

Core Safety Profile

Active substance:	Tamsulosin hydrochloride
Pharmaceutical form(s)/strength:	Modified release, 0.4mg capsules hard Prolonged release, 0.4mg film- coated tablets
P-RMS:	NL/H/PSUR/0014/002
Date of FAR:	08.11.2012

4.3 Contraindications

Hypersensitivity to tamsulosin hydrochloride, including drug-induced angioedema or to any of the excipients.

A history of orthostatic hypotension.

Severe hepatic insufficiency.

4.4 Special warnings and precautions for use

As with other α_1 -adrenoceptors antagonists, a reduction in blood pressure can occur in individual cases during treatment with /.../ 0,4, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

Before therapy with /.../0,4 is initiated, the patient should be examined in order to exclude the presence of other conditions, which can cause the same symptoms as benign prostatic hyperplasia. Digital rectal examination and, when necessary, determination of prostate specific antigen (PSA) should be performed before treatment and at regular intervals afterwards.

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

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin hydrochloride. IFIS may increase the risk of eye complications during and after the operation.

Discontinuing tamsulosin hydrochloride 1-2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit of treatment discontinuation has not yet been established. IFIS has also been reported in patients who had discontinued tamsulosin for a longer period prior to cataract surgery.

The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract surgery is scheduled is not recommended. During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract surgery are being or have been treated with tamsulosin in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

Tamsulosin hydrochloride should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4 (see section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

No interactions have been seen when tamsulosin hydrochloride was given concomitantly with either atenolol, enalapril-or theophylline. Concomitant cimetidine brings about a rise in

plasma levels of tamsulosin, whereas furosemide a fall, but as levels remain within the normal range posology need not be adjusted.

In vitro, neither diazepam nor propranolol, trichlormethiazide, chlormadinon, amitriptyline, diclofenac, glibenclamide, simvastatin and warfarin change the free fraction of tamsulosin in human plasma. Neither does tamsulosin change the free fractions of diazepam, propranolol, trichlormethiazide and chlormadinon.

Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin.

Concomitant administration of tamsulosin hydrochloride with strong inhibitors of CYP3A4 may lead to increased exposure to tamsulosin hydrochloride. Concomitant administration with ketoconazole (a known strong CYP3A4 inhibitor) resulted in an increase in AUC and Cmax of tamsulosin hydrochloride by a factor of 2.8 and 2.2, respectively.

Tamsulosin hydrochloride should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong and moderate inhibitors of CYP3A4.

Concomitant administration of tamsulosin hydrochloride with paroxetine, a strong inhibitor of CYP2D6, resulted in a Cmax and AUC of tamsulosin that had increased by a factor of 1.3 and 1.6, respectively, but these increases are not considered clinically relevant.

Concurrent administration of other α_1 -adrenoceptor antagonists could lead to hypotensive effects.

4.6 Pregnancy and lactation

~~Not applicable as /.../0,4 is intended for male patients only.~~

<Tradename> is not indicated for use in women.

Ejaculation disorders have been observed in short and long term clinical studies with tamsulosin. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure have been reported in the post authorization phase.”

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be aware of the fact that dizziness can occur.

4.8 Undesirable effects

System Organ Class	Common >1/100, <1/10	Uncommon >1/1000, 1/100	Rare >1/10,000,<1/1000	Very rare <1/10,000
Nervous system disorders	Dizziness (1.3%)	Headache	Syncope	
Cardiac disorders		Palpitations		
Vascular disorders		orthostatic hypotension		
Respiratory, thoracic and mediastinal disorders		Rhinitis		
Gastrointestinal disorders		Constipation, diarrhoea, nausea, vomiting		
Skin and subcutaneous tissue disorders		rash, pruritus, urticaria	angioedema	Stevens-Johnson syndrome
Reproductive system and breast disorders	ejaculation disorders			priapism
General disorders and administration site conditions		asthenia		

During cataract surgery a small pupil situation, known as Intraoperative Floppy Iris Syndrome (IFIS), has been associated with therapy of tamsulosin during post-marketing surveillance (see also section 4.4).

Post-marketing experience: In addition to the adverse events listed above, atrial fibrillation, arrhythmia, tachycardia and dyspnoea have been reported in association with tamsulosin use. Because these spontaneously reported events are from the worldwide post marketing experience, the frequency of events and the role of tamsulosin in their causation cannot be reliably determined.

The following reactions should be included in the table in the correct SOC and frequency category (not known): Vision blurred, visual impairment, epistaxis, ejaculation disorder, retrograde ejaculation, ejaculation failure, erythema multiforme, dermatitis exfoliative.

4.9 Overdose

Symptoms

Overdosage with tamsulosin hydrochloride can potentially result in severe hypotensive effects. Severe hypotensive effects have been observed at different levels of overdosing.

Treatment

In case of acute hypotension occurring after overdosage cardiovascular support should be given. Blood pressure can be restored and heart rate brought back to normal by lying the patient down. If this does not help then volume expanders and, when necessary, vasopressors could be employed. Renal function should be monitored and general supportive measures applied. Dialysis is unlikely to be of help as tamsulosin is very highly bound to plasma proteins.

Measures, 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.