Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Fintex 5 mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5 mg of the active ingredient Finasteride.
Also contains 90.962mg of Lactose Monohydrate.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated Tablet.

Blue, 7 mm, round biconvex, film-coated tablets marked “F5” on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

'Fintex' is 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.

'Fintex' causes regression of the enlarged prostate, improves urinary flow and improves the symptoms associated with BPH.

Patients with an enlarged prostate are the appropriate candidates for therapy with 'Fintex'.

4.2 Posology and method of administration

The recommended dosage 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. The risk of acute urinary retention is reduced within four months of treatment.

Use 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.

Use in the elderly

No dosage adjustment is required in elderly patients.

4.3 Contraindications

'Fintex' is not indicated for use in women or children. 'Fintex' is contra-indicated in the following: hypersensitivity to any component of this product; pregnancy - women when they are or may potentially be pregnant (see 4.6 'Pregnancy and lactation', Exposure to finasteride - risk to male foetus).

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.

Effects on prostate-specific antigen (PSA) and prostate cancer detection: No clinical benefit has yet been demonstrated in patients with prostate cancer treated with 'Fintex'. Patients with BPH and elevated PSA were monitored in controlled clinical studies with serial PSAs and prostate biopsies. In these BPH studies, 'Fintex' 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 'Fintex' or placebo. Digital rectal examination, as well as other evaluations for prostate cancer, should be performed on patients with BPH prior to initiating therapy with 'Fintex' 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 'Fintex'. A baseline PSA <4 ng/ml does not exclude prostate cancer.

'Fintex' 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 'Fintex' 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 3,000 patients in the four-year, double-blind, placebo-controlled 'Fintex' Long-term Efficacy and Safety Study (PLESS) confirmed that in typical patients treated with 'Fintex' 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 'Fintex'.

Percent free PSA (free to total PSA ratio) is not significantly decreased by 'Fintex' and remains constant even under the influence of 'Fintex'. When percent free PSA is used as an aid in the detection of prostate cancer, no adjustment is necessary.

Patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically important drug interactions have been identified. 'Fintex' 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, 'Fintex' 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.

4.6 Fertility, pregnancy and lactation

Pregnancy: 'Fintex' is contra-indicated in women when they are or may potentially be pregnant (see 4.3 'Contra-indications').

Because of the ability of Type II 5 α-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 was 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 α-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 α-reductase. It is for these reasons that 'Fintex' is contraindicated in women when they are or may potentially be pregnant.

The in utero effects of finasteride exposure during the period of embryonic and foetal development were evaluated in the rhesus monkey (gestation days 20-100), a species more predictive of human development than rats. Intravenous administration of finasteride to pregnant monkeys at doses as high as 800 ng/day (at least 60 to 120 times the highest estimated exposure of women to finasteride from semen of men taking 5 mg/day) resulted in no abnormalities in male foetuses. In confirmation of the relevance of the rhesus model for foetal development, oral administration of a very high dose of finasteride (2 mg/kg/day; 20 times the recommended human dose of 5 mg/day or approximately 1-2 million times the highest estimated exposure to finasteride from semen of men taking 5 mg/day) 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.

Exposure to finasteride - risk to male foetus

Women should not handle crushed or broken tablets of 'Fintex' 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). 'Fintex' tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed.

Lactation: 'Fintex' is not indicated for use in women. It is not known whether finasteride is excreted in human milk.

Small amounts of finasteride have been recovered from the semen in subjects receiving finasteride 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. When the patient’s sexual partner is or may potentially be pregnant, the patient is recommended to minimise exposure of his partner to semen.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

'Fintex' 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 disorders, decreased volume of ejaculate; breast tenderness, breast enlargement and rash.

There was no evidence of increased adverse experiences with increased duration of treatment with 'Fintex' and the incidence of new drug-related sexual adverse experiences decreased with duration of treatment.

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 'Fintex' and 1147 (24.4%) men receiving placebo. A greater number of high grade tumours (Gleason score 7-10) were detected on needle biopsy in patients in the 'Fintex' group, 280 (6.4%) vs 237 (5.1%). Additional analyses suggest that the increase in the prevalence of high-grade prostate cancer observed in the 'Fintex' group may be explained by a detection bias due to the effect of 'Fintex' on prostate volume. The relationship between long-term use of 'Fintex'and tumours with Gleason scores 7-10 is unknown.

Post-marketing experience

The following additional adverse experiences have been reported in post-marketing experience:

− 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 decrease in patients treated with 'Fintex'. 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 pretreatment value. Therefore, in typical patients treated with 'Fintex' for six months or more, PSA values should be doubled for comparison to normal ranges in untreated men. For clinical interpretation see 4.4 'Special warnings and special precautions for use', Effects on prostate-specific antigen (PSA) and prostate cancer detection.

No other difference was observed in patients treated with placebo or 'Fintex' in standard laboratory tests.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Finasteride is a competitive inhibitor of human 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 dependent upon the conversion of testosterone to DHT within the prostate. 'Fintex' is highly effective in reducing circulating and intraprostatic DHT. Finasteride has no affinity for the androgen receptor.

The effect of therapy with 'Fintex' on BPH-related urologic events (surgical intervention [e.g. transurethal resection of the prostate and prostatectomy] or acute urinary retention requiring catheterisation) has been assessed over a four-year period in 3,016 patients with moderate to severe symptoms of BPH in the 'Fintex' Long-term Efficacy and Safety Study (PLESS). In this double-blind, randomised, placebo-controlled multicentre study, treatment with 'Fintex' reduced the risk of total urologic 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.

Additional Clinical Studies

Information from a recently completed 7-year placebo-controlled trial that enrolled 18,882 men ≥ 55 years of age, with a normal digital rectal examination and a PSA of ≤ 3.0 ng/ml, may be relevant for men currently being treated with 'Fintex' for BPH. At the end of the study, 9060 men had prostate needle biopsy data available for analysis. In this study, prostate cancer was detected in 803 (18.4%) men receiving 'Fintex' and 1147 (24.4%) men receiving placebo. 'Fintex is not indicated to reduce the risk of developing prostate cancer (see 'Undesirable effects', Other long term data).

5.2 Pharmacokinetic properties

After 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 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 5 α-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 halflife of approximately 6 hours in men aged 18-60 years to 8 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 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. Dosage adjustment in nondialysed 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.

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

Tablet Core
Lactose monohydrate
Cellulose microcrystalline
Pregelatinised Maize Starch
Lauroyl Macrogol glycerides
Sodium starch glycollate Type A,
Magnesium stearate

Film Coat
Hypromellose 6cps
Titanium dioxide
Indigocarmine-lake
Macrogol 6000

6.2 Incompatibilities

None reported.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special storage precautions necessary.

6.5 Nature and contents of container

Blister (al/pvc), Blister (al/al) and HDPE container

Pack Sizes: Fintex tablets are supplied in packs of 10, 14, 28, 30, 50, 60, 90, 100 film-coated tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Women should not handle crushed or broken 'Fintex' Tablets when they are or may potentially be pregnant (see section 4.3 'Contra-indications' and section 4.6 'Pregnancy and lactation').

7 MARKETING AUTHORISATION HOLDER

Helsinn Birex Therapeutics Ltd
Damastown,
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8 MARKETING AUTHORISATION NUMBER

PA 915/16/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 26th September 2008

10 DATE OF REVISION OF THE TEXT