SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Omsula 0.4 mg prolonged-release capsules, hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release capsule, hard contains 0.4 mg tamsulosin hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release capsule, hard.

White or off-white pellets are filled in the capsules with size No. 2 (about 18 mm lengthwise and 6.3 mm in external diameter), which upper part is brown opaque, lower part is buff opaque.

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

Posology
One capsule daily.

Use in renal impairment
No dose adjustment is warranted in renal impairment (see section 4.4).

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

Paediatric population
There is no relevant use of Omsula in the paediatric population.
The safety and efficacy of tamsulosin in children <18 years have not been established. Currently

available data are described in section 5.1.

Method of administration
For oral use. 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 prolonged release of the active substance.

4.3 Contraindications

- Hypersensitivity to the active substance, including drug-induced angioedema 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-adrenoceptor 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 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 hydrochloride. IFIS may increase the risk of eye complications during and after the operation.

Discontinuing tamsulosin hydrochloride 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 the surgery.

The initiation of therapy with tamsulosin hydrochloride in patients for whom cataract or glaucoma surgery is scheduled is not recommended. 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 (e.g. ketoconazole) in patients with poor metaboliser CYP2D6 phenotype.

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

This medicine contains less than 1 mmol sodium (23 mg) per prolonged-release capsule, hard,

that is to say essentially ‘sodium-free’.

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, chlormadinone, 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.

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 (e.g. ketoconazole) in patients with poor metaboliser CYP2D6 phenotype.

Tamsulosin hydrochloride should be used with caution in combination with strong (e.g. ketoconazole) and moderate inhibitors (e.g. erythromycin) 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.

There is a theoretical risk of enhanced hypotensive effect when given concurrently with drugs which may reduce blood pressure, including anaesthetic agents and other α_1-adrenoceptor antagonists.

4.6 Fertility, pregnancy and lactation

Omsula 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 data is available on whether Omsula adversely affects the ability to drive or operate machines. However, in this respect patients should be aware of the fact that drowsiness, blurred vision, dizziness and syncope can occur.

4.8 Undesirable effects

The adverse reactions are described according to the MedDRA system organ class in the table below.

MedDRA System Organ Class	***Common*** *(≥1/100 to <1/10)*	***Uncommon*** *(≥1/1,000 to <1/100)*	***Rare*** *(≥1/10,000 to <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	Angioedema	Stevens-Johnson syndrome	Erythema multiforme*, Dermatitis exfoliative*
Reproductive system and breast disorders	Ejaculation disorders including retrograde ejaculation and ejaculation failure			Priapism	
General disorders and administration site conditions		Asthenia			

*observed post-marketing

As with other alpha-blockers, drowsiness, blurred vision or oedema can occur.

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 Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms
Overdosage with tamsulosin hydrochloride can potentially result in severe hypotensive effects, dizziness and malaise. Severe hypotensive effects have been observed at different levels of overdosing.
Acute overdose with 5 mg of tamsulosin 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.

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: Urologicals, Alpha-adrenoreceptor antagonists (preparations for the exclusive treatment of prostatic disease), ATC code: G04CA02

Mechanism of action
Tamsulosin binds selectively and competitively to the postsynaptic α_1-adrenoceptors, in particular to subtypes α_{1A} and α_{1D}. It brings about relaxation of prostatic and urethral smooth muscle, whereby tension is reduced.

Pharmacodynamic effects
Tamsulosin increases the maximum urinary flow rate by reducing smooth muscle tension in the prostate and urethra, thereby relieving obstruction.

It also improves the complex of irritative and obstructive symptoms in which bladder instability and tension of the smooth muscles of the lower urinary tract play an important role.

These effects on storage and voiding symptoms are maintained during long-term therapy. The need for surgery or catheterisation 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 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 H_2O 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 breakfast or the first meal of the day. 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 and volume of distribution is small (about 0.2 l/kg).

Biotransformation
Tamsulosin has a low first pass effect, being metabolised slowly. Most tamsulosin is present in plasma in the form of unchanged drug. It is metabolised in the liver. In rats, hardly any induction of microsomal liver enzymes was seen to be caused by tamsulosin.

In vitro results suggest that CYP3A4 and also CYP2D6 are involved in metabolism, with possible minor contributions to tamsulosin hydrochloride metabolism by other CYP isozymes. Inhibition of CYP3A4 and CYP2D6 drug metabolizing enzymes may lead to increased exposure to tamsulosin hydrochloride (see Section 4.4 and 4.5).

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

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

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

No dose adjustment is necessary in patients with renal impairment.

5.3 Preclinical safety data

Single and repeat dose toxicity studies were performed in mice, rats and dogs. In addition reproduction toxicity studies were performed 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 alpha-adrenergic blocking agents. 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 hyperprolactinaemia 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) dispersion 30 per cent (including:
polysorbate 80
sodium laurylsulfate)
Talc
Triethyl citrate
Calcium stearate

Capsule shell
Yellow iron oxide (E172)
Black iron oxide (E172)
Red iron oxide (E172)
Titanium dioxide (E171)
Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

30, 90 or 100 capsules are packed into clear or white opaque PVC/PVDC//Aluminium blisters.
The blisters are packed into folding box with a package leaflet.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Gedeon Richter Plc.
Gyömrői út 19-21.
1103 Budapest, Hungary

8 MARKETING AUTHORISATION NUMBER(S)

PL 04854/0134

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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07/01/2021