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SCHEDULING STATUS:

S4

PROPRIETARY NAME (AND DOSAGE FORM):

XATRAL XL 10 mg (Tablets)

COMPOSITION:

Each XATRAL XL 10 mg tablet contains:

10 mg of alfuzosin hydrochloride.

PHARMACOLOGICAL CLASSIFICATION:

A 5.2 Adrenolytics (sympatholytics)

PHARMACOLOGICAL ACTION:

Pharmacodynamics:

Alfuzosin hydrochloride 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 hydrochloride for the alpha$_1$-adrenoceptors located in the prostate, bladder base and prostatic urethra.

Alpha$_1$-adrenoceptor blockade decreases infra-vesical obstruction via a direct action on prostatic smooth muscle.

In vivo animal studies have shown that alfuzosin hydrochloride decreases urethral pressure and therefore, resistance to urine flow during micturition. Moreover, alfuzosin hydrochloride inhibits the hypertonic response of the urethra more readily than that of vascular muscle, and shows functional uroselectivity in experimental animals.

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

In addition, alfuzosin significantly increases the success rate of spontaneous voiding after catheter removal in men with an episode of acute urinary retention (AUR) related to benign prostatic hyperplasia (BPH).

Pharmacokinetics:

Alfuzosin hydrochloride is absorbed after oral administration, with a mean absolute bioavailability of 64 %.

The bioavailability of alfuzosin hydrochloride 10 mg once daily was similar to the immediate release formulation, 2,5 mg given three times daily, in middle aged healthy volunteers and the maximum plasma concentration was being achieved 9 hours after administration compared to 1,0 hour for the immediate release formulation.

CYP 3A4 is the principal hepatic enzyme isoform involved in the metabolism of alfuzosin.

The apparent elimination half-life is 9,1 hours.

Maximum blood levels and bioavailability are not affected by food intake.

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

Compared to subjects with normal renal function, mean Cmax and AUC values were about 5 % and 7 % increased in patients with mild to moderate renal impairment, without modification of the apparent elimination half-life. There are no data available on severe renal impairment.

The binding of alfuzosin hydrochloride to total proteins is about 90 %.

Alfuzosin hydrochloride undergoes extensive metabolism by the liver, with only 11 % of the parent compound being excreted as the unchanged product in the urine.
The majority of the metabolites, which are inactive, are excreted in the faeces (75 % to 91 %).

In subjects aged over 75 years, absorption of alfuzosin hydrochloride is more rapid and the peak levels are higher. Bioavailability may be increased and in some patients the volume of distribution is reduced. The elimination half-life remains unchanged.

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.

The pharmacokinetic profile of alfuzosin hydrochloride is not affected by chronic cardiac insufficiency.

INDICATIONS:

Treatment of functional symptoms of benign prostatic hyperplasia.

Adjunctive therapy with urethral catheterisation for acute urinary retention (AUR) related to benign prostatic hyperplasia (BPH).

CONTRAINDICATIONS:

Hypersensitivity to alfuzosin or any component.

Orthostatic hypotension.

Combination with other alpha$_1$-adrenoceptor blockers.

Hepatic insufficiency.

Severe renal insufficiency.

Not indicated for children.

WARNINGS:

In some subjects, in particular patients receiving antihypertensive medications, 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 usually transient, occur at the beginning of treatment, and do not usually prevent the continuation of treatment. The patient should be warned of the possible occurrence of such events.

Care should be taken when XATRAL XL 10 mg is administered to patients with symptomatic orthostatic hypotension.

INTERACTIONS:

Combinations contraindicated:

Alpha$_1$-adrenoceptor blockers (see CONTRAINDICATIONS).

Combinations to be taken into account:

- Antihypertensive drugs (see WARNINGS).
- Nitrates.
- General anaesthetics: Administration of general anaesthetics to a patient treated with XATRAL XL 10 mg may lead to a decrease in blood pressure.
- Potent CYP3A4 inhibitors such as ketoconazole, itraconazole and ritonavir since XATRAL XL 10 mg blood levels are increased.

Effects on the ability to drive and use machines:

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

DOSAGE AND DIRECTIONS FOR USE:

Benign prostatic hyperplasia (BPH): The recommended dose for XATRAL XL 10 mg tablets is one tablet daily to be taken after meals (as bioavailability in the fasting state is less than half that after a meal).

Acute urinary retention (AUR): One 10 mg tablet daily after a meal to be taken from the first day of catheterisation.

Tablets should be swallowed whole.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side Effects:

The following frequency rating is used, when applicable:

- very common : ≥ 1/10;
- common : ≥ 1/100 and < 1/10;
- uncommon : ≥ 1/1000 and < 1/100;
- rare : ≥ 1/10 000 and < 1/1000;
- very rare : ≤ 1/10 000.

Gastrointestinal disorders:

Common: Nausea, gastralgia

Uncommon: Diarrhoea, dry mouth

Central and peripheral nervous system disorders:

Common: Faintness/dizziness, headache

Uncommon: Vertigo, drowsiness, malaise

Cardiovascular disorders, general:

Uncommon: Tachycardia, symptomatic hypotension (postural), syncope, palpitations

Very rare: Angina pectoris in patients with pre-existing coronary artery disease (see SPECIAL PRECAUTIONS)

Unknown: Atrial fibrillation

Eye disorders:

Unknown: Intraoperative Floppy Iris Syndrome (IFIS) (see SPECIAL PRECAUTIONS).

Respiratory system disorders:

Uncommon: Rhinitis

Hepato-biliary disorders:

Unknown: Hepatocellular injury, cholestatic liver disease

Skin and appendages disorders:

Uncommon: Rash, pruritus

Very rare: Urticaria, angioedema

Body as a whole - general disorders:

Common: Asthenia

Uncommon: Flushes, oedema, chest pain

Reproductive system and breast disorders:

Unknown: Priapism

Special Precautions:

In coronary patients, XATRAL XL 10 mg (alfuzosin hydrochloride) should not be prescribed alone.

In patients with ischaemic heart disease/angina pectoris, the specific treatment for coronary insufficiency should be continued. If angina pectoris reappears or gets worse, XATRAL XL 10 mg should be discontinued.

Care should be taken when XATRAL XL 10 mg is administered to patients who have had a pronounced hypotensive response to another alpha$_1$-blocker.

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 some alpha$_1$-blockers (including XATRAL XL 10 mg).
Although the risk of this event with XATRAL XL 10 mg 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.

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.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

In case of overdosage, the patient should be hospitalised, kept in the supine position, and conventional treatment of hypotension should take place.

XATRAL XL 10 mg is not dialysable because of its high degree of protein binding.
Treatment is symptomatic and supportive.

IDENTIFICATION:

Round, biconvex three layer tablets, with one white layer between two yellow layers.

PRESENTATION:

Blister pack of 30 tablets.

STORAGE INSTRUCTIONS:

Store below 25 °C. Protect from moisture.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

35/5.2/0074

NAME AND BUSINESS ADDRESS OF HOLDER OF CERTIFICATE OF REGISTRATION:

sanofi-aventis south africa (pty) ltd

2 Bond Street

Midrand

1685

South Africa

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