

Tamsulosin Hydrochloride

URIMAX

COMPOSITION

Urimax- 0.2 Capsules

Each capsule contains

Tamsulosin hydrochloride200 mcg
(as modified release pellets)

Urimax- 0.4 Capsules

Each capsule contains

Tamsulosin hydrochloride....400 mcg
(as modified release pellets)

DOSAGE FORM

It is available as 0.2 mg/ 0.4 mg capsules

PHARMACOLOGY

Pharmacodynamics

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 BPH symptoms 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 tone is mediated by the sympathetic nervous stimulation of α_1 adrenoceptors, which are abundant in the prostate, prostatic capsule, prostatic urethra and bladder neck. Blockade of these adrenoceptors can cause smooth muscles in the bladder neck and prostate to relax, resulting in an improvement in urine flow rate and a reduction in symptoms of BPH.

Tamsulosin, an α_1 adrenoceptor blocking agent, exhibits selectivity for α_1 receptors in the human prostate. At least three discrete α_1 -adrenoceptor subtypes have been identified: α_{1A} , α_{1B} and α_{1D} ; their distribution differs between human organs and tissue. Approximately 70% of the α_1 -receptors in human prostate are of the α_{1A} subtype. Tamsulosin capsules are not intended for use as an antihypertensive drug.

Pharmacokinetics

Absorption: Absorption of tamsulosin HCl is essentially complete (>90%) following oral administration under fasting conditions. Tamsulosin HCl 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 capsules are administered with food.

Distribution: The mean steady-state apparent volume of distribution of tamsulosin HCl after intravenous administration to ten healthy male adults was 16L, which is suggestive of distribution into extracellular fluids in the body. 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 (20 to 600 ng/mL).

Metabolism: There is no enantiomeric bioconversion from tamsulosin HCl [R(-) isomer] to the S(+) isomer in humans. Tamsulosin HCl 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 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 HCl undergo extensive conjugation to glucuronide or sulfate prior to renal excretion.

Excretion: On administration of the radiolabeled dose of tamsulosin HCl to four healthy volunteers, 97% of the administered radioactivity was recovered, with urine (76%) representing the primary route of excretion compared to feces (21%) over 168 hours. Because of absorption rate-controlled pharmacokinetics with tamsulosin capsules, the apparent half-life of tamsulosin HCl is approximately 9 to 13 hours in healthy volunteers and 14 to 15 hours in the target population. Tamsulosin HCl undergoes restrictive clearance in humans, with a relatively low systemic clearance (2.88 L/h).

INDICATIONS

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

URIMAX capsules are not intended for use as an anti-hypertensive drug.

DOSAGE AND ADMINISTRATION

- 0.4 mg once daily with or without food at the same time every day. The capsule should be swallowed whole and should not be crunched or chewed.
- If the patient is unable to tolerate 0.4mg, then the patient should receive 0.2mg once daily.
- For patients who fail to respond to 0.4mg after 2-4 weeks of dosing, the dose can be increased to 0.8mg once daily
- If the drug administration is interrupted or discontinued for a few days due to any reason at either the 0.4 mg or 0.2 mg dose, therapy should be started again with the same dose.
- If the patient is receiving 0.8 mg once daily and the drug administration is interrupted or discontinued for few days due to any reason, therapy should be started again at 0.4 mg once daily.

CONTRAINDICATIONS

URIMAX capsules are contraindicated in patients known to be hypersensitive to tamsulosin HCl or any component of the formulation. Reactions have included skin rash, urticaria, pruritus, angioedema and respiratory symptoms.

WARNINGS AND PRECAUTIONS

Drug interactions

Tamsulosin is extensively metabolized, mainly by CYP3A4 and CYP2D6. **URIMAX** capsules 0.4 mg should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole). **URIMAX** capsules should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin), in combination with strong (e.g., paroxetine) or moderate (e.g., terbinafine) inhibitors of CYP2D6, in patients known to be CYP2D6 poor metabolizers particularly at a dose higher than 0.4 mg (e.g., 0.8 mg).

URIMAX capsules should be used with caution in combination with cimetidine, particularly at a dose higher than 0.4 mg (e.g., 0.8 mg).

URIMAX capsules should not be used in combination with other alpha adrenergic blocking agents

Caution is advised when alpha adrenergic blocking agents including **URIMAX** 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.

Caution should be exercised with concomitant administration of warfarin and **URIMAX** capsules

General

Priapism: Rarely (probably less than 1 in 50,000 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

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 **URIMAX** capsules and at regular intervals afterwards

Intraoperative Floppy Iris Syndrome: Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract surgery in some patients 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 alpha-1 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. The benefit of stopping alpha-1 blocker therapy prior to cataract surgery has not been established.

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 **URIMAX** capsules.

Information for patients

Patients should be told about the possible occurrence of symptoms related to postural hypotension such as dizziness and syncope when taking tamsulosin, and they should be cautioned about driving, operating machinery or performing hazardous tasks.

Patients should be advised not to crush, chew or open the **URIMAX** capsules.

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).

Patients should be advised that if they are considering cataract surgery, to tell their ophthalmologist that they have taken tamsulosin hydrochloride capsules.

Laboratory Tests

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

Renal impairment

Patients with renal impairment do not require any dosage adjustment in tamsulosin dosage.

Hepatic impairment

Patients with moderate hepatic dysfunction do not require any dosage adjustment in tamsulosin dosage.

Pregnancy

Category B.

URIMAX capsules are not indicated for use in women

Lactation

URIMAX capsules are not indicated for use in women.

Paediatric use

URIMAX capsules are not indicated for use in paediatric populations.

Geriatric use

Of the total number of subjects (1,783) in clinical studies of tamsulosin, 36% were 65 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects and the other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

UNDESIRABLE EFFECTS

The side-effects reported in $\geq 2\%$ of patients with tamsulosin HCl include abnormal ejaculation, back pain, chest pain, cough, diarrhoea, dizziness, headache, infection, nausea, tooth disorder, libido decreased, insomnia, somnolence, rhinitis, pharyngitis, sinusitis, asthenia, blurred vision.

Multiple testing for orthostatic hypotension was conducted in a number of studies. Because orthostasis was detected more frequently in tamsulosin-treated patients than in placebo recipients, there is a potential risk of syncope.

Priapism has been reported rarely during the post-marketing period. Allergic-type reactions such as skin rash, pruritus, urticaria, angioedema and respiratory symptoms have been reported with positive rechallenge in some cases. 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 α_1 blocker therapy.

OVERDOSAGE

Should overdose of tamsulosin HCl 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 HCl is 94% to 99% protein bound; therefore, dialysis is unlikely to be of benefit.

One patient reported an overdose of thirty 0.4 mg tamsulosin HCl capsules. Following the ingestion of the capsules, the patient reported a severe headache.

STORAGE AND HANDLING INSTRUCTIONS

Store in a cool dry place.

PACKAGING INFORMATION

Urimax- 0.2Blister pack of 10 capsules

Urimax- 0.4Blister pack of 15 capsules

Last updated July 2010