Tamsolin™

(TAMSULOSIN HCl)

0.4mg Capsules

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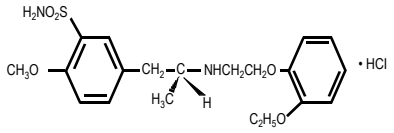
DESCRIPTION

Tamsolin (Tamsulosin HCl) is an antagonist of alpha$_{1A}$ adrenoceptors in the prostate.

Chemically, tamsulosin HCl is (-)-(*R*)-5-[2-[[2-(*o*-Ethoxyphenoxy) ethyl] amino] Propyl]-2- methoxybenzenesulfonamide, monohydrochloride.

Its molecular formula is $C_{20}H_{28}N_2O_5S$. HCl and structural formula is:



Tamsulosin HCl

QUALITATIVE AND QUANTITATIVE COMPOSITION

Tamsolin (Tamsulosin HCl) capsules are available for oral administration as:

Tamsolin 0.4mg Capsules
Each capsule contains:
Tamsulosin hydrochloride... 0.4mg
(as modified release pellets)

CLINICAL PHARMACOLOGY

Mechanism of Action

Tamsulosin binds selectively and competitively to postsynaptic α_1-adrenoceptors, in particular to subtypes alpha$_{1A}$ and alpha$_{1D}$. It brings about relaxation of prostatic and urethral smooth muscle resulting in an increase in urinary flow rate and a reduction in symptoms of benign prostatic hyperplasia (BPH). It also improves the irritative symptoms in which bladder instability plays an important role.

Pharmacokinetics

Absorption

Absorption of tamsulosin HCl is essentially complete (>90%) following oral administration under fasting conditions. 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 HCl capsules are administered with food. Taking tamsulosin HCl 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 HCl is extensively bound to human plasma proteins (94% to 99%), primarily alpha-1 acid glycoprotein (AAG), with linear binding over a wide concentration range. There is a minimal distribution to the brain, spinal cord and testes.

Metabolism

Tamsulosin HCl has a low first pass effect, being metabolized slowly. Tamsulosin HCl is extensively metabolized by cytochrome P450 enzymes in the liver. Most tamsulosin HCl is present in the plasma in the form of unchanged medicine.

Excretion

Tamsulosin HCl and its metabolites are mainly excreted in the urine with less than 10% of a dose being present in the form of unchanged medicine. After a single dose of tamsulosin HCl in the fed state and in the steady state in patients, elimination half-lives of about 10 and 13 hours respectively have been measured.

Special Populations

Geriatrics

Intrinsic clearance is independent of tamsulosin HCl 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 ($30 \leq Cl_{cr} < 70$ mL/min/1.73m^2) or moderate-severe ($10 \leq Cl_{cr} < 30$mL/min/1.73m^2)] do not require dose adjustment.

THERAPEUTIC INDICATIONS

Tamsolin (Tamsulosin HCl) is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

DOSAGE AND ADMINISTRATION

Tamsolin (Tamsulosin HCl) 0.4mg 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 0.4mg dose after two to four weeks of dosing, the dose of Tamsolin (Tamsulosin HCl) capsules can be increased to 0.8mg once daily. If Tamsolin (Tamsulosin HCl) capsules administration is discontinued or interrupted for several days at either the 0.4mg or 0.8mg dose, therapy should be started again with the 0.4mg once daily dose.

ADVERSE REACTIONS

The following adverse reactions have been reported during the use of tamsulosin HCl:

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

Nervous System:
Dizziness, somnolence, insomnia, decreased libido.

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

Digestive System:
Diarrhea, nausea, tooth disorder.

Urinogenital System:
Abnormal ejaculation

Special Senses:
Blurred vision

CONTRAINDICATIONS

Tamsulosin HCl is contraindicated in patients:

- With known hypersensitivity to tamsulosin HCl or to any excipient of the product.
- With a history of orthostatic hypotension.
- Taking other alpha-adrenergic blocking agents.
- With severe hepatic insufficiency.

Tamsulosin HCl is not indicated for use in:

- Women.
- The pediatric population.

PRECAUTIONS

- As with other alpha1-blockers, reduction in blood pressure can occur in individual cases during treatment with tamsulosin HCl, as a result of which, very rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.
- Before therapy with tamsulosin HCl is initiated, the patient should be examined in order to exclude the presence of other conditions which can cause the same symptoms as benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards.
- Patients with end stage renal disease (creatinine clearance <10mL/min/1.73m^2) should be approached with caution as these patients have not been studied.
- Patients should be advised about the possibility of priapism as a result of treatment with tamsulosin and other similar medications. Patients should be informed that this reaction is extremely rare, but if not brought to immediate medical attention, can lead to permanent erectile dysfunction (impotence).
- Intra-operative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients taking or who have previously been treated with alpha1 adrenoceptor antagonists.

Drug Interactions

- The pharmacokinetic interaction between cimetidine and tamsulosin HCl was investigated. The results indicate significant changes in tamsulosin HCl clearance (26% decrease) and AUC (44% increase). Therefore, tamsulosin HCl capsules should be used with caution in combination with cimetidine, particularly at doses higher than 0.4mg.
- Caution should be exercised with concomitant administration of warfarin and tamsulosin HCl.
- Tamsulosin HCl should be used with caution in combination with moderate or strong inhibitors of CYP2D6 (e.g., fluoxetine) or CYP3A4 (e.g., ketoconazole), particularly at doses higher than 0.4mg.

OVERDOSAGE

Acute overdose with 5mg tamsulosin HCl has been reported. Acute hypotension (systolic blood pressure 70mmHg), vomiting and diarrhea were observed, which were treated with fluid replacement and the patient could be discharged the same day.

If acute hypotension occurs after overdosage, cardiovascular support should be given and maintained. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this is insufficient then volume expanders and, when necessary, vasopressors could be administered. 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 to impede absorption, such as emesis, can be taken. When large quantities of tamsulosin HCl are involved, gastric lavage can be applied and activated charcoal and an osmotic laxative, such as sodium sulphate, can be administered.

STORAGE

Store below 30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

Tamsolin (Tamsulosin HCl) Capsules 0.4mg are available in blister pack of 20's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

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

Manufactured by:

Getz pharma (PVT) LIMITED
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29-30/27, K.I.A., Karachi, Pakistan

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