DATA SHEET

1. NAME OF THE MEDICINAL PRODUCT

Omnic 0.4 mg, modified release capsules, hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains as active ingredient tamsulosin hydrochloride 0.4 mg.

Excipient(s): For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Modified release capsule, hard

Orange/olive-green coded 0.4 and logo and 701

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of functional symptoms of benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration

Oral use

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

The capsule should be swallowed whole with a drink of water (about 150ml).

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

Pediatrics population

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

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 hydrochloride 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 Omnic 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 Omnic 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 and glaucoma 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 or glaucoma surgery is scheduled is not recommended.

Discontinuing tamsulosin 1-2 weeks prior to cataract or glaucoma surgery is anecdotally considered helpful, but the benefit and duration of stopping of therapy prior to ~~cataract~~ the surgery has not yet been established. IFIS has also been reported in patients who had discontinued tamsilosin for a longer period prior to the surgery.

During pre-operative assessment, surgeons and ophthalmic teams should consider whether patients scheduled for cataract or 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 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, nifedipine 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.

No interactions at the level of hepatic metabolism have been seen during *in vitro* studies with liver microsomal fractions (representative of the cytochrome P_{450}-linked drug metabolizing enzyme system), involving amitriptyline, salbutamol, glibenclamide and finasteride. Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin.

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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 Fertility, pregnancy and lactation

Omnic 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

Not known (cannot be estimated from the available data)	**Very rare <1/10,000**	**Rare >1/10,000,<1/1000**	**Uncommon >1/1000, <1/100**	**Common >1/100, <1/10**	**System Organ Class**
		syncope	headache	dizziness (1.3%)	Nervous system disorders
Vision blurred * Visual impairment *					Eye disorders
			palpitations		Cardiac disorders
			postural hypotension		Vascular disorders
Epistaxis*			rhinitis		Respiratory, thoracic and mediastinal disorders
Dry mouth*			constipation, diarrhoea, nausea, vomiting		Gastrointestinal disorders
Erythema multiforme* Dermatitis exfoliative*	Stevens-Johnson syndrome	angioedema	rash, pruritus, urticaria		Skin and subcutaneous tissue disorders
	priapism			ejaculation disorders, including retrograde ejaculation and ejaculation failure	Reproductive system and breast disorders
			asthenia		General disorders and administration site conditions

*observed post-marketing

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.

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. 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 the postsynaptic α_1-adrenoceptors, in particular to subtypes α_{1A} and $\alpha_{1D.}$ It brings about relaxation of prostatic and urethral smooth muscle.

Pharmacodynamic effects:
Omnic 0.4 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- adrenoceptor antagonists can reduce blood pressure by lowering peripheral resistance.
No reduction in blood pressure of any clinical significance was observed during studies with Omnic 0.4.

<u>Pediatrics population</u>

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 Omnic 0.4 mg after the usual breakfast. Tamsulosin shows linear kinetics.

After a single dose of Omnic 0.4 mg 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 drug. It is metabolized 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 a dose being present in the form of unchanged active substance.

After a single dose of Omnic 0.4 mg 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.

Tamsulosin (at doses expected to give exposure equivalent to 6 times that seen in man) suppressed mating behaviour and/or ejaculation function in male rats and, as a result, inhibited their fertility.

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

Capsule content: Microcrystalline Cellulose, Methacrylic acid - ethyl acrylate copolymer (1:1), Polysorbate 80, Sodium laurilsulfate, Triacetin, Calcium Stearate, Talc.

Capsule shell: Hard gelatin, Indigotine E132, Titanium dioxide E171, Yellow iron oxide E172, Red iron oxide E172.

6.2 Incompatibilities

Not applicable.

6.3 Special precautions for storage

Store in the original package. Store below *30^{o}C.*

7. MANUFACTURER

Astellas Pharma Europe B.V. The Netherlands

8. IMPORTER

CTS Ltd, 4 Haharash st, Hod Hasharon, Israel