Tamsulosin HCl

Tamsolin®

℞

400mcg Modified-Release Capsule

Alpha-Adrenoreceptor Antagonist

PRODUCT DESCRIPTION
Tamsulosin hydrochloride (Tamsolin®) 400 mcg Modified-Release Capsule is available as hard gelatin capsules having standard grey opaque cap and caramel opaque body printed Getz logo and 0.4 on shell containing white to off-white spherical pellets.

FORMULATION
Tamsulosin hydrochloride (Tamsolin®) capsules are available for oral administration as:

Each modified-release capsule contains:
Tamsulosin hydrochloride... 400mcg
(as modified release pellets)

CLINICAL PHARMACOLOGY
Mechanism of Action
Tamsulosin, an $alpha_1$ adrenoceptor blocking agent, exhibits selectivity for $alpha_1$ receptors in the human prostate. At least three discrete alpha1 adrenoceptor subtypes have been identified: $alpha_{1A}$, $alpha_{1B}$, and $alpha_{1D}$; their distribution differs between human organs and tissue. Approximately 70% of the $alpha_1$ receptors in the human prostate are of the $alpha_{1A}$ subtype.

Tamsulosin hydrochloride capsules are not intended for use as an antihypertensive drug.

Pharmacodynamics
Urologic pharmacodynamic effects have been evaluated in neurologically impaired pediatric patients and in adults with BPH.

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

Absorption
Absorption of Tamsulosin hydrochloride 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 (T_{max}) is reached by four to five hours under fasting conditions and by six to seven hours when Tamsulosin hydrochloride capsules are administered with food. Taking Tamsulosin hydrochloride capsules under fasted conditions results in a 30% increase in bioavailability (AUC) and 40% to 70% increase in peak concentrations (C_{max}) compared to fed conditions.

Distribution
Tamsulosin hydrochloride is extensively bound to human plasma proteins (94% to 99%), primarily alpha1 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, propranolol, trichlormethiazide, or chlormadinone. Likewise, Tamsulosin hydrochloride had no effect on the extent of binding of these drugs. There is a minimal distribution to the brain, spinal cord and testes.

Metabolism
Tamsulosin hydrochloride is extensively metabolized by cytochrome P450 enzymes in the liver and less than 10% of the dose is excreted in urine unchanged. Tamsulosin is extensively metabolized, mainly by CYP3A4 and CYP2D6 as well as via 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
Following intravenous or oral administration of an immediate-release formulation, the elimination half-life of Tamsulosin hydrochloride in plasma ranged from 5 to 7 hours. Because of absorption rate-controlled pharmacokinetics with Tamsulosin hydrochloride capsules, the apparent half-life of Tamsulosin hydrochloride is approximately 9 to 13 hours in healthy volunteers and 14 to 15 hours in target population.

Tamsulosin hydrochloride undergoes restrictive clearance in humans, with a relatively low systemic clearance (2.88 L/h).

Special Populations
Geriatrics (Age) Use
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 Impairment
Patients with renal impairment [mild-moderate ($30 \leq Clcr < 70$ mL/min/1.73m^2) or moderate-severe ($10 \leq Clcr < 30$mL/min/1.73m^2)] do not require dose adjustment.

Pediatric Use
Tamsulosin hydrochloride capsules are not indicated for use in pediatric populations.

Hepatic Impairment
Patients with moderate hepatic impairment do not require dose adjustment.

THERAPEUTIC INDICATIONS
Tamsulosin hydrochloride (Tamsolin®) capsules are indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

DOSAGE AND ADMINISTRATION
Tamsulosin hydrochloride (Tamsolin®) capsules 400mcg 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 400mcg dose after two to four weeks of dosing, the dose of Tamsulosin hydrochloride (Tamsolin®) capsules can be increased to 800mcg once daily. If Tamsulosin hydrochloride (Tamsolin®) capsules administration is discontinued or interrupted for several days at either the 400mcg or 800mcg dose, therapy should be started again with the 400mcg once daily dose.

CONTRAINDICATIONS
Tamsulosin hydrochloride capsules are contraindicated in patients known to be hypersensitive to Tamsulosin hydrochloride or any component of Tamsulosin hydrochloride capsules. Reactions have included skin rash, urticaria, pruritus, angioedema, and respiratory symptoms.

WARNINGS AND PRECAUTIONS
Orthostasis
The signs and symptoms of orthostasis (postural hypotension, dizziness, and vertigo) were detected more frequently in Tamsulosin hydrochloride 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 Tamsulosin hydrochloride capsules should be cautioned to avoid situations in which injury could result should syncope occur.

Priapism
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.

Screening for Prostate Cancer
Prostate cancer and BPH frequently co-exist; therefore, patients should be screened for the presence of prostate cancer prior to treatment with Tamsulosin hydrochloride capsules and at regular intervals afterwards.

Intraoperative Floppy Iris Syndrome
Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract and glaucoma surgery in some patients on or previously treated with alpha1 blockers, including Tamsulosin hydrochloride capsules.

Most reports were in patients taking the alpha1 blocker when IFIS occurred, but in some cases, the alpha1 blocker had been stopped prior to surgery. In most of these cases, the alpha1 blocker had been stopped recently prior to surgery (2 to 14 days), but in a few cases, IFIS was reported after the patient had been off the alpha1 blocker for a longer period (5 weeks to 9 months). IFIS is a variant of small pupil syndrome and is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs and potential prolapse of the iris toward the phacoemulsification incisions. The patient's ophthalmologist should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances.

IFIS may increase the risk of eye complications during and after the operation. The benefit of stopping alpha1 blocker therapy prior to cataract or glaucoma surgery has not been established. The initiation of therapy with Tamsulosin in patients for whom cataract or glaucoma surgery is scheduled is not recommended.

Sulfa Allergy
In patients with sulfa allergy, allergic reaction to Tamsulosin hydrochloride capsules has been rarely reported. If a patient reports a serious or life-threatening sulfa allergy, caution is warranted when administering Tamsulosin hydrochloride capsules.

PREGNANCY AND LACTATION
Tamsulosin hydrochloride capsules are not indicated for use in women.

DRUG INTERACTIONS
Cytochrome P450 Inhibition
Strong and Moderate Inhibitors of CYP3A4 or CYP2D6
Tamsulosin is extensively metabolized, mainly by CYP3A4 and CYP2D6.

Concomitant treatment with ketoconazole (a strong inhibitor of CYP3A4) resulted in an increase in the Cmax and AUC of Tamsulosin by a factor of 2.2 and 2.8, respectively . The effects of concomitant administration of a moderate CYP3A4 inhibitor (e.g., erythromycin) on the pharmacokinetics of Tamsulosin hydrochloride have not been evaluated.

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Concomitant treatment with paroxetine (a strong inhibitor of CYP2D6) resulted in an increase in the C_{max} and AUC of Tamsulosin by a factor of 1.3 and 1.6, respectively. A similar increase in exposure is expected in CYP2D6 poor metabolizers (PM) as compared to extensive metabolizers (EM). Since CYP2D6 PMs cannot be readily identified and the potential for significant increase in Tamsulosin exposure exists when Tamsulosin hydrochloride 400 mcg is co-administered with strong CYP3A4 inhibitors in CYP2D6 PMs, Tamsulosin hydrochloride 400mcg capsules should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole)

Cimetidine
Treatment with cimetidine resulted in a significant decrease (26%) in the clearance of Tamsulosin hydrochloride, which resulted in a moderate increase in Tamsulosin hydrochloride AUC (44%).

Other Alpha Adrenergic Blocking Agents
The pharmacokinetic and pharmacodynamic interactions between Tamsulosin hydrochloride capsules and other alpha adrenergic blocking agents have not been determined; however, interactions between Tamsulosin hydrochloride capsules and other alpha adrenergic blocking agents may be expected.

PDE5 Inhibitors
Caution is advised when alpha adrenergic blocking agents including Tamsulosin hydrochloride are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension.

Warfarin
Caution should be exercised with concomitant administration of warfarin and Tamsulosin hydrochloride capsules.

Nifedipine, Atenolol, Enalapril
Dosage adjustments are not necessary when Tamsulosin hydrochloride capsules are administered concomitantly with nifedipine, atenolol, or enalapril.

Digoxin and Theophylline
Dosage adjustments are not necessary when a Tamsulosin hydrochloride capsule is administered concomitantly with digoxin or theophylline.

Furosemide
Tamsulosin hydrochloride capsules had no effect on the pharmacodynamics (excretion of electrolytes) of furosemide.

ADVERSE REACTIONS
The following adverse reactions have been reported during the use of Tamsulosin hydrochloride:

Body as whole:
Headache, infection, asthenia, back pain, chest pain.

Nervous System:
Dizziness, somnolence, insomnia, decreased libido, erectile disorder (including priapism)

Respiratory System:
Rhinitis, pharyngitis, increased cough, sinusitis.

Digestive System:
Diarrhea, nausea, tooth disorder, vomiting, constipation.

Urinogenital System:
Abnormal ejaculation

Special Senses:
Blurred vision

Dermatological:
Rash, pruritis, angioedema.

OVERDOSE AND TREATMENT
Should overdosage of Tamsulosin hydrochloride capsules lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, then administration of intravenous fluids should be considered. If necessary, vasopressors should then be used and renal function should be monitored and supported as needed. Laboratory data indicate that Tamsulosin hydrochloride is 94% to 99% protein bound; therefore, dialysis is unlikely to be of benefit.

STORAGE CONDITIONS
Store at temperatures not exceeding 30°C.
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

Keep out of reach of children.

AVAILABILITY
Tamsulosin hydrochloride (Tamsolin®) capsules 400mcg in Alu-PVDC Blister pack x 10's (Box of 10's)

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to FDA: www.fda.gov.ph
The patient is advised to seek immediate medical attention at the first sign of adverse drug reaction.

REGISTRATION NUMBER: DR-XY38119.

DATE OF FIRST AUTHORIZATION / RENEWAL OF AUTHORIZATION
Initial: 23 June, 2010,
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2nd Renewal: 25 June,2020

DATE OF REVISION: 19 July, 2021

Please read the contents carefully before use.
This package insert is continually updated from time to time.

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