

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tamsulosin hydrochloride 400 micrograms modified-release capsules, hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains as active ingredient tamsulosin hydrochloride 400 micrograms.

For a full list of excipients, see Section 6.1

3 PHARMACEUTICAL FORM

Modified-release capsule, hard

Orange/olive-green capsule (19.3 x 6.4 mm). The capsules contain white to off-white pellets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration

Oral use

Posology

No dose adjustment is warranted in renal impairment. No dose adjustment is warranted in patients with mild to moderate hepatic insufficiency (see also 4.3 Contraindications).

Paediatric population

There is no relevant indication for use of tamsulosin in children.

The safety and efficacy of tamsulosine in children < 18 years have not been established. Currently available data are described in section 5.1.

Method of administration

One capsule daily, to be taken after breakfast or the first meal of the day.

The capsule must be swallowed whole and must not be crunched or chewed, as this interferes with the modified release of the active ingredient.

4.3 Contraindications

Hypersensitivity to the active substance, including drug-induced angio-oedema, or to any of the excipients listed in section 6.1.

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 tamsulosin, 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 tamsulosin 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 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 and glaucoma surgery in some patients on or previously treated with tamsulosin. IFIS may increase the risk of complications during and after the operation.

Discontinuing tamsulosin 1-2 weeks prior to cataract or glaucoma 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 in patients for whom cataract or glaucoma surgery is scheduled is not recommended.

During pre-operative assessment, cataract surgeons and ophthalmic teams should consider whether patients scheduled for cataract and glaucoma 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 should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype.

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

Excipients

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interactions

Paediatric population

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 C_{max} 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 C_{max} 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 -adrenoreceptor antagonist could lead to hypotensive effects.

4.6 Fertility, pregnancy and lactation

Tamsulosin 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 authorisation 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 (> 1/1 000, < 1/100) | Rare (> 1/10 000, < 1/1 000) | Very rare (< 1/10 000) | Not known (cannot be estimated from the available data) |
|--|--|---|------------------------------|--------------------------|---|
| Nervous system disorders | Dizziness (1.3%) | Headache | Syncope | | |
| Eye disorders | | | | | Vision blurred, visual impairment |
| Cardiac disorders | | Palpitations | | | |
| Vascular disorders | | Orthostatic hypotension | | | |
| Respiratory, thoracic and mediastinal Disorders | | Rhinitis | | | Epistaxis |
| Gastrointestinal disorders | | Constipation, diarrhoea, nausea, vomiting | | | Dry mouth |
| Skin and subcutaneous tissue disorders | | Rash, pruritus, urticaria | Angio-oedema | Stevens-Johnson syndrome | Erythema multiforme, dermatitis exfoliative |
| Reproductive systems and breast disorders | Ejaculation disorders, retrograde ejaculation, ejaculation failure | | | Priapism | |
| General | | Asthenia | | | |

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|---|--|--|--|--|--|
| disorders and administration site Conditions | | | | | |
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During cataract and glaucoma 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via IMB Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.

Website: www.imb.ie; e-mail: imbpharmacovigilance@imb.ie

4.9 Overdose

Symptoms

Overdosage with tamsulosin 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: α_1 -adrenoceptor antagonist, ATC code: GO4C AO2. Preparations for the exclusive treatment of prostatic disease

Mechanism of action

Tamsulosin binds selectively and competitively to postsynaptic α_{1A} adrenoreceptors, in particular to subtypes α_{1A} and α_{1D} . It brings about relaxation of prostatic and urethral smooth muscle.

Pharmacodynamic effects

Tamsulosin increases the maximum urinary flow rate. It relieves obstruction by relaxing smooth muscle in prostate and urethra thereby improving voiding symptoms.

It also improves the storage symptoms in which bladder instability plays an important role.

These effects on storage and voiding symptoms are maintained during long - term therapy. The need for surgery or catheterization is significantly delayed.

α_1 -adrenoceptors antagonists can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with tamsulosin.

Paediatric population

A double-blind, randomized, placebo-controlled, dose ranging study was performed in children with neuropathic bladder. A total of 161 children (with an age of 2 to 16 years) were randomized and treated at 1 of 3 dose levels of tamsulosin (low [0.001 to 0.002 mg/kg], medium [0.002 to 0.004 mg/kg], and high [0.004 to 0.008 mg/kg]), or placebo. The primary endpoint was number of patients who decreased their detrusor leak point pressure (LPP) to <40 cm H₂O based upon two evaluations on the same day. Secondary endpoints were: Actual and percent change from baseline in detrusor leak point pressure, improvement or stabilization of hydronephrosis and hydroureter and change in urine volumes obtained by catheterisation and number of times wet at time of catheterisation as recorded in catheterisation diaries. No statistically significant difference was found between the placebo group and any of the 3 tamsulosin dose groups for either the primary or any secondary endpoints. No dose response was observed for any dose level.

5.2 Pharmacokinetic properties

Absorption

Tamsulosin is absorbed from the intestine and is almost completely bioavailable. Absorption of tamsulosin is reduced by a recent meal. Uniformity of absorption can be promoted by the patient always taking tamsulosin after the same meal. Tamsulosin shows linear kinetics.

After a single dose of tamsulosin in the fed state, plasma levels of tamsulosin peak at around 6 hours and, in the steady state, which is reached by day 5 of multiple dosing, C_{max} in patients is about two thirds higher than that reached after a single dose. Although this was seen in elderly patients, the same finding would also be expected in young ones.

There is a considerable inter-patient variation in plasma levels both after single and multiple dosing.

Distribution

In man, tamsulosin is about 99% bound to plasma proteins. The volume of distribution is small (about 0.2 l/kg).

Biotransformation

Tamsulosin has a low first pass effect, being metabolized slowly. Most tamsulosin is present in plasma in the form of unchanged active substance. It is metabolised in the liver.

In rats, hardly any induction of microsomal liver enzymes was seen to be caused by tamsulosin.

None of the metabolites are more active than the original compound.

Elimination

Tamsulosin and its metabolites are mainly excreted in the urine with about 9% of the dose being present in the form of unchanged active substance.

After a single dose of tamsulosin in the fed state, and in the steady state in patients, elimination half-lives of about 10 and 13 hours respectively have been measured.

5.3 Preclinical safety data

Single and repeat dose toxicity studies were performed in mice, rats and dogs. In addition, reproduction toxicity in rats, carcinogenicity in mice and rats and in vivo and in vitro genotoxicity were examined.

The general toxicity profile, as seen with high doses of tamsulosin, is consistent with the known pharmacological actions of the α_1 -adrenoceptors antagonists.

At very high dose levels the ECG was altered in dogs. This response is considered to be not clinically relevant. Tamsulosin showed no relevant genotoxic properties.

Increased incidences of proliferative changes of mammary glands of female rats and mice have been reported. These findings, which are probably mediated by hyperprolactinemia and only occurred at high dose levels, are regarded as irrelevant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Content of capsule

Microcrystalline cellulose
Methacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30 per cent
Polysorbate 80
Sodium laurilsulfate
Triethyl citrate
Talc

Capsule body

Gelatine
Indigo carmine (E 132)
Titanium dioxide (E 171)
Yellow iron oxide (E 172)
Red iron oxide (E 172)
Black iron oxide (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Blister packs: Store in the original package.
Containers: Keep the container tightly closed.

6.5 Nature and contents of container

PVC/PE/PVDC/Aluminium blister packs in cardboard boxes and HDPE containers with PP child-resistant closures containing 10, 14, 20, 28, 30, 50, 56, 60, 90, 100 or 200 modified-release capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Synthon BV
Microweg 22
6545 CM Nijmegen
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA0840/013/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 January 2006

Date of last renewal: 23 March 2010

10 DATE OF REVISION OF THE TEXT

January 2021