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

For a 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
Alfuzosin HCl 2.5 mg film-coated 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 (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 insufficiency**
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 insufficiency**
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.

### 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.

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 tricuspid 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.

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 should not be used in patients suffering from incontinence due to overflow, anuria or prolonged renal insufficiency.
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp 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.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations contra-indicated:
- Alpha1-receptor blockers (see section 4.3).

Combinations to be taken into account:
- Antihypertensive drugs (see section 4.4)
- Nitrates (see section 4.4)
- Potent CYP3A4 inhibitors (such as itraconazole, ketoconazole and ritonavir) since alfuzosin blood levels are increased (see section 5.2).

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

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 (>1/10000 to ≤1/1000); very rare (≤1/10000), not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervous system disorders</td>
<td></td>
</tr>
<tr>
<td>Faintness/ dizziness</td>
<td>Common</td>
</tr>
<tr>
<td>Syncope</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Headache</td>
<td>Very rare</td>
</tr>
<tr>
<td>Vertigo</td>
<td>Not Known (Cannot be estimated from the available data)</td>
</tr>
<tr>
<td>Eye disorders</td>
<td></td>
</tr>
<tr>
<td>Vision abnormal</td>
<td>Common</td>
</tr>
<tr>
<td>Intraoperative floppy iris syndrome</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Cardiac disorders</td>
<td></td>
</tr>
<tr>
<td>Tachycardia, palpitations</td>
<td>Very rare</td>
</tr>
<tr>
<td>Angina pectoris in patients with pre-existing coronary artery disease</td>
<td>Not Known (Cannot be estimated from the available data)</td>
</tr>
<tr>
<td>Respiratory, thoracic and medicinal disorders</td>
<td></td>
</tr>
<tr>
<td>Rhinitis</td>
<td>Common</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
</tr>
<tr>
<td>Nausea, abdominal pain, diarrhoea, dry mouth</td>
<td>Very rare</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Not Known (Cannot be estimated from the available data)</td>
</tr>
<tr>
<td>Hepatobiliary disorders</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular injury, cholestatic liver disease</td>
<td>Not Known (Cannot be estimated from the available data)</td>
</tr>
</tbody>
</table>
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. 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 alf1-adrenoceptors.

In vitro pharmacological studies have documented the selectivity of alfuzosin for the alf1-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 α-adrenoceptors. Activation of α1-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 ($Q_{\text{max}}$) in patients with $Q_{\text{max}} \leq 15\text{ml/s}$ 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 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 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 $C_{\text{max}}$ 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

2 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, 100
Bottle pack: 100, 250, 1000

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
8 MARKETING AUTHORISATION NUMBER(S)

PL 16363/0300

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/09/2011

10 DATE OF REVISION OF THE TEXT

12/06/2015