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.

Tamsulosin Hydrochloride

1. NAME OF THE MEDICINAL PRODUCT
Tamsulosin 400 micrograms Modified-Release Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 400 micrograms of tamsulosin hydrochloride.
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Modified-release capsule, hard
Orange/olive-green capsule, with the black printed mark “SJ 0.4”
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
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.
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).
The safety and efficacy of tamsulosin in children <18 years have not been established. Currently available data are described in section 5.1.

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.
4.5. Interaction with other medicinal products and other forms of interaction
No interactions have been observed when tamsulosin has been given concomitantly with atenolol, enalapril, 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. 

*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 chlormadinone.

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 
α1-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
See Table.

4.9. Overdose
Acute overdose with 5 mg tamsulosin hydrochloride has been reported. Acute hypotension (systolic blood pressure 70 mm Hg), vomiting and diarrhoea were observed, which were treated with fluid replacement and the patient could be discharged the same day. 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.

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.

<table>
<thead>
<tr>
<th>Nervous system disorders</th>
<th>Common (&gt;1/100, &lt;1/10)</th>
<th>Uncommon (&gt;1/1000, &lt;1/100)</th>
<th>Rare (&gt;1/10000, &lt;1/1000)</th>
<th>Very rare (&lt;1/10000)</th>
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<tbody>
<tr>
<td>Dizziness</td>
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<td>Headache</td>
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<td>Syncope</td>
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<td>Cardiac disorders</td>
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<td>Palpitations</td>
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<td>Vascular disorders</td>
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<td>Orthostatic hypotension</td>
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<td>Gastrointestinal disorders</td>
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<td>Constipation, diarrhoea, nausea, vomiting</td>
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<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Rash, itching, urticaria</td>
<td>Angio-oedema</td>
<td>Stevens-Johnson syndrome</td>
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<td>Reproductive systems and breast disorders</td>
<td>Ejaculation disorders</td>
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<td>General disorders and administration site conditions</td>
<td>Asthenia</td>
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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: α1A adrenoreceptor antagonist. ATC code: G04CA02

Mechanism of action
Tamsulosin binds selectively and competitively to postsynaptic α1A 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.

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 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 Cmax 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 more than 99% bound to plasma proteins and the 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 the dose being present in unchanged form.

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 excipient(s)
Microcrystalline cellulose (Avicel PH101), Eudragit L30D-55, Polysorbate 80, Sodium lauryl sulphate, Sodium lauryl sulphate, Triacetin, Calcium Stearate, Talc
Empty gelatin capsule

6.2. Incompatibilities
Not applicable.

6.3. Shelf life
4 years.

6.4. Special precautions for storage
Blister packs: Store in the original package. Store below 25°C.

6.5 Nature and contents of container
Aluminium / aluminium foil blister packs containing 30 Capsules

6.6. Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER
SAJA Pharmaceuticals
Saudi Arabian Japanese pharmaceutical company limited
Jeddah – Saudi Arabia
Under license from ASTELLAS PHARMA INC
Tokyo-Japan

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8. MARKETING AUTHORISATION NUMBER(S)
2000/370/01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
20/05/1421

10. DATE OF REVISION OF THE TEXT
March 2013