

Prostreat

(Tamsulosin HCl)

پروسٹریٹ

COMPOSITION

Each **PROSTREAT** 0.4 mg capsule contains 0.4mg of tamsulosin hydrochloride (as slow release pellets).

MECHANISM OF ACTION

Tamsulosin, an alpha1 adrenoceptor blocking agent, exhibits selectivity for alpha1 receptors in the human prostate. At least three discrete alpha1-adrenoceptor subtypes have been identified: alpha1A, alpha1B and alpha1D; their distribution differs between human organs and tissue. Approximately 70% of the alpha1-receptors in human prostate are of the alpha1A subtype.

Tamsulosin binds selectively and competitively to alpha1A adrenoreceptors, which convey smooth muscle contraction. Tamsulosin increases the maximum urinary flow rate by relaxing prostatic and urethral smooth muscle, thus relieving symptoms of benign prostatic hyperplasia.

Tamsulosin also improves the irritative and obstructive symptoms in which the contraction of smooth muscle in the lower urinary tract plays an important role.

PHARMACOKINETIC

Absorption

Absorption of tamsulosin hydrochloride from **PROSTREAT** capsules 0.4 mg is essentially complete (>90%) following oral administration under fasting conditions. Tamsulosin hydrochloride exhibits linear kinetics following single and multiple dosing, with achievement of steady-state concentrations by the fifth day of once-a-day dosing.

Effect of Food

The time to maximum concentration (Tmax) is reached by four to five hours under fasting conditions and by six to seven hours when **PROSTREAT** capsules are administered with food.

Taking **PROSTREAT** capsules under fasted conditions results in a 30% increase in bioavailability (AUC) and 40% to 70% increase in peak concentrations (Cmax) compared to fed conditions.

Distribution

In humans, tamsulosin is more than 99% bound to plasma proteins.

Biotransformation

Tamsulosin hydrochloride is extensively metabolized by cytochrome P450 enzymes in the liver and less than 10% of the dose is excreted in urine unchanged. In vitro results indicate that CYP3A4 and CYP2D6 are involved in metabolism of tamsulosin as well as some minor participation of other CYP isoenzymes. Inhibition of hepatic drug-metabolizing enzymes may lead to increased exposure to tamsulosin. The metabolites of tamsulosin hydrochloride undergo extensive conjugation to glucuronide or sulfate prior to renal excretion.

Excretion

Tamsulosin and its metabolites are mainly excreted in the urine with about 9% of the dose being present in unchanged form.

The elimination half-life of tamsulosin in patients is approximately 10 hours (when taken after a meal) and 13 hours in the steady state.

Special Populations

Geriatrics

Cross-study comparison of **PROSTREAT** capsules overall exposure (AUC) and half-life indicate that the pharmacokinetic disposition of tamsulosin hydrochloride may be slightly prolonged in geriatric males compared to young, healthy male volunteers.

Renal Dysfunction

Patients with renal impairment do not require an adjustment in **PROSTREAT** (tamsulosin hydrochloride) capsules dosing. However, patients with endstage renal disease (creatinine clearance of <10 mL/min/1.73m²) have not been studied.

Hepatic Dysfunction

Patients with moderate hepatic dysfunction do not require an adjustment in **PROSTREAT** capsules dosage. **PROSTREAT** has not been studied in patients with severe hepatic dysfunction.

INDICATIONS

PROSTREAT (tamsulosin hydrochloride) capsules are indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

DOSAGE AND ADMINISTRATION

PROSTREAT capsules 0.4 mg once daily is recommended as the dose for the treatment of the signs and symptoms of BPH. It should be administered approximately one-half hour following the same meal each day.

For those patients who fail to respond to the 0.4 mg dose after two to four weeks of dosing, the dose of **PROSTREAT** capsules can be increased to 0.8 mg once daily. The 0.8 mg dose should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole).

If **PROSTREAT** capsules administration is discontinued or interrupted for several days at either the 0.4 mg or 0.8 mg dose, therapy should be started again with the 0.4 mg once daily dose.

UNDESIRABLE EFFECTS

	Common (>1/100, <1/10)	Uncommon (>1/1 000, <1/100)	Rare >1/10 000, (<1/1 000)	Very rare (<1/10 000)
Nervous system disorders	Dizziness	Headache	Syncope	
Cardiac disorders		Tachycardia		
Vascular disorders		Orthostatic hypotension		
Respiratory, thoracic and mediastinum-related disorders		Rhinitis		
Gastrointestinal disorders		Constipation, diarrhoea, nausea, vomiting		
Skin and subcutaneous tissue disorders		Rash, itching, urticaria	Angio-oedema	
Reproductive systems and breast disorders		Abnormal ejaculation		Priapism
General disorders and administration site conditions		Asthenia		

Post-Marketing Experience

Allergic-type reactions such as skin rash, urticaria, pruritus, angioedema and respiratory symptoms have been reported with positive rechallenge in some cases. Priapism has been reported rarely. Infrequent reports of palpitations, hypotension, skin desquamation, constipation and vomiting have been received during the post-marketing period. During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported in association with alpha-1 blocker therapy.

DRUG INTERACTIONS

Alpha-adrenergic blocking agents

The pharmacokinetic and pharmacodynamic interactions between **PROSTREAT** capsules and other alpha-adrenergic blocking agents may be expected. Therefore, **PROSTREAT** capsules should not be used in combination with other alpha-adrenergic blocking agents.

Nifedipine, Atenolol & Enalapril

PROSTREAT capsules 0.4 mg for seven days followed by **PROSTREAT** capsules 0.8 mg for another seven days resulted in no clinically significant effects on blood pressure and pulse rate compared to placebo. Therefore, dosage adjustments are not necessary.

Warfarin

A definitive drug-drug interaction study between tamsulosin hydrochloride and warfarin was not conducted. Results from limited in vitro and in vivo studies are inconclusive. Therefore, caution should be exercised with concomitant administration of warfarin and **PROSTREAT** capsules.

Digoxin and Theophylline

Dosage adjustments are not necessary when a **PROSTREAT** capsule is administered concomitantly with digoxin or theophylline.

Furosemide

Furosemide produced an 11% to 12% reduction in tamsulosin hydrochloride Cmax and AUC, these changes are expected to be clinically insignificant and do not require adjustment of the **PROSTREAT** capsules dosage.

Cimetidine

PROSTREAT capsules should be used with caution in combination with cimetidine, particularly at doses higher than 0.4 mg.

Strong Inhibitors of CYP3A4 or CYP2D6

PROSTREAT capsules should be used with caution in combination with moderate or strong inhibitors of CYP2D6 (e.g., fluoxetine & paroxetine) or CYP3A4 (e.g., ketoconazole), particularly at doses higher than 0.4 mg.

PRECAUTIONS

Carcinoma of the prostate

Carcinoma of the prostate and BPH frequently co-exist. Patients should be evaluated prior to the start of **PROSTREAT** capsules therapy to rule out the presence of carcinoma of the prostate.

Intraoperative Floppy Iris Syndrome

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients treated with alpha-1 blockers, including **PROSTREAT** capsules.

Sulfa Allergy

In patients with sulfa allergy, allergic reaction to **PROSTREAT** (tamsulosin hydrochloride) capsules has been rarely reported. If a patient reports a serious or life threatening sulfa allergy, caution is warranted when administering **PROSTREAT** capsules.

Laboratory Tests

No laboratory test interactions with **PROSTREAT** capsules are known. Treatment with **PROSTREAT** capsules for up to 12 months had no significant effect on prostate-specific antigen (PSA).

Pregnancy

PROSTREAT capsules are not indicated for use in women.

Nursing Mothers

PROSTREAT capsules are not indicated for use in women.

Geriatric Use

Clinical experiences has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Pediatric Use

PROSTREAT capsules are not indicated for use in pediatric populations.

WARNINGS

- Doses of **PROSTREAT** higher than 0.4 mg (e.g., 0.8 mg) should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole).
- The signs and symptoms of orthostasis (postural hypotension, dizziness and vertigo) were detected more frequently in **PROSTREAT** capsule-treated patients than in placebo recipients. As with other alpha-adrenergic blocking agents there is a potential risk of syncope.
- Patients beginning treatment with **PROSTREAT** capsules should be cautioned to avoid situations where injury could result should syncope occur.
- Rarely (probably less than one in fifty thousand patients), tamsulosin, like other alpha1 antagonists, has been associated with priapism (persistent painful penile erection unrelated to sexual activity). Because this condition can lead to permanent impotence if not properly treated, patients must be advised about the seriousness of the condition.

OVERDOSE

Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed which were treated with fluid replacement and the patient could be discharged the same day. In case of acute hypotension occurring after overdosage cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this does not help then volume expanders, and when necessary, vasopressors could be employed. Renal function should be monitored and general supportive measures applied. Dialysis is unlikely to be of help as tamsulosin is very highly bound to plasma proteins. Measures, such as emesis, can be taken to impede absorption. When large quantities are involved, gastric lavage can be applied and activated charcoal and an osmotic laxative, such as sodium sulphate, can be administered.

CONTRAINDICATIONS

- Hypersensitivity to tamsulosin hydrochloride or any component of **PROSTREAT** capsules.
- History of orthostatic hypotension.
- Severe hepatic insufficiency.
- Tamsulosin HCl is not indicated for use in women and pediatric population

PRESENTATION

PROSTREAT 0.4mg slow release capsule: 1 x 10's/pack.

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Manufactured by:
AsianContinental (Pvt.) Ltd.
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Karachi-Pakistan.

خوراک:

ڈاکٹر کی ہدایت کے مطابق۔

ہدایات:

دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

دھوپ اور نمی سے بچائیں۔

بچوں کی پہنچ سے دور رکھیں۔

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