XATRAL Tablets® Abridged Prescribing Information:

1-NAME & PRESENTATION: Xatral® XL 10 mg, prolonged-release tablets

2. Therapeutic INDICATIONS:

- Treatment of the functional symptoms of benign prostatic hypertrophy.
- Adjunctive treatment for vesical catheterization in acute urinary retention associated with benign prostatic hypertrophy.

3. DOSAGE & POSOLOGY OF ADMINISTRATION:

Oral use.

The recommended dosage is one 10 mg tablet daily, to be taken immediately after the evening meal.

Adjunctive treatment for vesical catheterization in acute urinary retention associated with benign

prostatic hypertrophy:

The recommended dosage is one 10 mg tablet daily, to be taken after a meal, starting on the day of

insertion of the urethral catheter.

The treatment is administered for 3 to 4 days including 2 to 3 days during catheterization and 1 day

following catheter removal.

4. SPECIAL POPULATION: cautious should be there with elderly patients.

4. CONTRA-INDICATIONS:

This medicinal product must not be administered in the following situations:

hypersensitivity to alfuzosin and/or any of the other ingredients;

postural hypotension;

liver failure;

severe kidney failure (creatinine clearance < 30 ml/min); in combination with ritonavir.

5-WARNINGS & PRECAUTIONS: This medicinal product must be used with caution in patients treated with antihypertensives or nitrate

derivatives.

Use of this medicinal product is not recommended with antihypertensive alpha-blockers (see

section 4.5).

In some subjects, orthostatic 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.

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 antihypertensive

medication).

There is a risk of ischemic strokes, particularly in elderly patients with pre-existing asymptomatic or symptomatic disorders of cerebral circulation (such as cardiac arrhythmia, atrial fibrillation or a history of transient ischemic attack) due to the fact that hypotension may develop following alfuzosin administration

The patient should be warned of the possible occurrence of such events.

Care should be taken, particularly in the elderly. The risk of developing hypotension and related symptoms may be greater in elderly patients.

As with all alpha-1 blockers, this medicine should be used with caution in patients with acute heart failure.

Patients with congenital prolonged QTc interval, or a history of prolonged QTc interval or who are being treated with medicines that increase the QTc interval should be monitored before and during treatment.

The combination of alfuzosin and potent CYP3A4 inhibitors (e.g. itraconazole, ketoconazole, protease inhibitors, clarithromycin, telithromycin and nefazodone) must be avoided (see section 4.5). Alfuzosin must not be used in combination with CYP3A4 inhibitors that are known to prolong the QTc interval (e.g. itraconazole and clarithromycin). If this treatment is initiated, alfuzosin treatment should be temporarily discontinued.

Rarely, alfuzosin, like other alpha-1 blockers, has been associated with priapism (persistent painful penile erection unrelated to sexual activity). Rapid patient management (sometimes involving surgery) is essential. Priapism may lead to permanent impotence if not properly treated.

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 cases have also been reported with other alpha-1 blockers, therefore a possible class effect cannot be ruled out. Considering that IFIS can be the cause of additional technical difficulties during cataract operations, the surgeon must be informed of any history or current use of alpha-1 blockers before the eye surgery, even if the risk of IFIS occurring with alfuzosin is low.

Given the lack of data on safety in patients with severe kidney failure (creatinine clearance < 30 mL/min), Xatral LP 10 mg prolonged-release tablets should not be administered to these patients.

This medicinal product contains castor oil, which can cause gastrointestinal disorders (mild laxative effect, diarrhea).

Care should be taken when alfuzosin is administered to patients who have experienced marked hypotension following administration of another alpha-1 blocker.

In coronary patients, alfuzosin should not be prescribed alone. The specific treatment for coronary insufficiency should be continued. If angina pectoris reappears or worsens, alfuzosin should be

discontinued.
Use with PDE5 inhibitors: concomitant administration of Xatral LP 10 mg with a phosphodiesterase type 5 inhibitor (e.g. sildenafil, tadalafil or vardenafil) can cause symptomatic hypotension in certain patients

6. INTERACTIONS:

Contraindicated combinations

 Ombitasvir + paritaprevir

The combined therapy causes an increase in plasma alfuzosin concentrations due to decreased alfuzosin liver metabolism.

Inadvisable combinations

 Antihypertensive alpha-blockers (doxazosin, prazosin, urapidil)

Increased hypotensive effect. Higher risk of severe postural hypotension.

 Potent CYP3A4 inhibitors (boceprevir, clarithromycin, cobicistat, erythromycin, itraconazole, ketoconazole, nelfinavir, posaconazole, ritonavir, telaprevir, telithromycin, nefazodone, voriconazole)

There is a risk of increased plasma alfuzosin concentrations and increased undesirable effects. (See section 4.4)

Combinations requiring precautions for use

 Phosphodiesterase type 5 inhibitors (avanafil, sildenafil, tadalafil, vardenafil)

There is a risk of orthostatic hypotension, particularly in elderly subjects.

Treatment should be initiated at the lowest recommended dose and adjusted gradually if necessary.

Combinations to be taken into account

 Antihypertensive drugs except alpha-blockers

Increased hypotensive effect. Higher risk of severe postural hypotension.

 Dapoxetine

There is a risk of increased undesirable effects, particularly dizziness or syncope.

 Blood pressure-lowering drugs

There is a risk of enhanced hypotension, particularly orthostatic

7. PREGNANCY AND LACTATION: The therapeutic indication does not apply to women.

It is not known whether alfuzosin is safe during pregnancy nor whether it is excreted in breast milk.

8. EFFECTS ON ABILITY TO DRIVE: There are no available data on the effect of alfuzosin on the ability to drive vehicles.

Special caution must be exercised by patients who drive and use machines due to the risk of orthostatic hypotension, dizzy spells, asthenia and visual disturbances, particularly at the beginning of treatment.

9. ADVERSE REACTIONS:

Common (≥1% - <10%); Uncommon (≥0.1% - <1%); Very rare (<0.01%).

Nervous system disorders:

Common: lightheadedness, dizziness, faintness, headache,

Uncommon: dizzy spells, drowsiness.

Heart disorders:

Uncommon: tachycardia, palpitations, postural hypotension, syncope,

Very rare: angina pectoris in patients with a history of coronary artery disease

Respiratory, thoracic and mediastinal disorders:

Uncommon: nasal congestion.

Gastrointestinal disorders:

Common: nausea, abdominal pain,

Uncommon: diarrhea, dry mouth.

Skin and subcutaneous tissue disorders:

Uncommon: skin rashes, pruritus,

Very rare: urticaria, angioedema.

Systemic disorders:

Common: asthenia,

Uncommon: flushing, edema, chest pain (see Section 4.4).

Hepatobiliary disorders:

Systemic disorders:

Common: asthenia,

Uncommon: flushing, edema, chest pain (see Section 4.4).

Hepatobiliary disorders:

Unknown incidence: hepatocellular injury, cholestatic hepatitis.

Reproductive system and breast disorders:

o Unknown incidence: priapism.

10.Overdose: In the event of overdose, the patient should be hospitalized and kept lying down.

Standard treatment for hypotension should be instituted.

As alfuzosin is highly protein bound, it is not easily dialyzable.

11.Pharmacodynamics: Alfuzosin is an orally active quinazoline derivative. It is a selective antagonist of post-synaptic alpha-1 adrenoreceptors. Pharmacological studies conducted in vitro have confirmed the selectivity of alfuzosin for alpha-1 adrenoreceptors located in the prostate, bladder trigone and

urethra.

Alpha-blockers decrease infravesical obstruction via direct action on prostatic smooth muscle.

In vivo studies in animals have shown that alfuzosin reduces urethral pressure thereby lowering resistance to urine flow during micturition. A study in conscious rats showed a greater effect on urethral pressure than the effect on blood pressure.

Placebo-controlled studies in patients with benign prostatic hypertrophy showed that alfuzosin:

· significantly increases urine flow rate by a mean of 30% in patients with a flow rate of ≤15 ml/s. This improvement is observed from the first dose,

· significantly reduces detrusor pressure and increases volume, producing the desire to void,

· significantly reduces the residual urine volume.

These effects lead to an improvement in irritative and obstructive urinary symptoms. They have no negative effect on sexual function.

Furthermore, maximum urinary flow rate remains significantly increased 24 hours after dosing.

In the ALFAUR study, the effect of alfuzosin on the return of normal voiding was evaluated in 357 men over the age of 50 with a first painful episode of acute urinary retention (AUR) associated with benign prostatic hypertrophy (BPH), and a residual urine volume of between 500 and 1500 ml during catheter insertion and for the first hour following catheterization. In this double-blind, randomized, multicenter study in two parallel groups comparing 10 mg/day alfuzosin prolonged-release with placebo, evaluation of the return to normal voiding was conducted 24 hours after catheter removal, in the morning, after at least two days of alfuzosin treatment.

Treatment with alfuzosin significantly increased ($p = 0.012$) the rate of successful voiding postcatheter removal in patients with a first episode of AUR, i.e. 146 patients with successful voiding (61.9%) in the alfuzosin group versus 58 (47.9%) in the placebo group.

12. MARKETING AUTHORIZATION HOLDER: Sanofi-aventis France- 82, avenue Raspail 94250 Gentilly, France. Abbreviated Prescribing Information based on the local SmPC as of July 2019. Always refer to the full Summary of Product Characteristics (SmPC) before prescribing.