

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Alfuzosin HCl 2.5 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 2.5 mg alfuzosin hydrochloride.

Excipient with known effect:

Each film-coated tablet contains 61.05 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet

White to off-white round, biconvex, film-coated tablets debossed with 'X' on one side and '31' on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of the functional symptoms of benign prostatic hyperplasia (BPH).

4.2 Posology and method of administration

Posology

Adults

The usual dose is one tablet three times daily. The dose may be increased to a maximum of 4 tablets (10 mg) per day depending on the clinical response.

Elderly and treated hypertensive patients

As a routine precaution when prescribing alfuzosin to elderly patients (aged over 65 years) and the treated hypertensive patient, the initial dose should be 1 tablet in the morning and 1 tablet in the evening.

Renal impairment

In patients with renal insufficiency, as a precaution, it is recommended that the dosing be started at Alfuzosin HCl 2.5mg twice daily adjusted according to clinical response.

Hepatic impairment

In patients with mild to moderate hepatic insufficiency, it is recommended that therapy should commence with a single dose of Alfuzosin HCl 2.5 mg Tablets/day to be increased to Alfuzosin HCl 2.5 mg Tablets twice daily according to clinical response.

Alfuzosin HCl 2.5 mg tablets are contraindicated in patients with severe hepatic insufficiency (see section 4.3).

Paediatric population:

Efficacy of alfuzosin has not been demonstrated in children aged 2 to 16 years (see section 5.1). Therefore, alfuzosin is not indicated for use in paediatric population.

Method of administration

Alfuzosin HCl 2.5 mg film-coated tablets should be swallowed whole. The first dose should be given just before bedtime.

4.3 Contraindications

- Hypersensitivity to the active substance alfuzosin, another quinazolines (eg: terazosine, doxazosine) or to any of the excipients.
- History of orthostatic hypotension.
- Combination with other alfa1-blockers and / or dopamine receptor agonists.
- Severe hepatic insufficiency

4.4 Special warnings and precautions for use

Blood pressure should be monitored at the start of treatment. A reduction in blood pressure may arise in individual cases.

Alfuzosin HCl should be given with caution to patients who are on antihypertensive medication or nitrates.

In some subjects postural hypotension may develop, with or without symptom (dizziness, fatigue, sweating) within a few hours following administration. These effects are transient, occur in the beginning of treatment and do not usually prevent the continuation of treatment.

Pronounced drop in blood pressure has been reported in post-marketing surveillance in patients with pre-existing risk factors (such as underlying cardiac diseases and/or concomitant treatment with anti-hypertensive medication). The risk of developing hypotension and related adverse reactions may be greater in elderly patients (see section 4.8). The patient should be warned of the possible occurrence of such events.

In cases of orthostatic hypotension the patient should lie or sit down until the symptoms have disappeared.

Care should be taken when alfuzosin is administered to patients who have had a pronounced hypotensive response to another alpha-1-blocker.

In coronary patients, the specific treatment for coronary insufficiency should be continued. If angina pectoris reappears or worsens, alfuzosin should be discontinued.

As with all alpha-1-blockers, alfuzosin should be used with caution in patients with acute cardiac failure.

- lung oedema due to mitral or tricuspidal stenosis,
- high output cardiac failure,
- cardiac failure due to pulmonary embolism or pericardial effusion

Patients with congenital QTc prolongation, with a known history of acquired QTc prolongation or who are taking drugs known to increase the QTc interval should be evaluated before and during the administration of alfuzosin

The patient should be examined prior to treatment with alfuzosin to exclude other conditions, which may cause the same symptoms as benign prostatic hyperplasia. A digital rectal examination should be performed prior to treatment and regularly during treatment. A prostate specific antigen (PSA) test should also be carried out if required.

Concomitant use of alfuzosin and potent CYP3A4 inhibitors (such as itraconazole, ketoconazole, protease inhibitors, clarithromycin, telithromycin and nefazodone) should be avoided (see section 4.5). Alfuzosin should not be used concomitantly with CYP3A4 inhibitors that are known to increase the QTc interval (e.g. itraconazole and clarithromycin) and a temporary interruption of alfuzosin treatment is recommended if treatment with such medicinal products is initiated.

The 'Intraoperative Floppy Iris Syndrome' (IFIS, a variant of small pupil syndrome) has been observed during cataract surgery in some patients on or previously treated with tamsulosin. Isolated reports have also been received with other alpha-1 blockers and the possibility of a class effect cannot be excluded. As IFIS may lead to increased procedural complications during the cataract operation current or past use of alpha-1 blockers should be made known to the ophthalmic surgeon in advance of surgery.

Alfuzosin, like other alpha adrenergic antagonist, has been associated with priapism (persistent painful penile erection unrelated to sexual activity; see section 4.8). Because this condition can lead to permanent impotence if not properly treated, patients should be advised to seek immediate assistance in the event of an erection that persists longer than 4 hours.

Alfuzosin should not be used in patients suffering from incontinence due to overflow, anuria or prolonged renal insufficiency.

Alfuzosin HCl contains lactose

Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Patients should be warned that the tablet should be swallowed whole. Any other mode of administration, such as crunching, crushing, chewing, grinding or pounding to powder should be prohibited. These actions may lead to inappropriate release and absorption of the drug and therefore possible early adverse reactions.

Alfuzosin HCl Contains sodium:

This medicinal product contains less than 1 mmol (23 mg) of sodium per tablet, that is to say it is essentially 'sodium-free.'

4.5 Interaction with other medicinal products and other forms of interaction

Combinations contra-indicated:

- Alpha1-receptor blockers (see section 4.3).

Concomitant use not recommended:

- Potent CYP3A4 inhibitors such as itraconazole, ketoconazole, protease inhibitors, clarithromycin, telithromycin and nefazodone since alfuzosin blood levels may be increased (see section 4.4)

Combinations to be taken into account:

- Antihypertensive drugs (see section 4.4)
- Nitrates (see section 4.4)
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The administration of general anaesthetics to patients receiving Alfuzosin HCl 2.5mg film-coated tablets could cause profound hypotension. It is recommended that Alfuzosin HCl 2.5mg Tablets be withdrawn 24 hours before surgery.

No pharmacokinetic interaction has been observed in healthy volunteers between alfuzosin and the following drugs: warfarin and digoxin,

4.6 Fertility, Pregnancy and lactation

This section is not applicable given the therapeutic indications.

4.7 Effects on ability to drive and use machines

No data are available concerning the effect on ability to drive or use machines. Side-effects such as, vertigo, dizziness or asthenia may occur, in particular, at the start of treatment. This should be taken into consideration when driving vehicles or using machines.

4.8 Undesirable effects

Tabulated list of adverse reactions

The adverse reactions considered at least possibly related to treatment are listed below by body system organ class and absolute frequency. Frequencies are defined as very common ($\geq 1/10$); common ($>1/100$ to $<1/10$); uncommon ($>1/10000$ to $\leq 1/1000$); very rare ($\leq 1/10000$), not known (cannot be estimated from the available data).

System Organ Class	Frequency			
	Common	Uncommon	Very rare	Not Known (Cannot be estimated from the available data)

Blood and lymphatic system disorders				Neutropenia thrombocytopenia
Nervous system disorders	Faintness/ dizziness, headache, vertigo	Syncope, drowsiness		
Eye disorders		vision abnormal		Intraoperative floppy iris syndrome
Cardiac disorders		tachycardia, palpitations,	Angina pectoris in patients with pre-existing coronary artery disease	Atrial fibrillation
Vascular disorders	Hypotension (postural)	Flushing		
Respiratory, thoracic and medicinal disorders		rhinitis		
Gastrointestinal disorders	nausea, abdominal pain, diarrhoea, dry mouth			vomiting
Hepatobiliary disorders			hepatotoxicity	Hepatocellular injury, cholestatic liver disease
Reproductive system and breast disorders				Priapism
Skin and subcutaneous tissue disorders		rashe pruritus,	urticaria, angioedema	
General disorders and administration site conditions	Asthenia, malaise	Oedema, chest pain		

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

4.9 Overdose

In case of overdosage, the patient should be hospitalised, kept in the supine position, and conventional treatment of hypotension should take place. In case of significant hypotension, the appropriate corrective treatment may be a vasoconstrictor that acts directly on vascular muscle fibres. Alfuzosin is not easily dialysable because of its high degree of protein binding. Gastric lavage is a possibility followed by administration of activated carbon and a laxative.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: alpha adrenoreceptor antagonists
ATC code: G04CA01

Alfuzosin is an orally active quinazoline derivative. It is a selective, peripherally acting antagonist of post synaptic alfa1-adrenoceptors.

In vitro pharmacological studies have documented the selectivity of alfuzosin for the alpha1-adrenoceptors located in the prostate, bladder base and prostatic urethra.

Clinical manifestations of Benign Prostatic Hypertrophy are associated with infra vesical obstruction which is triggered by both anatomical (static) and functional (dynamic) factors. The functional component of obstruction arises from the tension of prostatic smooth muscle which is mediated by α -adrenoceptors. Activation of alfa1-adrenoceptors stimulates smooth muscle contraction, thereby increasing the tone of the prostate, prostatic capsule, prostatic urethra and bladder base, and, consequently, increasing the resistance to bladder outflow. This in turn leads to outflow obstruction and possible secondary bladder instability.

Alpha-blockade decreases infra vesical obstruction via a direct action on prostatic smooth muscle.

In vivo, animal studies have shown that alfuzosin decreases urethral pressure and therefore, resistance to urine flow during micturition. Moreover, alfuzosin

inhibits the hypertonic response of the urethra more readily than that of vascular muscle and shows functional uroselectivity in conscious normotensive rats by decreasing urethral pressure at doses that do not affect blood pressure.

In man, alfuzosin improves voiding parameters by reducing urethral tone and bladder outlet resistance, and facilitates bladder emptying.

In placebo controlled studies in BPH patients, alfuzosin significantly increases peak flow rate (Q_{\max}) in patients with $Q_{\max} \leq 15\text{ml/s}$ by a mean of 30%. This improvement is observed from the first dose, significantly reduces the detrusor pressure and increases the volume producing a strong desire to void, significantly reduces the residual urine volume.

These favourable urodynamic effects lead to an improvement of lower urinary tract symptoms ie. filling (irritative) as well as voiding (obstructive) symptoms.

Paediatric population

Alfuzosin is not indicated for use in the paediatric population (see section 4.2). Efficacy of alfuzosin hydrochloride was not demonstrated in the two studies conducted in 197 patients 2 to 16 years of age with elevated detrusor leak point pressure ($LPP \geq 40\text{ cm H}_2\text{O}$) of neurologic origin. Patients were treated with alfuzosin hydrochloride 0.1 mg/kg/day or 0.2 mg/kg/day using adapted paediatric formulations.

5.2 Pharmacokinetic properties

Alfuzosin HCl 2.5mg Tablets are well absorbed with a mean bioavailability of 64%, peak plasma levels are generally reached in 0.5-6 hours. The kinetics are linear within the therapeutic dosage. The kinetic profile is characterised by large inter-individual variations in plasma concentrations. The half-life is 3 – 5 hours. The plasma-protein binding of alfuzosin is approximately 90%. Alfuzosin is metabolised by the liver and is primarily excreted in urine and faeces. None of the metabolites found in humans has a pharmacodynamic action. The pharmacokinetic profile is not influenced by concurrent ingestion of food.

Absorption in patients older than 75 years is more rapid and plasma levels are higher. Biological availability may be higher, while for some patients the distribution volume is reduced. The elimination half-life remains unchanged. The distribution volume and metabolic clearance of alfuzosin is increased with renal insufficiency through an increase of the free fraction. Chronic renal insufficiency, even where this is severe (creatinine clearance between 15 and 40 ml/minute) is not negatively influenced by alfuzosin.

A twofold increase of C_{\max} levels and a threefold increase in the AUC have been observed in patients with severe hepatic insufficiency. The biological availability is increased in comparison with healthy volunteers. The pharmacokinetic profile of alfuzosin is not influenced by chronic cardiac insufficiency.

Metabolic interactions: CYP3A4 is the principal hepatic enzyme isoform involved in the metabolism of alfuzosin (see section 4.5)

5.3 Preclinical safety data

In vitro, alfuzosin prolonged the action potential duration and QT interval duration at a clinically relevant concentration.
No other data of therapeutic relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Sodium starch glycolate (Type A)

Cellulose microcrystalline

Lactose monohydrate

Povidone

Magnesium stearate

Coating:

Hypromellose

Macrogol 400

Titanium dioxide (E 171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions

6.5 Nature and contents of container

Alfuzosin HCl is packed in PVC / PVdC- Aluminium foil blister packs or (HDPE) bottle packs with polypropylene closure.

Pack sizes:

Blister pack: 15, 30, 50, 60, 90 and 100 film-coated tablets

Bottle pack: 100, 250 and 1000 film-coated tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Milpharm Limited
1 Roundwood Avenue,
Stockley Park,
Uxbridge,
UB11 1AF
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 16363/0300

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/12/2024

10 DATE OF REVISION OF THE TEXT

14/04/2026