# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDINICAL PRODUCT

UROMAX® 0.4 mg MR modified release hard gelatin capsule

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active Ingredient:**

Each capsule contains 0.4 mg Tamsulosin Hydrochloride.

**Excipient:**

In each gelatin capsule;

Sodium hydroxide 0.088 mg

For excipients see 6.1.

## 3. PHARMACEUTICAL FORM

Modified release transparent blue hard gelatin capsule.

## 4. CLINICAL PROPERTIES

### 4.1. Therapeutic indications

It is indicated for the treatment of lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH).

### 4.2. Posology and method of administration

**Posology, application frequency and duration:**

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

**Method of Application:**

The capsule should be swallowed whole and not crushed or chewed, as this may affect the altered release of the active substance.

**Additional information on special populations:**

**Kidney failure:**

There is no need for dose adjustment in renal failure.

**Liver failure:**

No dose adjustment is required in mild to moderate hepatic impairment (see section 4.3).

**Pediatric population:**

There is no indication for the use of UROMAX® in children.

**Geriatric population:**

A significant portion of patients treated in tamsulosin clinical studies were 65 years of age or older. In these studies and other reported clinical experience, no overall differences in safety and efficacy were observed between these patients and younger patients, but it cannot be excluded that some older individuals may be more sensitive.

## 4.3. Contraindications

- Hypersensitivity to tamsulosin hydrochloride or any of the excipients, including drug-induced angioedema.
- Orthostatic hypotension history
- Severe liver failure
- Tamsulosin hydrochloride should not be used in combination with strong CYP3A4 inhibitors (e.g. ketoconazole) (see section 4.5).

## 4.4. Special warnings and precautions for use

As with other α1-adrenoceptor antagonists, a decrease in blood pressure may occur in some individuals during UROMAX® treatment; as a result, syncope may rarely occur. When the first signs of orthostatic hypotension (dizziness, weakness) appear, the patient should sit or lie down until the symptoms disappear.

Before starting treatment with UROMAX®, the patient should be examined and the presence of other conditions that may cause the same symptoms caused by benign prostatic hyperplasia should be excluded. Digital rectal examination and, when necessary, prostate-specific antigen (PSA) determination should be performed before treatment and at regular intervals thereafter.

Treatment of patients with severe renal impairment (creatinine clearance below 10 mL/min) should be approached with caution, as there are no studies on these patients.

Intraoperative Floppy Iris Syndrome (IFIS; a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery in some patients who are currently taking or have previously taken tamsulosin hydrochloride. IFIS may increase the risk of eye complications during and after surgery.

There is anecdotal evidence that discontinuing tamsulosin hydrochloride 1-2 weeks before cataract or glaucoma surgery is beneficial; however, the usefulness of discontinuing treatment has not yet been determined. IFIS has also been reported in patients who stopped taking tamsulosin long before surgery.

It is not recommended to initiate tamsulosin hydrochloride therapy in patients scheduled for cataract or glaucoma surgery. During pre-operative evaluation, surgeons and ophthalmology teams should examine whether patients scheduled for cataract or glaucoma surgery are currently or previously treated with tamsulosin and take necessary precautions regarding IFIS treatment during surgery. (see Section 4.5)

Caution should be exercised when using tamsulosin hydrochloride in combination with moderate CYP3A4 inhibitors (e.g. erythromycin).

## 4.5. Interactions with other medicinal products and other forms of interaction

Interaction studies have been conducted only in adults.

No interaction has been observed when tamsulosin hydrochloride was given with atenolol, enalapril or theophylline. Concomitant administration of cimetidine increases plasma tamsulosin levels, while administration of furosemide decreases them; however, in both cases, tamsulosin levels remain within normal limits, so no dose adjustment is necessary.

In vitro, diazepam, propranolol, trichlormethiazide, chlormadinone, amitriptyline, diclofenac, glibenclamide, simvastatin and warfarin do not alter the free fractions of tamsulosin in human plasma. Tamsulosin does not alter the free fractions of diazepam, propranolol, trichlormethiazide and chlormadinone. However, diclofenac and warfarin may increase the rate of elimination of tamsulosin.

Co-administration of tamsulosin hydrochloride with strong CYP3A4 inhibitors may result in increased systemic exposure to tamsulosin hydrochloride. Co-administration with ketoconazole (a known strong CYP3A4 inhibitor) resulted in 2.8- and 2.2-fold increases in AUC and Cmax of tamsulosin hydrochloride, respectively. Because CYP2D6 poor metabolizers cannot be easily identified, and because there is a potential for significant

increase in systemic tamsulosin hydrochloride exposure when tamsulosin hydrochloride is administered with strong CYP3A4 inhibitors in CYP2D6 poor metabolizers, tamsulosin hydrochloride should not be given in combination with strong CYP3A4 inhibitors. Caution should be exercised when using tamsulosin hydrochloride in combination with moderate CYP3A4 inhibitors (erythromycin).

Co-administration of tamsulosin hydrochloride with paroxetine, a strong CYP2D6 inhibitor, resulted in 1.3- and 1.6-fold increases in tamsulosin hydrochloride Cmax and AUC, respectively; however, these increases are not considered to be of clinical significance.

Concomitant administration with other alpha1-adrenoceptor antagonists may lead to hypotensive effects.

**Additional information on special populations**

**Pediatric population:**

No interaction studies have been conducted in the pediatric population.

## 4.6. Pregnancy and Lactation

**Women of childbearing potential/Birth control (Contraception)**

UROMAX® is not indicated for use in women.

**Pregnancy**

UROMAX® is not indicated for use in women.

**Lactation**

UROMAX® is not indicated for use in women.

**Reproductive ability/Fertility**

UROMAX® is not indicated for use in women.

Ejaculation disorders have been observed in short- and long-term clinical studies conducted with tamsulosin. In the post-licensing period, ejaculation disorders, retrograde ejaculation and ejaculation failure events have been reported.

## 4.7. Effects on the ability to drive and use machines

No studies have been conducted on the effects on the ability to drive a car or operate machinery. However, patients should be warned that drowsiness, blurred vision, dizziness and syncope may occur. Patients with such a condition should avoid activities such as driving or operating machinery.

## 4.8. Undesirable effects

The prevalence of the following undesirable effects according to the MedDRA convention is as follows: Very common (≥1/10); 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**

Common: Dizziness (1.3%)

Uncommon: Headache

Rare: Syncope

**Eye diseases**

Unknown: Blurred vision*, visual impairment*

**Cardiac diseases**

Uncommon: Palpitations

**Vascular diseases**

Uncommon: Orthostatic hypotension

**Respiratory, thoracic disorders and mediastinal diseases**

Uncommon: Rhinitis

Unknown: Epistaxis*

**Gastrointestinal diseases**

Uncommon: Constipation, diarrhoea, nausea, vomiting

Unknown: Dry mouth

**Skin and subcutaneous tissue diseases**

Uncommon: Rash, pruritus, urticaria

Rare: Angioedema

Very rare: Stevens-Johnson syndrome

Unknown: Erythma multiforme*, Dermatitis exfoliative*

**Reproductive system and breast diseases**

Common: Ejaculation disorders (including retrograde ejaculation and ejaculation failure)

Very rare: Priapism

**General disorders and diseases related to the application area**

Uncommon: Asthenia

*Side effects seen after marketing

As with other alpha-blockers, dizziness or edema may occur.

In post-marketing surveillance studies, a condition of small pupils known as Intraoperative Floppy Iris Syndrome (IFIS) has been associated with tamsulosin treatment during cataract and glaucoma surgery (see also Section 4.4).

Post-marketing experience: In addition to the adverse events listed above, atrial fibrillation, arrhythmia, tachycardia, and dyspnea have been reported in association with tamsulosin use.

Because these spontaneously reported events relate to post-marketing experience worldwide, the frequency of these events and the role played by tamsulosin in their cause cannot be reliably defined.

## 4.9. Overdose and its treatment

Symptoms:

Tamsulosin hydrochloride overdose may result in potentially severe hypotensive effects. Severe hypotensive effects have been observed in varying degrees of overdose.

Treatment:

If acute hypotension occurs after overdose, cardiovascular support should be provided. Blood pressure and heart rate can return to normal by placing the patient in a supine position. If this measure is not sufficient, volume expanders and, if necessary,

vasopressors can be used. Renal functions should be monitored and general supportive measures taken. Because tamsulosin is so highly bound to plasma proteins, dialysis is unlikely to be helpful.

Precautions such as inducing vomiting can be taken to prevent absorption. When large amounts are ingested, gastric lavage may be performed and activated charcoal, as well as an osmotic laxative such as sodium sulfate, may be administered.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamics properties

Pharmacotherapeutic group : Alpha-adrenoreceptor antagonists

ATC Code : G04CA02 - Preparations used only in prostate disease

Mechanism of action:

Tamsulosin binds selectively and competitively to postsynaptic α1-adrenoreceptors, particularly the α1A and α1D receptor subtypes. It allows the smooth muscles of the prostate and urethra to relax.

Pharmacodynamic effects:

UROMAX® increases the maximum urine flow rate. It relieves obstruction by relaxing the smooth muscles of the prostate and urethra, thus improving urination symptoms.

Tamsulosin also provides improvement in storage symptoms in which bladder instability plays an important role.

These effects on urine storage and urination symptoms are persistent over long-term treatment. The need for surgical intervention or catheterization is significantly delayed.

α1-adrenoreceptor antagonists may also lower blood pressure by reducing peripheral resistance. No clinically significant decreases in blood pressure were observed during studies with UROMAX®.

## 5.2 Pharmacokinetic properties

Absorbation:

Tamsulosin is absorbed from the intestine and has almost complete bioavailability.

The absorption of tamsulosin is reduced by recently eaten meals.

Uniformity of absorption can be achieved by having patients always take UROMAX® after the same meal.

After a single dose of UROMAX® taken under a fed state, tamsulosin plasma concentrations peak at approximately 6 hours. The Cmax level in patients at steady state on the 5th day of multiple dosing is approximately two-thirds higher than that achieved with a single dose. Although this has been seen in elderly patients, the same finding would be expected in young people as well.

There is significant interpatient variation in plasma levels after both single-dose and multiple-dose administration.

Distribution:

Tamsulosin is approximately 99% bound to plasma proteins in humans and has a low volume of distribution (approximately 0.2 L/kg).

Biotransformation:

Tamsulosin has a low first-pass effect and is slowly metabolized.

The majority of tamsulosin is present in plasma in the form of unchanged active substance.

Tamsulosin is metabolized in the liver.

It was observed that liver microsomal enzymes were not induced by tamsulosin in rats.

*In vitro* results suggest that CYP3A4 as well as CYP2D6 are involved in the metabolism of tamsulosin hydrochloride, with other CYP isozymes possibly making minor contributions to metabolism. Inhibition of drug-metabolizing enzymes CYP3A4 and CYP2D6 may result in increased systemic tamsulosin hydrochloride exposure (see sections 4.4 and 4.5).

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

Elimination:

Tamsulosin and its metabolites are excreted mainly in the urine. Approximately 9% of the administered dose is found as unchanged active substance in the urine.

After a single dose of UROMAX® in patients on a fed stomach and at steady state, the elimination half-life was measured to be approximately 10 and 13 hours, respectively.

Linearity/Non-linearity:

Tamsulosin shows linear kinetics.

### 5.3 Preclinical safety data

Single-dose and repeated-dose toxicity studies were conducted in mice, rats and dogs. Additionally, reproductive toxicity in rats, carcinogenicity in mice and rats, and genotoxicity *in vivo* and *in vitro* were also studied.

The overall toxicity profile seen at high doses of tamsulosin is consistent with the known pharmacological effects of α1-adrenoreceptor antagonists.

ECG changes occurred in dogs at very high dose levels. This response is not thought to be of clinical significance. Tamsulosin did not show significant genotoxic properties.

An increased incidence of proliferative changes has been reported in the mammary glands of female rats and mice. These findings, which are probably mediated by hyperprolactinemia and occur only at high doses, are considered to be of no significance.

## 6. PHARMACEUTICAL PROPERTIES

### 6.1 List of Excipients

Microcrystalline cellulose

Purified water

Magnesium stearate

Methacrylic acid-ethyl acrylate copolymer (1:1)

Sodium hydroxide

Triacetin

Talc

Titanium dioxide

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

The shelf life of UROMAX® is 24 months as packaged. This period does not include cases where the packaging has been opened.

**6.4 Special precautions for storage**

It should be stored at room temperature below 25°C, in its original packaging.

**6.5 The nature and content of the packaging**

UROMAX® 0.4 mg MR Modified Release Hard Gelatin Capsule, PVC/PVDC/ Aluminum foil blisters.

In cardboard boxes containing 30 capsules.

**6.6 Disposal of residual human medicinal product material and other special precautions**

No special requirements.

Unused products or waste materials must be disposed of in accordance with the "Control of Medical Waste" and "Control of Packaging and Packaging Waste" regulations.

**7. LICENSE HOLDER**

Drogsan İlaçları San. ve Tic. A.Ş.
Oğuzlar Mah. 1370. Sok 7/3
06520 Balgat- ANKARA

**8. LICENSE NUMBER**

221 / 19

## 9. FIRST LICENSE DATE/LICENSE RENEWAL DATE

First license date: 14.10.2009

License renewal date: 18.02.2015

## 10. RENEWAL DATE OF SPC

14.01.2014