coloured, apple-shaped, film-coated tablets.

CLINICAL PARTICULARS
Therapeutic indications: FINASID® is indicated for the treatment and control of benign prostatic hyperplasia (BPH) in patients with and enlarged prostate 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.

Posology and method of administration:
The recommended adult dose is one 5 mg tablet daily, with or without food. Although early improvement in symptoms may be seen, treatment for at least six months may be necessary to assess whether a beneficial response has been achieved. Thereafter, treatment should be continued long term.
No dosage adjustment is required in the elderly or in patients with varying degrees of renal insufficiency (creatinine clearances as low as 9 ml/min).
There are no data available in patients with hepatic insufficiency.
FINASID® is contra-indicated in children.

Contra-indications:
Hypersensitivity to any component of this product; women who are or may potentially be pregnant; children.

Special warnings and special precautions for use
General: Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy.
Effects on prostate-specific antigen (PSA) and prostate cancer detection: No clinical benefit has yet been demonstrated in patients with prostate cancer treated with FINASID®.
Digital rectal examination, as well as other evaluations for prostate cancer, should be carried out on patients with BPH prior to initiating therapy with FINASID® and periodically thereafter. Generally, when PSA assays are performed 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 FINASID®. A baseline PSA <4 ng/ml does not exclude prostate cancer.
FINASID® 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 in patients with BPH treated with FINASID® 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 FINASID® 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 finasteride should be carefully evaluated, including consideration of non-compliance to therapy with FINASID®.
Percent free PSA (free to total PSA ratio) is not significantly decreased by FINASID® and remains constant even under the influence of FINASID®. When percent free PSA is used as an aid in the detection of prostate cancer, no adjustment is necessary.

Interaction with other medicaments and other forms of interaction:
No clinically important drug interactions have been identified. FINASID® does not appear to significantly affect the cytochrome P450-linked drug metabolising enzyme system. Compounds which have been tested in man include propranolol, digoxin, glibenclamide, warfarin, theophylline, and antipyrine and no clinically meaningful interactions were found.
Other concomitant therapy: Although specific interaction studies were not performed in clinical studies, FINASID® was used concomitantly with ACE inhibitors, alpha-blockers, beta-blockers, calcium channel blockers, cardiac nitrates, diuretics, H2 antagonists, HMG-CoA reductase inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and paracetamol, quinolones and benzodiazepines without evidence of clinically significant adverse interactions.

Pregnancy and lactation: Pregnancy Group x
Pregnancy:
FINASID® is contra-indicated in women who are or may potentially be pregnant.
Because of the ability of Type II 5 ∝-reductase inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including finasteride, may cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman.
In animal developmental studies, dose-dependent development of hypospadias were observed in the male offspring of pregnant rats given finasteride at doses ranging from 100 µg/kg/day to 100 mg/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 ∝-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 ∝-reductase. It is for these reasons that FINASID® is contra-indicated in women who are or may potentially be pregnant.
No effects were seen in female offspring exposed *in utero* to any dose of finasteride.
Exposure to finasteride - risk to male foetus: Women should not handle crushed or broken tablets of FINASID® 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'). FINASID® tablets are coated and 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 FINASID® 5 mg/day. 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 (e.g. by use of a condom) or discontinue FINASID®.
Lactation: FINASID® is not indicated for use in women. It is not known whether finasteride is excreted in human milk.

Effects on ability to drive and use machines:
None reported.

Undesirable effects:
FINASID® is well tolerated. In controlled clinical studies where patients received 5 mg of finasteride over periods of up to four years, the following adverse reactions were considered possibly, probably or definitely drug-related and occurred with a frequency greater than placebo and greater than or equal to 1%; impotence, decreased libido, ejaculation disorder, decreased volume of ejaculate; breast enlargement, breast tenderness and rash. There was no evidence of increased adverse experiences with increased duration of treatment with FINASID® and the incidence of new drug-related sexual adverse experiences decreased with duration of treatment.
The following additional adverse experiences have been reported in post-marketing experiences:
- hypersensitivity reactions, including pruritus, urticaria and swelling of the lips and face.
- testicular pain.

Laboratory test findings: 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 generally decrease in patients treated with FINASID®. In most patients, a rapid decrease in PSA levels stabilise to a new baseline. The post-treatment baseline approximates half of the pre-treatment value. Therefore, in typical patients treated with FINASID® for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men.
For clinical interpretation see 'Special warnings and precautions for use'.
Effects on prostate-specific antigen (PSA) and prostate cancer detection: No other difference was observed in patients treated with placebo or FINASID® in standard laboratory test.

Overdose:
No specific treatment of overdosage with FINASID® is recommended. Patients have received single doses of FINASID® up to 400 mg and multiple dose of FINASID® up to 80 mg/day for up to three months without any adverse effects.

PHARMACOLOGICAL PROPERTIES:
Pharmacodynamic properties
Finasteride is a competitive inhibitor of human 5 ∝-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 dependent upon the conversion of testosterone to DHT within the prostate. FINASID® is highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor.
In clinical studies of patients with moderate to severe symptoms of BPH, an enlarged prostate on digital rectal examination and low residual urinary volumes, FINASID® 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 (range 0-34), a sustained regression in prostate volume of approximately 20% and a sustained increase in urinary flow rate.

Pharmacokinetic properties:
After an oral dose of ^{14}C-finasteride in man, 39% of the dose was excreted in the urine in the form of metabolites (virtually o unchanged drug was excreted in the urine), and 57% of total dose was excreted in the faeces. Two metabolites have been identified which possess only a small fraction of the Type II 5 ∝-reductase activity of finasteride.
The oral bioavailability of finasteride is approximately 80%, relative to an intravenous reference dose, and is unaffected by food. Maximum plasma concentrations are reached approximately two hours after dosing and the absorption is complete within 6-8 hours. Protein binding is approximately 93%. Plasma clearance and the volume of distribution are approximately 165 ml/min and 76 l, respectively.
In the elderly, the elimination rate of finasteride is somewhat decreased. Half-life is prolonged from a mean half-life of approximately six hours in men aged 18-60 years to eight 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 chronic renal impairment, whose creatinine clearance ranged from 9-55 ml/min, the disposition of a single dose of ^{14}C-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. 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.

Preclinical safety data:
No further information provided.

PHARMACEUTICAL PRECAUTIONS
List of excipients
Cellulose, Microcrystalline (E460)
Docusate sodium
Lactose monohydrate
Magnesium stearate (E572)
Pregelatinised maize starch
Sodium starch glycollate Type A
Yellow Iron oxide (E172)
Hydroxypropylcellulose (E463)
Indigo carmine aluminium lake (E132)
Hypromellose (E464)
Talc
Titanium dioxide (E171)

Incompatibilities: None reported.

Expiration date:
Do not use this drug after the expiry date given on the package.

Special precautions for storage:
Store below 30°C. Store in the original package.

Nature and contents of container:
White opaque PVC/PVDC blisters lidded with aluminium foil; packs of 30 tablets.

Instructions for use/handling:
Women should not handle crushed or broken FINASID® Tablets when they are or may potentially be pregnant (see 'Contra-indications, 'Pregnancy and lactation', Exposure to finasteride - risk to male foetus).

THIS IS A MEDICAMENT
– A drug is a product which acts on your health and its consumption could be dangerous when you do not follow the instructions.
– Follow strictly the doctor's prescriptions, the method of use and the instructions of the pharmacist who sold the medicament.
– The doctor and the pharmacist know the medicine, its benefits and risks.
– Do not by yourself interrupt the period of treatment prescribed for you.
– Do not repeat the same prescription without consulting your doctor.
– Keep out of the reach of children.

Manufactured by:
SAJA Pharmaceuticals Co., Ltd.
Saudi Arabian Japanese Pharmaceutical Company

Revision Date: Mar. 2007 25BFNAA