TAMUSIN®

ٹیموسن ۰.۴ ملی گرام

(tamsulosin hydrochloride) 0.4 mg Capsules

(ٹیمسولوسین ہائیڈروکلورائیڈ)

Prescribing Information

DESCRIPTION

Tamsulosin hydrochloride is an antagonist of alpha1A adrenoceptors in the prostate. Tamsulosin hydrochloride is (-)-(R)-5-[2-[[2-(0 Ethoxyphenoxy) ethyl]amino]propyl]-2-methoxybenzenesulfonamide, monohydrochloride. Tamsulosin hydrochloride is a white crystalline powder that melts with decomposition at approximately 230°C. It is sparingly soluble in water and methanol, slightly soluble in glacial acetic acid and ethamol, and practically insoluble an ether.

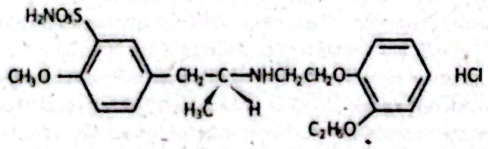
The empirical formula of tamsulosin hydrochloride is C20H28N2O55 ' HCl. The molecular weight of tamsulosin hydrochloride is 444.98. Its structural formula is:

INDICATIONS

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

TAMUSIN Capsules are not indicated for the treatment of hypertension.

TAMUSIN is for use by men only. TAMUSIN is not indicated for use in women.



DOSAGE & ADMINISTRATION

TAMUSIN Capsule 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 TAMUSIN Capsule can be increased to 0.8 mg once daily. If TAMUSIN 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.

CONTRAINDICATIONS

TAMUSIN Capsules are contraindicated in patients known to be hypersensitive to tamsulosin hydrochloride or any component of TAMUSIN .

CLINICAL PHARMACOLOGY

The symptoms associated with benign prostatic hyperplasia (BPH) are related to bladder outlet obstruction, which is comprised of two underlying components' static and dynamic. The static component is related to an increase in prostate size caused, in part, by a proliferation of smooth muscle cells in the prostatic stroma. However, the severity of BPHsymptoms and the degree of urethral obstruction do not correlate well with the size of the prostate. The dynamic component is a function of an increase in smooth muscle tone in the prostate and bladder neck leading to constriction of the bladder outlet. Smooth muscle toneis mediated by the sympathetic nervous stimulation of alpha, adrehoceptors, which are abundant in the prostate, prostatic capsule, prostatic urethra, and bladder neck. Blockade of these adrenoceptors can cause smooth muscles in the bladder nech and prostate to relax, resulting in an improvement in urine flow rate and a reduction in symptoms of BPH.

Tamsulosin, an alpha, adrenoceptor blocking agent, exhibits selectivity for alpha, receptors in the human prostate. At least three discrete alpha,- 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.

SIDE EFFECTS: in some cases Dizziness, unusual weakness, drowsiness, trooble sleeping, blurred vision, runny nose, or problems ejaculating may occur. If any of these effects persist or worsen, tell your doctor promptly.

Pharmacokinetics

The pharmacokinetics of tamsulosin hydrochloride have been evaluated in adult healthy volunteers and patients with BPH after single and/or multiple administration withrdoses ranging from 0.1 mg to 1 mg.

Absorption

Absorption of tamsulosin hydrochloride from TAMUSIN Capsules 0.4 mg is essentialiy 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 TAMUSIN Capsules are administered with food. Taking TAMUSIN 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

The mean steady-state apparent volume of distribution of tamsulosin hydrochloride after intraenous administration to ten healthy male adaults was 16 L, which is suggestive of distribution into extracellular fluids in the body. Tamsulosin hydrochloride is extensively bound to human plasma protein (94% to 99%),primarily alpha-1 acid glycoprotein (AAG), with linear binding over a wide concentration range (20 to 600 ng/mL). The results of two-way in vitro studies indicate that the binding of tamsulosin hydrochloride to human plasma proteins is not affected by amitriptyline, diclofenac, glyburide, simvastatin plus simvastatin-hydroxy acid metabolite, warfarin, diazepam, ppropranolol, ichlormethiazide, or chlormadinone. Likewise, tamsulosin hydrochloride had no effect on the extent of binding of these drugs.

Metabolism

There is no enantiomeric bioconversion from tamsulosin hydrochloride [R(-) isomer] to the S(+) isomer in humans. Tamsulosin hydrochloride is extensively metabolized by cytochrome P450 enzymes in the liver and less than 10% of the dose is excreted in urine

unchanged. However, the pharmacokinetic profile of the metabolites in humans has not been established. In vitro results indicate that CYP3A4 and CYP 2D6 are involved inmetabolism 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 lucuronide or sulfate prior to renal excretion. Incubations with human liver microsomes showed no evidence of clinically significant metabolic interactions between tamsulosin ydrochloride and amitriptyline, albuterol (beta agonist), glyburide (glibenclamide) and finasteride (5alpha-reductase inhibitor for treatment of BPH). However, results of the in vitro testing of the tamsulosin hydrochride interaction with diclofenac and warfarin were equivocal.

Excretion

On administration of the radiolabeled dose of tamsulosin hydrochloride to four healthy volunteers, 97% pf the administered radioactivity was recovered, with urine (76%) representing the primary route of excretion compared to feces (21%) over 168 hours. Following intravenous or oral administration of an immediate-relaase formulation, the elimination half-life of tamsulosin hydrochloride in plasma rangeti from five to seven hours Because of absorption rate-controlled pharmacokinetics with (tamsulosin hydrochloride) Capsules, The apparent half-life of tamsulosin hydrochloride approximately 9 to 13 hours in healthy volunteers and 14 to 15 hours in the target population. Tamsulosin hydrochloride undergoes restrictive clearance in humans, with a relatively low systemic clearance (2.88 L/h).

Special Populations

Geriatrics (Age)

Cross-study comparison of TAMUSIN Capsules overall exposure (AUC) and half-life indicates that the pharmacokinetic disposition of tamsulosin hydrochloride may be slightly prolonged in geriatric males compared to young, healthy male volunteers. Intrinsic clearance is independent of tamsulosin hydrochloride binding to AAG, but diminishes with age, resulting in a 40% overall higher exposure (AUC) in subjects of age 55 to 75 years compared to subjects of age 20 to 32 years.

Renal Dysfunction The pharmacokinetics of tamsulosin hydrochloride have been compared in 6 subjects with mild-moderate (30<CLcr<70 mL/min/1.73m2) or moderate-severe (10<CLcr <30 mL/min/1.73m2) renal impairment and 6 normal subjects (Clcr <90 mL/min/1.73m2), while a change in the overall plasma concentration of tamsulosin hydrochloride was observed as the result of altered binding to AAG, the unbound (active) concentration of tamsulosin hydrochloride, as well as the intrinsic clearance remained relatively constant. Therefore, patients with renal impairment do not require an adjustment in Tamusin (tamsulos in hydrochloride) Capsules dosing. However,patients with endstage renal disease (Clcr <10 mL/min/1.73m2) have not been studied.

Hepatic Dysfunction

The pharmacokinetics of tamsulosin hydrochloride have been compared in 8 subjects with moderate hepatic dysfunction (Child-Pugh's lassification. Grades A and B) and 8 normal subjects. While a change in the overall plasma concentration of tamsulosin hydrochloride was observed as the result of altered binding to AAG, the unbound (active) concentration of tamsulosin hydrochloride does not change significantly, with only a modest (32%) change in intrinsic clearance of unbound tamsulosin hydrochloride. Therefore, patients with moderate hepatic dysfunction do not require an adjustment in tamsulosin dosage.

Tamsulosin has not been studied in patients with severe hepatic dysfunction.

Drug-Drug Interactions

Nifedipine, Atenolol, Enalapril

In three studies in hypertensive subjects (age range 47-79 years) whose blood pressure was controlled with stable doses of Procardia XL®, atenolol, or enalapril for at least three months, tamsulosin Capsules 0.4 mg for seven days followed by tamsulosin Capsules 0.8 mg for another seven days (n=5 pes study) resulted in no clinically significant effects on blood pressure and pulse rate compared to placebo (n=4 per study). Therefore, dosage adjustments are not necessary when TAMUSIN Capsules are administered concomitantly with atenolol, or enalapril.

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 TAMUSIN Capsules.

Digoxin and Theophylline

In two studies in healthy volunteers (n=10 per study; age range (19-39 years) receiving tamsulosin Capsuls 0.4 mg/day for two days, followed by TAMUSIN Capsules 0.8 mg/day for five to eight days, single intravenous doses of digoxin 0.5 mg or theophylline 5 mg/kg resulted in no change in the pharmacokinetics of digoxin or theophylline. Therefore dosage adjustments are not necessary when a TAMUSIN is administered concomitantly with digoxin or theophylline.

Pack Size 2x10 Blister Pack.

Store at 25°C (77°F); excursions permitted to 15°-30°C (59°-86°F).

Keep TAMUSIN and all medicines out of reach of children.

Manufactured By:
Aims Pharmaceuticals
Plot # 291, Industrial Triangle, Kahuta Road,
Islamabad-Pakistan