PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1 NAME OF THE MEDICINE
URILOSIN 0,4 modified-release capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains tamsulosin hydrochloride 0,4 mg.
Sugar free.
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Modified-release capsules.
Hard gelatine capsules with orange coloured body and olive coloured cap.
The capsule is filled with white to off-white pellets.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
URILOSIN 0,4 is indicated for the treatment of functional symptoms of benign prostatic hyperplasia (BPH) in adult males. Efficacy in children with neurogenic bladder has not been demonstrated.

4.2 Posology and method of administration
Posology
One capsule daily to be taken after breakfast or the first meal of the day.

Special populations
Renal impairment
No dose adjustment is warranted in renal impairment.
Hepatic impairment
No dose adjustment is warranted in patients with mild to moderate hepatic insufficiency (see section 4.3).
Paediatric population
There is no indication for use of URILOSIN 0,4 in children.
The safety and efficacy of tamsulosin in children < 18 years have not been established.

Method of administration
Oral use.
The capsule should be swallowed whole and must not be crunched or chewed, as this will interfere with the sustained release property of the active ingredient.

4.3 Contraindications
- Hypersensitivity to tamsulosin hydrochloride or to any of the excipients of URILOSIN 0,4 (see section 6.1).
- A history of orthostatic hypotension.
- Severe hepatic insufficiency.
- URILOSIN 0,4 should not be used in combination with strong inhibitors of CYP3A4, e.g. ketoconazole (see section 4.5).

4.4 Special warnings and precautions for use
Orthostatic hypotension
A decrease in blood pressure can take place during therapy with URILOSIN 0,4 as a result of which orthostatic hypotension and 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 URILOSIN 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.

Severe renal impairment
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.

Intraoperative Floppy Iris Syndrome
The "Intraoperative Floppy Iris Syndrome" (IFIS, a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery in some patients previously treated with tamsulosin as in URILOSIN 0,4. IFIS may increase the risk of eye complications during and after the operation. Discontinuing URILOSIN 0,4 one to two 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 eye surgery.

Cataract or glaucoma surgery
The initiation of therapy with URILOSIN 0,4 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 URILOSIN 0,4 in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

Inhibitors of CYP3A4
URILOSIN 0,4 should not be given in combination with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype.
URILOSIN 0,4 should be used with caution in combination with moderate inhibitors of CYP3A4 (see section 4.5).

Cimetidine
URILOSIN 0,4 should be used with caution in combination with cimetidine, particularly at doses higher than 0,4 mg.

Alpha adrenergic blockers
URILOSIN 0,4 should not be used in combination with other alpha-adrenergic blockers. Caution is advised when alpha adrenergic blockers, including URILOSIN 0,4 are co-administered with PDE-5 inhibitors. Both alpha-adrenergic blockers and PDE- inhibitors are vasodilators that can lower blood pressure. Concomitant use of these two medicine classes can potentially cause symptomatic hypotension.

Warfarin
Caution should be exercised with concomitant administration of warfarin and URILOSIN 0,4.

Priapism
URILOSIN 0,4 has been associated with priapism. Because this condition can lead to permanent impotence if not properly treated, patients must be advised about the seriousness of the condition (see Section 4.8).

Screening for prostate cancer
Prostate cancer and BPH frequently co-exist; therefore, patients should be screened for the presence of prostate cancer before treatment with URILOSIN 0,4 and at regular intervals afterwards.

Sulfa allergy
There have been reports of allergic reactions to tamsulosin, as in URILOSIN 0,4 in patients with a sulfa allergy. If a patient reports a serious or life-threatening sulfa allergy, caution is warranted when taking URILOSIN 0,4.

URILOSIN 0,4 is intended for adult male patients only.

4.5 Interaction with other medicines and other forms of interaction
No interactions have been seen when tamsulosin hydrochloride (as in URILOSIN 0,4) 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 in patients with poor metaboliser CYP2D6 phenotype. Tamsulosin hydrochloride should be used with caution in combination with moderate inhibitors 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.
Concurrent administration of other α1-adrenoreceptor antagonists could lead to hypotensive effects.

Paediatric population
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation
URILOSIN 0,4 is not indicated for use in women.

Fertility
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 authorisation 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
a. Summary of the safety profile
The side effects are presented below according to system organ class and with the following frequencies: frequent, less frequent or frequency unknown.

b. Tabulated summary of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Nervous system disorders	Frequent	Dizziness, drowsiness, lethargic
	Less frequent	Headache, syncope, depression, nervousness, sleep disturbances, vertigo, hallucinations, paraesthesia
Eye disorders	Frequency unknown	Vision blurred, visual impairment
Ear and labyrinth disorders	Less frequent	Tinnitus
Endocrine disorders	Less frequent	Diaphoresis
Cardiac disorders	Less frequent	Palpitations, tachycardia
Vascular disorders	Less frequent	Orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Less frequent	Rhinitis, nasal congestion, chest pain, dyspnoea, epistaxis
Gastrointestinal disorders	Less frequent	Constipation, diarrhoea, nausea, vomiting
	Frequency unknown	Dry mouth
Skin and subcutaneous tissue disorders	Less frequent	Rash, pruritus, urticaria, angio-oedema, Stevens-Johnson syndrome, alopecia, arthralgia, lichen planus
	Frequency unknown	Erythema multiforme, dermatitis exfoliative
Renal and urinary disorders	Less frequent	Urinary frequency and incontinence
Reproductive system and breast disorders	Frequent	Ejaculation disorders, retrograde ejaculation, ejaculation failure
	Less frequent	Priapism, impotence
Hepatobiliary disorders	Less frequent	Pancreatitis
General disorders and administration site conditions	Less frequent	Asthenia
Investigations	Less frequent	Abnormal liver enzyme values

c. Description of selected adverse reactions
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, dysrhythmia, 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 medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9 Overdose
Symptoms
Overdosage with URILOSIN 0,4 may result in severe hypotensive effects. Severe hypotensive effects have been observed at different levels of overdosing.
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, activated charcoal and an osmotic laxative, such as sodium sulphate, can be administered.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Category and class: A34 Others.
Pharmacotherapeutic group: α1-adrenoceptor antagonist, ATC code: G04CA02. Preparations for the exclusive treatment of prostatic disease.
Mechanism of action
Tamsulosin binds selectively and competitively to the postsynaptic alpha$_1$-adrenoceptors in particular to the subtype alpha$_{1A}$ and alpha$_{1D}$. It brings about relaxation of the prostatic and urethral smooth muscle.
Pharmacodynamic properties
Tamsulosin increases the maximum urine flow rate. It relieves obstruction by relaxing the smooth muscle in the prostate and urethra.
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 catheterisation is significantly delayed.
Alpha$_1$- blockers can reduce blood pressure by lowering peripheral resistance. Tamsulosin is not intended for use as an antihypertensive medicine.

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 improved by the patient always taking tamsulosin after the same meal. 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 younger patients.
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 medicine. 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 medicine metabolising enzymes may lead to increased exposure to tamsulosin hydrochloride (see section 4.4).
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 the dose being present in the form of unchanged medicine.
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.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Content of capsule
Microcrystalline cellulose
Methacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30 per cent
Polysorbate 80
Sodium laurilsulfate
Triethyl citrate
Talc
Capsule body
Gelatine
Indigo carmine (E 132)
Titanium dioxide (E 171)
Yellow iron oxide (E 172)
Red iron oxide (E 172)
Black iron oxide (E 172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store at or below 25 °C.
Blister packs: Store in the original package.
Containers: Keep the container tightly closed.

6.5 Nature and contents of container
PVC/PE/PVDC/Aluminium blister packs in cardboard boxes and HDPE containers with polypropylene child-resistant closures containing 10, 14, 20, 28, 30, 50, 56, 60, 90, 100 or 200 modified-release capsules. Not all pack sizes may be marketed.

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

7 HOLDER OF CERTIFICATE OF REGISTRATION
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8 REGISTRATION NUMBER
56/34/0989

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
08 October 2024

10 DATE OF REVISION OF THE TEXT
N.A