

Pharmacode position may change as per Supplier's m/c requirement & additional small pharma code may appear on the front / back panel



SUMMARY OF PRODUCT CHARACTERISTICS

DUTABIT 0.5
Dutasteride Soft Capsules 0.5 mg
Rx Only

NAME OF THE MEDICINAL PRODUCT: Dutasteride Soft Capsules 0.5 mg

(TRADE) NAME OF PRODUCT: DUTABIT 0.5

STRENGTH : 0.5 mg.

PHARMACEUTICAL DOSAGE FORM: Soft Capsules.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Dutasteride Soft Capsules 0.5 mg: Each Capsule contains Dutasteride Ph. Eur. 0.5 mg.

PHARMACEUTICAL FORM:

Dull yellow, opaque, oblong shaped, size '6' soft gelatin capsule containing clear colorless to pale yellow viscous oil.

CLINICAL PARTICULARS

Therapeutic indications

Monotherapy: Dutasteride is indicated for the treatment and control of symptomatic benign prostatic hyperplasia (BPH) in men with an enlarged prostate to improve symptoms, reduce the risk of acute urinary retention, and reduce the risk of the need for BPH-related surgery.

Combination With Alpha-Blocker: Dutasteride in combination with the alpha-blocker tamsulosin is indicated for the treatment of symptomatic BPH in men with an enlarged prostate.

Posology and method of administration

Adult Males (Including Elderly): Recommended Dose: 1 capsule (0.5 mg) taken orally once a day.

Although an improvement may be observed at an early stage, treatment for at least 6 months may be necessary in order to assess objectively whether a satisfactory response to the treatment can be achieved.

Treatment of BPH: Dutasteride can be administered alone or in combination with the α -blocker, tamsulosin (0.4 mg).

Renal Impairment: The effect of renal impairment on dutasteride pharmacokinetics has not been studied. However, no adjustment in dosage is anticipated for patients with renal impairment.

Hepatic Impairment: The effect of hepatic impairment on dutasteride pharmacokinetics has not been studied so caution should be used in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the use of dutasteride is contraindicated.

Administration: Capsules should be swallowed whole and not chewed or opened, as contact with the capsule contents may result in irritation of the oropharyngeal mucosa. Dutasteride may be taken with or without food.

Contraindications

Dutasteride is contraindicated in patients with known hypersensitivity to dutasteride, other 5-alpha reductase inhibitors, or any component of the preparation. (see List of Excipients).

Dutasteride is contraindicated for use in women and children and adolescents (see Pregnancy and Lactation).

Dutasteride is contraindicated in patients with severe hepatic impairment.

Special warnings and precautions for use

General: Lower urinary tract symptoms of BPH can be indicative of other urological diseases, including prostate cancer. Patients should be assessed to rule out other urological diseases prior to treatment with Dutasteride. Patients with a large residual urinary volume and/or severely diminished urinary flow may not be good candidates for 5 α -reductase inhibitor therapy, and should be carefully monitored for obstructive uropathy.

Exposure of Women and Children: Dutasteride is absorbed through the skin; therefore, women and children and adolescents must avoid contact with leaking capsules. If contact is made with leaking capsules, the contact area should be washed immediately with soap and water. Women who are pregnant or may be pregnant should not handle Dutasteride because of the possibility of absorption of dutasteride and the potential risk of a foetal anomaly to a male foetus.

Blood Donation: Men being treated with dutasteride should not donate blood until at least 6 months have passed following their last dose. The purpose of this deferred period is to prevent administration of dutasteride to a pregnant female transfusion recipient.

Hepatic Impairment: Dutasteride was not studied in patients with liver disease. Caution should be used in the administration of dutasteride to patients with mild to moderate hepatic impairment.

Effects on Prostate-Specific Antigen (PSA) and Prostate Cancer Detection: Digital rectal examination, as well as other evaluations for prostate cancer, should be performed on patients with BPH prior to initiating therapy with dutasteride and periodically, thereafter.

Serum PSA concentration is an important component of the screening process to detect prostate cancer. Dutasteride causes a decrease in mean serum PSA levels by approximately 50% after 6 months of treatment.

Patients receiving Dutasteride should have a new PSA baseline established after 6 months of treatment with Dutasteride. It is recommended to monitor PSA values regularly, thereafter. Any confirmed increase from lowest PSA level while on Dutasteride may signal the presence of prostate cancer (particularly high grade cancer) or non-compliance to therapy with Dutasteride, and should be carefully evaluated, even if those values are still within the normal range for men not taking a 5 α -reductase inhibitor. In the interpretation of a PSA value for a patient taking Dutasteride, previous PSA values should be sought for comparison.

Treatment with Dutasteride does not interfere with the use of PSA as a tool to assist in the diagnosis of prostate cancer after a new baseline has been established.

Total serum PSA levels return to baseline within 6 months of discontinuing treatment.

The ratio of free to total PSA remains constant even under the influence of Dutasteride. If clinicians elect to use percent free PSA as an aid in the detection of prostate cancer in men undergoing Dutasteride therapy, no adjustment to its value is necessary.

Increased Risk of High-Grade Prostate Cancer: In men aged 50 to 75 years with a prior negative biopsy for prostate cancer and a baseline PSA between 2.5 ng/mL and 10.0 ng/mL taking AVODART in the 4-year Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial, there was an increased incidence of Gleason score 8-10 prostate cancer compared with men taking placebo (AVODART 1.0% versus placebo 0.5%). In a 7-year placebo controlled clinical trial with another 5-alpha reductase inhibitor (finasteride 5 mg, PROSCAR), similar results for Gleason score 8-10 prostate cancer were observed (finasteride 1.8% versus placebo 1.1%).

5-alpha reductase inhibitors may increase the risk of development of high-grade prostate cancer. Whether the effect of 5-alpha reductase inhibitors to reduce prostate volume, or study related factors, impacted the results of these studies has not been established.

Men taking Dutasteride should be regularly evaluated for prostate cancer risk including PSA testing.

Interaction with other medicinal products and other forms of interaction

Dutasteride is metabolised by human cytochrome P450 isoenzyme CYP3A4. Therefore, blood concentrations of dutasteride may increase in the presence of inhibitors of CYP3A4.

Decrease in clearance of dutasteride when co-administered with the CYP3A4 inhibitors verapamil (37%) and diltiazem (44%). In contrast no decrease in clearance when amlodipine, another calcium channel antagonist, was co-administered with dutasteride. A decrease in clearance and subsequent increase in exposure to dutasteride, in the presence of CYP3A4 inhibitors, is unlikely to be clinically significant due to the wide margin of safety (up to 10 times the recommended dose has been given to patients for up to six months); therefore no dose adjustment is necessary.

Dutasteride is not metabolized by human cytochrome P450 isoenzymes CYP1A2, CYP2A6, CYP2E1, CYP2C8, CYP2C9, CYP2C19, CYP2B6, and CYP2D6.

Dutasteride neither inhibits human cytochrome P450 drug-metabolizing enzymes nor induces cytochrome P450 isoenzymes CYP1A, CYP2B, and CYP3A in rats and dogs.

Dutasteride does not displace warfarin, diazepam, acenocoumrol, phenprocoumon, or phenytoin from plasma protein, nor do these model compounds displace dutasteride. Compounds that have been tested for drug interactions in man include tamsulosin, terazosin, warfarin, digoxin, and cholestyramine, and no clinically significant pharmacokinetic or pharmacodynamic interactions have been observed.

No clinically significant adverse interactions were observed when dutasteride was co-administered with anti-hyperlipidemics, angiotensin-converting enzyme (ACE) inhibitors, beta-adrenergic blocking agents, calcium channel blockers, corticosteroids, diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), phosphodiesterase Type V inhibitors, and quinolone antibiotics.

Pregnancy and lactation

Fertility: The clinical significance of dutasteride's effect on semen characteristics for an individual patient's fertility is not known.

Pregnancy: Dutasteride is contraindicated for use by women. Dutasteride has not been studied in women because preclinical data suggests that the suppression of circulating levels of dihydrotestosterone may inhibit the development of the external genital organs in a male foetus carried by a woman exposed to dutasteride.

Lactation: It is not known whether dutasteride is excreted in breast milk.

Effects on ability to drive and use machines

Based on the pharmacodynamic properties of dutasteride, treatment with dutasteride would not be expected to interfere with the ability to drive or operate machinery.

A/s: 210 x 300 mm ■ Black

	Product Name	Component	Item Code	Date & Time
	Dutabit	Leaflet	P1537142	04.12.2024 & 02.30 PM
	Customer / Country	Version No.	Reason Of Issue	Reviewed / Approved by
Malaysia_Unit 1	01	NEW		
Team Leader	Kiran Kumar	Dimensions	No. of Colours : 01	
Initiator	Shirisha N	210 x 300 mm		
Artist:	Advnt (Kiran)	Pharmacode		
Additional Information :				Sign / Date

Undesirable effects

Adverse drug reactions are listed as follows by system organ class and frequency. Frequencies are defined as: Very common, common, uncommon, rare and very rare including isolated reports.

Immune System Disorders: Very Rare: Allergic reaction, including rash, pruritus, urticaria and angioedema.

Psychiatric Disorders: Very Rare: Depressed mood.

Skin and Subcutaneous Tissue Disorders: Rare: Alopecia (primarily body hair loss), hypertrichosis.

Reproductive System and Breast Disorders: Very Rare: Testicular pain and swelling.

Overdose:

In volunteer studies, single doses of dutasteride up to 40 mg/day (80 times the therapeutic dose) for 7 days have been administered without significant safety concerns. In clinical studies, doses of 5 mg daily have been administered to patients for 6 months with no additional adverse effects to those seen at therapeutic doses of 0.5 mg. There is no specific antidote for dutasteride therefore, in cases of suspected overdosage, symptomatic and supportive treatment should be given as appropriate.

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Testosterone-5 α -reductase inhibitors. ATC Code: G04CB02.

Pharmacology:

Pharmacodynamics:

Dutasteride reduces circulating levels of dihydrotestosterone (DHT) by inhibiting both type 1 and 2, 5 α -reductase isoenzymes which are responsible for the conversion of testosterone to 5 α -DHT.

Effects on DHT/Testosterone: Effect of daily doses of Dutasteride on the reduction on DHT is dose dependent and is observed within 1-2 weeks (85% and 90% reduction, respectively).

Effect on Prostate Volume: Significant reductions in prostate volume have been detected as early as 1 month after initiation of treatment and reductions continued through month 24.

Reduction of the size of prostate leads to improvement of symptoms and a decreased risk for acute urinary retention (AUR) and BPH-related surgery.

PHARMACOKINETIC PROPERTIES

Absorption: Dutasteride is administered orally in solution as a soft gelatin capsule. Following administration of a single 0.5-mg dose, peak serum concentrations of Dutasteride occur within 1-3 hours.

Absolute bioavailability in man is approximately 60% relative to a 2-hour IV infusion. The bioavailability of dutasteride is not affected by food.

Distribution: Dutasteride has a large volume of distribution (300-500 L). Dutasteride is highly bound to plasma proteins (>99.5%). Following daily dosing, dutasteride serum concentrations achieve 65% of steady-state concentration after 1 month and approximately 90% after 3 months.

Steady-state serum concentrations (C_{ss}) of approximately 40 ng/mL are achieved after 6 months of dosing 0.5 mg once a day. Similarly to serum, dutasteride concentrations in semen achieved steady state at 6 months. After 52 weeks of therapy, semen dutasteride concentrations averaged 3.4 ng/mL (range 0.4-14 ng/mL). Dutasteride partitioning from serum into semen averaged 11.5%.

Biotransformation: Dutasteride is metabolized by the human cytochrome P450 (CYP450) enzyme CYP450 3A4 to 2 minor mono-hydroxylated metabolites, but it is not metabolized by CYP1A2, CYP2A6, CYP2E1, CYP2C8, CYP2C9, CYP2C19, CYP2B6 or CYP2D6.

In human serum, following dosing to steady-state, unchanged dutasteride, 3 major metabolites (4'-hydroxydutasteride, 1,2-dihydrodutasteride and 6-hydroxydutasteride) and 2 minor metabolites (6,4'-dihydroxydutasteride and 15-hydroxydutasteride) have been detected.

Elimination: Dutasteride is extensively metabolized. Following oral dosing of dutasteride 0.5mg/day to steady-state in humans, 1-15.4% (mean of 5.4%) of the administered dose is excreted as dutasteride in the faeces. The remainder is excreted in the faeces as 4 major metabolites comprising 39%, 21%, 7% and 7% each of drug-related material and 6 minor metabolites (<5% each).

Only trace amounts of unchanged dutasteride (<0.1% of the dose) are detected in human urine.

At therapeutic concentrations, the terminal half-life (t_{1/2}) of dutasteride is 3-5 weeks. Serum concentrations remain detectable (>0.1 ng/mL) for up to 4-6 months after discontinuation of treatment.

Linearity/Non-linearity: Dutasteride pharmacokinetics can be described as 1st order absorption process and 2 parallel elimination pathways, 1 saturable (concentration-dependent) and 1 non saturable (concentration-independent).

At low serum concentrations (<3 ng/mL), dutasteride is cleared rapidly by both the concentration dependent and concentration-independent elimination pathways. Single doses of \leq 5 mg showed evidence of rapid clearance and a short t_{1/2} of 3-9 days.

At serum concentrations, >3 ng/mL, dutasteride is cleared slowly (0.35-0.58 L/hr) primarily by linear, non-saturable elimination with terminal t_{1/2} of 3-5 weeks. At therapeutic concentrations, following repeat dosing of 0.5 mg/day, the slower clearance dominates,

and the total clearance is linear and concentration-independent.

Elderly: Exposure of dutasteride, represented by area under the concentration-time curve (AUC) and peak plasma concentration (C_{max}) values, was not statistically different between age groups.

No differences in drug effect as measured by DHT reduction between age groups.

No dutasteride dose adjustment based on age is necessary.

Renal Impairment: The effect of renal impairment on dutasteride pharmacokinetics has not been studied. However, <0.1% of a steady-state 0.5-mg dose of dutasteride is recovered in human urine, so no adjustment in dosage is anticipated for patients with renal impairment.

Hepatic Impairment: The effect on the pharmacokinetics of dutasteride in hepatic impairment has not been studied.

PHARMACEUTICAL PARTICULARS

List of Excipients:

Glycerol Monocaprylocaprate, Butylated Hydroxy Toluene (E321), Gelatin (160 Bloom), Glycerol, Titanium Dioxide (E171), Iron oxide yellow (E172), Triglycerides, Medium chain.

Incompatibilities

Not applicable.

Shelf life

24 months.

Special precautions for storage

Do not store above 30°C.

Nature and contents

Blister of white opaque PVC/PVDC containing 10 capsules, packed into cartons of 30 capsules.

Manufacturer



AUROBINDO

APL Health Care Limited,
Unit I, Sy. No. 410/P, 411/P, 458/P, Plot No. S-1/B,
TSIIC SEZ Green Industrial Park, Polepally,
Jadcherla Mandal, Mahabub Nagar,
Telangana, 509302, India .

Product Registration Holder in Malaysia

Synerrv Sdn Bhd, SO-29-2, Menara 1,
KL ECO City, Jalan Bangsar,
KG Haji Abdullah Hukum,
59200 Kuala Lumpur,
Wilayah Persekutuan Kuala Lumpur,
Malaysia.

DATE OF PREPARATION OF THIS LEAFLET

4 December 2024