Product Monograph

[Pr]ratio-TAMSULOSIN

(tamsulosin hydrochloride)

Sustained-release Capsules 0.4mg

Selective Antagonist of
$Alpha_{1A}$ Adrenoreceptor Subtype in the Prostate

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tamsulosin hydrochloride
0.4 mg Sustained-release Capsules

THERAPEUTIC CLASSIFICATION
Selective Antagonist of $Alpha_{1A}$ Adrenoreceptor Subtype in the Prostate

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Oral	Sustained Release Capsule 0.4 mg	None. *For a complete listing see the Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

ratio-TAMSULOSIN (tamsulosin hydrochloride) is indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH).

Geriatrics (> 65 years of age):
Tamsulosin hydrochloride has been found to be a safe and effective $alpha_1$ adrenoceptor antagonist when administered at therapeutic doses (0.4 mg once daily) to patients over the age of 65 years.

Pediatrics:
Tamsulosin hydrochloride sustained-release capsules is not indicated for use in children.

CONTRAINDICATIONS

ratio-TAMSULOSIN (tamsulosin hydrochloride) is contraindicated in patients known to have hypersensitivity including drug induced angioedema to tamsulosin or any component of the ratio-TAMSULOSIN sustained-release formulation. For a completer listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

WARNINGS AND PRECAUTIONS

As with all alpha$_1$-adrenoceptor antagonists, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin hydrochloride sustained-release, as a result of which, 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.

Patients beginning treatment with tamsulosin should be cautioned to avoid situations where injury could result should syncope occur (see ADVERSE REACTIONS).

General
Tamsulosin hydrochloride is not indicated for the treatment of hypertension.

Carcinoma of the Prostate
Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases frequently co-exist. Patients should be evaluated to rule out the presence of carcinoma of the prostate.

Orthostatic Hypotension
While syncope is the most severe orthostatic symptom of alpha$_1$-adrenoceptor antagonists, , other symptoms can occur (dizziness and postural hypotension). In the two U.S., studies (Studies 1 and 2), orthostatic testing was conducted at each visit. Postural hypotension was reported in three patients (0.6%) receiving tamsulosin.

In 2102 patients included in U.S., European, and Japanese placebo-controlled clinical studies, 0.3% of patients receiving tamsulosin experienced postural hypotension, 10.2% experienced dizziness, and 0.7% experienced vertigo; patients receiving placebo experienced postural hypotension, dizziness, and vertigo at rates of 0.1%, 7.2%, and 0.4%, respectively.

Patients in occupations in which orthostatic hypotension could be dangerous should be treated with caution.

If hypotension occurs, the patient should be placed in the supine position and, if this measure is inadequate, volume expansion with intravenous fluids or vasopressor therapy may be used. A transient hypotensive response is not a contraindication to further therapy with tamsulosin.

Hepatic
The treatment of patients with severe hepatic impairment should be approached with caution as no studies have been conducted in this patient population. Patients with mild to moderate hepatic dysfunction do not require an adjustment in tamsulosin dosage.

Renal
The treatment of patients with severe renal impairment (creatinine clearance of <10mL/min) should be approached with caution, as these patients have not been studied.

Intraoperative Floppy Iris Syndrome:

During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported during post-marketing surveillance in association with alpha-1 blocker therapy, including tamsulosin. Most reports to date were in patients taking tamsulosin when IFIS occurred, but in some cases, tamsulosin has been stopped prior to surgery. In most of these cases, tamsulosin 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 tamsulosin for a longer period. This variant of small pupil syndrome 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, including tamsulosin, prior to cataract surgery has not been established.

Special Populations

Pregnant Women: Tamsulosin sustained-release is not indicated for use in women. Studies in pregnant rats and rabbits at daily doses of 300 and 50 mg/kg, respectively (30,000 and 5,000 times the anticipated human dose), revealed no evidence of harm to the fetus. There are no adequate data on the use of tamsulosin in pregnant women; therefore the potential risk from the use of tamsulosin during pregnancy in humans is unknown.

Nursing Women:
Tamsulosin is not indicated for use in women.

Pediatrics:
Tamsulosin sustained-release is not indicated for use in children.

Geriatrics (> 65 years of age): There were no pharmacokinetic studies conducted in geriatric patients with tamsulosin. Cross-study comparisons of overall exposure (AUC) and half-life of tamusolin capsules indicate that the pharmacokinetic disposition of tamsulosin may be slightly prolonged in geriatric males compared to young healthy male volunteers. However, tamsulosin capsules has been found to be a safe and effective $alpha_1$-adrenoceptor antagonist when administered at therapeutic doses to patients over the age of 65 years.

Gender effects:

Tamsulosin sustained-release is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated in women.

Monitoring and Laboratory Tests:

No laboratory test interactions with tamsulosin are known. Treatment with tamsulosin for up to 3 months had no significant effect on prostate specific antigen (PSA).

Information for the patient (See PART III: CONSUMER INFORMATION):

Patients should be advised not to crush or chew or open tamsulosin sustained-release capsules. These capsules are specially formulated to control the delivery of tamsulosin HCl to the blood stream.

There are no specific studies conducted with tamsulosin sustained-release and the ability to drive vehicles or use machinery. However patients should be advised that dizziness can occur with tamsulosin sustained-release, requiring caution in people who must drive, operate machinery, or perform hazardous tasks.

Patients should be advised about the possibility of priapism as a result of treatment with tamsulosin sustained-release 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).

ADVERSE REACTIONS

The incidence of treatment emergent adverse events has been ascertained from six short-term U.S. and European placebo-controlled clinical trials in which daily doses of 0.1 to 0.8 mg tamsulosin were used. These studies evaluated safety in 1783 patients treated with tamsulosin and 798 patients administered placebo. The data suggest that tamsulosin is generally well tolerated at daily dose levels ranging from 0.1 to 0.8 mg.

Adverse events seen were generally mild, transient, and self-limiting. Table 1 summarizes the treatment emergent adverse events occurring in ≥1% of patients receiving either tamsulosin or placebo during these six short-term, (U.S. and European) placebo-controlled trials.

No new types of AEs were apparent after long-term treatment with tamsulosin. Those AEs reported with the higher incidence by patients receiving tamsulosin compared to those receiving placebo in the short-term studies were reported with a similar pattern in the long-term studies.

Clinical Trial Adverse Drug Reactions

Table 1: Treatment Emergent Adverse Events Occurring in ≥1% of Tamsulosin or Placebo Patients During Short-term (U.S. and European) Placebo-controlled Trials[a]

Body System/Adverse Event	Tamsulosin (N=1783)	Placebo (N=798)
Body as a Whole		
Headache	14.7%	15.5%
Infection	7.9%	6.8%
Pain	7.6%	7.3%
Asthenia	6.1%	5.0%
Back Pain	6.2%	4.5%
Abdominal Pain	3.4%	4.3%
Chest Pain	3.3%	3.1%
Accidental Injury	2.1%	3.0%
Flu Syndrome	2.1%	2.9%
Neck Pain	1.0%	1.1%
Fever	1.0%	1.0%
Chills	0.7%	1.0%
Malaise	0.4%	1.1%
Cardiovascular System		
Hypertension	0.9%	1.1%
Digestive System		
Diarrhea	4.4%	4.4%
Dyspepsia	3.8%	5.4%

Nausea	2.6%	2.9%
Constipation	1.3%	1.4%
Tooth Disorder	1.1%	0.9%
Metabolic and Nutritional Disorders		
Peripheral Edema	0.8%	1.0%
Musculoskeletal System		
Arthralgia	3.0%	3.3%
Myalgia	1.7%	2.1%
Arthritis	1.1%	1.0%
Nervous System		
Dizziness	11.8%	8.9%
Somnolence	2.5%	1.5%
Insomnia	1.7%	0.6%
Hypertonia	1.1%	1.5%
Libido Decreased	1.2%	0.9%
Paresthesia	0.4%	1.1%
Respiratory System		
Rhinitis	11.6%	6.9%
Pharyngitis	4.3%	3.9%
Cough Increased	3.1%	2.4%
Sinusitis	2.1%	1.3%
Dyspnea	1.1%	1.1%
Lung Disorder	1.1%	0.9%
Skin and Appendages		
Rash	1.8%	1.8%
Pruritus	1.0%	1.0%
Sweating	1.1%	0.8%
Urogenital System		
Abnormal Ejaculation	8.7%	0.5%
Urinary Tract Infection	1.5%	0.4%
Dysuria	1.2%	1.3%
Impotence	1.2%	1.5%

[a] Adverse events from patients given 0.1 to 0.8 mg tamsulosin daily were pooled.

Adverse reactions occurring in <1% of the tamsulosin and placebo patient population include amblyopia, with a frequency of 0.6% and 0.2%, respectively.

Tamsulosin hydrochloride has not been associated with any clinically significant changes in the urinalysis or the routine biochemical and hematologic tests.

Table 2 shows the treatment emergent adverse events from which ≥0.5% of the patients administered tamsulosin (N=1783) placebo (N=798) discontinued U.S. and European short-term, placebo-controlled clinical studies. The most frequent adverse events resulting in discontinuation of tamsulosin treatment were dizziness, asthenia, abnormal ejaculation, and chest pain.

Table 2: Description of Discontinuations Occurring in ≥0.5% of Tamsulosin or Placebo Patients in U.S. and European Short-term Placebo-controlled Clinical Studies[a]

Body System/Adverse Event	Tamsulosin (N=1783)	Placebo (N=798)
Body as a Whole		
Asthenia	0.7%	0.6%

Headache	0.4%	0.6%
Chest Pain	0.5%	0.3%
Nervous System		
Dizziness	1.4%	0.9%
Urogenital System		
Abnormal Ejaculation[b]	0.6%	0%

[a] Adverse events from patients given 0.1 to 0.8 mg tamsulosin daily were pooled.

[b] Abnormal ejaculation includes ejaculation failure, ejaculation disorder, retrograde ejaculation and ejaculation decrease. Abnormal ejaculation was dose related in U.S. studies: 8.4% in 0.4 mg group, 18.1% in 0.8 mg group. Withdrawal from these clinical studies of tamsulosin because of abnormal ejaculation was also dose dependent 1.6% in the 0.8 mg group, and no patients in the 0.4 mg or placebo groups.

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported during the use of tamsulosin hydrochloride at a frequency of :

>1% AND < 10%:
Nervous System Disorders: dizziness

> 0.1% AND < 1%:
Cardiac disorders: palpitations
Gastrointestinal Disorders: constipation, diarrhea, nausea, and vomiting
General disorders and administration site conditions: asthenia
Nervous systems disorders: headache
Reproductive system and breast disorders: abnormal ejaculation
Respiratory, thoracic and mediastinal disorders: rhinitis
Skin and subcutaneous tissue disorders: rash, pruritus, urticaria
Vascular disorders: postural hypotension

> 0.01% AND < 0.1%:
syncope, angioedema

< 0.01%:
priapism

During cataract surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported during post-marketing surveillance in association with alpha-1 blocker therapy, including tamsulosin (See **WARNINGS AND PRECAUTIONS**).

DRUG INTERACTIONS

Overview

The pharmacokinetic and pharmacodynamic interactions between tamsulosin and other alpha-adrenergic blocking agents have not been determined. However, interactions may be expected and caution should be exercised with concomitant administration of tamsulsoin capsules and alpha-adrenergic blocking agents.

No clinically significant drug-drug interactions were observed when tamsulosin 0.4 mg or 0.8 mg was administered with one of the following therapeutic agents: nifedipine, atenolol, enalapril, digoxin, furosemide or theophylline.

Drug-Drug Interactions

Nifedipine, Atenolol, Enalapril:
No dosage adjustments are necessary when tamsulosin is administered concomitantly with Procardia XL® (nifedipine), atenolol, or enalapril. In three studies in hypertensive subjects (age range 47 to 79 years) whose blood pressure was controlled with stable doses of Procardia XL® (nifedipine), atenolol or enalapril for at least three months, tamsulosin 0.4 mg capsules for seven days followed by tamsulosin 0.8 mg capsules for another seven days (n=8 per study) resulted in no clinically significant effects on blood pressure and pulse rate compared to placebo (n=4 per study).

Warfarin:
A definitive drug-drug interaction study between tamsulosin 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 tamsulosin capsules.

Digoxin and Theophylline:
No dosage adjustments are necessary when tamsulosin is administered concomitantly with digoxin or theophylline. In two studies in healthy volunteers (n=10 per study; age range 19 - 39 years), receiving tamsulosin capsules 0.4 mg/day for two days, followed by tamsulosin 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

Furosemide:
No dosage adjustments are necessary when tamsulosin is administered concomitantly with furosemide. The pharmacokinetic and pharmacodynamic interaction between tamsulosin capsules 0.8 mg/day (steady-state) and furosemide 20 mg intravenously (single dose) was evaluated in ten healthy volunteers (age range 21 to 40 years). Tamsulosin capsules had no effect on the pharmacodynamics (excretion of electrolytes) of furosemide. While furosemide produced a 11% to 12% reduction in tamsulosin C_{max} and AUC, these changes are expected to be clinically insignificant and do not require adjustment of the tamsulosin dosage.

Cimetidine:
The effects of cimetidine at the highest recommended dose (400 mg every six hours for six days) on the pharmacokinetics of a single tamsulosin 0.4 mg capsules dose was investigated in ten healthy volunteers (age range 21 - 38 years). Treatment with cimetidine resulted in a moderate increase in tamsulosin AUC (44%) due to a significant decrease (26%) in the clearance of tamsulosin. Therefore, tamsulosin capsules should be used with caution in combination with cimetidine, particularly at doses higher than 0.4 mg.

Drug-Laboratory Interactions
No laboratory test interactions with tamsulosin sustained-release are known. Treatment with tamsulosin sustained-release for up to 3 months had no significant effect on prostate specific antigen (PSA).

DOSAGE AND ADMINISTRATION

Dosing Considerations

Tamsulosin hydrochloride 0.4 mg once daily is recommended as the dose for the treatment of signs and symptoms of BPH.

Depending on individual patient symptomatology and/or flow rates, the does may be adjusted to 0.8 mg once daily. If tamsulosin administration is discontinued or interrupted for several days at either the 0.4 mg or 0.8 mg dose, therapy should be reinstituted, beginning with the 0.4 mg once daily dose.

Missed Dose

If a dose of tamsulosin is missed, the missed dose can be taken later the same day. If a day is missed, the missed dose should be skipped and the regular dosing schedule should be resumed. Doses must not be doubled.

Administration

Tamsulosin should be administered approximately one-half hour following the same meal each day.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Should overdosage of tamsulosin (tamsulosin hydrochloride) sustained-release lead to hypotension (see **WARNING AND PRECAUTIONS**), 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 is 94% to 99% protein bound: therefore, dialysis is unlikely to be of benefit.

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.

Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mmHg), vomiting and diarrhoea were observed, which were treated with fluid replacement and the patient was discharged the same day. One patient reported an overdose of 30 X 0.4 mg tamsulosin capsules. Following the ingestion of the capsules, the patient reported a headache judged to be severe and probably drug-related that resolved the same day.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Tamsulosin (tamsulosin hydrochloride) an alpha$_1$ adrenoceptor (AR) blocking agent, exhibits selectivity for alpha$_1$ receptors in the human prostate. At least three discrete alpha1 adrenoreceptor subtypes have been identified: alpha$_{1A}$, alpha$_{1B}$ and alpha$_{1D}$; their distribution differs between human organs and tissue. Approximately 70% of the alpha$_1$-receptor in human prostate are of the alpha$_{1A}$ subtype .

Pharmacodynamics:
The symptoms associated with benign prostatic hyperplasia (BPH) are related to bladder outlet obstruction, which is comprised of two underlying components: the 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 alpha$_1$ adrenoceptors, which are abundant in the prostate, prostatic capsule, prostatic urethra, and bladder neck. Blockade of these adrenoreceptors 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 sustained-release (tamsulosin hydrochloride) is not intended for use as an antihypertensive drug.

Pharmacokinetics
The pharmacokinetics of tamsulosin have been evaluated in adult healthy volunteers and patients with BPH with doses ranging from 0.1 mg to 1 mg.

Absorption:

Absorption of tamsulosin from the tamsulosin 0.4 mg sustained-release formulation is essentially complete (>90%) following oral administration under fasted conditions. Time to maximum concentration (T_{max}) is reached by four to five hours under fasted conditions and by six to seven hours when tamsulosin is administered with food. The delay in T_{max} when tamsulosin is administered with food has the desirable effect of smoothing the tamsulosin plasma concentration profile, thereby reducing fluctuation of the plasma peak and trough concentrations with multiple dosing. Taking tamsulosin under fasted conditions results in a 30% increase in bioavailability (AUC) and 40% to 70% increase in peak concentration (C_{max}) compared to fed conditions. The effects of food on the pharmacokinetics of tamsulosin are consistent regardless of whether tamsulosin is taken with a light breakfast or a high-fat breakfast. (Table 3)

Table 3: Mean Pharmacokinetic Parameters Following Daily (Q.D.) Dosing with Tamsulosin 0.4mg Once Daily or 0.8 mg Once Daily with a Light Breakfast, High Fat Breakfast or Fasted.

Pharmacokinetic Parameter	0.4 mg q.d. to healthy volunteers (age range 18-32 years)	0.8 mg q.d. to healthy volunteers (age range 55-75 years)

	Light Breakfast	Fasted	Light Breakfast	High Fat Breakfast	Fasted
AUC (ng·hr/mL)	151	199	440	449	557
T_{max} (hours)[1]	6.0	4.0	7.0	6.5	5.0
C_{max} (ng/mL)	10.1	17.1	29.8	29.1	41.6
C_{min} (ng/mL)	3.8	4.0	12.3	13.5	13.3
C_{max}/C_{min} Ratio	3.1	5.3	2.7	2.5	3.6

AUC: area under the tamsulosin plasma time curve over the dosing interval; T_{max}: median time-to-maximum concentration; C_{max}: observed maximum tamsulosin plasma concentration; C_{min}: observed minimum concentration. Coefficients of variation (%CV) for C_{max} and AUC generally ranged from 35%-53%, collectively.
[1]median

Distribution:
The mean steady-state apparent volume of distribution of tamsulosin after intravenous administration to ten healthy male adults was 16 liters, which is suggestive of distribution into extracellular fluids in the body. Additionally, whole body autoradiographic studies in mice, rats and dogs indicate that tamsulosin is widely distributed to most tissues including kidney, prostate, liver, gall bladder, heart, aorta, and brown fat, and minimally distributed to the brain, spinal cord, and testes.

Tamsulosin is extensively bound to human plasma proteins (94% to 99%), primarily alpha-1-acid glycoprotein (AAG) in humans, with linear binding over a wide concentration range (20 to600 ng/mL). The results of two-way *in-vitro* studies indicate that the binding of tamsulosin 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 had no effect on the extent of binding of these drugs.

Metabolism: Tamsulosin is extensively metabolized by cytochrome P450 enzymes (CYP3A) in the liver, followed by extensive glucuronide or sulfate conjugation of metabolites. On administration of a dose of radiolabelled tamsulosin 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. Less than 10% of the dose was recovered as unchanged (parent) compound in the urine.

Metabolites of tamsulosin do not contribute significantly to tamsulosin adrenoreceptor antagonist activity. Furthermore, there is no enantiomeric bioconversion from tamsulosin [R(-) isomer] to the S(+) isomer in studies with mice, rats, dogs, and humans.

Incubations with human liver microsomes showed no evidence of clinically significant interactions between tamsulosin and drugs which are known to interact or be metabolized by hepatic enzymes, such as amitriptyline, diclofenac, albuterol (beta agonist), glyburide (glibenclamide), finasteride (5 alpha-reductase inhibitor for treatment of BPH), and warfarin.

Excretion: Tamsulosin undergoes restrictive clearance in humans, with a relatively low systemic clearance (2.88 L/h). Tamsulosin exhibits linear pharmacokinetics following single or multiple dosing of tamsulosin resulting in a proportional increase in C_{max} and AUC at therapeutic doses. Intrinsic clearance is independent of tamsulosin 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.

Following intravenous or oral administration of an immediate-release formulation, the elimination half-life of tamsulosin in plasma ranged from five to seven hours. Because of absorption rate-controlled pharmacokinetics with the tamsulosin sustained-release formulation, the apparent half-life of tamsulosin increases to approximately 9 to 13 hours in healthy volunteers and to 14 to 15 hours in the target population.

Special Populations and Conditions

Pediatrics: Tamsulosin is not indicated for use in children. Pharmacokinetics have not been evaluated in pediatrics.

Geriatrics: There were no pharmacokinetic studies conducted in geriatric patients with tamsulosin sustained-release. Cross-study comparisons of overall exposure (AUC) and half-life of tamsulosin capsules indicate that the pharmacokinetic disposition of tamsulosin may be slightly prolonged in geriatric males compared to young healthy male volunteers. However, tamsulosin capsules have been found to be a safe and effective $alpha_1$-adrenoreceptor antagonist when administered at therapeutic doses to patients over the age of 65 years.

Gender Effects: Tamsulosin sustained-release is not indicated for use in women. Pharmacokinetics have not been evaluated in women.

Hepatic Insufficiency: The pharmacokinetics of tamsulosin have been compared in subjects with hepatic dysfunction (n=8) and in normal subjects (n=8). While a change in the overall plasma concentration of tamsulosin was observed as the result of altered binding to AAG, the unbound (active) concentration of tamsulosin does not change significantly with only a modest (32%) change in intrinsic clearance of unbound tamsulosin. Therefore, patients with mild to moderate hepatic dysfunction do not require an adjustment in tamsulosin dosage.

Renal Insufficiency: The pharmacokinetics of tamsulosin have been compared in subjects with moderate (n=6) or severe (n=6) renal impairment and in normal subjects (n=6). While a change in the overall plasma concentration of tamsulosin was observed as the resuit of altered binding to AAG, the unbound (active) concentration of tamsulosin, as well as the intrinsic clearance, remained relatively constant. Therefore, patients with such renal impairment do not require an adjustment in tamsulosin dosing. Patients with end stage renal disease (Cl_{cr} <10mL/min) have not been studied.

STORAGE AND STABILITY

Store at room temperature (15°C - 30°C).

DOSAGE FORMS, COMPOSTION AND PACKAGING

ratio-TAMSULOSIN (tamsulosin hydrochloride) sustained-release capsules are supplied as a hard gelatin capsule with an orange body and olive green cap, with a black line at each end of the capsule and “TSL 0.4” printed in black ink on the cap. Available in bottles of 100 capsules, bottles of 500 capsules and blister packs of 30 capsules.

Each sustained-release capsule contains: tamsulosin hydrochloride 0.4 mg.

Nonmedicinal ingredients: methacrylic acid-ethyl acrylate copolymer (polysorbate 80, sodium laurilsulfate) microcrystalline cellulose, talc, and triethylcitrate. The capsule shells are composed of: black iron oxide, FD&C Blue No.2, gelatin, red iron oxide, titanium dioxide, yellow iron oxide. Capsule imprinting ink contains: antifoam, black iron oxide, shellac glaze, and soya lectin.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

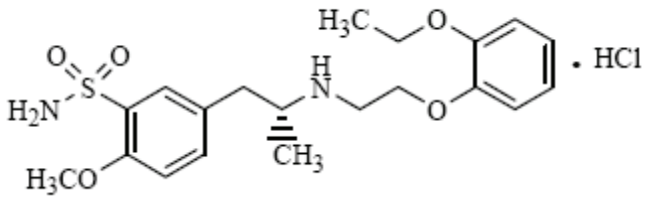
Drug Substance

Common name: Tamsulosin Hydrochloride

Chemical name: *R(-)*-5-[2-[[2-(2-Ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzene sulfonamide, monohydrochloride

Molecular formula and molecular mass: $C_{20}H_{28}N_2O_5S$•HCl; 444.98

Structural formula:



Description:

Tamsulosin HCl occurs as white crystals that melt with decomposition at approximately 230°C. It is sparingly soluble in water and in methanol, slightly soluble in glacial acetic acid and in ethanol, and practically insoluble in ether.

CLINICAL TRIALS

Successful bioequivalence studies were conducted between Flomax® (Boehringer Ingelheim, Canada) and ratio-TAMSULOSIN. The results of the bioequivalence studies are summarized in the tables below.

Single dose study under fasting conditions

A blind, randomized, 2-way crossover, bioequivalence study of ratio-TAMSULOSIN Capsules and Flomax® Capsules (Boehringer Ingelheim, Canada) administered as 1 x 0.4 mg capsule in healthy males under fasting conditions (n=28, age=18 to 55 years) was conducted and demonstrates the bioequivalency of ratio-TAMSULOSIN and Flomax®.

Tamsulosin Hydrochloride
(1 x 0.4 mg) From
measured data

Geometric Mean
Arithmetic Mean (CV %)

Parameter	Test* ratio-TAMSULOSIN	Reference† Flomax®	% Ratio of Geometric Means	90% Confidence Interval
AUC_T (pg·h/mL)	207853.76 226716.73 (37.87)	216440.38 237186.15 (40.59)	96.03	91.35-100.96
AUC_I (pg·h/mL)	217340.28 239392.32 (40.90)	223905.23 246964.06 (42.49)	97.07	92.30-102.08
C_{MAX} (pg/mL)	15844.84 16810.93 (30.57)	17551.24 18319.33 (27.25)	90.28	84.74-96.18
T_{MAX}§ (h)	5.24 (34.59)	4.83 (23.97)		
$T_{½}$§ (h)	12.30 (36.51)	11.94 (23.10)		

* ratio-TAMSULOSIN (tamsulosin hydrochloride SR Capsules) by ratiopharm inc.
† Flomax® Capsules are manufactured by Boehringer Ingelheim Canada, and were purchased in Canada.
§ Expressed as the arithmetic mean (CV%).

Single dose study under fed conditions

A blind, randomized, 2-way crossover, bioequivalence study of ratio-TAMSULOSIN Capsules and Flomax® Capsules (Boehringer Ingelheim, Canada) administered as 1 x 0.4 mg capsule in healthy males under fed conditions (n=26, age=18 to 55 years) was conducted and demonstrates the bioequivalency of ratio-TAMSULOSIN and Flomax®.

Tamsulosin Hydrochloride (1 x 0.4 mg) From measured data **Geometric Mean** **Arithmetic Mean (CV %)**				
Parameter	**Test*** ratio-TAMSULOSIN	**Reference†** Flomax®	**% Ratio of Geometric Means**	**90% Confidence Interval**
AUC_T (pg·h/mL)	178629.54 199868.74 (49.59)	176939.95 197812.67 (48.59)	100.95	95.27-106.98
AUC_I (pg·h/mL)	186899.66 211647.44 (53.13)	185069.27 211628.51 (55.81)	100.99	95.17-107.16
C_{MAX} (pg/mL)	9644.15 10405.19 (38.82)	9889.42 10521.57 (33.91)	97.52	89.30-106.50
T_{MAX}§ (h)	8.79 (45.25)	9.13 (44.11)		
$T_{½}$§ (h)	11.66 (21.48)	11.65 (34.59)		

* ratio-TAMSULOSIN (tamsulosin hydrochloride SR Capsules) by ratiopharm inc.

† Flomax® Capsules are manufactured by Boehringer Ingelheim Canada, and were purchased in Canada.

§ Expressed as the arithmetic mean (CV%).

Multiple dose study: 7 days, Fasting Conditions

A blind, randomized, 2-way crossover, bioequivalence study of ratio-TAMSULOSIN Capsules and Flomax® Capsules (Boehringer Ingelheim, Canada) administered as 1 x 0.4 mg capsule daily for 7 consecutive days in healthy males under fasting conditions (n=23, age=18 to 55 years) was conducted and demonstrates the bioequivalency of ratio-TAMSULOSIN and Flomax®.

Tamsulosin Hydrochloride (1 x 0.4 mg) From measured data **Geometric Mean** **Arithmetic Mean (CV %)**				
Parameter	**Test*** ratio-TAMSULOSIN	**Reference†** Flomax®	**% Ratio of Geometric Means**	**90% Confidence Interval**
AUC_{tau} (pg·h/mL)	192272.18 212874.51 (44.74)	190123.03 213653.55 (45.37)	101.13	93.97-108.84
C_{MAX} (pg/mL)	18732.87 20470.43 (42.92)	19707.90 21678.58 (43.48)	95.05	87.35-103.43
C_{MIN} (pg/mL)	3078.07 3686.66 (62.43)	2967.09 3563.60 (61.52)	103.74	93.88-114.63
T_{MAX}§ (h)	4.79 (18.48)	4.65 (20.36)		

* ratio-TAMSULOSIN (tamsulosin hydrochloride SR Capsules) by ratiopharm inc.

† Flomax® Capsules are manufactured by Boehringer Ingelheim Canada, and were purchased in Canada.

§ Expressed as the arithmetic mean (CV%).

The bioequivalence studies prove bioequivalence between ratio-TAMSULOSIN and Flomax®.

DETAILED PHARMACOLOGY

Four large placebo-controlled clinical studies and one large active-controlled clinical study comprising 2296 patients (1003 received tamsulosin 0.4 mg once daily, 491 received tamsulosin 0.8 mg once daily, and 802 were control patients) were conducted in the U.S. and Europe. These studies support the once daily tamsulosin dose of 0.4 mg and 0.8 mg.

Tamsulosin was extensively studied in two U.S. placebo-controlled, double-blind, 13-week, multicenter studies (Study 1 and Study 2) that included 1486 men with the signs and symptoms of BPH. The validated Total AUA Symptom Score questionnaire evaluated irritative (frequency, urgency and nocturia) and obstructive (hesitancy, incomplete emptying, intermittency, and weak stream) symptoms. Decreases in scores are consistent with improvements in symptoms.

Peak urine flow rate was measured at all visits, and increased peak urine flow rate values over Baseline are consistent with decreased urinary obstruction.

In Study 1, peak urine flow rate was measured during the estimated time of peak plasma concentration (4 to 8 hours after dosing). In Study 2, peak urine flow rate was measured at the estimated time of peak plasma concentration for the first two weeks of the double-blind treatment (4 to 8 hours after dosing), and at the estimated time of trough plasma concentration (24 to 27 hours after dosing) thereafter. In both studies, patients were randomized to either placebo, tamsulosin 0.4 mg once daily or tamsulosin 0.8 mg once daily groups. Patients in tamsulosin 0.8 mg once daily treatment groups received a dose of 0.4 mg once daily for one week before increasing to the 0.8 mg once daily dose.

Table 4: Mean Changes from Baseline to Endpoint in Total AUA Symptom Score (0-35) and Peak Urine Flow Rate (mL/sec)

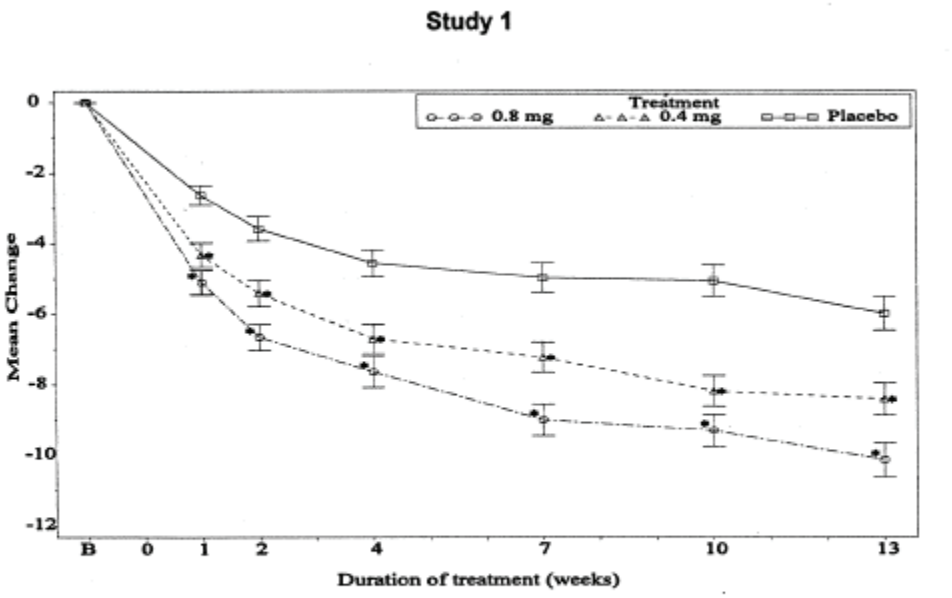
	Total AUA Symptom Score		Peak Urine Flow Rate	
	Mean Baseline Value	Mean Change	Mean Baseline Value	Mean Change
Study 1 †				
Tamsulosin 0.8 mg once daily	19.9 n=247	-9.6* n=237	9.57 n=247	1.78* n=247
Tamsulosin 0.4 mg once daily	19.8 n=254	-8.3* n=246	9.46 n=254	1.75* n=254
Placebo	19.6 n=254	-5.5 n=246	9.75 n=254	0.52 n=253
Study 2 ‡				
Tamsulosin 0.8 mg once daily	18.2 n=244	-5.8* n=238	9.96 n=244	1.79* n=237
Tamsulosin 0.4 mg once daily	17.9 n=248	-5.1* n=244	9.94 n=248	1.52 n=244
Placebo	19.2 n=239	-3.6 n=235	9.95 n=239	0.93 n=235

* Statistically significant difference from placebo (p-value $\leq$0.050; Bonferroni-Holm multiple test procedure)
† Peak urine flow rate measured 4 to 8 hours post dose at endpoint
‡ Peak urine flow rate measured 24 to 27 hours post dose at endpoint

Mean total AUA Symptom Score at Endpoint was improved relative to Baseline in Study 1 and Study 2 in both tamsulosin treatment groups (Table 4). Both treatment groups were statistically significantly improved (p-value ≤0.050) compared to placebo.

At the initial evaluation one week after dosing, a reduction in symptoms had occurred, with significant improvements from Baseline compared to placebo in the mean Total AUA Symptom Score in both tamsulosin treatment groups for Study 1 (Figure 1). The improvements persisted for the duration of the study.

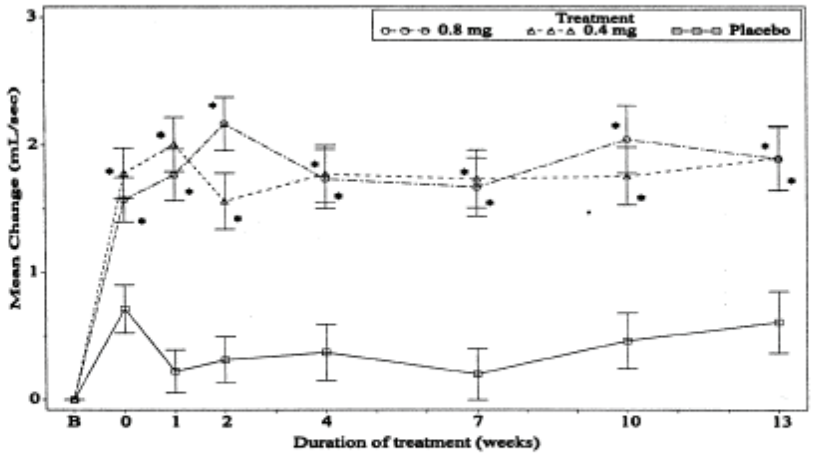
FIGURE 1. Mean (±S.E.) Change from Baseline in Total AUA Symptom Score (0-35)



* indicates significant difference from placebo (p-value≤0.050).
B=Baseline determined approximately one week prior to the initial dose of double-blind medication at Week 0.
Note: Patients in the 0.8 mg treatment group received 0.4 mg for the first week.
Note: Total AUA Symptom Scores range from 0 to 35.

Patients treated with tamsulosin had an increase in peak urine flow rate that was statistically significant (p-value ≤0.050) 4 to 8 hours after the initial dose of therapy (Figure 2). This improvement in the patients treated with tamsulosin was also evident throughout the duration of clinical studies in both the 0.4 mg once daily and 0.8 mg once daily dosing groups.

FIGURE 2: Mean (±S.E.) Increase in Peak Urine Flow Rate (mL/sec)
Study 1



* indicates significant difference from placebo (p-value≤0.050).
B=Baseline determined approximately one week prior to the initial dose of double-blind medication at week 0.
Note: The uroflowmetry assessments at week 0 were recorded four to eight hours after patients received the first dose of double-blind medication.
Note: Patients in the 0.8 mg treatment group received 0.4 mg for the first week.

Patients in this study completed a validated Quality of Life assessment questionnaire covering the following topics: "physical discomfort," "worry about health," "bothersomeness of condition," and "time kept from doing things". Both tamsulosin treatment groups experienced statistically significant (p-value ≤0.050) improvements from Baseline to Endpoint compared with patients in the placebo treatment group. A subgroup analysis of the effect of tamsulosin on blood pressure of normotensive patients and uncontrolled hypertensive patients did not reveal any clinically significant blood pressure lowering effect of tamsulosin 0.4 or 0.8 mg once daily compared with placebo (Table 5) . A similar lack of blood pressure lowering effect was also seen in controlled hypertensive (Baseline diastolic blood pressure <90 mmHg).

Table 5: Mean Change in Blood Pressure (mmHg) from Baseline to Final Visit in Study 1

		Normotension			Hypertension (Uncontrolled)*		
	Treatments	**n**	**Mean Baseline Value**	**Mean Change**	**n**	**Mean Baseline Value**	**Mean Change**
Systolic Blood Pressure (mmHg)	Tamsulosin 0.8 mg once daily	170	127	-1.9	40	146	-10.2
	Tamsulosin 0.4 mg once daily	182	127	-2.7	37	145	-7.2
	Placebo	172	127	1.3	41	147	-8.4
Diastolic Blood Pressure (mmHg)	Tamsulosin 0.8 mg once daily	170	80	0.1	40	96	-8.5
	Tamsulosin 0.4 mg once daily	182	80	0.0	37	96	-7.2
	Placebo	172	80	1.2	41	98	-8.6

*Hypertensive patients whose average of the last two diastolic measurements in the sitting position during the single-blind placebo evaluation period regardless of the treatment the patient was taking was ≥90mmHg.

A total of 1547 patients with the signs and symptoms of BPH involved in the U.S. and European short-term trials continued therapy with tamsulosin in controlled and uncontrolled follow-up studies examining long-term efficacy and safety which support the use of tamsulosin for over one year in the treatment of BPH.

Results from a long-term, U.S. placebo-controlled, double-blind extension of Study 1 showed that, in the 269 patients treated with tamsulosin, both Total AUA Symptom Score and Peak Urine Flow Rate continued to show improvement (p-value $\leq$0.050) from Baseline for one year.

TOXICOLOGY

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Rats administered doses up to 43 mg/kg/day in males and 52 mg/kg/day in females had no increases in tumour incidence with the exception of a modest increase in the frequency of mammary gland fibroadenomas in female rats receiving doses $\geq$5.4 mg/kg ($P<0.015$). The highest doses of tamsulosin evaluated in the rat carcinogenicity study produced systemic exposures (AUC) in rats 3 times the exposures in men receiving doses of 0.8 mg/day.

Mice were administered doses up to 127 mg/kg/day in males and 158 mg/kg/day in females. There were no significant tumour findings in male mice. Female mice treated for 2 years with the two highest doses of 45 and 158 mg/kg/day had statistically significant increases in the incidence of mammary gland fibroadenomas ($P<0.0001$) and adenocarcinomas ($P<0.0075$). The highest dose levels of tamsulosin evaluated in the mice carcinogenicity study produced systemic exposures (AUC) in mice 8 times the exposures in men receiving dose of 0.8 mg/day.

The increased incidences of mammary gland neoplasms in female rats and mice were considered secondary to tamsulosin-induced hyperprolactinemia. It is not known if tamsulosin elevates prolactin in humans. The relevance for human risk of the findings of prolactin-mediated endocrine tumours in rodents is not known.

Tamsulosin produced no evidence of mutagenic potential *in vitro* in the Ames reverse mutation test, mouse lymphoma thymidine kinase assay and chromosomal aberration assays in Chinese hamster ovary cells or human lymphocytes. There were no mutagenic effects in the *in vivo* sister chromatid exchange and mouse micronucleus assay.

Studies in rats revealed significantly reduced fertility in males dosed with single or multiple daily doses of 300 mg/kg/day of tamsulosin (AUC exposure in rats about 50 times the human exposure at a dose of 0.8mg/day). The mechanism of decreased fertility in male rats is considered to be an effect of the compound on the vaginal plug formation possibly due to changes of semen content or impairment of ejaculation. The effects on fertility were reversible showing improvement by 3 days after a single dose and 4 weeks after multiple dosing. Effects on fertility in males were completely reversed within nine weeks of discontinuation of multiple dosing. Multiple doses of 10 and 100 mg/kg/day tamsulosin (1/5 and 16 times the anticipated human AUC exposure) did not significantly alter fertility in male rats. Effects of tamsulosin on sperm counts or sperm function have not been evaluated.

Studies in female rats revealed significant reductions in fertility after single or multiple dosing with 300 mg/kg/day of the R-isomer or racemic mixture of tamsulosin, respectively. In female rats, the reductions in fertility after single doses were considered to be associated with impairments in fertilization. Multiple dosing with 10 or 100 mg/kg/day of the racemic mixture did not significantly alter fertility in female rats

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PART III: CONSUMER INFORMATION

[Pr]ratio-TAMSULOSIN
tamsulosin hydrochloride
0.4 mg sustained-release capsules

This leaflet is part III of a three-part "Product Monograph" published when ratio-TAMSULOSIN was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ratio-TAMSULOSIN. Contact your doctor or pharmacist if you have any questions about the drug.

Please read this leaflet before you start taking **ratio-TAMSULOSIN** (tamsulosin hydrochloride). Also, read it each time you renew your prescription, just in case new information has been added.

ABOUT THIS MEDICATION

What this medication is used for:

- ratio-TAMSULOSIN is for use by men only.
- Your physician has prescribed ratio-TAMSULOSIN because you have a medical condition called benign prostatic hyperplasia or BPH. This occurs only in men.

What it does:
ratio-TAMSULOSIN acts by relaxing muscles in the prostate and bladder neck at the site of the obstruction, resulting in improved urine flow, and reduced BPH symptoms.

What is BPH? BPH is an enlargement of the prostate gland. After age 50, most men develop enlarged prostates. The prostate is located below the bladder. As the prostate enlarges, it may slowly restrict the flow of urine. This can lead to symptoms such as:

- having a weak urinary system;
- a sensation of not emptying your bladder completely after you finish urinating;
- pushing or straining to begin urination;
- stopping and starting again several times when urinating;
- urinating again less than 2 hours after you finish urinating;
- finding it difficult to postpone urination;
- frequent sleep interruption caused by a need to urinate.

When it should not be used:
You should not use **ratio-TAMSULOSIN** if you are allergic (hypersensitive) to tamsulosin or any of the other ingredients in **ratio-TAMSULOSIN**. Hypersensitivity may present as sudden local swelling of the soft tissues of the body (e.g. the throat or tongue), difficult breathing and/or itching and rash (angioedema).

What the medicinal ingredient is:
Tamsulosin hydrochloride.

What the non-medicinal ingredients are:
Methacrylic acid-ethyl acrylate copolymer (polysorbate 80, sodium laurilsulfate), microcrystalline cellulose, talc, and triethylcitrate. The capsule shells are composed of: black iron oxide, FD&C Blue No.2, gelatin, red iron oxide, titanium dioxide, yellow iron oxide. Capsule imprinting ink contains: antifoam, black iron oxide, shellac glaze, and soya lectin.

What dosage forms it comes in:
Sustained-Release Capsules

WARNINGS AND PRECAUTIONS

Rarely, fainting can occur during the use of ratio-TAMSULOSIN, as with other medicinal products of this type. At the first signs of dizziness or weakness you should sit or lie down until they have disappeared.

ratio-TAMSULOSIN should not be used in women or children.

BEFORE you use **ratio-TAMSULOSIN** talk to your doctor or pharmacist :

- if you suffer from severe liver problems;
- if you suffer from fainting due to reduced blood pressure when changing posture (going to sit or stand up);
- if you have kidney problems;
- if you have previously taken **ratio-TAMSULOSIN** and became unwell;
- if you are going to drive, operate machinery or perform hazardous tasks.

You must see your doctor regularly. While taking **ratio-TAMSULOSIN**, you must have regular checkups. Follow your doctor's advice about when to have these checkups.

If you are undergoing eye surgery because of cloudiness of the lens (cataract) please inform your eye specialist that you are using or have used **ratio-TAMSULOSIN**. The specialist can then take appropriate precautions with respect to medication and surgical techniques to be used. Ask your doctor whether or not you should temporarily stop taking this medicine when undergoing eye surgery because of a cloudy lens.

INTERACTIONS WITH THIS MEDICATION

Taking **ratio-TAMSULOSIN** with other medicines from the same class ($alpha_1$-adrenoceptor blockers) may cause an unwanted decrease in blood pressure.

Please tell your doctor or pharmacist if you are taking or have recently taken cimetidine or any other medicines, including medicines obtained without a prescription.

PROPER USE OF THIS MEDICINE

Usual dose:
Follow your doctor's advice about how to take **ratio-TAMSULOSIN**. You should take one capsule (0.4 mg) approximately one-half hour following the same meal each day.

Do not crush, chew, or open capsules of **ratio-TAMSULOSIN** sustained-release formulation. These capsules are specially formulated to control the delivery of tamsulosin hydrochloride to the blood stream.

Do not share **ratio-TAMSULOSIN** with anyone else; it was prescribed only for you.

If you interrupt your treatment for several days or more, resume treatment after consulting with your physician.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Taking too many **ratio-TAMSULOSIN** capsules may lead to an unwanted decrease in blood pressure and an increase in heart rate, with feelings of faintness. Contact your doctor immediately if you have taken too much **ratio-TAMSULOSIN**.

Missed dose:

You may take your daily **ratio-TAMSULOSIN** capsule later the same day if you have forgotten to take it as recommended. If you have missed a day, just continue to take your daily capsule as prescribed. Never take a double dose to make up for the forgotten capsule.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all prescription drugs, **ratio-TAMSULOSIN** may cause side effects. Side effects due to **ratio-TAMSULOSIN** may include:

Common (1-10%):
Dizziness, particularly when getting up from a seated or lying position.

Some men may experience dizziness or fainting caused by a decrease in blood pressure after taking **ratio-TAMSULOSIN.** Although these symptoms are unlikely, you should avoid driving or hazardous tasks for 12 hours after the initial dose.

Uncommon (0.1-1%):
Headache, palpitations (a feeling of rapid beating of the heart that may be more forceful), reduced blood pressure e.g. when getting up quickly from a seated or lying position sometimes associated with dizziness; runny or blocked nose (rhinitis), diarrhea, feeling sick and vomiting, constipation, weakness (asthenia), rashes, itching and hives (urticaria), abnormal ejaculation. The latter means that semen does not leave the body via the urethra, but instead goes into the bladder. This phenomenon is harmless.

Rare (0.01-0.1%):
Rarely, fainting can occur during the use of **ratio-TAMSULOSIN**, as with other medicinal products of this type. At the first signs of dizziness or weakness you should sit or lie down until they have disappeared.

Sudden local swelling of the soft tissues of the body (e.g. the throat or tongue), difficulty breathing and/or itching and rash, often as an allergic reaction (angioedema). If you suspect such symptoms, call your doctor or go to an Emergency Room as soon as possible.

Very rare (<0.01%):
Priapism (painful prolonged unwanted erection for which immediate medical treatment is required).

There have been reports that **ratio-TAMSULOSIN** and similar medications have caused prolonged, painful erection of the penis, which is unrelieved by sexual intercourse or masturbation. This condition, if untreated, can lead to permanent inability to have an erection. If you suspect such symptoms, call your doctor or go to an Emergency Room as soon as possible.

If you are undergoing eye surgery because of cloudiness of the lens (cataract) and are already taking or have previously taken **ratio-TAMSULOSIN**, the pupil may dilate poorly and the iris (the coloured circular part of the eye) may become floppy during the procedure.

This is not a complete list of side effects. For any unexpected effects while taking ratio-TAMSULOSIN, contact your doctor or pharmacist. immediately, so that these effects may be properly addressed.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Dizziness, particularly when getting up from a seated or lying position		√	
Uncommon	Palpitations (feeling of rapid beating of the heart that may be more forceful)		√	
	Rashes, itching and hives (urticaria)			√
	Reduced blood pressure e.g. when getting up quickly from a seated or lying position, sometimes associated with dizziness		√	
Rare	Fainting			√
	*Sudden local swelling of the soft tissues of the body (e.g. the throat or tongue), difficulty breathing and/or itching and rash (angioedema)			√
Very Rare	*Priapism (painful prolonged unwanted erection)			√

* If you suspect such symptoms, call your doctor or go to an Emergency Room as soon as possible.

HOW TO STORE IT

Store between 15ºC and 30ºC.

Keep ratio-TAMSULOSIN and all medicines out of the reach of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to:**
    Canada Vigilance Program
    Health Canada
    Postal Locator 0701D
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals may be obtained by contacting the sponsor, Teva Canada Limited., at:

1-800-268-4127 ext. 5005 (English);

1-877-777-9117 (French)

or druginfo@tevacanada.com

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