Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tamsulosin 0.4 mg Modified Release Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains tamsulosin hydrochloride 0.4 mg.

For a full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Modified-release capsule, hard.

Light green/yellow capsule. The capsules contain white to slightly yellowish 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

One capsule a day after breakfast or the first meal of the day. The capsule is swallowed whole with a glass of water while standing or sitting (not lying down). The capsule should not be broken or pulled apart as this may have an effect on the release of the long-acting active ingredient.

4.3 Contraindications

Hypersensitivity to tamsulosin, including drug-induced angio-oedema, or to any of the excipients.
Orthostatic hypotension observed earlier (history of orthostatic hypotension).
Severe hepatic insufficiency.

4.4 Special warnings and precautions for use

The use of tamsulosin may lower blood pressure, which in rare cases may cause fainting. If initial symptoms of orthostatic hypotension start to appear (dizziness, weakness), then the patient should sit or lie down until the symptoms have gone.

The patient should be examined before commencement of therapy with tamsulosin to exclude the presence of other conditions that can produce similar symptoms to those of BPH. The prostate should be examined via the rectum and, if necessary, the PSA count determined prior to commencement of treatment and again later at regular intervals.

The treatment of severely renally impaired patients(creatinine clearance of < 10 ml/min) should be approached with caution as these patients have not been studied.

Angio-oedema has been rarely reported after the use of tamsulosin. Treatment should be discontinued immediately, the patient should be monitored until disappearance of the oedema, and tamsulosin should not be re-administered.

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. IFIS may lead to increased procedural complications during the operation. The initiation of therapy with tamsulosin in patients for whom cataract surgery is scheduled is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract surgery is anecdotally considered helpful, but the benefit and duration of requirement of stopping the therapy prior to cataract surgery has not yet been established.

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.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions have been observed when tamsulosin has been given concomitantly with atenolol, enalapril, nifedipine or theophylline. Concomitant cimetidine raises, and concomitant furosemide lowers, plasma concentrations of tamsulosin but, as the concentration of tamsulosin remains within the normal range, posology need not be altered.

Tamsulosin has not been found to interact with amitriptyline, salbutamol, glibenclamide or finasteride during *in vitro* studies with liver microsomal fractions (representing the cytochrome P450-linked metabolising enzyme system). Diclofenac and Warfarin may increase the elimination rate of tamsulosin.

Concurrent administration with another α_1-adrenoreceptor antagonist may lower blood pressure.

4.6 Pregnancy and lactation

Tamsulosin is intended for males only.

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

	Common (>1/100, <1/10)	Uncommon (>1/1 000, <1/100)	Rare (>1/10 000, <1/1 000)	Very rare (<1/10 000)
Nervous system disorders	Dizziness	Headache	Syncope	
Cardiac disorders		Palpitations		
Vascular disorders		Orthostatic hypotension		
Respiratory, thoracic and mediastinum-related disorders		Rhinitis		
Gastrointestinal disorders		Constipation, diarrhoea, nausea, vomiting		
Skin and subcutaneous tissue disorders		Rash, pruritus urticaria	Angio-oedema	Stevens-Johnson syndrome

Reproductive systems and breast disorders	ejeculation 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.

4.9 Overdose

No cases of acute overdose have been reported. However, acute hypotension could theoretically occur after overdose in which case 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.

If large quantities of the medicinal product are involved, gastric lavage may be performed and activated charcoal and an osmotic laxative, such as sodium sulphate, may be given.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
α_{1A} adrenoreceptor antagonist, ATC code: G04CA02.
The medicinal product is only used for the treatment of prostatic conditions.

Mechanism of action
Tamsulosin binds selectively and competitively to postsynaptic α_{1A} adrenoreceptors, which convey smooth muscle contraction**,** thereby relaxing prostatic and urethral smooth muscle.

Pharmacodynamic effects
Tamsulosin increases the maximum urinary flow rate by relaxing prostatic and urethral smooth muscle, thus relieving obstruction.

The medicinal product also improves the irritative and obstructive symptoms in which the contraction of smooth muscle in the lower urinary tract plays an important role.

Alpha-blockers can reduce blood pressure by lowering peripheral resistance. No reduction in blood pressure of any clinical significance was observed during studies with tamsulosin in normotensive patients.

The medicinal product's effect on storage and voiding symptoms are also maintained during long-term therapy, as a result of which the need for surgical treatment is significantly postponed.

5.2 Pharmacokinetic properties

Absorption
Tamsulosin is rapidly absorbed from the intestines and its bioavailability is almost complete. Absorption is slowed down if a meal has been eaten before taking the medicinal product. Uniformity of absorption can be assured by always taking tamsulosin after breakfast.
Tamsulosin shows linear kinetics.
Peak plasma levels are achieved at approximately six hours after a single dose of tamsulosin taken after a full meal. The steady state is reached by day five of multiple dosing, when C_{max} in patients is about two-thirds higher than that reached after a single dose. Although this has been demonstrated only in the elderly, the same result would also be expected in younger patients.
There are huge inter-patient variations in plasma levels of tamsulosin, both after single as well as multiple dosing.

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

Biotransformation
Tamsulosin has a low first pass metabolic effect. Most tamsulosin is found unaltered in plasma. The substance is metabolised in the liver.

In studies on rats, tamsulosin was found to cause only a slight induction of microsomal liver enzymes. The metabolites are not as effective and toxic as the active medicinal product itself.

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

The elimination half-life of tamsulosin in patients is approximately 10 hours (when taken after a meal) and 13 hours in the steady state.

5.3 Preclinical safety data

Toxicity after a single dose and multiple dosing has been investigated in mice, rats and dogs. Reproductive toxicity has also been investigated in rats, carcinogenicity in mice and rats, and genotoxicity *in vivo* and *in vitro*.

The common toxicity profile found with large doses of tamsulosin is equivalent to the pharmacological effect associated with alpha adrenergic antagonists.
Changes in ECG readings were found with very large doses in dogs. This is not, however, assumed to be of any clinical significance. Tamsulosin has not been found to have any significant genotoxic properties.

Greater proliferative changes in the mammary glands of female rats and mice have been discovered on exposure to tamsulosin. These findings, which are probably indirectly linked to hyperprolactinaemia and only occur as a result of large doses having been taken, are considered clinically insignificant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Content of capsule
Microcrystalline cellulose (E460)
Polyacrylate
Metacrylic acid-ethyl acrylate copolymer (1:1)
Polysorbate 80 (E433)
Sodium laurilsulfate
Talc (E553b)
Colloidal anhydrous silica (E551)

Capsule shell
Gelatine (E441)
Patent Blue V (E131)
Titanium dioxide (E171)
Yellow iron oxide (E172)
Red iron oxide (E172)
Black iron oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

2 years

6.4 Special precautions for storage

Store below 30 º C

6.5 Nature and contents of container

PVDC/TE/PVC//Al blister

Pack sizes:
10, 20, 30, 50, 60, 90 or 100 capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Stichting Registratiebeheer
Locatellikade 1
4076 AZ Amsterdam
The Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1319/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

The date of first authorisation: 10th August 2007.

10 DATE OF REVISION OF THE TEXT

October 2010