SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Alfuzosin Hydrochloride 2.5mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5mg alfuzosin hydrochloride.

Excipients with known effect: Each tablet contains 61 mg lactose anhydrous.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablets.

White round, film coated tablet for oral administration marked “ALZ” on one side and “2,5” on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Alfuzosin is indicated in the treatment of the functional symptoms of benign prostatic hypertrophy.

4.2 Posology and method of administration

Alfuzosin hydrochloride 2.5mg tablets should be swallowed whole. The first dose should be given just before bedtime.

Adults
The usual dose is one tablet three times daily. The dose may be increased to a maximum of 4 tablets (10mg) 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 insufficiency
In patients with renal insufficiency, as a precaution, it is recommended that the dosing be started at alfuzosin hydrochloride 2.5mg tablets twice daily adjusted according to clinical response.

Hepatic insufficiency
In patients with mild to moderate hepatic insufficiency, it is recommended that therapy should commence with a single dose of alfuzosin hydrochloride 2.5mg

tablets/day to be increased to alfuzosin hydrochloride 2.5mg Tablets twice daily according to clinical response.

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 the paediatric population.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients (see section 6.1).
- History of orthostatic hypotension.
- Combination with other alpha-1 receptor blockers.
- Concomitant administration with ritonavir alone or in combination with ombitasvir/paritaprevir, lopinavir and nirmatrelvir (see Section 4.5).
- Severe hepatic insufficiency.

4.4 Special warnings and precautions for use

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As with all alpha-1 blockers in some subjects, in particular patients receiving antihypertensive medications or nitrates, postural hypotension with or without symptoms (dizziness, fatigue, sweating) may develop within a few hours following administration. In such cases, the patient should lie down until the symptoms have completely disappeared. These effects are transient, occur at 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, see section 4.8). The risk of developing hypotension and related adverse reactions may be greater in elderly patients. The patient should be warned of the possible occurrence of such events.

As with all alpha1-receptor blockers, alfuzosin should be used with caution in patients with acute cardiac failure.

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

Treatment should be initiated gradually in patients with hypersensitivity to alpha-1-blockers. Alfuzosin should be administered carefully to patients being treated with antihypertensive medication or nitrates (see section 4.5). Blood pressure should be monitored regularly, especially at the beginning of treatment.

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.

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.

Prolonged erections and priapism have been reported with alpha-1 blockers including alfuzosin in post marketing experience. If priapism is not treated immediately, it could result in penile tissue damage and permanent loss of potency, therefore the patient should seek immediate medical assistance (see section 4.8).

Precautions

In coronary patients, the specific treatment for coronary insufficiency should be continued. If angina pectoris reappears or worsens alfuzosin hydrochloride 2.5 mg tablets should be discontinued.

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 alpha1-blockers.Although the risk of this event with alfuzosin appears very low, ophthalmic surgeons should be informed in advance of cataract surgery of current or past use of alpha-1-blockers, as IFIS may lead to increased procedural complications. The ophthalmologists should be prepared for possible modifications to their surgical technique

Excipients
Alfuzosin hydrochloride 2.5 mg tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
This medicine contains less than 1mmol sodium (23mg) per tablet, that is to say essentially 'sodium free'

4.5 Interactions with other medicinal products and other forms of interaction

Combinations contraindicated:

- Alpha-1-receptor blockers (see section 4.3)

Concomitant use not recommended:

- Potent CYP3A4 inhibitors such as itraconazole, ketoconazole, protease inhibitors(e.g. ritonavir), 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)

The administration of general anaesthetics to patients receiving alfuzosin hydrochloride 2.5mg tablets could cause profound hypotension. It is recommended that alfuzosin hydrochloride 2.5mg tablets be withdrawn 24 hours before surgery.

Other forms of interaction
No pharmacodynamic or pharmacokinetic interaction has been observed in healthy volunteers between alfuzosin and the following drugs: warfarin, digoxin, hydrochlorothiazide and atenolol.

4.6 Pregnancy and lactation

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

4.7 Effects on ability to drive and use machines

There are no data available on the effect on driving vehicles. Adverse reactions such as vertigo, dizziness and asthenia may occur essentially at the beginning of treatment. This has to be taken into account when driving vehicles and operating machinery.

4.8 Undesirable effects

Classification of expected frequencies:
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).

- **Cardiac disorders**
  Uncommon: tachycardia, palpitations, palpitations, hypotension (postural)
  Very rare: angina pectoris in patients with pre-existing coronary artery disease (see section 4.4.)
  Not known: atrial fibrillation

- **Eye disorders**
  Uncommon: vision abnormal
  Not known: intraoperative floppy iris syndrome (see section 4.4)

- **General disorders and administration site conditions**
  Common: asthenia, malaise
  Uncommon:, flushes, oedema, chest pain

- **Gastro-intestinal disorders**
  Common: nausea, abdominal pain,
  Uncommon: diarrhoea, dry mouth
  Not known: vomiting

- **Hepatobiliary disorders**
  Not known: hepatocellular injury, cholestatic liver disease

- **Nervous system disorders**
  Common: faintness/dizziness, vertigo, headache
  Uncommon: drowsiness, syncope
  Not known: cerebral ischemic disorders in patients with underlying cerebrovascular disturbances

- **Reproductive system and breast disorders**
  Not known: priapism

- **Respiratory, thoracic and mediastinal disorders**
  Uncommon: rhinitis

- **Skin and subcutaneous tissue disorders**
  Uncommon: rash, pruritus
  Very rare: urticaria, angioedema

- **Vascular disorders**
  Common: hypotension (postural)
  Uncommon: flushing

- **Blood and lymphatic system disorders**
  Not known: neutropenia, thrombocytopenia

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 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 dialysable because of its high degree of protein binding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: alpha adrenoreceptor antagonists
ATC code: G04C A01

Alfuzosin is an orally active quinazoline derivative. It is a selective, peripherally acting antagonist of post synaptic alpha$_1$-adrenoceptors.

In vitro pharmacological studies have documented the selectivity of alfuzosin for the alpha 1-adrenoreceptors 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 alpha-adrenoceptors. Activation of alpha 1-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} less than or equal to 15ml/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).

5.2 Pharmacokinetic properties

Alfuzosin Hydrochloride 2.5mg Tablets are well absorbed with a mean bioavailability of 64%, peak plasma levels are generally reached in 0.5-3 hours. Kinetics within the therapeutic range are linear. The kinetic profile is characterised by large interindividual fluctuations in plasma concentrations. The terminal half-life is 3-5 hours. Alfuzosin is 90% protein bound in plasma, 68.2% to human serum albumin and 52.5% to human serum alpha-glycoprotein. It is partially metabolised and excreted mainly in the bile and faeces.

None of the metabolites found in man has any pharmacodynamic activity. The pharmacokinetic profile is not affected by taking Alfuzosin Hydrochloride 2.5mg Tablets with food.

In subjects over 75 years, absorption is more rapid and peak plasma levels are higher. Bioavailability may be increased and in some patients the volume of distribution is reduced. The elimination half-life does not change.

The volume of distribution and clearance of alfuzosin are increased in renal insufficiency, with or without dialysis, owing to an increase in the free fraction.

Chronic renal insufficiency even when severe (creatinine clearance between 15 and 40 mls/min) is not adversely affected by alfuzosin.

In patients with severe hepatic insufficiency, the elimination half-life is prolonged. A two-fold increase in Cmax values and a three-fold increase in the AUC is observed. Bioavailability is increased compared with healthy volunteers.

The pharmacokinetic profile of alfuzosin is not affected 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

No data of therapeutic relevance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core: Microcrystalline cellulose, lactose, povidone, sodium starch glycollate, magnesium stearate.

Coating: Methylhydroxypropylcellulose, polyethylene glycol 400, titanium dioxide suspension (E171).

6.2 Incompatibilities

Not known.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30ºC. Store in the original package

6.5 Nature and contents of container

Boxes with 30, 60 or 90 tablets in pvc/foil blister strips.

PP containers with 30, 60, 90 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

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

7 MARKETING AUTHORISATION HOLDER

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