Avozaq SR 0,4 mg
Pharma Dynamics (Pty) Ltd

Each hard gelatin capsule contains 0,40 mg tamsulosin hydrochloride.

Clinical Approved: 07 February 2025

Registration Approval: 03 June 2025

APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

AVOZAQ SR 0,4 mg hard gelatin capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains 0,40 mg tamsulosin hydrochloride.

AVOZAQ SR 0,4 mg capsules are sugar free

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Sustained-release hard gelatin capsule, with an orange body and olive cap containing white to off white pellets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AVOZAQ SR 0,4 mg 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.

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4.2 Posology and method of administration

Posology

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

Special populations

Renal impairment

No dose adjustment is warranted in renal impairment.

Hepatic impairment

In patients with mild to moderate hepatic insufficiency, no dose adjustment is warranted (see section 4.3).

Paediatric population

AVOZAQ SR 0,4 mg is not indicated in children.

The safety and efficacy of tamsulosin hydrochloride in children under the age of 18 have not been established.

Method of administration

AVOZAQ SR 0,4 mg is to be taken orally, swallowed whole, without crushing or chewing, as this will affect the sustained release properties of the active ingredient.

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4.3 Contraindications

- hypersensitivity to tamsulosin hydrochloride or to any of the ingredients of AVOZAQ SR 0,4 mg (see section 6.1)
- patients with a history of orthostatic hypotension
- patients with hepatic insufficiency
- combination therapy with strong inhibitors of CYP3A4 such as ketoconazole (see section 4.5)

4.4 Special warnings and precautions for use

A decrease in blood pressure can occur in individual cases during AVOZAQ SR 0,4 mg therapy, 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.

Prior to initiating therapy with AVOZAQ SR 0,4 mg, 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 with AVOZAQ SR 0,4 mg and at regular intervals afterwards.

Treatment should be approached with caution in patients with severe renal impairment (creatinine clearance of <10 mL/min), as this patient group has not been studied.

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In some patients previously treated with tamsulosin as in AVOZAQ SR 0,4 mg, the “Intraoperative Floppy Iris Syndrome” (IFIS, a variant of small pupil syndrome) has been observed during cataract and glaucoma surgery. IFIS may increase the risk of eye complications during and after the operation. Although the discontinuation of AVOZAQ SR 0,4 mg 1 to 2 weeks prior to cataract or glaucoma surgery is anecdotally considered helpful, the benefit of treatment discontinuation has not yet been established as IFIS has also been reported in patients who had discontinued AVOZAQ SR 0,4 mg for a longer period prior to eye surgery.

In patients for whom cataract or glaucoma surgery is scheduled, initiation of therapy with AVOZAQ SR 0,4 mg 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 AVOZAQ SR 0,4 mg in order to ensure that appropriate measures will be in place to manage the IFIS during surgery.

Combination therapy with strong inhibitors of CYP3A4 in patients with poor metaboliser CYP2D6 phenotype, is not recommended.

Caution is recommended when AVOZAQ SR 0,4 mg is taken in combination with strong and moderate inhibitors of CYP3A4 (see section 4.5).

AVOZAQ SR 0,4 mg is intended for adult male patients only.

Priapism

Tamsulosin has been associated with priapism (persistent painful penile erection unrelated to sexual activity). Because this condition can lead to permanent impotence if not properly treated, patients must be advised about the seriousness of the condition.

Sulphur Allergy

In patients with sulphur allergy, allergic reaction to tamsulosin as in AVOZAQ SR 0,4 mg has been rarely reported. If a patient reports a serious or life-threatening sulphur allergy, caution is warranted when administering AVOZAQ SR 0,4 mg capsules.

4.5 Interaction with other medicines and other forms of interaction

No interactions have been seen when tamsulosin as in AVOZAQ SR 0,4 mg was given concomitantly with either atenolol, enalapril, nifedipine, digoxin or theophylline.

When AVOZAQ SR 0,4 mg is taken concomitantly with cimetidine, a rise in plasma levels of tamsulosin occur.

In vitro, neither diazepam, propranolol, trichlormethiazide, chlormadinone, amitriptyline, diclofenac, glibenclamide, simvastatin or warfarin change the free fraction of tamsulosin in human plasma. Tamsulosin does not change the free fractions of diazepam, propranolol, trichlormethiazide and chlormadinone.

Diclofenac and warfarin, however, may increase the elimination rate of tamsulosin, as in AVOZAQ SR 0,4 mg. A definitive medicine interaction study between tamsulosin hydrochloride and warfarin was not conducted. Results from limited *in vitro* and *in vivo* studies are inconclusive. Caution should be exercised with concomitant administration of warfarin and AVOZAQ SR 0,4 mg capsules.

Concomitant administration of AVOZAQ SR 0,4 mg 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. Since CYP2D6 poor metabolisers cannot be readily identified and the potential for significant increase in tamsulosin hydrochloride exposure exists when AVOZAQ SR 0,4 mg is co-administered with strong CYP3A4 inhibitors in CYP2D6 poor metabolisers, AVOZAQ SR 0,4 mg should not be given in combination with strong inhibitors of CYP3A4 (see section 4.3). AVOZAQ SR 0,4 mg should be given with caution in combination with moderate inhibitors of CYP3A4.

AVOZAQ SR 0,4 mg capsules should be used with caution in combination with moderate inhibitors of CYP3A4 (e.g., erythromycin).

Concomitant administration of AVOZAQ SR 0,4 mg with paroxetine, a strong inhibitor of CYP2D6, resulted in an increased C_{max} and AUC by a factor of 1,3 and 1,6, respectively. These increases are not considered clinically relevant.

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Other Alpha Adrenergic Blocking medicines

Concurrent administration of other alpha$_1$-adrenoceptor antagonists could lead to hypotensive effects.

The pharmacokinetic and pharmacodynamic interactions between AVOZAQ SR 0,4 mg and other alpha adrenergic blocking medicines have not been determined; however, interactions between AVOZAQ SR 0,4 mg capsules and other alpha adrenergic blocking agents may be expected.

PDE5 Inhibitors

Caution is advised when alpha adrenergic blocking medicines including AVOZAQ SR 0,4 mg are co-administered with PDE5 inhibitors. Alpha-adrenergic blockers and PDE5 inhibitors are both vasodilators that can lower blood pressure. Concomitant use of these two medicine classes can potentially cause symptomatic hypotension.

Furosemide

AVOZAQ SR 0,4 mg had no effect on the pharmacodynamics (excretion of electrolytes) of furosemide. While furosemide produced an 11 % to 12 % reduction in tamsulosin hydrochloride C_{max} and AUC, these changes are expected to be clinically insignificant and do not require adjustment of the dosage. Concomitant use with furosemide brings about a fall, but as levels remains within the normal range dosages need not to be changed.

4.6 Fertility, pregnancy, and lactation

AVOZAQ SR 0,4 mg is not indicated for use in women.

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Fertility

Ejaculation disorders have been observed in short- and long-term clinical studies with tamsulosin, as in AVOZAQ SR 0,4 mg. Events of ejaculation disorder, retrograde ejaculation and ejaculation failure may occur.

4.7 Effects on ability to drive and use machines:

No data is available on whether AVOZAQ SR 0,4 mg adversely affects the ability to drive or operate machinery. However, patients should be aware of the fact that dizziness, blurred vision, visual impairment, or Intraoperative Floppy Iris Syndrome (IFIS) may occur and should not engage in these activities until they know how AVOZAQ SR 0,4 mg affects them.

4.8 Undesirable effects

a). Tabulated summary of adverse reactions

System Organ Class	**Frequency**	**Side effects**
Nervous system disorders	Frequent Less frequent	Dizziness, somnolence, insomnia Headache, syncope
Eye disorders	Frequency unknown	Blurred vision, visual impairment, intraoperative floppy iris syndrome (IFIS)
Cardiac disorders	Less frequent Frequency unknown	Palpitations Atrial fibrillation, dysrhythmia, tachycardia

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Vascular disorders	Less frequent	Orthostatic hypotension
Respiratory, thoracic, and mediastinal disorders	Less frequent Frequency unknown	Rhinitis, pharyngitis, cough increased, sinusitis Epistaxis, dyspnoea
Gastrointestinal disorders	Less frequent Frequency unknown	Constipation, diarrhoea, nausea, vomiting, tooth disorder Dry mouth
Skin and subcutaneous tissue disorders	Less frequent Frequency unknown	Rash, pruritus, urticaria, angioedema, Stevens-Johnson Syndrome Erythema multiforme, exfoliative dermatitis, skin desquamation
Reproductive system and breast disorders	Frequent Less frequent	Ejaculation disorders, retrograde ejaculation, ejaculation failure, libido decreased Priapism
General disorders and administrative site conditions	Less frequent	Asthenia, infection, back pain, chest pain

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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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
By reporting side effects, you can help provide more information on the safety of AVOZAQ 0,4 mg SR. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za, to ensure safety of the product.

4.9 OVERDOSE

Signs and symptoms:

Overdosage with AVOZAQ SR 0,4 mg may result in severe hypotensive effects. Severe hypotensive effects have been observed at different levels of overdosing. The highest dose of tamsulosin as in AVOZAQ SR 0,4 mg accidentally given to a single patient was 12 mg, resulting in headache but not requiring hospitalisation.

Management of overdose:

Cardiovascular support should be given in cases of acute hypotension occurring after overdosage. By lying the patient down, blood pressure can be restored, and heart rate brought back to normal. 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

Pharmacotherapeutic group: Urologicals: Drugs used in benign prostatic hypertrophy.

ATC code: G04CA02.

Pharmacological classification: A 34 Other

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 and an improvement of the urinary flow.

Pharmacodynamic effects

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 0,4 mg capsule after the same meal. After a single dose of tamsulosin 0,4 mg capsule taken after a meal, plasma levels of tamsulosin peak at around 6 hours. 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 males, tamsulosin is about 99 % bound to plasma proteins and volume distribution is small (about 0,21 L/kg).

Biotransformation

Tamsulosin has a low first pass effect, being metabolised 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 parent compound.

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Elimination

Tamsulosin and its metabolites are mainly excreted in the urine with about 9 % of a dose being present in the form of unchanged medicine. The elimination half-life after a single dose is about 10 hours. The elimination half-life in the steady state is about 13 hours. The lowering of the dose in renal impairment is not warranted.

Linearity/non-linearity

Kinetics of tamsulosin is linear.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium stearate

Colloidal hydrous silica

Dibutyl sebacate

Microcrystalline cellulose

Metacrylic acid – ethyl acrylate copolymer dispersion (methacrylic acid, ethyl acrylate copolymer, sodium lauryl sulfate, polysorbate)

Polysorbate 80

Capsules

Black iron oxide

Gelatin

Indigotine – FD&C Blue 2

Titanium dioxide

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Red iron oxide

Yellow iron oxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C in a cool, dry place

Keep blister strips in outer carton until required for use.

6.5 Nature and contents of container

Capsules are packed into PVC/PVDC – Aluminium blisters consisting of 10 or 15 capsules per blisters. These blisters are packed into an outer carton with a leaflet.

Pack sizes: 10, 20, 30, 50, 90, 100 capsules*.

* Not all pack sizes will be marketed.

6.6 Special precautions for disposal

No special precautions.

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7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

Tel: + 27 21 707 7000

or 0860-PHARMA (742 762)

8. REGISTRATION NUMBER

57/34/0289

9. DATE OF FIRST AUTHORISATION

03 June 2025