ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Xatral 2.5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains

Alfuzosin hydrochloride .....5 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Treatment of the functional symptoms of benign prostatic hypertrophy.

4.2. Posology and method of administration

Posology

Oral use.

Adults

The recommended dosage is one Xatral 5 mg tablet three times daily.

Elderly patients or patients treated for hypertension

As a systematic precaution, it is recommended that treatment be started with one Xatral 2.5 mg tablet morning and evening and that the dosage then be increased on the basis of the patient's individual response, without exceeding the maximum dosage of four Xatral 2.5 mg tablets daily.

Patients with liver failure

It is recommended that treatment be started with one Xatral 2.5 mg tablet per day and that the dosage then be increased on the basis of the patient's individual response, without exceeding the maximum dosage of one Xatral 2.5 mg tablet twice daily.

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

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

- Hypersensitivity to alfuzosin or any of the excipients mentioned in section 6.1
- Orthostatic hypotension
- Severe liver failure (class C in the Child-Pugh classification)
- Severe kidney failure (creatinine clearance <30 mL/min)
- Concomitant administration of ritonavir alone or in combination with ombitasvir, paritaprevir, lopinavir or nirmatrelvir (see section 4.5).

4.4. Special warnings and precautions for use

Special warnings

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 anti-hypertensive 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 (see section 4.8).

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). Since this condition can lead to permanent impotence if not properly treated, rapid patient management (sometimes involving surgery) is essential.

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.

This medicinal product contains lactose. Therefore, it is not recommended for use in patients with galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption syndrome (rare hereditary diseases).

This medicinal product contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

Precautions for use

Care should be taken when alfuzosin is administered to patients who have had a pronounced hypotensive response to another alpha1-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 2.5 mg with a phosphodiesterase type 5 inhibitor (e.g. sildenafil, tadalafil or vardenafil) can cause symptomatic hypotension in certain patients (see section 4.5). To reduce the risk of orthostatic hypotension, patients must be stabilised under alpha-blocker treatment before initiating treatment with a phosphodiesterase type 5 inhibitor.

In addition, treatment with the phosphodiesterase-type 5 inhibitor should be started at the lowest possible dose.

4.5. Interaction with other medicinal products and other forms of interaction

Drugs that induce orthostatic hypotension

In addition to antihypertensive agents, numerous drugs can cause orthostatic hypotension. These include nitrate derivatives, phosphodiesterase type-5 inhibitors, alpha 1 receptor blockers for urological conditions, imipramine antidepressants and phenothiazine neuroleptics, dopamine agonists and levodopa.
Concomitant use could therefore increase the frequency and intensity of this adverse effect. Refer to the interactions specific to each group, with the corresponding obligations.

Contraindicated combinations

+ **Ritonavir alone or in combination with ombitasvir/paritaprevir, lopinavir or nirmatrelvir (see section 4.3).**

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

Inadvisable combinations

+ **Antihypertensive alpha-blockers (doxazosin, prazosin, urapidil)**

There is a risk of severe orthostatic hypotension due to an enhanced hypotensive effect.

+ **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**

There is a risk of severe orthostatic hypotension due to an enhanced hypotensive effect.

+ **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.

4.6. Fertility, pregnancy and lactation

Pregnancy and breast-feeding

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.

4.7. Effects on ability to drive and use machines

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.

4.8. Undesirable effects

Undesirable effects are classified by frequency based on the following convention: very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1 000, <1/100); rare (≥1/10 000, <1/1 000); very rare (<1/10 000); frequency not known (cannot be estimated from the available data).

	FREQUENCY			
SYSTEM ORGAN CLASS	**Common (≥1% - <10%)**	**Uncommon (≥0.1% - <1%)**	**Very rare (<0.01%)**	**Not known**
Cardiac disorders		tachycardia, palpitations	angina pectoris in patients with a history of coronary artery disorders	atrial fibrillation
Eye disorders		abnormal vision		intraoperative floppy iris syndrome
General disorders and administration site conditions	asthenia, malaise	oedema, chest pain		
Gastrointestinal disorders	nausea, abdominal pain, diarrhoea, dry mouth,	vomiting		
Hepatobiliary disorders				hepatocellular injury, hepatic cholestasis
Nervous system disorders	dizziness, vertigo, light-headedness, headache	syncope, drowsiness		ischemic stroke in patients with underlying cerebrovascular disorders
Reproductive system and breast disorders				priapism
Respiratory, thoracic and mediastinal disorders		nasal congestion		
Skin and subcutaneous tissue disorders		skin eruption, pruritus	urticaria, angioedema	

Vascular disorders	orthostatic hypotension (see section 4.4)	flushing		
Blood and lymphatic system disorders				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 French national reporting system, i.e.: Agence nationale de sécurité du médicament et des produits de santé (ANSM) under "Réseau des Centres Régionaux de Pharmacovigilance" (Network of Regional Pharmacovigilance Centres) - Website: https://signalement.social-sante.gouv.fr/

4.9. Overdose

If overdose occurs, the patient should be hospitalised and kept in the supine position. Conventional treatment of hypotension should be instituted. If severe hypotension occurs, a vasoconstrictor agent that acts directly on the vascular muscle fibres can be used.

Alfuzosin is highly protein-bound and is therefore not easily dialyzable.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Alpha-blockers, ATC code: G04CA01 - G: genito urinary system and sex hormones.

Alfuzosin is an orally active quinazoline derivative. It is a selective antagonist of post-synaptic alpha-1-adrenergic receptors. In vitro pharmacological studies have confirmed that alfuzosin is selective for alpha-1-adrenergic receptors located in the prostate, bladder base and urethra.

Alpha-blockers decrease infravesical obstruction via direct action on prostatic smooth muscle. In vivo animal studies have shown that alfuzosin reduces urethral pressure, thereby lowering resistance to urine flow during micturition. A study in alert rats showed a greater effect of alfuzosin on urethral pressure than on blood pressure.

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

- significantly increases urine flow 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, with no negative effect on sexual function.

Paediatric population

Alfuzosin is not indicated for use in the paediatric population (see section 4.2).

The efficacy of alfuzosin hydrochloride was not demonstrated in 2 studies conducted in 197 patients aged between 2 and 16 years with increased detrusor pressure (≥40 cm H_2O) caused by a neurological disorder. Patients were treated with 0.1 mg/kg/day or 0.2 mg/kg/day of alfuzosin hydrochloride using adapted paediatric formulations.

5.2. Pharmacokinetic properties

Alfuzosin has a mean bioavailability of 64%. Peak plasma concentrations are reached approximately 1.5 hours after administration (with a range of 0.5 to 6 hours).

Pharmacokinetic characteristics within the therapeutic range are linear. The pharmaceutical profile is characterised by large inter-individual fluctuations.

The elimination half-life of alfuzosin is approximately 4.8 hours in healthy volunteers.

Alfuzosin is approximately 90% plasma protein bound.

Alfuzosin is extensively metabolised in the liver, with only 11% of the parent compound excreted unchanged in the urine.

The majority of the metabolites (which are inactive) are excreted in the faeces (75% to 90%).

Concomitant intake of food does not affect the pharmacokinetic pattern of the drug.

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

In patients with severe liver failure, the elimination half-life is prolonged. Bioavailability is increased compared with healthy volunteers.

The volume of distribution and clearance of alfuzosin are increased in renal failure, with or without dialysis, due to an increase in the free fraction. No dose adjustment is required for patients with kidney failure whose creatinine clearance is over 30 mL/min.

The pharmacokinetic profile of alfuzosin is not affected by chronic heart failure.

5.3. Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Microcrystalline cellulose, povidone, calcium hydrogen phosphate dihydrate, magnesium stearate, hydrogenated castor oil

Film-coating: hypromellose, titanium dioxide, Propylene glycol

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Store the blisters in the outer packaging, in order to protect from light and moisture.

6.5. Nature and contents of container

30 tablets in (PVC/aluminium) blisters.

60 tablets in (PVC/aluminium) blisters.

90 tablets in (PVC/aluminium) blisters.

100 tablets in (PVC/aluminium) blisters.

6.6. Special precautions for disposal and other handling

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

Sanofi Winthrop Industrie
82 avenue Raspail
94250 Gentilly
France

8. MARKETING AUTHORISATION NUMBER(S)

- 34009 330 160-1 2: 30 film-coated tablets in (PVC/aluminium) blisters
- 34009 330 161-8 0: 60 film-coated tablets in (PVC/aluminium) blisters
- 34009 556 232-3 6: 90 film-coated tablets in (PVC/aluminium) blisters
- 34009 330 162-4 1: 100 film-coated tablets in (PVC/aluminium) blisters

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01/2026

10. DATE OF REVISION OF THE TEXT

To be filled in subsequently by the Marketing Authorisation Holder