SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fuzatal® XL 10mg prolonged release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged release tablet contains 10 mg of alfuzosin hydrochloride

Excipient with known effect:
Each tablet contains 8 mg of lactose monohydrate.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged release tablet.

White, round, bevelled-edges tablets.

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

Adults
The recommended dose is one 10 mg tablet daily to be taken after a meal.

Renal impairment
In patients with mild to moderate renal impairment (creatinine clearance > 30 ml/min), it is recommended to start treatment with a lower dose, to be increased to 10 mg depending on clinical response.

Alfuzosin 10 mg prolonged-release tablets should not be given to patients with severely impaired renal function (creatinine clearance < 30 ml/min) as there are no clinical safety data available for this patient group (see section 4.4).

Hepatic impairment
In patients with mild to moderate hepatic impairment, it is recommended not to use Alfuzosin 10 mg prolonged release tablets. After careful medical consideration, a preparation containing a lower dose of alfuzosin hydrochloride might be considered appropriate.

Alfuzosin given as 10 mg prolonged release tablets are contraindicated in patients with severe hepatic impairment (see section 4.3).
Alfuzosin 10 mg prolonged release tablets must not be divided to achieve lower dose in patients with mild to moderate hepatic impairment. Preparations containing a lower dosage should be used. Refer to the corresponding product information for dosing instructions.

Paediatric population

The efficacy of alfuzosin has not been demonstrated in children aged 2 to 16 years (see section 5.1).Therefore, alfuzosin 10 mg prolonged release tablets is not indicated for use in the paediatric population.There is no relevant indication for use of Alfuzosine 10 mg prolonged release tablets in children.
Method of administration
Oral adminstration.
The prolonged-release tablet should be swallowed whole with a sufficient amount of fluid (e.g. a glass of water). The tablets must not be crushed, chewed or divided (see section 4.4).

The first dose should be taken at bedtime. The prolonged-release tablet 10 mg should be taken immediately after the same meal each day.

4.3 Contraindications

- Hypersensitivity to alfuzosin, other quinazolines (e.g. terazosin, doxazosin) or any of the excipients listed in section 6.1;
- History of orthostatic hypotension;
- Severe hepatic impairment;
- Combination with other alpha1-blockers (see section 4.5).

4.4 Special warnings and precautions for use

- The patient should be examined before commencement of therapy with alfuzosin to exclude the presence of other conditions that can produce similar symptoms to those of BPH.
- Alfuzosin 10 mg should not be administered to patients with severely impaired renal function (creatinine clearance < 30 ml/min) as there are no clinical safety data available for this patient group.
- Alfuzosin should be given with caution to patients treated with antihypertensive medicinal products or nitrates. Blood pressure should be monitored regularly, especially at the beginning of treatment.
- In some subjects postural hypotension may develop, with or without symptoms (dizziness, fatigue, sweating) within a few hours following administration. These effects are usually transient occur at the beginning of treatment and do not usually prevent the continuation of treatment. In such cases, the patient should lie down until the symptoms have completely disappeared.
- .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). Caution should be exercised when prescribing alfuzosin to elderly patients. The patient should be warned of the possible occurrence of such events.

- Caution should be exercised when alfuzosin is administered to patients who have responded with pronounced hypotension to other alpha1-blockers.
- Treatment should be initiated gradually in patients with hypersensitivity to other α1-receptor blockers.
- As with all α1-receptor blockers, alfuzosin should be used with caution in patients with acute cardiac failure.
- In cardiac patients the treatment of coronary insufficiency should continue taking into account that the concomitant administration of nitrates and alfuzosin may increase the risk of occurrence of hypotension. Alfuzosin should be discontinued if angina pectoris recurs or worsens.
- Patients with congenital QTc prolongation, a known history of acquired QTc prolongation or who are taking medicinal products known to increase the QTc interval should be evaluated before and during the administration of alfuzosin.
- 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, even though the risk of this event with alfuzosin appears to be very low.
- Patients should be instructed to swallow the tablets whole. Other methods of administration such as crunching, crushing, grinding, pounding or chewing the tablet should be avoided. Incorrect administration may lead to undesirable release and absorption of the active substance, with a risk of early undesirable effects.

Excipient(s)

Lactose

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

4.5 Interaction with other medicinal products and other forms of interaction

Contraindicated combinations

- Alpha -1 receptor blocking agents
  Increased hypotensive effect. Risk of severe orthostatic hypotension.

Combinations to be taken into account

- Potent CYP3A4 inhibitors (ketoconazole, itraconazole, ritonavir, clarithromycin, erythromycin)

Increase the plasma concentration of alfuzosin and increase the risk of undesirable effects.

- Antihypertensive drugs (see section 4.4)
  antihypertensive effect and risk of increased hypotension (cumulative effect).
- Nitrate preparations (see section 4.4).

Administration of a general anaesthetic to a patient being treated with alfuzosin may lead to profound hypotension. It is recommended that the tablets be withdrawn 24 hours before surgery.

4.6 Fertility, pregnancy and lactation

Due to the type of indication this section is not applicable.

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."

Adverse reactions such as vertigo, dizziness or asthenia may occur, especially at the beginning of treatment. This should be taken into account when driving or using machines.

4.8 Undesirable effects

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 (≥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).

	Frequency			
	Common	Uncommon	Very rare	Not known
Blood and lymphatic system disorders				Neutropenia, Thrombocytopenia
Nervous system disorders	Dizziness/faintness, headache, vertigo	Syncope, Somnolence		Stroke in patients with underlying cerebrovascular disorders

	Frequency			
	Common	Uncommon	Very rare	Not known
Eye disorders		Visual disturbance		Intraoperative floppy iris syndrome (IFIS) (see section 4.4)
Cardiac disorders		Tachycardia, palpitations	Aggravation or recurrence of angina pectoris in patients with pre-existing coronary artery disease (see section 4.4)	Atrial fibrillation
Vascular disorders	Orthostatic (postural) hypotension (initially, primarily with a too high dose or if treatment is resumed after a short interruption of therapy) (see section 4.4)	Hot flushes		
Respiratory, thoracic and mediastinaldisorders		Rhinitis		
Gastrointestinal disorders	Nausea, abdominal pain, diarrhoea dry mouth	Vomiting		
Hepatobiliary disorders				Hepatocellular injury, cholestatic liver disease
Skin and subcutaneous tissue disorders		Skin rashes, pruritus	Angiooedema, urticaria	
Reproductive system and breast disorders				Priapism
General disorders and administration site conditions	Asthenia, malaise	Oedema, chest pains (see section 4.4)		

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 the Yellow Card Scheme at: 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 overdose, the patient should be admitted to hospital, kept in the supine position and given normal support therapy for hypotension.

In case of significant hypotension, the appropriate antidote is a vasoconstrictor that acts directly on the smooth muscle in the blood vessels such as noradrenaline.

Gastric lavage and/or administration of medicinal charcoal should be considered. Alfuzosin is difficult to dialyse, due to the high degree of protein binding.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group :alpha -adrenoreceptor antagonist, ATC code : G04CA01

Alfuzosin, which is a racemate, is an orally acting quinazoline derivative which selectively blocks post-synaptic alpha1-receptors.
In vitro studies have confirmed the selectivity of alfuzosin for alpha1-adrenoreceptors located in the prostate, the trigonum vesicae and the prostatic urethra.
The clinical manifestations of BPH are associated with infravesical obstruction, the mechanism of which comprises both anatomical (static) and functional (dynamic) factors. The functional component of obstruction depends on prostatic smooth muscle contraction which is mediated by alpha1-adrenoreceptors: activation of alpha1-adrenoreceptors stimulates smooth muscle contraction, thereby increasing the tone of the prostate, prostatic capsule, prostatic urethra and bladder neck and, consequently, increasing resistance to bladder outflow, leading to outflow obstruction and possibly secondary bladder instability.

Alpha blockade decreases infravesical obstruction through its direct action on prostatic smooth muscle, decreasing resistance to bladder flow and allowing the BPH patient to urinate better.

In vivo animal studies have shown that alfuzosin decreases urethral pressure and thus resistance to urinary flow during urination. In addition, alfuzosin more readily inhibits the hypertonic response of the urethra than that of the vascular muscle, demonstrating functional uroselectivity in conscious normotensive rats by decreasing urethral pressure at doses that do not affect blood pressure.

In humans, alfuzosin improves the voiding of water by reducing the urethral muscle tone, with reduction in the resistance to outflow from the bladder, making it easier to empty the bladder.

A lower frequency of acute urinary retention has been observed in patients treated with alfuzosin than in untreated patients.

In placebo-controlled studies of BPH patients alfuzosin has:

- significantly increased maximum urinary flow (Qmax) in patients with Qmax <15 ml/s by an average of 30%. This improvement was observed from the first dose,
- significantly reduced the detrusor pressure and increased the volume producing a strong desire to void,
- significantly reduced the residual urine volume.

The effect on peak flow is maintained for 24 hours after intake.

These urodynamic effects lead to an improvement of Lower Urinary Tract Symptoms (LUTS), i.e. filling (irritative) as well as voiding (obstructive) symptoms, which has been clearly demonstrated.

A lower frequency of acute urinary retention is observed in the alfuzosin-treated patient than in the untreated patient.

In a double-blind, placebo-controlled study involving 357 patients with acute urinary retention secondary to benign prostatic hyperplasia, alfuzosin 10 mg/day increased the success rate of spontaneous voiding after catheter removal at 2-3 days in males: 146 spontaneous voiding (61.9%) for alfuzosin versus 58 (47.9%) for the placebo group (p=0.012).
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≥40 cm H2O) 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 has linear pharmacokinetic properties within the therapeutic dose range. The peak plasma concentration is reached approx. 5 hours after administration. The kinetic profile is characterised by large inter-individual fluctuations in plasma concentrations. Absorption is increased when the medication is administered after a meal.

Metabolic interactions:
CYP3A4 is the major hepatic isoenzyme involved in the metabolism of alfuzosin. Ketoconazole is a potent inhibitor of CYP3A4.
Repeated daily doses of 200 mg ketoconazole, for 7 days, resulted in a 2.11-fold increase in Cmax and a 2.46-fold increase in AUCfinal of 10 mg alfuzosin administered once daily under fed conditions.

Other parameters such as tmax and t½ were not modified.
Repeated administration for 8 days of 400 mg ketoconazole increased the alfuzosin Cmax 2.3-fold and the AUCfinal and AUC 3.2-fold and 3-fold, respectively (see sections 4.4 and 4.5).
Absorption
After the first dose (fed) the mean maximum plasma concentration was 7.72 ng/ml, AUCinf was 127 ng x h/ml (fed), and tmax was 6.69 h (fed). Under steady state conditions (fed) the mean AUC over the dosing interval (AUCτ) was 145 ng x h/ml, mean Cmax was 10.6 ng/ml and Cmin was 3.23 ng/ml.

Distribution
The binding rate of alfuzosin to plasma protein is approx. 90%. Alfuzosin's distribution volume is 2.5 l/kg in healthy volunteers. It has been shown to preferentially distribute in the prostate in comparison to plasma.

Elimination
The apparent elimination half-life is approx. 8 hours. Alfuzosin is extensively metabolised in the liver, (through various routes), metabolites are eliminated via renal excretion and probably also via biliary excretion. Of an oral dose, 75-91% is excreted in the faeces, 35% in unmodified form and the rest as metabolites, which indicates some degree of biliary excretion. About 10% of the dose is excreted in the urine in its unmodified form. None of the metabolites is pharmacologically active.

Renal impairment
In patients with renal impairment, whether or not on dialysis, volume of distribution and clearance increase with reduced renal function, possibly owing to a decreased degree of protein binding. The half-life, however, is unchanged. This change in the pharmacokinetic profile is not considered clinically relevant. Therefore, this does not necessitate a dosing adjustment in patient with mild to moderate renal insufficiency insufficiency (creatinine clearance > 30 ml/min, see sections 4.2 and 4.4)

Hepatic impairment
In patients with severe hepatic impairment the half-life is prolonged. The peak plasma concentration is doubled and the bioavailability increases in relation to that in young, healthy volunteers. Alfuzosin 10 mg prolonged release tablets are contraindicated in hepatic insufficiency (see section 4.3).

Chronic heart failure
Chronic heart failure does not affect the pharmacokinetic profile of alfuzosin.

Elderly patients
Compared to healthy middle-aged volunteers, pharmacokinetic parameters (Cmax and AUC) are not increased in elderly patients.

5.3 Preclinical safety data

Pre-clinical data reveal no special hazard for humans based on conventional studies on safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential or reproductive toxicity for males.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Hypromellose (E464)

Povidone K25

Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

For bottles (HDPE):
Shelf life after first opening: 1 year

6.4 Special precautions for storage

Keep the blister in the outer carton in order to protect from light.

Store below 30°C.

6.5 Nature and contents of container

10, 28, 30, 50, 90 or 100 tablets in blister packs (PVC/PVDC/Aluminium) or 100 tablets in bottles (HDPE).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited
Ridings Point
Whistler Drive
Castleford
WF10 5HX
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/1074

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

27/09/2007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24/11/2010

10 DATE OF REVISION OF THE TEXT

30/01/2023