

TAMSULOSIN HYDROCHLORIDE- tamsulosin hydrochloride capsule

Coupler LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TAMSULOSIN HYDROCHLORIDE CAPSULES safely and effectively. See full prescribing information for TAMSULOSIN HYDROCHLORIDE CAPSULES.

TAMSULOSIN HYDROCHLORIDE capsules, for oral use
Initial U.S. Approval: 1997

INDICATIONS AND USAGE

- Tamsulosin hydrochloride capsules are an alpha₁ adrenoceptor antagonist indicated for treatment of the signs and symptoms of benign prostatic hyperplasia (1)
- Tamsulosin hydrochloride capsules are not indicated for the treatment of hypertension (1)

DOSAGE AND ADMINISTRATION

- 0.4 mg once daily taken approximately one-half hour following the same meal each day. Tamsulosin hydrochloride capsules should not be crushed, chewed or opened. (2)
- Can be increased to 0.8 mg once daily for patients who fail to respond to the 0.4 mg dose after 2 to 4 weeks of dosing (2)
- If discontinued or interrupted for several days, therapy should start again with the 0.4 mg once-daily dose (2)

DOSAGE FORMS AND STRENGTHS

- Capsules: 0.4 mg (3)

CONTRAINDICATIONS

- Contraindicated in patients known to be hypersensitive to tamsulosin hydrochloride or any component of tamsulosin hydrochloride capsules (4, 6.2)

WARNINGS AND PRECAUTIONS

- Advise patients about the possibility of symptoms related to postural hypotension and to avoid situations where injury could result should syncope occur (5.1)
- Should not be used in combination with strong inhibitors of CYP3A4. Use with caution in combination with moderate inhibitors of CYP3A4, with strong or moderate inhibitors of CYP2D6, in patients known to be CYP2D6 poor metabolizers, or in combination with other cytochrome P450 inhibitors. (5.2, 7.1, 12.3)
- Should not be used in combination with other alpha adrenergic blocking agents (5.2, 7.2, 12.3)
- Exercise caution with concomitant administration of warfarin (5.2, 7.4, 12.3)
- Advise patients about the possibility and seriousness of priapism (5.3)
- Intraoperative Floppy Iris Syndrome has been observed during cataract and glaucoma surgery in some patients. Advise patients considering cataract or glaucoma surgery to tell their ophthalmologist that they have taken tamsulosin hydrochloride capsules. (5.5)
- Advise patients to be screened for the presence of prostate cancer prior to treatment and at regular intervals afterwards (5.4)

ADVERSE REACTIONS

- The most common adverse events (≥2% of patients and at a higher incidence than placebo) with the 0.4 mg dose or 0.8 mg dose were headache, dizziness, rhinitis, infection, abnormal ejaculation, asthenia, back pain, diarrhea, pharyngitis, chest pain, cough increased, somnolence, nausea, sinusitis, insomnia, libido decreased, tooth disorder, and blurred vision (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Aurobindo Pharma USA, Inc. at 1-866-850-2876 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Tamsulosin hydrochloride capsules 0.4 mg should not be used with strong inhibitors of CYP3A4 (e.g., ketoconazole). Tamsulosin hydrochloride capsules should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin), in combination with strong (e.g., paroxetine) or moderate (e.g., terbinafine) inhibitors of CYP2D6, or in patients known to be CYP2D6 poor metabolizers,

particularly at a dose higher than 0.4 mg (e.g., 0.8 mg). (5.2, 7.1, 12.3)

- Concomitant use of PDE5 inhibitors with tamsulosin can potentially cause symptomatic hypotension. (5.2, 7.3, 12.3)

-----**USE IN SPECIFIC POPULATIONS**-----

- Pediatric Use: Not indicated for use in pediatric populations. (8.4, 12.3)
- Geriatric Use: No overall differences in efficacy or safety vs. younger patients, but greater sensitivity of some older adults cannot be ruled out (8.5, 12.3)
- Renal Impairment: Has not been studied in patients with end-stage renal disease (8.6, 12.3)
- Hepatic Impairment: Has not been studied in patients with severe hepatic impairment (8.7, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 9/2021

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Tamsulosin hydrochloride capsules are indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) [see *Clinical Studies (14)*]. Tamsulosin hydrochloride capsules are not indicated for the treatment of hypertension.

2 DOSAGE AND ADMINISTRATION

Tamsulosin hydrochloride capsules 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. Tamsulosin hydrochloride capsules should not be crushed, chewed or opened.

For those patients who fail to respond to the 0.4 mg dose after 2 to 4 weeks of dosing, the dose of tamsulosin hydrochloride capsules can be increased to 0.8 mg once daily. Tamsulosin hydrochloride capsules 0.4 mg should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole) [see *Warnings and Precautions (5.2)*].

If tamsulosin hydrochloride capsules administration is discontinued or interrupted for several days at either the 0.4 mg or 0.8 mg dose, therapy should be started again with the 0.4 mg once-daily dose.

3 DOSAGE FORMS AND STRENGTHS

Capsule: 0.4 mg are olive green opaque/orange opaque size '0' hard gelatin capsules imprinted with 'D' on cap and '53' on body with black edible ink filled with white to off-white beadlets.

4 CONTRAINDICATIONS

Tamsulosin hydrochloride capsules are contraindicated in patients known to be hypersensitive to tamsulosin hydrochloride or any component of tamsulosin hydrochloride capsules. Reactions have included skin rash, urticaria, pruritus, angioedema, and respiratory symptoms [see *Adverse Reactions (6.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Orthostasis

The signs and symptoms of orthostasis (postural hypotension, dizziness, and vertigo) were detected more frequently in tamsulosin hydrochloride capsule-treated patients than in placebo recipients. As with other alpha adrenergic blocking agents there is a potential risk of syncope [see *Adverse Reactions (6.1)*]. Patients beginning treatment with tamsulosin hydrochloride capsules should be cautioned to avoid situations in which injury could result should syncope occur.

5.2 Drug Interactions

Tamsulosin is extensively metabolized, mainly by CYP3A4 and CYP2D6. Tamsulosin hydrochloride capsules 0.4 mg should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole) [see *Drug Interactions (7.1)* and *Clinical Pharmacology (12.3)*]. Tamsulosin hydrochloride capsules should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin), in combination with strong (e.g., paroxetine) or moderate (e.g., terbinafine) inhibitors of CYP2D6, in patients known to be CYP2D6 poor metabolizers particularly at a dose higher than 0.4 mg (e.g., 0.8 mg) [see *Drug Interactions (7.1)* and *Clinical Pharmacology (12.3)*].

Tamsulosin hydrochloride capsules should be used with caution in combination with cimetidine, particularly at a dose higher than 0.4 mg (e.g., 0.8 mg) [see *Drug Interactions (7.1)* and *Clinical Pharmacology (12.3)*].

Tamsulosin hydrochloride capsules should not be used in combination with other alpha adrenergic blocking agents [see *Drug Interactions (7.2)* and *Clinical Pharmacology (12.3)*].

Caution is advised when alpha adrenergic blocking agents including tamsulosin hydrochloride are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension [see *Drug Interactions (7.3)* and *Clinical Pharmacology (12.3)*].

Caution should be exercised with concomitant administration of warfarin and tamsulosin hydrochloride capsules [see *Drug Interactions (7.4)* and *Clinical Pharmacology (12.3)*].

5.3 Priapism

Rarely (probably less than 1 in 50,000 patients), tamsulosin, like other alpha

α_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.

5.4 Screening for Prostate Cancer

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

5.5 Intraoperative Floppy Iris Syndrome

Intraoperative Floppy Iris Syndrome (IFIS) has been observed during cataract and glaucoma surgery in some patients on or previously treated with alpha α_1 blockers, including tamsulosin hydrochloride capsules [see *Adverse Reactions (6.2)*].

Most reports were in patients taking the alpha α_1 blocker when IFIS occurred, but in some cases, the alpha α_1 blocker had been stopped prior to surgery. In most of these cases, the alpha α_1 blocker had been stopped recently prior to surgery (2 to 14 days), but in a few cases, IFIS was reported after the patient had been off the alpha α_1 blocker for a longer period (5 weeks to 9 months). IFIS is a variant of small pupil syndrome and is characterized by the combination of a flaccid iris that billows in response to intraoperative irrigation currents, progressive intraoperative miosis despite preoperative dilation with standard mydriatic drugs and potential prolapse of the iris toward the phacoemulsification incisions. The patient's ophthalmologist should be prepared for possible modifications to their surgical technique, such as the utilization of iris hooks, iris dilator rings, or viscoelastic substances.

IFIS may increase the risk of eye complications during and after the operation. The benefit of stopping alpha α_1 blocker therapy prior to cataract or glaucoma surgery has not been established. The initiation of therapy with tamsulosin in patients for whom cataract or glaucoma surgery is scheduled is not recommended.

5.6 Sulfa Allergy

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

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reactions rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

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 hydrochloride capsules were used. These studies evaluated safety in 1783 patients treated with tamsulosin hydrochloride capsules and 798 patients administered placebo. Table 1 summarizes the treatment-emergent adverse events that occurred in $\geq 2\%$ of patients receiving either tamsulosin hydrochloride capsules 0.4 mg or 0.8 mg and at an incidence numerically higher than that in the placebo group during two 13-week U.S. trials (US92-03A and US93-01) conducted in 1487 men.

Table 1 Treatment-Emergent ¹Adverse Events Occurring in $\geq 2\%$ of Tamsulosin Hydrochloride Capsules or Placebo Patients in Two U.S. Short-Term Placebo-Controlled Clinical Studies

BODY SYSTEM/ADVERSE EVENT	TAMSULOSIN HYDROCHLORIDE CAPSULES GROUPS		PLACEBO n=493
	0.4 mg n=502	0.8 mg n=492	
BODY AS WHOLE			
Headache	97 (19.3%)	104 (21.1%)	99 (20.1%)
Infection ²	45 (9%)	53 (10.8%)	37 (7.5%)
Asthenia	39 (7.8%)	42 (8.5%)	27 (5.5%)
Back pain	35 (7%)	41 (8.3%)	27 (5.5%)
Chest pain	20 (4%)	20 (4.1%)	18 (3.7%)
NERVOUS SYSTEM			
Dizziness	75 (14.9%)	84 (17.1%)	50 (10.1%)
Somnolence	15 (3%)	21 (4.3%)	8 (1.6%)
Insomnia	12 (2.4%)	7 (1.4%)	3 (0.6%)
Libido decreased	5 (1%)	10 (2%)	6 (1.2%)
RESPIRATORY SYSTEM			
Rhinitis ³	66 (13.1%)	88 (17.9%)	41 (8.3%)
Pharyngitis	29 (5.8%)	25 (5.1%)	23 (4.7%)
Cough increased	17 (3.4%)	22 (4.5%)	12 (2.4%)
Sinusitis	11 (2.2%)	18 (3.7%)	8 (1.6%)
DIGESTIVE SYSTEM			
Diarrhea	31 (6.2%)	21 (4.3%)	22 (4.5%)
Nausea	13 (2.6%)	19 (3.9%)	16 (3.2%)
Tooth disorder	6 (1.2%)	10 (2%)	7 (1.4%)
UROGENITAL SYSTEM			
Abnormal ejaculation	42 (8.4%)	89 (18.1%)	1 (0.2%)
SPECIAL SENSES			
Blurred vision	1 (0.2%)	10 (2%)	2 (0.4%)

¹A treatment-emergent adverse event was defined as any event satisfying one of the following criteria:

The adverse event occurred for the first time after initial dosing with double-blind study medication;

- The adverse event was present prior to or at the time of initial dosing with double-blind study medication and subsequently increased in severity

during double-blind treatment; or

- The adverse event was present prior to or at the time of initial dosing with double-blind study medication, disappeared completely, and then reappeared during double-blind treatment.

²Coding preferred terms also include cold, common cold, head cold, flu, and flu-like symptoms.

³Coding preferred terms also include nasal congestion, stuffy nose, runny nose, sinus congestion, and hay fever.

Signs and Symptoms of Orthostasis

In the two U.S. studies, symptomatic postural hypotension was reported by 0.2% of patients (1 of 502) in the 0.4 mg group, 0.4% of patients (2 of 492) in the 0.8 mg group, and by no patients in the placebo group. Syncope was reported by 0.2% of patients (1 of 502) in the 0.4 mg group, 0.4% of patients (2 of 492) in the 0.8 mg group, and 0.6% of patients (3 of 493) in the placebo group. Dizziness was reported by 15% of patients (75 of 502) in the 0.4 mg group, 17% of patients (84 of 492) in the 0.8 mg group, and 10% of patients (50 of 493) in the placebo group. Vertigo was reported by 0.6% of patients (3 of 502) in the 0.4 mg group, 1% of patients (5 of 492) in the 0.8 mg group, and by 0.6% of patients (3 of 493) in the placebo group.

Multiple testing for orthostatic hypotension was conducted in a number of studies. Such a test was considered positive if it met one or more of the following criteria: (1) a decrease in systolic blood pressure of ≥ 20 mmHg upon standing from the supine position during the orthostatic tests; (2) a decrease in diastolic blood pressure ≥ 10 mmHg upon standing, with the standing diastolic blood pressure < 65 mmHg during the orthostatic test; (3) an increase in pulse rate of ≥ 20 bpm upon standing with a standing pulse rate ≥ 100 bpm during the orthostatic test; and (4) the presence of clinical symptoms (faintness, lightheadedness/lightheaded, dizziness, spinning sensation, vertigo, or postural hypotension) upon standing during the orthostatic test.

Following the first dose of double-blind medication in Study 1, a positive orthostatic test result at 4 hours post-dose was observed in 7% of patients (37 of 498) who received tamsulosin hydrochloride capsules 0.4 mg once daily and in 3% of the patients (8 of 253) who received placebo. At 8 hours post-dose, a positive orthostatic test result was observed for 6% of the patients (31 of 498) who received tamsulosin hydrochloride capsules 0.4 mg once daily and 4% (9 of 250) who received placebo (Note: patients in the 0.8 mg group received 0.4 mg once daily for the first week of Study 1).

In Studies 1 and 2, at least one positive orthostatic test result was observed during the course of these studies for 81 of the 502 patients (16%) in the tamsulosin hydrochloride capsules 0.4 mg once-daily group, 92 of the 491 patients (19%) in the tamsulosin hydrochloride capsules 0.8 mg once-daily group, and 54 of the 493 patients (11%) in the placebo group.

Because orthostasis was detected more frequently in tamsulosin hydrochloride capsules-treated patients than in placebo recipients, there is a potential risk of syncope [see *Warnings and Precautions (5.1)*].

Abnormal Ejaculation

Abnormal ejaculation includes ejaculation failure, ejaculation disorder, retrograde ejaculation, and ejaculation decrease. As shown in Table 1, abnormal ejaculation was associated with tamsulosin hydrochloride capsules administration and was dose-related in the U.S. studies. Withdrawal from these clinical studies of tamsulosin hydrochloride capsules because of abnormal ejaculation was also dose-dependent, with 8 of 492 patients (1.6%) in the 0.8 mg group and no patients in the 0.4 mg or placebo groups discontinuing treatment due to abnormal ejaculation.

Laboratory Tests

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

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of tamsulosin hydrochloride capsules. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Decisions to include these reactions in labeling are typically based on one or more of the following factors: (1) seriousness of the reaction, (2) frequency of reporting, or (3) strength of causal connection to tamsulosin hydrochloride capsules.

Allergic-type reactions such as skin rash, urticaria, pruritus, angioedema, and respiratory symptoms have been reported with positive rechallenge in some cases. Priapism has been reported rarely. Infrequent reports of dyspnea, palpitations, hypotension, atrial fibrillation, arrhythmia, tachycardia, skin desquamation including reports of Stevens-Johnson syndrome, erythema multiforme, dermatitis exfoliative, constipation, vomiting, dry mouth, visual impairment, and epistaxis have been received during the postmarketing period.

During cataract and glaucoma surgery, a variant of small pupil syndrome known as Intraoperative Floppy Iris Syndrome (IFIS) has been reported in association with alpha₁ blocker therapy [see *Warnings and Precautions (5.5)*].

7 DRUG INTERACTIONS

7.1 Cytochrome P450 Inhibition

Strong and Moderate Inhibitors of CYP3A4 or CYP2D6

Tamsulosin is extensively metabolized, mainly by CYP3A4 and CYP2D6.

Concomitant treatment with ketoconazole (a strong inhibitor of CYP3A4) resulted in an

increase in the C_{max} and AUC of tamsulosin by a factor of 2.2 and 2.8, respectively [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*]. The effects of concomitant administration of a moderate CYP3A4 inhibitor (e.g., erythromycin) on the pharmacokinetics of tamsulosin hydrochloride have not been evaluated [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

Concomitant treatment with paroxetine (a strong inhibitor of CYP2D6) resulted in an increase in the C_{max} and AUC of tamsulosin by a factor of 1.3 and 1.6, respectively [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*]. A similar increase in exposure is expected in CYP2D6 poor metabolizers (PM) as compared to extensive metabolizers (EM). Since CYP2D6 PMs cannot be readily identified and the potential for significant increase in tamsulosin exposure exists when tamsulosin hydrochloride 0.4 mg is co-administered with strong CYP3A4 inhibitors in CYP2D6 PMs, tamsulosin hydrochloride capsules 0.4 mg should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole) [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

The effects of concomitant administration of a moderate CYP2D6 inhibitor (e.g., terbinafine) on the pharmacokinetics of tamsulosin hydrochloride have not been evaluated [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

The effects of co-administration of both a CYP3A4 and a CYP2D6 inhibitor with tamsulosin hydrochloride capsules have not been evaluated. However, there is a potential for significant increase in tamsulosin exposure when tamsulosin hydrochloride 0.4 mg is co-administered with a combination of both CYP3A4 and CYP2D6 inhibitors [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

Cimetidine

Treatment with cimetidine resulted in a significant decrease (26%) in the clearance of tamsulosin hydrochloride, which resulted in a moderate increase in tamsulosin hydrochloride AUC (44%) [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

7.2 Other Alpha Adrenergic Blocking Agents

The pharmacokinetic and pharmacodynamic interactions between tamsulosin hydrochloride capsules and other alpha adrenergic blocking agents have not been determined; however, interactions between tamsulosin hydrochloride capsules and other alpha adrenergic blocking agents may be expected [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

7.3 PDE5 Inhibitors

Caution is advised when alpha adrenergic blocking agents including tamsulosin hydrochloride are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two drug classes can potentially cause symptomatic hypotension [see *Warnings and Precautions (5.2) and Clinical Pharmacology (12.3)*].

7.4 Warfarin

A definitive drug-drug interaction study between tamsulosin hydrochloride and warfarin was not conducted. Results from limited *in vitro* and *in vivo* studies are inconclusive. Caution should be exercised with concomitant administration of warfarin and tamsulosin hydrochloride capsules [see *Warnings and Precautions (5.2)* and *Clinical Pharmacology (12.3)*].

7.5 Nifedipine, Atenolol, Enalapril

Dosage adjustments are not necessary when tamsulosin hydrochloride capsules are administered concomitantly with nifedipine, atenolol, or enalapril [see *Clinical Pharmacology (12.3)*].

7.6 Digoxin and Theophylline

Dosage adjustments are not necessary when a tamsulosin hydrochloride capsule is administered concomitantly with digoxin or theophylline [see *Clinical Pharmacology (12.3)*].

7.7 Furosemide

Tamsulosin hydrochloride capsules had no effect on the pharmacodynamics (excretion of electrolytes) of furosemide. While furosemide produced an 11% to 12% reduction in tamsulosin hydrochloride C_{max} and AUC, these changes are expected to be clinically insignificant and do not require adjustment of the tamsulosin hydrochloride capsules dosage [see *Clinical Pharmacology (12.3)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Tamsulosin hydrochloride is not indicated for use in women. There are no adequate data on the developmental risk associated with the use of tamsulosin hydrochloride in pregnant women. No adverse developmental effects were observed in animal studies in which tamsulosin hydrochloride was administered to rats or rabbits during the period of organogenesis (GD 7 to 17 in the rat and GD 6 to 18 in the rabbit) [see *Data*].

In the U.S. general population, the estimated background risk of major birth defects and of miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Administration of tamsulosin hydrochloride to pregnant female rats during the period of

organogenesis at dose levels up to approximately 50 times the human therapeutic AUC exposure (300 mg/kg/day) revealed no evidence of harm to the fetus. Administration of tamsulosin hydrochloride to pregnant rabbits during the period of organogenesis at dose levels up to 50 mg/kg/day produced no evidence of fetal harm.

8.2 Lactation

Tamsulosin hydrochloride is not indicated for use in women. There are no data on the presence of tamsulosin hydrochloride in human milk, the effects of tamsulosin hydrochloride on the breastfed infant, or the effects of tamsulosin hydrochloride on milk production. Tamsulosin hydrochloride is present in the milk of lactating rats [see *Data*] .

Data

Oral administration of radiolabeled tamsulosin hydrochloride to rats demonstrated that tamsulosin hydrochloride and/or its metabolites are excreted into the milk of rats.

8.3 Females and Males of Reproductive Potential

Infertility

Males

Abnormal ejaculation including ejaculation failure, ejaculation disorder, retrograde ejaculation, and ejaculation decrease has been associated with tamsulosin hydrochloride [see *Clinical Trials Experience (6.1)*] .Studies in rats revealed significantly reduced fertility in males considered to be due to impairment of ejaculation, which was reversible [see *Nonclinical Toxicology (13.1)*] .

Females

Tamsulosin hydrochloride is not indicated for use in women. Female fertility in rats was significantly reduced, considered to be due to impairment of fertilization [see *Nonclinical Toxicology (13.1)*] .

8.4 Pediatric Use

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

Efficacy and positive benefit/risk of tamsulosin hydrochloride was not demonstrated in two studies conducted in patients 2 years to 16 years of age with elevated detrusor leak point pressure (>40 cm H₂O) associated with known neurological disorder (e.g., spina bifida). Patients in both studies were treated on a weight-based mg/kg schema (0.025 mg, 0.05 mg, 0.1 mg, 0.2 mg, or 0.4 mg tamsulosin hydrochloride) for the reduction in detrusor leak point pressure below 40 cm H₂O. In a randomized, double-blind, placebo-controlled, 14-week, pharmacokinetic, safety and efficacy study in 161 patients, no statistically significant difference in the proportion of responders was observed between groups receiving tamsulosin hydrochloride and placebo. In an open-label, 12-month safety study, 87 patients were treated with tamsulosin hydrochloride. The most frequently reported adverse events (≥5%) from the pooled data of both studies were urinary tract infection, vomiting, pyrexia, headache, nasopharyngitis, cough, pharyngitis,

influenza, diarrhea, abdominal pain, and constipation.

8.5 Geriatric Use

Of the total number of subjects (1783) in clinical studies of tamsulosin, 36% were 65 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and the other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out [see *Clinical Pharmacology (12.3)*].

8.6 Renal Impairment

Patients with renal impairment do not require an adjustment in tamsulosin hydrochloride capsules dosing. However, patients with end-stage renal disease ($CL_{cr} < 10$ mL/min/1.73 m²) have not been studied [see *Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

Patients with moderate hepatic impairment do not require an adjustment in tamsulosin hydrochloride capsules dosage. Tamsulosin hydrochloride has not been studied in patients with severe hepatic impairment [see *Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

Should overdose of tamsulosin hydrochloride capsules lead to hypotension [see *Warnings and Precautions (5.1)* and *Adverse Reactions (6.1)*], support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be accomplished by keeping the patient in the supine position. If this measure is inadequate, then administration of intravenous fluids should be considered. If necessary, vasopressors should then be used and renal function should be monitored and supported as needed. Laboratory data indicate that tamsulosin hydrochloride is 94% to 99% protein bound; therefore, dialysis is unlikely to be of benefit.

11 DESCRIPTION

Tamsulosin hydrochloride is an antagonist of alpha_{1A} adrenoceptors in the prostate.

Tamsulosin hydrochloride is (-)-(R)-5-[2-[[2-(o-Ethoxyphenoxy) ethyl]amino]propyl]-2-methoxybenzenesulfonamide, monohydrochloride. Tamsulosin hydrochloride USP is a white or almost white crystalline powder that melts with decomposition at approximately 230°C. It is sparingly soluble in water and methanol, slightly soluble in glacial acetic acid and ethanol, and practically insoluble in ether.

The molecular formula of tamsulosin hydrochloride is C₂₀H₂₈N₂O₅S • HCl. The molecular weight of tamsulosin hydrochloride is 444.98. Its structural formula is:

Each tamsulosin hydrochloride capsule, USP for oral administration contains tamsulosin hydrochloride USP 0.4 mg, and the following inactive ingredients: calcium stearate, FD&C Blue 2, gelatin, iron oxide red, iron oxide yellow, microcrystalline cellulose, methacrylic acid and ethyl acrylate copolymer dispersion, sodium lauryl sulfate, talc, triacetin, and titanium dioxide. The capsules are printed with SW-9008 Black Ink containing black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

Meets USP dissolution test 10.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The symptoms associated with benign prostatic hyperplasia (BPH) are related to bladder outlet obstruction, which is comprised of two underlying components: static and dynamic. The static component is related to an increase in prostate size caused, in part, by a proliferation of smooth muscle cells in the prostatic stroma. However, the severity of BPH symptoms and the degree of urethral obstruction do not correlate well with the size of the prostate. The dynamic component is a function of an increase in smooth muscle tone in the prostate and bladder neck leading to constriction of the bladder outlet. Smooth muscle tone is mediated by the sympathetic nervous stimulation of alpha₁adrenoceptors, which are abundant in the prostate, prostatic capsule, prostatic urethra, and bladder neck. Blockade of these adrenoceptors can cause smooth muscles in the bladder neck and prostate to relax, resulting in an improvement in urine flow rate and a reduction in symptoms of BPH.

Tamsulosin, an alpha₁adrenoceptor blocking agent, exhibits selectivity for alpha₁receptors in the human prostate. At least three discrete alpha₁adrenoceptor subtypes have been identified: alpha_{1A}, alpha_{1B}, and alpha_{1D}; their distribution differs between human organs and tissue. Approximately 70% of the alpha₁receptors in the human prostate are of the alpha_{1A}subtype.

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

12.2 Pharmacodynamics

Urologic pharmacodynamic effects have been evaluated in neurologically impaired pediatric patients and in adults with BPH [*see Use in Specific Populations (8.4) and Clinical Studies (14)*].

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, 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 tumor 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 hydrochloride evaluated in the rat carcinogenicity study produced systemic exposures (AUC) in rats 3 times the exposures in men receiving the maximum therapeutic dose 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 tumor 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 hydrochloride 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 hydrochloride-induced hyperprolactinemia. It is not known if tamsulosin hydrochloride capsules elevate prolactin in humans. The relevance for human risk of the findings of prolactin-mediated endocrine tumors in rodents is not known.

Tamsulosin hydrochloride produced no evidence of mutagenic potential *in vitro* in the Ames reverse mutation test, mouse lymphoma thymidine kinase assay, unscheduled DNA repair synthesis 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 hydrochloride (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 hydrochloride (1/5 and 16 times the anticipated human AUC exposure) did not significantly alter fertility in male rats. Effects of tamsulosin hydrochloride 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 hydrochloride, 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.

16 HOW SUPPLIED/STORAGE AND HANDLING

Tamsulosin Hydrochloride Capsules USP, 0.4 mg are olive green opaque/orange opaque size '0' hard gelatin capsules imprinted with 'D' on cap and '53' on body with black edible ink filled with white to off-white beadlets.

Bottles of 100	NDC 65862-598-01
Bottles of 500	NDC 65862-598-05
3 x 10 Unit-dose Capsules	NDC 65862-598-10

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Preserve in tight container. Avoid excessive moisture.

Keep tamsulosin hydrochloride capsules and all medicines out of reach of children.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information)

- **Hypotension**

Advise the patient about the possible occurrence of symptoms related to postural hypotension, such as dizziness, when taking tamsulosin hydrochloride capsules, and they should be cautioned about driving, operating machinery, or performing hazardous tasks [see *Warnings and Precautions (5.1)*].

- **Drug Interactions**

Advise the patient that tamsulosin hydrochloride should not be used in combination with strong inhibitors of CYP3A4 [see *Warnings and Precautions (5.2)* and *Drug Interactions (7.1)*].

- **Priapism**

Advise the patient about the possibility of priapism as a result of treatment with tamsulosin hydrochloride 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) [see *Warnings and Precautions (5.3)*].

- **Screening for Prostate Cancer**

Prostate cancer and BPH frequently co-exist; therefore, screen patients for the presence of prostate cancer prior to treatment with tamsulosin hydrochloride capsules and at regular intervals afterwards [see *Warnings and Precautions (5.4)*].

- **Intraoperative Floppy Iris Syndrome**

Advise the patient when considering cataract or glaucoma surgery to tell their ophthalmologist that they have taken tamsulosin hydrochloride capsules [see *Warnings*].

and Precautions (5.5)] .

- **Administration**

Advise the patient that tamsulosin hydrochloride capsules should not be crushed, chewed or opened [see Dosage and Administration (2)].

FDA-approved Patient Labeling

Patient labeling is provided at the end of this prescribing information.

Distributed by:

Aurobindo Pharma USA, Inc.
279 Princeton-Hightstown Road
East Windsor, NJ 08520

Manufactured by:

Aurobindo Pharma Limited
Hyderabad-500 032, India

Revised: 09/2021

PATIENT INFORMATION

Tamsulosin Hydrochloride Capsules, USP (tam soo' loe sin hye" droe klor' ide)

Read the Patient Information that comes with tamsulosin hydrochloride capsules before you start taking them and each time you refill your prescription. The information may have changed. This leaflet does not take the place of discussions with your doctor about your medical condition or your treatment.

What are tamsulosin hydrochloride capsules?

Tamsulosin hydrochloride capsules are a prescription alpha-blocker medicine used to treat the signs and symptoms of benign prostatic hyperplasia (BPH), a condition your doctor may refer to as an enlarged prostate.

- Tamsulosin hydrochloride capsules are not for women.
- Tamsulosin hydrochloride capsules are not for children.

Who should not take tamsulosin hydrochloride capsules?

Do not take tamsulosin hydrochloride capsules if you are allergic to any of its ingredients. See the end of this leaflet for a complete list of ingredients in tamsulosin hydrochloride capsules.

What should I tell my doctor before using tamsulosin hydrochloride capsules?

Before taking tamsulosin hydrochloride capsules, tell your doctor about all your medical conditions, including:

- any kidney or liver problems.
- any history of low blood pressure.
- any allergies to sulfa or any other medicines.
- if you are planning to have cataract or glaucoma surgery.

Tell your doctor about all the medicines you take, including:

- any prescription medicines, including blood pressure medicines.
- any non-prescription medicines, including vitamins and herbal supplements.

Some of your other medicines may affect the way tamsulosin hydrochloride capsules work. Especially tell your doctor if you take a medicine for high blood pressure. You should not take tamsulosin hydrochloride capsules if you are already taking certain blood pressure medicines.

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How should I take tamsulosin hydrochloride capsules?

- Take tamsulosin hydrochloride capsules exactly as prescribed by your doctor.
- Do not crush, chew, or open tamsulosin hydrochloride capsules.
- Take tamsulosin hydrochloride capsules one time each day, about 30 minutes after the same meal each day. For example, you may take tamsulosin hydrochloride capsules 30 minutes after dinner each day.
- If you miss a dose of tamsulosin hydrochloride capsule, take it as soon as you remember. If you miss your dose for the whole day, continue with your next dose on your regular schedule. Do not take two doses at the same time.
- If you stop or forget to take tamsulosin hydrochloride capsules for several days, talk with your doctor before starting again.
- If you take more tamsulosin hydrochloride capsules than prescribed, call your doctor right away.

What are the possible side effects of tamsulosin hydrochloride capsules?

Possible side effects of tamsulosin hydrochloride capsules may include:

- **Decreased blood pressure when changing positions.** Tamsulosin hydrochloride capsules may cause a sudden drop in blood pressure upon standing, especially after

the first dose or when changing doses.

Symptoms may include:

- fainting
- dizziness
- lightheadedness

Change positions slowly from lying down to sitting up or from a sitting to a standing position until you learn how you react to tamsulosin hydrochloride capsules. If you begin to feel dizzy, sit or lie down until you feel better. If the symptoms are severe or do not improve, call your doctor.

- **Allergic reactions.** Make your doctor aware of any allergic reactions you may experience while taking tamsulosin hydrochloride capsules.

Allergic reactions may include:

- rash
- itching
- hives

Rare and more serious allergic reactions may also occur. **Get medical help right away if you have any of the following reactions:**

- swelling of face, tongue, or throat
- difficulty breathing
- blistering of the skin

- **A painful erection that will not go away.** Tamsulosin hydrochloride capsules can cause a painful erection (priapism), which cannot be relieved by having sex. If this happens, get medical help right away. If priapism is not treated, you may not be able to get an erection in the future.

- **Eye problems during cataract or glaucoma surgery.** During cataract or glaucoma surgery, a condition called intraoperative floppy iris syndrome (IFIS) can happen if you take or have taken tamsulosin hydrochloride capsules. If you need to have cataract or glaucoma surgery, be sure to tell your surgeon if you take or have taken tamsulosin hydrochloride capsules.

Common side effects of tamsulosin hydrochloride capsules may include:

- runny nose
- dizziness
- decreased semen

These are not all the possible side effects with tamsulosin hydrochloride capsules. Tell your doctor if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088, or by visiting www.fda.gov/medwatch.

What should I avoid while taking tamsulosin hydrochloride capsules?

Avoid driving, operating machinery, or other dangerous activities, until you know how tamsulosin hydrochloride capsules affect you. Tamsulosin hydrochloride capsules may cause a sudden drop in blood pressure upon standing, especially after the first dose or when changing doses. See **“What are the possible side effects of tamsulosin hydrochloride capsules?”**

How do I store tamsulosin hydrochloride capsules?

Store tamsulosin hydrochloride capsules at room temperature 20° to 25°C (68° to 77°F). Short-term exposure to higher or lower temperatures [from 59°F (15°C) to 86°F (30°C)] is acceptable. Ask your doctor or pharmacist if you have any questions about storing your capsules.

Keep tamsulosin hydrochloride capsules and all medicines out of the reach of children.

General information

This medicine was prescribed for you by your doctor for your condition. Do not use it for another condition. Do not give tamsulosin hydrochloride capsules to other people, even if they have the same symptoms that you have. They may harm them.

While taking tamsulosin hydrochloride capsules, you must have regular checkups. Follow your doctor’s advice about when to have these checkups.

BPH can occur with other more serious conditions, including prostate cancer. Therefore, ask your doctor about screening for prostate cancer prior to treatment with tamsulosin hydrochloride capsules and at regular intervals afterwards.

This patient information leaflet summarizes the most important information about tamsulosin hydrochloride capsules. If you would like more information, talk with your doctor. You can ask your pharmacist or doctor for information about tamsulosin hydrochloride capsules that is written for health professionals. For more information call Aurobindo Pharma USA, Inc. at 1-866-850-2876.

What are the ingredients in tamsulosin hydrochloride capsules?

- Active Ingredient: tamsulosin hydrochloride
- Inactive Ingredients: calcium stearate, FD&C Blue 2, gelatin, iron oxide red, iron oxide yellow, microcrystalline cellulose, methacrylic acid and ethyl acrylate copolymer dispersion, sodium lauryl sulfate, talc, triacetin, and titanium dioxide. The capsules are printed with SW-9008 Black Ink containing black iron oxide, butyl alcohol, dehydrated alcohol, isopropyl alcohol, potassium hydroxide, propylene glycol, shellac, and strong ammonia solution.

Distributed by:
Aurobindo Pharma USA, Inc.
 279 Princeton-Hightstown Road
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Manufactured by:
Aurobindo Pharma Limited
 Hyderabad-500 032, India

Revised: 09/2021



TAMSULOSIN HYDROCHLORIDE

tamsulosin hydrochloride capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:67046-0829(NDC:65862-598)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TAMSULOSIN HYDROCHLORIDE (UNII: 11SV1951MR) (TAMSULOSIN - UNII:G3P28OML5I)	TAMSULOSIN HYDROCHLORIDE	0.4 mg

Inactive Ingredients

Ingredient Name	Strength
CALCIUM STEARATE (UNII: 776XM7047L)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
GELATIN, UNSPECIFIED (UNII: 2G86QN327L)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
METHACRYLIC ACID AND ETHYL ACRYLATE COPOLYMER (UNII: NX76LV5T8J)	

SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
TALC (UNII: 7SEV7J4R1U)	
TRIACETIN (UNII: XHX3C3X673)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERROSFERRIC OXIDE (UNII: XM0M87F357)	
BUTYL ALCOHOL (UNII: 8PJ61P6TS3)	
ALCOHOL (UNII: 3K9958V90M)	
ISOPROPYL ALCOHOL (UNII: ND2M416302)	
POTASSIUM HYDROXIDE (UNII: WZH3C48M4T)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
SHELLAC (UNII: 46N107B71O)	
AMMONIA (UNII: 5138Q19F1X)	

Product Characteristics

Color	green (Olive Green Opaque) , orange (Orange Opaque)	Score	no score
Shape	CAPSULE	Size	21mm
Flavor		Imprint Code	D;53
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:67046-0829-3	30 in 1 BLISTER PACK; Type 0: Not a Combination Product	11/06/2024	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA202433	11/06/2024	

Labeler - Coupler LLC (119003108)

Establishment

Name	Address	ID/FEI	Business Operations
Coupler LLC		119003108	repack(67046-0829)