PRODUCT MONOGRAPH

[Pr] MYLAN-TAMSULOSIN

(tamsulosin hydrochloride)

Sustained-release Capsules 0.4 mg

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

Mylan Pharmaceuticals ULC
85 Advance Road
Toronto, Ontario
M8Z 2S6

Date of Preparation:
June 3, 2009

Control No. 130335

Table of Contents

PART I: HEALTH PROFESSIONAL INFORMATION 3
SUMMARY PRODUCT INFORMATION 3
INDICATIONS AND CLINICAL USE 3
CONTRAINDICATIONS 3
WARNINGS AND PRECAUTIONS 4
ADVERSE REACTIONS 6
DRUG INTERACTIONS 10
DOSAGE AND ADMINISTRATION 11
OVERDOSAGE 12
ACTION AND CLINICAL PHARMACOLOGY 12
STORAGE AND STABILITY 16
DOSAGE FORMS, COMPOSITION AND PACKAGING 16

PART II: SCIENTIFIC INFORMATION 17
PHARMACEUTICAL INFORMATION 17
CLINICAL TRIALS 17
DETAILED PHARMACOLOGY 25
TOXICOLOGY 25
REFERENCES 27

PART III: CONSUMER INFORMATION 28

Pr MYLAN-TAMSULOSIN

(tamsulosin hydrochloride)

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Oral	Sustained-release Capsules 0.4 mg	*For a complete listing see Dosage Forms, Composition and Packaging section.*

INDICATIONS AND CLINICAL USE

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

Geriatrics:

Tamsulosin hydrochloride has been found to be a safe and effective $alpha_1$ adrenoreceptor antagonist when administered at therapeutic doses (0.4 mg and 0.8 mg once daily) to patients over the age of 65 years.

Pediatrics:

MYLAN-TAMSULOSIN is not indicated for use in children.

CONTRAINDICATIONS

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) is contraindicated in patients known to be hypersensitive to tamsulosin or any component of the MYLAN-TAMSULOSIN sustained-release formulation. For a complete listing, see the Dosage Forms, Composition and Packaging section of the product monograph.

WARNINGS AND PRECAUTIONS

The signs and symptoms of orthostasis (postural hypotension, dizziness and vertigo) were detected more frequently in tamsulosin hydrochloride-treated patients than in placebo recipients. As with other alpha-adrenergic blocking agents, there is a potential risk of syncope (see ADVERSE REACTIONS).

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

Very rarely tamsulosin, like other alpha$_1$ 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 (See WARNINGS AND PRECAUTIONS, General, Information For The Patient).

General

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) is not indicated for the treatment of hypertension.

Information For The Patient (see PART III: CONSUMER INFORMATION)

Patients should be told that dizziness can occur with MYLAN-TAMSULOSIN, requiring caution in people who must drive, operate machinery, or perform hazardous tasks. Patients should be advised not to crush, chew, or open the capsules of MYLAN-TAMSULOSIN sustained-release formulation. These capsules are specially formulated to control the delivery of tamsulosin HCl to the blood stream.

Patients should be advised about the possibility of priapism as a result of treatment with MYLAN-TAMSULOSIN Capsules 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).

Carcinogenesis and Mutagenesis

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 prior to the start of MYLAN-TAMSULOSIN (tamsulosin hydrochloride) therapy to rule out the presence of carcinoma of the prostate.

Orthostatic Hypotension

While syncope is the most severe orthostatic symptom of tamsulosin hydrochloride, other symptoms can occur (dizziness and postural hypotension). In the two U.S. double-blind, placebo-controlled studies (Studies 1 and 2), orthostatic testing was conducted at each visit. Postural hypotension was reported in three patients (0.6%) receiving tamsulosin hydrochloride.

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 particular 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 MYLAN-TAMSULOSIN.

Peri-operative Considerations

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 had 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:

MYLAN-TAMSULOSIN is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated 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. Tamsulosin hydrchloride is neither indicated nor recommended for use in women.

Nursing Women:

MYLAN-TAMSULOSIN is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated in women.

Pediatrics:

MYLAN-TAMSULOSIN is not indicated for use in children.

Geriatrics:

Cross-study comparisons of tamsulosin hydrochloride overall exposure (AUC) and half-life indicate that the pharmacokinetic disposition of tamsulosin may be slightly prolonged in geriatric males compared to young healthy male volunteers. However, tamsulosin hydrochloride has been found to be a safe and effective $alpha_1$ adrenoreceptor antagonist when administered at therapeutic doses (0.4 mg and 0.8 mg once daily) to patients over the age of 65 years.

Gender Effects:

MYLAN-TAMSULOSIN 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 hydrochloride are known. Treatment with tamsulosin hydrochloride for up to 12 months had no significant effect on prostate specific antigen (PSA).

ADVERSE REACTIONS

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

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.

TABLE 1. TREATMENT EMERGENT ADVERSE EVENTS OCCURRING IN ≥ 1% OF TAMSULOSIN OR PLACEBO PATIENTS DURING SHORT-TERM (U.S. AND EUROPEAN) PLACEBO-CONTROLLED TRIALS[1]

([1]Adverse events from patients given 0.1-0.8 mg tamsulosin daily were pooled)

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%

BODY SYSTEM / ADVERSE EVENT	TAMSULOSIN (N=1783)	PLACEBO (N=798)
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%
Pruritis	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%

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[1]

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[2]	0.6%	0%

[1] Adverse events from patients given 0.1-0.8 mg tamsulosin daily were pooled.
[2] 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 hydrochloride 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.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

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

Abnormal Hematologic and Clinical Chemistry Findings

No data is available.

Post-Market Adverse Drug Reactions

The following adverse reactions have been reported during the use of tamsulosin hydrochloride: Dizziness, abnormal ejaculation and, less frequently, headache, asthenia, postural hypotension, palpitations and rhinitis.

Gastrointestinal reactions such as nausea, vomiting, diarrhea and constipation can occasionally occur.

Hypersensitivity reactions such as rash, pruritus, and urticaria can occur occasionally, angioedema has been rarely reported.

Syncope has been reported rarely. Priapism has been reported very rarely.

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

DRUG INTERACTIONS

Overview

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

Drug-Drug Interactions

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

Nifedipine, Atenolol, Enalapril:

No dosage adjustments are necessary when tamsulosin hydrochloride is administered concomitantly with Procardia XL® (nifedipine), atenolol, or enalapril. In three studies in hypertensive subjects (age range 47-79 years) whose blood pressure was controlled with stable doses of Procardia XL® (nifedipine), atenolol or enalapril for at least three months, tamsulosin hydrochloride 0.4 mg for seven days followed by tamsulosin hydrochloride 0.8 mg 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 hydrochloride capsules.

Digoxin and Theophylline:

No dosage adjustments are necessary when tamsulosin hydrochloride is administered concomitantly with digoxin or theophylline. In two studies in healthy volunteers (n=10 per study; age range 19-39 years), receiving tamsulosin hydrochloride 0.4 mg/day for two days, followed by tamsulosin hydrochloride 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 hydrochloride is administered concomitantly with furosemide. The pharmacokinetic and pharmacodynamic interaction between tamsulosin hydrochloride 0.8 mg/day (steady-state) and furosemide 20 mg intravenously (single dose) was evaluated in ten healthy volunteers (age range 21-40 years). Tamsulosin hydrochloride 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 hydrochloride 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 hydrochloride 0.4 mg 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 hydrochloride capsules should be used with caution in combination with cimetidine, particularly at doses higher than 0.4 mg.

Drug-Food Interactions

The effects of food on the pharmacokinetics of tamsulosin are consistent regardless of whether tamsulosin hydrochloride is taken with a light breakfast or a high fat breakfast (see **ACTION AND CLINICAL PHARMACOLOGY,** Absorption, Table 3)**.**

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Recommended Dose and Dosage Adjustment

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) 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.

Depending on individual patient symptomatology and/or flow rates, the dose may be adjusted to 0.8 mg once daily.

If MYLAN-TAMSULOSIN administration is discontinued or interrupted for several days at either the 0.4 or 0.8 mg dose, therapy should be reinstituted, beginning with the 0.4 mg once daily dose.

Administration

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) should be administered approximately one-half hour following the same meal each day.

OVERDOSAGE

Should overdosage of MYLAN-TAMSULOSIN (tamsulosin hydrochloride) lead to hypotension, (see WARNINGS 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.

One patient reported an overdose of 30 0.4 mg capsules of tamsulosin hydrochloride. 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

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) is not intended for use as an antihypertensive drug.

Mechanism of Action

Tamsulosin, an $alpha_1$ adrenoreceptor blocking agent, exhibits selectivity for $alpha_1$ receptors in the human prostate. At least three discrete $alpha_1$ 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 $alpha_1$ adrenoreceptors, 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.

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 hydrochloride 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 hydrochloride is administered with food. The delay in T_{max} when tamsulosin hydrochloride 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 hydrochloride 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 hydrochloride 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 HYDROCHLORIDE 0.4 MG ONCE DAILY OR 0.8 MG ONCE DAILY WITH A LIGHT BREAKFAST, HIGH FAT BREAKFAST OR FASTED.

Pharmacokinetics 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.
Coefficient 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 to 600 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/Excretion:

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 radiolabeled dose of 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.

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 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 hydrochloride 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.

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.

Special Populations and Conditions

Geriatrics:

Cross-study comparisons of tamsulosin hydrochloride overall exposure (AUC) and half-life indicate that the pharmacokinetic disposition of tamsulosin may be slightly prolonged in geriatric males compared to young healthy male volunteers. However, tamsulosin hydrochloride has been found to be a safe and effective $alpha_1$ adrenoreceptor antagonist when administered at therapeutic doses (0.4 mg and 0.8 mg once daily) to patients over the age of 65 years.

Pediatrics:

MYLAN-TAMSULOSIN is not indicated for use in children.

Gender Effects:

MYLAN-TAMSULOSIN is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated in women.

Hepatic Insufficiency

The treatment of patients with severe hepatic impairment should be approached with caution as no studies have been conducted in this patient population.

Renal Insufficiency

The treatment of severely renally impaired patients (creatinine clearance of <l0 mL/min) should be approached with caution, as these patients have not been studied.

Pregnant Women:

MYLAN-TAMSULOSIN is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated 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. Tamsulosin hydrchloride is neither indicated nor recommended for use in women.

Nursing Women:

MYLAN-TAMSULOSIN is not indicated for use in women. Safety, effectiveness, and pharmacokinetics have not been evaluated in women.

STORAGE AND STABILITY

Store at room temperature (15-30°C).

DOSAGE FORMS, COMPOSITION AND PACKAGING

MYLAN-TAMSULOSIN (tamsulosin hydrochloride) sustained-release capsules 0.4 mg are hard gelatin capsules with orange coloured body and olive coloured cap, the cap and body both have one black line at the top. The cap is imprinted with the code TSL 0.4 with black ink. The capsule is filled with white to off-white pellets. MYLAN-TAMSULOSIN sustained-release capsules are supplied in HDPE bottles of 100 capsules.

Each capsule of MYLAN-TAMSULOSIN Sustained-release Formulation for oral administration contains tamsulosin hydrochloride 0.4 mg, and the following **non-medicinal ingredients** (in alphabetical order): indigo carmine – FD&C Blue 2, iron oxide black, iron oxide red, iron oxide yellow, gelatin, methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30 per cent (contains polysorbate 80 and sodium laurylsulfate), microcrystalline cellulose (Grade 101), purified water, talc, titanium dioxide, triethyl citrate.

Capsule imprinting ink contains (in alphabetical order): black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac and strong ammonia solution.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

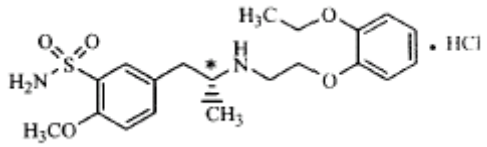
Proper name: Tamsulosin hydrochloride

Chemical name: (-)-(R)-5-[2-[[2-o-ethoxyphenoxy)ethyl]amino]propyl]-2-methoxybenzenesulfonamide monohydrochloride.

Molecular formula: $C_{20}H_{28}N_2O_5S.HCl$.

Molecular mass: 444.98.

Structural formula:



Physicochemical properties: Tamsulosin hydrochloride 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.

pH (7.5 mg/mL): 5.20

pKa: 8.37 (secondary amine). 10.23 (sulfonamide)

CLINICAL TRIALS

Four large placebo-controlled clinical studies and one large active-controlled clinical study comprising 2296 patients (1003 received tamsulosin hydrochloride 0.4 mg once daily, 491 received tamsulosin hydrochloride 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 hydrochloride dose of 0.4 mg and 0.8 mg.

Tamsulosin hydrochloride 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 hydrochloride 0.4 mg once daily or tamsulosin hydrochloride 0.8 mg once daily groups. Patients in tamsulosin hydrochloride 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)

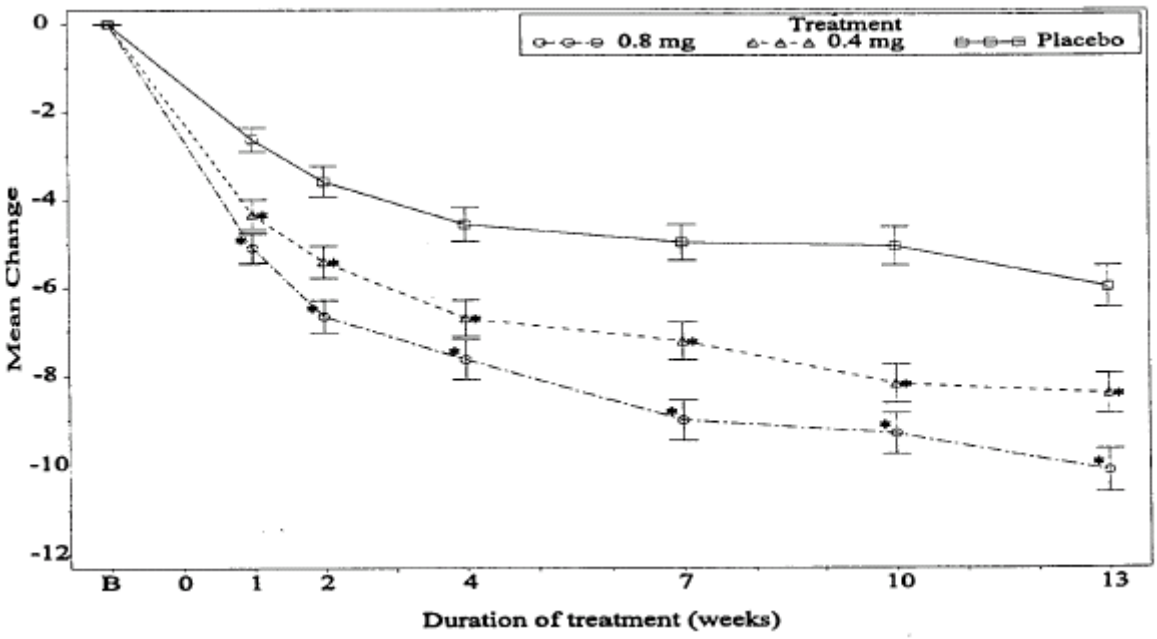
	Total AUA Symptom Score		Peak Urine Flow Rate	
	Mean Baseline Value	Mean Change	Mean Baseline Value	Mean change
Study 1 †				
Tamsulosin hydrochloride 0.8 mg once daily	19.9 n=247	-9.6* n=237	9.57 n=247	1.78* n=247
Tamsulosin hydrochloride 0.4 mg once daily	19.8 n=254	-8.3* n=246	9.46 n=254	1.75* n=254
Placebo	19.6 n=254	-5.5 n=246	9.75 n=254	0.52 n=253
Study 2 ‡				
Tamsulosin hydrochloride 0.8 mg once daily	18.2 n=244	-5.8* n=238	9.96 n=244	1.79* n=237
Tamsulosin hydrochloride 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 ≤ 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 hydrochloride 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 hydrochloride treatment groups for Study 1 (Figure 1). The improvements persisted for the duration of the study.

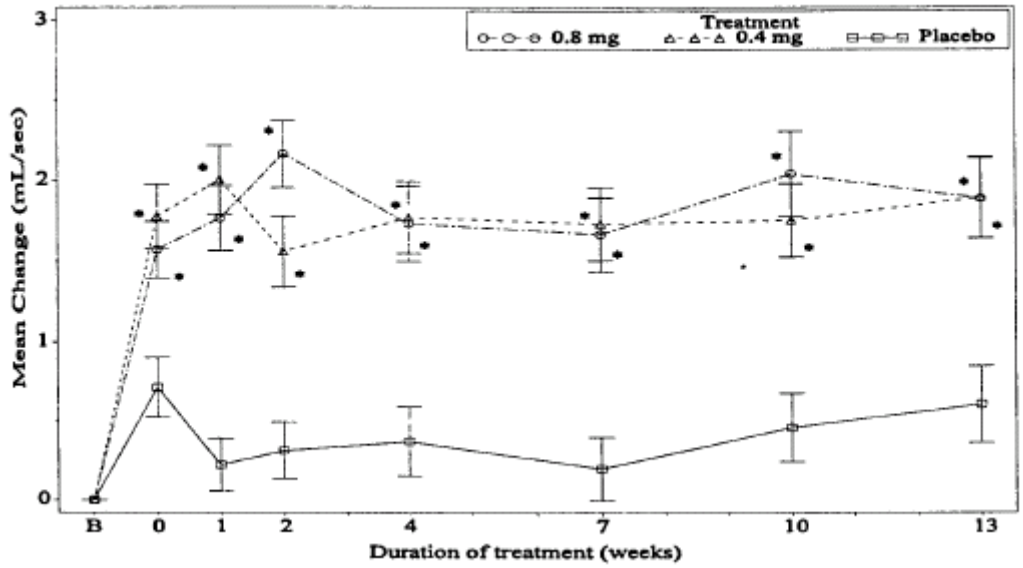
FIGURE 1. Mean (±S.E.) Change from Baseline in Total AUA Symptom Score (0-35)
Study 1



* 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: 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 hydrochloride 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 hydrochloride 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 hydrochloride 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 hydrochloride on blood pressure of normotensive patients and uncontrolled hypertensive patients did not reveal any clinically significant blood pressure lowering effect of tamsulosin hydrochloride 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 hypertensives (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 hydrochloride 0.8 mg once daily	170	127	-1.9	40	146	-10.2
	Tamsulosin hydrochloride 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 hydrochloride 0.8 mg once daily	170	80	0.1	40	96	-8.5
	Tamsulosin hydrochloride 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 ≥ 90 mmHg.

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 hydrochloride in controlled and uncontrolled follow-up studies examining long-term efficacy and safety which support the use of tamsulosin hydrochloride 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 hydrochloride, both Total AUA Symptom Score and Peak Urine Flow Rate continued to show improvement (p-value ≤ 0.050) from Baseline for one year.

Renal Dysfunction

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 result 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 hydrochloride dosing. Patients with end stage renal disease (Cl_{cr} < 10mL/min)

have not been studied.

Hepatic Dysfunction

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 hydrochloride dosage.

Bioequivalence Studies

Fasting Conditions

A comparative bioavailability study of Tamsulosin 0.4 mg Capsules (Mylan Pharmaceuticals ULC, Canada) and Flomax® 0.4 mg Capsules (Boehringer Ingelheim (Canada) Ltd.) was conducted in 39 healthy male volunteers under fasting conditions.

A summary of the comparative bioavailability data is presented below:

Tamsulosin (1 x 0.4 mg) From measured data **uncorrected for potency** Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test*	Reference†	% Ratio of Geometric Means	90% Confidence Interval
AUC_{72} (ng·h/mL)	201.1420 223.104(52.4710)	198.436 220.766 (50.7530)	101.4	95.08 – 108.06
AUC_{∞} (ng·h/mL)	207.1585 230.698 (54.2133)	204.0777 227.594 (52.0497)	101.5	95.21 – 108.23
C_{max} (ng/mL)	15.2889 16.395(37.6950)	16.1090 17.374 (39.4488)	94.9	86.76 – 103.82
T_{max}§ (h)	5.00 (2.00–8.00)	*5.00* (3.00–8.00)		
$T_{½}$ (h)	12.53 (28.3946)	12.75 (31.3583)		

* Mylan-Tamsulosin (Tamsulosin hydrochloride) 0.4 mg sustained release capsules (Mylan Pharmaceuticals ULC, Canada)
† Flomax® (Boehringer Ingelheim (Canada) Ltd., purchased in Canada)
§ Expressed as the median (range) only
 Expressed as the arithmetic mean (CV%) only

Fed Conditions

A comparative bioavailability study of Tamsulosin 0.4 mg Capsules (Mylan Pharmaceuticals ULC, Canada) and Flomax® 0.4 mg Capsules (Boehringer Ingelheim (Canada) Ltd.) was conducted in 42 healthy male volunteers under fed conditions.

A summary of the comparative bioavailability data is presented below:

Tamsulosin (1 x 0.4 mg) From measured data **uncorrected for potency** Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test*	Reference†	% Ratio of Geometric Means	90 % Confidence Interval
AUC_{72} (ng·h/mL)	196.127 222.074 (51.42)	177.507 200.212 (50.86)	110.5	105.26 – 116.58
AUC_{∞} (ng·h/mL)	209.577 236.938 (52.51)	188.198 212.555 (52.68)	111.5	105.66 – 117.43
C_{max} (ng/mL)	10.282 (40.20)	9.288 (37.41)	109.7	102.20 – 119.21
T_{max}§ (h)	9.00 (3.00–24.00)	9.00 (3.00–24.00)		
$T_{½}$€ (h)	12.93 (25.4)	12.56 (18.50)		

* Mylan-Tamsulosin (Tamsulosin hydrochloride) 0.4 mg sustained release capsules (Mylan Pharmaceuticals ULC, Canada)
† Flomax® (Boehringer Ingelheim (Canada) Ltd., purchased in Canada)
§ Expressed as the median (range) only
€ Expressed as the arithmetic mean (CV%) only

Steady State Conditions

A comparative bioavailability study of Tamsulosin HCl 0.4 mg capsules (Mylan Pharmaceuticals ULC, Canada) and Flomax® 0.4 mg capsules (Boehringer Ingelheim Ltd., Canada) was conducted in 32 healthy male volunteers under fasting, steady state conditions.

A summary of the comparative bioavailability data is presented below:

Tamsulosin (1 x 0.4 mg) From measured data **uncorrected for potency** Geometric Mean Arithmetic Mean (CV %)				
Parameter	Test*	Reference†	% Ratio of Geometric Means	90% Confidence Interval
AUC_{tau} (ng·h/mL)	216.074 230.329 (37.203)	219.296 234.807 (38.361)	98.5	95.1 - 102.1
C_{max} (ng/mL)	18.554 19.323 (28.304)	19.628 20.589 (31.162)	94.5	89.80-99.50
C_{min} (ng/mL)	4.073 4.46 (57.054)	4.071 4.42 (53.960)	100.0	92.40-108.30
T_{max}§ (h)	5.00 (2.00 – 7.00)	5.00 (3.00 – 9.00)		
FL¶ (%)	166.5 (34.2891)	174.9 (29.4821)		

* Mylan-Tamsulosin (Tamsulosin hydrochloride) 0.4 mg sustained release capsules (Mylan Pharmaceuticals ULC, Canada)
† Flomax®, (Boehringer Ingelheim, Canada), purchased in Canada
§ Expressed as the median (range) only
¶ Expressed as the arithmetic mean (CV%) only

DETAILED PHARMACOLOGY

Refer to ACTION AND CLINICAL PHARMACOLOGY.

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 ≥ 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 the maximum therapeutic 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 the maximum therapeutic 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 hydrochloride 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 with the maximum therapeutic dose). 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.

REFERENCES

1. McGrath, J.C., Lepor H., Wyllit M.G. Report of a unique meeting between the alpha-blocker subcommittee and pharmaceutical industry. Urol 48(5), 1996.

2. Price D.T., Lomasney J.W., Allen L.F., Caron M.G., Lefkowitz. Identification, quantification, and localization of mRNA for three distinct alpha$_1$ adrenergic receptor subtypes in human prostate. J Urol 1993; 150:546-551.

3. Hatano A., Takahashi H., Tamaki M., Komeyama T., Koizumi T., Takeda M. Pharmacological evidence of distinct α_1 - adrenoceptor subtypes mediating the contraction of human prostatic urethra and peripheral artery. Br J Pharmacol 1994; 113:723-728.

4. Moriyama N., Hamada K., Takanashi M., Kurimoto S., Kimura K., Inagaki O. Evaluation of α_1 - adrenoceptor subtypes in human hypertrophied prostate using [^{3}H]YM617, an α_1-selective antagonist. Acta Histochem Cytochem 1994; 27 (3):219-225.

5. Faure C., Pimoule C., Vallancien G., Langer S.Z., Graham D. Identification of α_1 - adrenoceptor subtypes present in the human prostate. Life Sci 1994;54(21):1595-1605.

6. Michel M.C., Insel P.A. Comparison of cloned and pharmacologically defined rat tissue α_1 - adrenoceptor subtypes. Naunyn-Schmiedebergs Arch Pharmacol 1994;350(2):136-142.

7. Yamada S., Suzuki M., Tanaka C., Mori R., Kimura R., Inagaki O. Comparative study on α_1 - adrenoceptor antagonist binding in human prostate and aorta. Clinical and Experimental Pharmacol and Physiol 1994;21:405-411.

8. Boehringer Ingelheim (Canada) Ltd., Product Monograph, Flomax®, Date of Preparation: May 28, 1998, Date of Revision: December 20, 2005, Control #101886.

PART III: CONSUMER INFORMATION

[Pr] MYLAN-TAMSULOSIN
(tamsulosin hydrochloride)

This leaflet is part III of a three-part "Product Monograph" published when MYLAN-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 MYLAN-TAMSULOSIN. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Your doctor has prescribed MYLAN-TAMSULOSIN because you have a medical condition called benign prostatic hyperplasia or BPH. This occurs only in men.

MYLAN-TAMSULOSIN is for use by men only.

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 stream;
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.

What it does:
MYLAN-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.

When it should not be used:
Do not use MYLAN-TAMSULOSIN if you are allergic to tamsulosin or any component of the MYLAN-TAMSULOSIN sustained-release formulation (see 'What the important non-medicinal ingredients are' listed below).

What the medicinal ingredient is:
tamsulosin hydrochloride

What the important non-medicinal ingredients are:

Non-medicinal ingredients (in alphabetical order): indigo carmine – FD&C Blue 2, iron oxide black, iron oxide red, iron oxide yellow, gelatin, methacrylic acid – ethyl acrylate copolymer (1:1) dispersion 30 per cent (contains polysorbate 80 and sodium laurilsulfate), microcrystalline cellulose (Grade 101), purified water, talc, titanium dioxide, triethylcitrate.

Capsule imprinting ink contains (in alphabetical order): black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac and strong ammonia solution.

What dosage forms it comes in:
Sustained – Release Capsules. Each capsule contains 0.4 mg tamsulosin hydrochloride.

WARNINGS AND PRECAUTIONS

Before you use MYLAN-TAMSULOSIN, tell your doctor or pharmacist:

If you suffer from fainting due to reduced blood pressure.
If you suffer from severe liver problems.
If you have kidney problems.
If you have or ever had prostate cancer.

What you need to know while taking MYLAN-TAMSULOSIN:

You must see your doctor regularly. While taking MYLAN-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 MYLAN-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 under going eye surgery because of cloudy lens.
You should avoid driving or hazardous tasks for 12 hours after the initial dose or after your doctor recommends an increase in dose.

INTERACTIONS WITH THIS MEDICATION

Drug that may interact with MYLAN-TAMSULOSIN include warfarin, cimetidine and alpha-adrenergic blocking agents (alfuzosin, doxazosin, prazosin, terazosin).

Tell your doctor and pharmacist what prescription and non-prescription medications, vitamins, nutritional supplements and herbal products that you are taking.

PROPER USE OF THIS MEDICATION

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

Usual dose:
The recommended dose for MYLAN-TAMSULOSIN is 0.4 mg once daily.

Follow your doctor's advice about how to take MYLAN-TAMSULOSIN. You should take it approximately 30 minutes following the same meal every day.

If you discontinued or interrupt your treatment for several days or more, resume treatment at one capsule/day, after consulting

with your doctor.

Do not crush, chew, or open capsules of MYLAN-TAMSULOSIN Sustained-release Formulation. These capsules are specially formulated to control the delivery of tamsulosin HCl to the blood stream.

Overdose:
You should take MYLAN-TAMSULOSIN as prescribed by your doctor. If you suspect that you took too many capsules, contact your doctor.

Missed Dose:

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and go back to the regular dosing schedule. Do not double dosage.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all prescription drugs, MYLAN-TAMSULOSIN may cause side effects. Side effects due to MYLAN-TAMSULOSIN may include dizziness, weakness/loss of strength (asthenia), headache, runny nose, heart palpitations (feeling of heart beating fast), ejaculatory problems, nausea, diarrhoea, vomiting, constipation, rashes, itching and hives. In some cases side effects may decrease or disappear while the patient continues to take MYLAN-TAMSULOSIN.

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

Extremely rarely, MYLAN-TAMSULOSIN Capsules 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 taking or have taken MYLAN-TAMSULOSIN, you should inform your surgeon. MYLAN-TAMSULOSIN may cause your pupil to dilate poorly and the iris (the coloured circular part of the eye) may become floppy during the procedure. By warning your surgeon in advance, he will be able to use a slightly different technique to make the surgery easier.

You should discuss side effects with your doctor before taking MYLAN-TAMSULOSIN and anytime you think you are having a side effect.

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/ lighheadedness upon rising		√	
	Abnormal ejaculation		√	
Uncommon	Headache		√	
	Heart palpitations		√	
	Weakness/loss of strength (asthenia)		√	
	Itchiness			√
	Hives			√
Serious and Rare	Fainting			√
	Swelling of the face, eyes, lips, tongue and/or throat, hands or feet (angioedema).			√
Very Rare	Prolonged painful erection of penis			√

This is not a complete list of side effects. For any unexpected effects while taking MYLAN-TAMSULOSIN, contact your doctor or pharmacist.

HOW TO STORE IT

Store at room temperature (15-30°C).

Keep MYLAN-TAMSULOSIN and all medicines out of reach of children.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada collects information on serious and unexpected effects of drugs . If you suspect you have had a serious or unexpected reaction to this drug you may notify Health Canada by:

toll-free telephone: 866-234-2345
toll-free fax 866-678-6789
By email: cadrmp@hc-sc.gc.ca

By regular mail:
National AR Centre
Marketed Health Products Safety and Effectiveness Information Division
Marketed Health Products Directorate
Tunney's Pasture, AL 0701C
Ottawa ON K1A 0K9

NOTE: Before contacting Health Canada, you should contact your physician or pharmacist.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found by contacting the sponsor, Mylan Pharmaceuticals ULC, at: 1-800-575-1379.

This leaflet was prepared by:
Mylan Pharmaceuticals ULC
85 Advance Road
Toronto, Ontario
M8Z 2S6

Date of preparation: June 3, 2009