INSTRUCTION
for medical use of the medicinal product
OMIX

Composition:
active ingredient: tamsulosin hydrochloride;
1 capsule contains 0.4 mg of tamsulosin hydrochloride;
excipients: microcrystalline cellulose, methacrylate copolymer dispersion, hypromellose (hydroxypropyl methylcellulose), propylene glycol, talc, magnesium stearate, sodium laurylsulfate; capsule shell: titanium dioxide (E 171), quinoline yellow (E 104), carmoisine (E 122), ponceau 4R (E 124), gelatine.
Pharmaceutical form. Prolonged-release capsules, hard.
Basic physical and chemical properties: hard-shell gelatine cylinder capsules, with white opaque body and red opaque cap, containing white to off-white granules.
Pharmacotherapeutic group. Drugs used in benign prostatic hypertrophy. α_1-adrenoreceptor antagonists. ATC code G04C A02.
Pharmacological properties.
Pharmacodynamics.
Omix selectively and concurrently blocks postsynaptic α_1-adrenoreceptors, in particular α_{1A} and α_{1D}, present in prostate smooth muscles, neck of urinary bladder and prostatic part of the urethra. This leads to lowering of prostate smooth muscle tone, neck of urinary bladder, prostatic part of the urethra and improvement of urine excretion. At the same time, obstruction and irritation symptoms, associated with benign prostatic hyperplasia, are reduced (difficulty to start urine stream, loosening of urine stream, post-urination dripping, sensation of bladder incomplete emptying, frequent uresiesthesia, nocturnal uresiesthesia, urgent need for urination).
Usually, therapeutic effects develop within 2 weeks after the initiation of administration. These effects are maintained during long-term therapy and significantly postpone surgery or catheterisation.
α_1-adrenoreceptor antagonists can decrease blood pressure by lowering peripheral vascular tone. Tamsulosin at a daily dose of 0.4 mg does not induce clinically significant decrease of blood pressure.
Pharmacokinetics.
Absorption: tamsulosin is well absorbed from gastrointestinal tract and its bioavailability is almost 100 %. Tamsulosin absorption is slower after meals. Homogeneity of absorption is achieved only if patient receives Omix at the same time after meals. Tamsulosin pharmacokinetics is linear.
Following administration of single doses of Omix after meals, tamsulosin peak plasma concentration is achieved after 6 hours and stable concentration is achieved at Day 5 after daily administration. C_{max} is approximately two third higher than the value achieved after administration of a single dose.
Distribution: in men, tamsulosin bounds to plasma proteins by approximately 99 %. Drug distribution volume is not significant (approximately 0.2 L/kg).
Metabolism: tamsulosin hydrochloride does not undergo first-pass metabolism and is slowly metabolized in the liver with the formation of pharmacologically active metabolites which maintain high selectivity to α_1-adrenoreceptors. Major part of the active substance is present in the blood unchanged.
Elimination: tamsulosin and its metabolites are excreted from the body mostly in the urine. Approximately 9 % of the dose remains as unchanged active substance.
Following single administrations of Omix after meals and during stable blood plasma concentration, the half-lives are approximately 10 and 13 hours respectively.

Clinical particulars.

Indications.

Therapy of functional lower urinary tract disorders in benign prostatic hyperplasia.

Contraindications.

Hypersensitivity reactions, including drug-induced angioedema, to tamsulosin hydrochloride or to any of the excipients; history of orthostatic hypotension; severe hepatic impairment.

Interaction with other medicinal products and other forms of interaction.

No interactions have been reported in cases of co-administration of tamsulosin hydrochloride with atenolol, enalapril, or theophylline. Co-administration with cimetidine increases, and with furosemide decreases tamsulosin plasma concentration; however, as far as these levels remain in normal range, special dose adjustment may not be necessary.

During *in vitro* studies, diazepam, propranolol, trichlormethiazide, chlormadinone, amitriptyline, diclofenac, glibenclamide, simvastatin and warfarin have no effect on free tamsulosin fraction in human blood plasma. Similarly tamsulosin does not affect free fraction level of diazepam, propranolol, trichlormethiazide and chlormadinone in human blood plasma.

However, diclofenac and warfarin may increase the rate of elimination of tamsulosin.

Co-administration of tamsulosin hydrochloride with potent CYP3A4 inhibitors can potentiate the effect of tamsulosin hydrochloride. Co-administration with ketoconazole (known potent CYP3A4 inhibitor) resulted in the increase of C_{max} and AUC to 2.2 and 2.8 respectively.

Tamsulosin hydrochloride should not be administered in combination with potent CYP3A4 inhibitors in patients with low CYP2D6 metabolism.

Tamsulosin hydrochloride should be used with caution in combination with potent and moderate CYP3A4 inhibitors.

Concomitant administration of tamsulosin hydrochloride and paroxetine (potent CYP2D6 inhibitor) leads to the increase of C_{max} and AUC to 1.3 and 1.6 respectively, however it is not clinically significant.

Co-administration with other α_1-adrenoblockers may potentiate hypotensive effect.

Special warnings and precautions for use.

As with other α_1-adrenoblockers, in some cases of Omix administration, the drug may decrease blood pressure, sometimes resulting in loss of consciousness. When first signs of orthostatic hypotension appear (dizziness, weakness), the patient should take supine position until above mentioned symptoms resolve.

Before starting therapy with the drug, patients should undergo medical examination to determine other co-morbidities which are able to induce symptoms similar to benign prostatic hyperplasia. Prior to therapy, a rectal examination of prostate gland should be conducted and, if necessary, prostate-specific antigen test (PSA) should be done before initiation of therapy and at regular intervals during treatment.

Caution should be exercised when prescribing to patients with severe renal insufficiency (creatinine clearance – <10 ml / min), as no clinical studies have been performed with tamsulosin hydrochloride in such patients.

In some patients who received or receive tamsulosin during cataract and glaucoma surgery intraoperative floppy iris syndrome (IFIS, variant of constricted pupil syndrome) was reported, which can increase the incidence of complications during the surgery.

Usually, 1-2 weeks prior to surgical removal of cataract and glaucoma, tamsulosin should be discontinued, however, therapeutic effectiveness of tamsulosin discontinuation is not well established yet. The atonic pupil syndrome was also reported in patients who stopped tamsulosin long time before surgery for cataracts.

In patients before elective surgery for cataract or glaucoma, tamsulosin hydrochloride should not be initiated. When preparing for surgery, surgeons and ophthalmologists should find out whether the patient has been taking (or is taking) tamsulosin in order to prevent possible complications associated with IFIS.

Tamsulosin hydrochloride should not be administered concomitantly with potent CYP3A4 inhibitors to the patients who are poor CYP2D6 metabolizers.
Tamsulosin hydrochloride should be used with caution in combination with potent and moderate CYP3A4 inhibitors (see Section "Interaction with other medicinal products and other forms of interaction").
There have been reports of allergic reactions to tamsulosin in patients with a history of allergy to sulfonamides. Caution should be exercised when using tamsulosin hydrochloride in patients who have previously been allergic to sulfonamides.

Pregnancy and lactation.

Omix is not indicated to treat female patients.

Fertility.

During clinical studies of short and long-term administration of tamsulosin there were reports of ejaculation impairment. Cases of ejaculation impairment, retrograde ejaculation and inadequate ejaculation were noted during post-marketing period.

Effect on ability to drive and use machines.

Effect on ability to drive and use machines has not been studied. However patients should be aware of possible dizziness.

Dosage and administration.

Recommended dose for adults – 1 capsule once daily after breakfast or after the first meal. The capsule should be swallowed whole without breaking or chewing, as this will interfere with the modified release of the active ingredient.
Patients with renal insufficiency do not need dose adjustment. Patients with mild to moderate hepatic impairment do not need dose adjustment (see also "Contraindications").

Paediatric population.

The drug is not indicated to treat children.
The safety and efficacy of tamsulosin in children has not been evaluated.

Overdose.

Symptoms.

An overdose of tamsulosin hydrochloride may cause severe hypotensive effects. Severe hypotensive effects were noted at various degrees of overdose.

Treatment.

If sudden drop in blood pressure occurs due to overdose, maintenance therapy aimed at restoring of cardiovascular function (for example, a patient should take supine position) should be used. Should this measure be deemed ineffective, an infusion therapy is conducted and vasopressor agents are administered. Renal function monitoring and general maintenance therapy are required. Due to high tamsulosin's binding to blood plasma proteins, haemodialysis is hardly reasonable.
Vomiting can be manually induced to stop further drug absorption. During overdose with considerable amount of drug, the patient should undergo gastric lavage using activated charcoal and low osmotic cathartic agents, such as sodium sulfate.

Undesirable effects.

CNS disorders: dizziness, headache, syncope.
Eye disorders: blurred vision*, impaired vision.*
Cardiovascular disorders: palpitations, orthostatic hypotension.
Respiratory disorders: rhinitis, nose bleeding.*
Gastrointestinal disorders: constipations, diarrhoea, nausea, vomiting.
Skin and subcutaneous tissue disorders: rash, itching, urticaria, angioedema, Stevens–Johnson syndrome, erythema multiforme*, exfoliative dermatitis*.
Reproductive system disorders: ejaculation impairment, including retrograde ejaculation and inadequate ejaculation.
General disorders: asthenia.

* - were observed during post-registration period.
Cases of intraoperative floppy iris syndrome (constricted pupil syndrome) during post-operative period after cataract and glaucoma surgery were reported in patients who received tamsulosin (see Section "Special warnings and precautions for use").
Post-marketing experience: in addition to the above-mentioned adverse reactions, cases of atrial fibrillation, arrhythmia, tachycardia and dyspnoea have been reported. As these cases were reported spontaneously, the frequency of reports and the role of tamsulosin in those cases cannot be reliably established.
Colorants carmoisine (E 122) and ponceau 4R (E 124), which are part of the capsule shell, can cause allergic reactions.
Shelf-life. 3 years.
Storage.
Store in the original packaging below 30 ^{0}C. Keep away from children.
Package.
10 capsules in a blister. 1 or 3 blisters in a cardboard pack.
Prescription status.
℞.
Manufacturer / applicant.
Group of Pharmaceutical Companies "Lekhim"
Private Joint Stock Company "Technolog"
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