1. NAME OF THE MEDICINAL PRODUCT
Finasid 5 mg Film-coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
One film-coated tablet contains 5 mg finasteride
Excipient: lactose monohydrate (90.95 mg)
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Blue-coloured, apple shaped, film-coated tablet

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
FINASID are indicated for the treatment and control of benign prostatic hyperplasia (BPH) 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 reduce need for surgery including transurethral resection of the prostate (TURP) and prostatectomy.
FINASID should be administered in patients with an enlarged prostate (prostate volume above ca. 40 ml).
5α reductase inhibitors is not approved for prevention of prostate cancer

4.2 Posology and method of administration
For oral use only.
The recommended dosage is one 5 mg tablet daily with or without food. The tablet should be swallowed whole and must not be divided or crushed (See section 6.6). Even though improvement can be seen within a short time, treatment for at least 6 months may be necessary in order to determine objectively whether a satisfactory response to treatment has been achieved.

Dosage in the elderly
Dosage adjustments are not necessary although pharmacokinetic studies have shown that the elimination rate of finasteride is slightly decreased in patients over the age of 70.

4.3 Contraindications
Hypersensitivity to finasteride or to any of the excipients.
Contra-indicated in women and children (see sections 4.4, 4.6 and 6.6)
Pregnancy - Use in women when they are or may potentially be pregnant (see 4.6 Pregnancy and lactation, Exposure to finasteride - risk to male fetus).

4.4 Special warnings and precautions for use
General:
- Patients with large residual urine volume and/or severely diminished urinary flow should be carefully monitored for obstructive uropathy.
- Consultation of an urologist should be considered in patients treated with finasteride.
- Obstruction due to trilobular growth pattern of the prostate should be excluded before starting treatment with finasteride.
- There is no experience in patients with liver insufficiency. Since finasteride is metabolised in the liver (see section 5.2). Caution is advised in patients with decreased hepatic function as the plasma-levels of finasteride may be increased in such patients.
- This medicinal product contains lactose-monohydrate. Patients with rare hereditary problems of
galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

- To avoid obstructive complications it is important that patients with large residual urine and/or heavily decreased urinary flow are carefully controlled. The possibility of surgery should be an option.

**Effects on prostate-specific antigen (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 serum 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 or placebo.

Digital rectal examination, and, if necessary, determination of prostate-specific-antigen (PSA) in serum should be carried out on patients prior to initiating therapy with finasteride and periodically during treatment to rule out prostate Cancer. 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.

Finasteride 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 patients with BPH treated with finasteride 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 finasteride for six months or more, PSA values should be doubled for comparison with normal ranges in untreated men. This adjustment preserves the sensitivity or 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 finasteride therapy.

Percent free PSA (free to total PSA ratio) is not significantly decreased by finasteride and 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 is necessary.

- 5α reductase inhibitors may increase the risk of development of high grade prostate cancer.

Women who are pregnant or may become pregnant should not handle crushed or broken finasteride tablets because of the possibility of absorption of finasteride and the subsequent potential risk to a male foetus. Finasteride tablets have a film coating which prevents contact with the active ingredient provided that the tablets have not been broken or crushed (see sections 4.6 and 6.6).

**Evaluation for other urological disease:**

Prior to initiating therapy with finasteride, perform appropriate evaluation to rule out other urological conditions, including prostate cancer that might mimic benign prostatic hyperplasia (BPH).

**Drug/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. In most patients, a rapid decrease in PSA is seen within the first months of therapy, after which time PSA levels stabilize to a new baseline. The post-treatment baseline approximates half of the pre-treatment value. Therefore, in typical patients treated with finasteride for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men.
ed men. For clinical interpretation, see 4.4 Special warnings and precautions for use, Effects on PSA and prostate cancer detection.

*Breast cancer in men*

Breast cancer has been reported in men taking FINASID 5mg during clinical trials and 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.

**Pediatric use**

FINASID is not indicated for use in children. Safety and effectiveness in children have not been established.

*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 medicinal products and other forms of interaction**

No clinically significant drug interactions have been identified. Finasteride does not appear to significantly affect the cytochrome P450-linked drug metabolizing enzyme system. The following medicinal products have been investigated in man, and no clinically meaningful interactions have been found: propanolol, digoxin, glibenclamide, warfarin, theophylline and antipyrine and no clinically meaningful interactions were found.

**4.6 Pregnancy and lactation**

**Pregnancy:** FINASID is contra indicated in women when they are or may potentially be pregnant (see section 4.3).

Because of the ability of 5α-Reductase-inhibitors to inhibit conversion of testosterone to dihydrotestosterone, these drugs, including FINASID, might cause abnormalities of the external genitalia of a male foetus when administered to a pregnant woman (See section 5.3 and section 6.6).

**Exposure to FINASID - risk to male foetus.**

Women who are pregnant or may become pregnant should not handle FINASID tablets especially if crushed or broken because of the possibility of absorption of FINASID and the subsequent potential risk to a male foetus (see section 6.6).

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 FINASID 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 FINASID. When the patient’s sexual partner is or may potentially be pregnant, the patient is recommended to minimise exposure of his partner to semen.

**Lactation:** FINASID are not indicated for use in women. It is not known whether FINASID is excreted in breast milk.

**4.7 Effects on ability to drive and use machines**

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

**4.8 Undesirable effects**

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. The frequencies of undesirable effects are following: very common (1/10), common (1/100 to <1/10), uncommon (1/1,000 to <1/100), rare (1/10,000 to 1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

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

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency: adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigations</td>
<td></td>
</tr>
<tr>
<td>Common: decreased volume of ejaculate</td>
<td></td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
</tr>
<tr>
<td>Unknown: palpitation</td>
<td></td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
</tr>
<tr>
<td>Uncommon: rash</td>
<td></td>
</tr>
<tr>
<td>Unknown: pruritus, urticaria</td>
<td></td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
</tr>
<tr>
<td>Unknown: hypersensitivity reactions including swelling of the lips and face</td>
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</tbody>
</table>
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 FINASID and 1147 (24.4%) men receiving placebo. In the FINASID 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 FINASID group may be explained by a detection bias due to the effect of FINASID 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.

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 is seen within the first months of therapy, after which time PSA levels stabilize 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 details and clinical interpretation See section 4.4 (Paragraph Effects on prostate specific antigen (PSA) and prostate Cancer detection).

4.9 Overdose
Patients have received Single doses of FINASID up to 400 mg and multiple doses up to 80 mg/day without adverse effects. There is no specific recommended treatment of overdose of FINASID.
The Medical Therapy of Prostatic Symptoms (MTOPS) Trial was a 4- to 6-year study in 3047 men with symptomatic BPH who were randomised to receive FINASID 5 mg/day, doxazosin 4 or 8 mg/day*, the combination of FINASID 5 mg/day and doxazosin 4 or 8 mg/day*, or placebo. The primary endpoint was time to clinical progression of BPH, defined as a 4 point confirmed increase from baseline in symptom score, acute urinary retention, BPH-related renal insufficiency, recurrent urinary tract infections or urosepsis, or incontinence. Compared to placebo, treatment with FINASID, doxazosin, or combination therapy resulted in a significant reduction in the risk of clinical progression of BPH by 34 (p=0.002), 39 (p<0.001), and 67% (p<0.001), respectively.

The majority of the events (274 out of 351) that constituted BPH progression were confirmed 4 point increases in symptom score; the risk of symptom score progression was reduced by 30 (95% CI 6 to 48%), 46 (95% CI 25 to 60%), and 64% (95% CI 48 to 75%) in the FINASID, doxazosin, and combination groups, respectively, compared to placebo. Acute urinary retention accounted for 41 of the 351 events of BPH progression; the risk of developing acute urinary retention was reduced by 67 (p=0.011), 31 (p=0.296), and 79% (p=0.001) in the FINASID, doxazosin, and combination groups, respectively, compared to placebo. Only the FINASID and combination therapy groups were significantly different from placebo.

* Titrated from 1 mg to 4 or 8 mg as tolerated over a 3-week period

In this study the safety and tolerability profile of combined treatment was broadly similar to the profile of each of the drugs taken separately. However, undesirable effects concerning the "nervous system" and "uro-genital system" organ classes were observed more frequently when the two drugs were used in combination (see section 4.8).

### 5.2 Pharmacokinetic properties

**Absorption:**
The bioavailability of FINASID is approx. 80%. Peak
plasma concentrations are reached approx. 2 hours after drug intake, and absorption is complete after 6-8 hours.

**Distribution:**
Binding to plasma proteins is approx. 93%. Clearance and volume of distribution are approx. 165 ml/min (70-279 ml/min) and 76 l (44-96 l), respectively. Accumulation of small amounts of FINASID is seen on repeated administration. After a daily dose of 5 mg the lowest steady-state concentration of FINASID has been calculated to be 8-10 ng/ml, which remains stable over time.

**Biotransformation:**
FINASID is metabolised in the liver. FINASID does not significantly affect the cytochrome P 450 enzyme system. Two metabolites with low 5α-reductase-inhibiting effects have been identified.

**Elimination:**
The plasma half-life averages 6 hours (4-12 hours) (in men >70 years of age, 8 hours, range 6-15 hours). After administration of radioactively labelled FINASID, approx. 39% (32-46%) of the given dose is excreted in the urine in the form of metabolites. Virtually no unchanged FINASID is recovered in the urine. Approximately 57% (51-64%) of the total dose is excreted in the faeces.

FINASID has been found to cross the blood-brain barrier. Small amounts of FINASID have been recovered in the seminal fluid of treated. In 2 studies of healthy subjects (n=69) receiving FINASID 5 mg/day for 6-24 weeks, FINASID concentrations in semen ranged from undetectable (<0.1 ng/ml) to 10.54 ng/ml. In an earlier study using a less sensitive assay, FINASID concentrations in the semen of 16 subjects receiving FINASID 5 mg/day ranged from undetectable (<1.0 ng/ml) to 21 ng/ml. Thus, based on a 5-ml ejaculate volume, the amount of FINASID in semen was estimated to be 50- to 100-fold less than the dose of FINASID (5 μg) that had no effect on circulating DHT levels in men (see also section 5.3.).

In patients with chronic renal impairment, whose creatinine clearance ranged from 9-55 ml/min, the disposition of a single dose of 14C-FINASID was not different from that in healthy volunteers (see section 4.2). 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.

### 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 FINASID). The clinical relevance of these findings is unclear.

As with other 5-alpha-reductase inhibitors, feminisation of male rat foetuses has been seen with administration of FINASID in the gestation period. Intravenous administration of FINASID to pregnant rhesus monkeys at doses up to 800 ng/day during the entire period of embryonic and fetal development resulted in no abnormalities in male fetuses. This does is about 60 to 120 times higher than the estimated amount in semen of a man who have taken 5 mg FINASID, 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 FINASID 2 mg/kg/day (the systemic exposure (AUC) of monkeys was slightly higher (3x) than that of men who have taken 5 mg FINASID, or approximately 1 to 2 million times the estimated amount of FINASID in semen) to pregnant monkeys resulted in external genital abnormalities in male fetuses. No other abnormalities were observed in male foetuses and no FINASID-related abnormalities were observed in female foetuses at any dose.

### 6. PHARMACEUTICAL PARTICULARS

#### 6.1 List of excipients

Lactose monohydrate, Hydroxypropylcellulose
6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Do not store above 30°C.
Store in the original package

6.5 Nature and contents of container
An opaque white (PVC –PVDC /Aluminium) Blister
The FINASID 5mg tablets are packed in blister packs of 30 tablets

6.6 Special precautions for disposal and other handling
Women who are pregnant or may become pregnant should not handle FINASID tablets especially if crushed or broken because of the possibility of absorption of FINASID and the subsequent potential risk to a male foetus (see section 4.6).
Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER
SAJA Pharmaceuticals
Saudi Arabian Japanese pharmaceutical company limited
Jeddah – Saudi Arabia

For any information about FINASID, please contact
Saudi Arabian Japanese pharmaceutical company limited
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P.O. Box: 42600, Jeddah 21551, KSA
Tel: + 966 2 645 0303
www.sajaonline.net

8. MARKETING AUTHORISATION NUMBER(S)
08-370-44

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
1429-07-10