(Official logo of the French National Agency for Medicines and Health Products Safety)

REPUBLIC OF FRANCE

[stamp]
October 18, 2018

[date stamped]
Saint-Denis **October 15, 2018**

Sanofi Aventis France
82, avenue Raspail
94250 Gentilly, France

Division	Division of Medicines used in Cardiology, Rheumatology, Stomatology, Endocrinology, Gynecology, Urology, Pulmonology, ENT, and Allergology
Unit	Endocrinology, Gynecology, Urology, Pulmonology, ENT, and Allergology
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CIS	**6 044 360 9**
NL	**NL 24386**
Procedure No.	**APN_6862**
Outgoing Mail No.	2018100900219

ANSM reference to be used in all correspondence:
Dossier No. 2017120900082/V4IINAT-2017-12-00030

Dear Sir/Madam,

In your letter dated December 08, 2017, and received on December 08, 2017, in accordance with the provisions of Commission Regulation (EC) No. 1234/2008 of 24 November 2008 and the guidelines relating to its implementation, you submitted an application for the following type of variation:

- ☐ IB
- ☒ II
- ☐ Grouped variations
- ☐ Grouped variations[1]

to the Marketing Authorization for the proprietary medicinal product:

Xatral LP 10 mg prolonged-release tablets

concerning:

C.I.4-Change(s) in the Summary of Product Characteristics, Labeling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data.

I am pleased to inform you that your application has been approved. Please find enclosed the Decision amending the Marketing Authorization of the proprietary medicinal product.

An appeal against this Decision may be lodged before the competent administrative court within two months from date of receipt. Please be sure to indicate the ANSM reference in all correspondence.

(French formal ending to correspondence)

[stamp]
Division of Medicines used in Cardiology, Rheumatology, Stomatology, Endocrinology, Gynecology, Urology, Pulmonology, ENT, and Allergology

(Original French document *signed)*

Céline Druet
Deputy Director

[1] Translator's note: Repeated in original French document.

References

NL	CIS
NL 24386	6 044 360 9

Decision

amending the Marketing Authorization of the proprietary medicinal product:

Xatral LP 10 mg prolonged-release tablets

THE DIRECTOR GENERAL OF THE FRENCH NATIONAL AGENCY FOR MEDICINES AND HEALTH PRODUCTS SAFETY

Considering the Commission Regulation (EC) No. 1234/2008 of 24 November 2008 concerning the examination of variations to the terms of Marketing Authorizations for medicinal products for human use and veterinary medicinal products as well as the guidelines relating to its implementation;

Considering the French Public Health Code, Part V, and particularly articles L.5121-8, L.5121-20, R.5121-21 *et seq.*;

Considering the Marketing Authorization granted on November 30, 1999, as amended;

Considering the application for a change to the Marketing Authorization submitted by:

Sanofi-Aventis France

on December 08, 2017

and concerning:

the following sections in the Summary of Product Characteristics:

- ☐ 1. Name of the medicinal product
- ☐ 2. Qualitative and quantitative composition
- ☐ 3. Pharmaceutical form
- ☐ 4.1. Therapeutic indications
- ☐ 4.2. Posology and method of administration
- ☒ 4.3. Contraindications
- ☐ 4.4. Special warnings and precautions for use
- ☒ 4.5. Interaction with other medicinal products and other forms of interaction
- ☐ 4.6. Fertility, pregnancy and lactation
- ☐ 4.7. Effects on ability to drive and use machines
- ☒ 4.8. Undesirable effects
- ☐ 4.9 Overdose
- ☐ 5.1. Pharmacodynamic properties
- ☐ 5.2. Pharmacokinetic properties
- ☐ 5.3. Preclinical safety data
- ☐ 6.1. List of excipients
- ☐ 6.2. Incompatibilities
- ☐ 6.3. Shelf life
- ☐ 6.4. Special precautions for storage
- ☐ 6.5. Nature and contents of container
- ☐ 6.6. Special precautions for disposal and other handling

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- ☐ 7. Marketing Authorization Holder
- ☐ 8. Marketing Authorization Number(s)
- ☐ General classification for supply

the following section(s) in Annex II:

- ☐ A Manufacturer(s) of the biological active substance(s) and manufacturer(s) responsible for batch release
- ☐ B. Conditions or restrictions regarding supply and use
- ☐ C. Other conditions and requirements of the Marketing Authorization
- ☐ D. Conditions or restrictions with regard to the safe and effective use of the medicinal product
- ☐ E. Specific obligation to complete post-authorization measures for the Marketing Authorization under exceptional circumstances
- ☐ F. Qualitative and quantitative composition in excipients

As well as the corresponding sections in the Package Leaflet and Labeling;

Considering the interim measure notified on February 02, 2018;

Considering the justification provided by the applicant on April 06, 2018, in response to the aforementioned notification;

HAS DECIDED

Article 1

The Marketing Authorization for the proprietary medicinal product **Xatral LP 10 mg prolonged-release tablets** by **Sanofi-Aventis France** is amended.

Article 2

The product information annexed to this Decision supersedes the corresponding information in the Annexes to the current Marketing Authorization.

Article 3

The concerned party is hereby notified of this Decision.

October 15, 2018
[date stamped]

[stamp]
Division of Medicines used in Cardiology,
Rheumatology, Stomatology,
Endocrinology, Gynecology, Urology,
Pulmonology, ENT, and Allergology

(Original French document *signed)*

Céline Druet
Deputy Director

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Xatral LP 10 mg prolonged-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Alfuzosin hydrochloride ..... 10 mg

For one prolonged-release tablet.

Excipient with known effect: hydrogenated castor oil.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release tablets.

4. CLINICAL PARTICULARS

4.1. 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.

4.2. Posology and method of administration

Posology

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.

Pediatric patients

Since the efficacy of alfuzosin has not been demonstrated in children aged between 2 and 16 years (see Section 5.1), it should not be used in pediatric patients.

Method of administration

The tablet must be swallowed whole with a glass of water (see Section 4.4).

4.3. Contraindications

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

- Hypersensitivity to alfuzosin and/or any of the other excipients mentioned in Section 6.1;
- Postural hypotension;
- Liver failure;
- Severe kidney failure (creatinine clearance < 30 mL/min);
- In combination with potent CYP3A4 inhibitors (see section 4.5);
- In combination with ombitasvir and paritaprevir (see section 4.5).

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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).

Some patients may experience postural hypotension within a few hours following administration, possibly with symptoms (dizzy spells, fatigue, sweating). If this occurs, patients should remain lying down until the symptoms have completely subsided.

These effects are usually transient, occur at the beginning of treatment and do not generally prevent continued treatment.

A marked drop in blood pressure has been reported in post-marketing surveillance in patients with pre-existing risk factors (such as underlying cardiac disease and/or concomitant treatment with anti-hypertensive medication).

There is a risk of stroke, 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 onset of hypotension following administration of alfuzosin (see Section 4.8).

Patients should be warned of the possible occurrence of these events.

Caution is recommended, particularly in the elderly. The risk of hypotension and related symptoms may be higher 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.

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 small pupil syndrome variant) has been observed during cataract surgery in some patients previously or currently 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).

Precautions for use

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

In patients with coronary disease, alfuzosin should not be prescribed alone. Specific heart failure treatment should be continued. If angina pectoris recurs or worsens, alfuzosin treatment 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 (see Section 4.5).

To reduce the risk of postural hypotension, patients must be stabilized 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.

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Patients should be informed that the tablets must be swallowed whole. They must not be crunched, chewed, crushed or ground into a powder.

Doing so could lead to inappropriate release and absorption of the medicinal product, consequently causing undesirable effects which may be of early onset.

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

Drugs that induce postural hypotension
In addition to antihypertensive agents, numerous drugs can cause postural 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

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

There is a risk of increased plasma alfuzosin concentrations and increased undesirable effects.

+ **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)**

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

Combinations requiring precautions for use

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

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

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

Combinations to be taken into consideration

+ **Antihypertensives except alpha-blockers**

There is a risk of severe postural 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 postural.

4.6. Fertility, pregnancy and lactation

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.

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 postural hypotension, dizzy spells, asthenia and visual disturbances, particularly at the beginning of treatment.

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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				intraoperative floppy iris syndrome
General disorders and administration site conditions	asthenia malaise	edema, chest pain		
Gastrointestinal disorders	nausea, abdominal pain	diarrhea, dry mouth, vomiting		
Hepatobiliary disorders				hepatocellular injury, hepatic cholestasis
Nervous system disorders	dizzy spells, lightheadedness, headache	syncope, dizziness, drowsiness		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 rash, pruritus	urticaria, angioedema	
Vascular disorders		postural hypotension (see section 4.4) flushing		

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Blood and lymphatic system disorders				neutropenia, thrombocytopenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 Centers) - Website: www.ansm.sante.fr.

4.9. Overdose

If overdose occurs, the patient should be hospitalized 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 fibers 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.

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

In the ALFAUR study, the effect of alfuzosin on the return to 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 prolonged-release alfuzosin 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 post-catheter 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.

Pediatric patients

Alfuzosin should not be used in pediatric patients (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 pediatric formulations.

5.2. Pharmacokinetic properties

Alfuzosin

Alfuzosin hydrochloride is approximately 90% plasma protein bound.

Alfuzosin is extensively metabolized 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 feces (75 to 90%).

The pharmacokinetic pattern of alfuzosin is unchanged in patients with chronic heart failure.

Prolonged-release formulation

The mean value of the relative bioavailability is 104.4% following administration of a 10 mg dose *versus* the immediate-release formulation at a dose of 7.5 mg (2.5 mg three times daily) in middle-aged healthy volunteers. Peak plasma concentrations are reached 9 hours after administration compared to 1 hour for the immediate-release formulation.

The apparent elimination half-life is 9.1 hours.

Studies have shown that bioavailability is increased when the medicinal product is administered after a meal (see section 4.2).

Compared to healthy 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 are moderately increased in patients with moderate renal impairment (creatinine clearance > 30 mL/min), with no change in elimination half-life.

Dose adjustment is, therefore, not necessary in patients with renal failure with a creatinine clearance of > 30 mL/min.

5.3. Preclinical safety data

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Hypromellose, hydrogenated castor oil, ethylcellulose, yellow iron oxide, colloidal hydrated silica, magnesium stearate, mannitol, povidone, microcrystalline cellulose.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

No special precautions for storage.

6.5. Nature and contents of container

28 tablets in (PVC/aluminum) blisters.

30 tablets in (PVC/aluminum) blisters.

50 tablets in (PVC/aluminum) blisters.

90 tablets in (PVC/aluminum) blisters.

100 tablets in (PVC/aluminum) blisters.

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6.6. Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORIZATION HOLDER

Sanofi-Aventis France
82 avenue Raspail
94250 Gentilly, France

8. MARKETING AUTHORIZATION NUMBERS

- 34009 351 104 3 5: 28 tablets in (PVC/aluminum) blisters.
- 34009 351 106 6 4: 30 tablets in (PVC/aluminum) blisters.
- 34009 561 623 7 6: 50 tablets in (PVC/aluminum) blisters.
- 34009 387 233 8 0: 90 tablets in (PVC/aluminum) blisters.
- 34009 561 624 3 7: 100 tablets in (PVC/aluminum) blisters.

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

To be filled in subsequently by the Marketing Authorization holder

10. DATE OF REVISION OF THE TEXT

To be filled in subsequently by the Marketing Authorization holder

11. DOSIMETRY

Not applicable.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Not applicable.

GENERAL CLASSIFICATION FOR SUPPLY

List I

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

A.1 Name and address of the manufacturer(s) of the biological active substance(s)

Not applicable.

A.2 Name and address of the manufacturer(s) responsible for batch release

Sanofi Winthrop Industrie
30-36 avenue Gustave Eiffel
37000 Tours, France

OR

Sanofi Synthelabo Limited
Edgefield Avenue
Fawdon, Newcastle on Tyne
Tyne & Wear NE3 3TT
United Kingdom

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

List I

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORIZATION

Not applicable.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

Not applicable.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORIZATION MEASURES FOR THE MARKETING AUTHORIZATION UNDER EXCEPTIONAL CIRCUMSTANCES

Not applicable.

F. QUALITATIVE AND QUANTITATIVE COMPOSITION IN EXCIPIENTS

Hypromellose	203.76 mg
Hydrogenated castor oil	41.40 mg
Ethylcellulose	5.00 mg
Yellow iron oxide	0.40 mg
Colloidal hydrated silica	2.80 mg
Magnesium stearate	4.17 mg
Mannitol	10.00 mg
Povidone	7.92 mg
Microcrystalline cellulose	65.00 mg

ANNEX IIIA

LABELING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

NATURE/TYPE OUTER PACKAGING OR IMMEDIATE PACKAGING

Outer packaging.

1. NAME OF THE MEDICINAL PRODUCT

Xatral LP 10 mg prolonged-release tablets

Alfuzosin hydrochloride

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Alfuzosin hydrochloride ..... 10 mg

For one prolonged-release tablet.

3. LIST OF EXCIPIENTS

Excipients with known effect: Hydrogenated castor oil

4. PHARMACEUTICAL FORM AND CONTENTS

Prolonged-release tablets.

Box of 28, 30, 50, 90 or 100 tablets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Not applicable.

8. EXPIRY DATE

EXP {MM/YYYY}

9. SPECIAL STORAGE CONDITIONS

Not applicable.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

Not applicable.

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11. NAME AND ADDRESS OF THE MARKETING AUTHORIZATION HOLDER

Marketing Authorization Holder

Sanofi-Aventis France
82 avenue Raspail
94250 Gentilly, France

Operating Company

Sanofi-Aventis France
82 avenue Raspail
94250 Gentilly, France

12. MARKETING AUTHORIZATION NUMBERS

Marketing Authorization No.:

13. BATCH NUMBER

Batch {number}

14. GENERAL CLASSIFICATION FOR SUPPLY

List I

15. INSTRUCTIONS ON USE

Not applicable.

16. INFORMATION IN BRAILLE

The Decision of May 07, 2018, in application of Article R. 5121-138 of the French Public Health Code published in the Official Journal of the Republic of France of May 22, 2018 must be complied with.

17. UNIQUE IDENTIFIER – 2D BAR CODE

2D bar code carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC: {number} [CIP code]

SN: {number} [serial number]

PICTOGRAM TO APPEAR ON THE OUTER PACKAGING OR, WHERE THERE IS NO OUTER PACKAGING, ON THE IMMEDIATE PACKAGING

[Pictogram relative to teratogenic or fetotoxic effects]

If applicable, the pictogram mentioned in section III of Article R. 5121-139 of the French Public Health Code (teratogenic or fetotoxic effects) must be affixed in accordance with the application decree stipulated in the same article.

[Pictogram relative to effects on the ability to drive]

The pictogram mentioned in section II of Article R.5121-139 of the French Public Health code (effects on the ability to drive) must comply with the decree stipulated in the same article.

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

NATURE/TYPE BLISTERS/STRIPS

Blisters (PVC/Aluminum).

1. NAME OF THE MEDICINAL PRODUCT

Xatral LP 10 mg prolonged-release tablets

Alfuzosin hydrochloride

2. NAME OF THE MARKETING AUTHORIZATION HOLDER

Sanofi-Aventis France

3. EXPIRY DATE

EXP {MM/YYYY}

4. BATCH NUMBER

Batch {number}

5. OTHER

Not applicable.

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MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

NATURE/TYPE SMALL IMMEDIATE PACKAGING UNITS

Not applicable.

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Not applicable.

2. METHOD OF ADMINISTRATION

Not applicable.

3. EXPIRY DATE

Not applicable.

4. BATCH NUMBER

Not applicable.

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

Not applicable.

6. OTHER

Not applicable.

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ANNEX IIIB

PACKAGE LEAFLET: INFORMATION FOR THE USER

Name of the medicinal product

Xatral LP 10 mg prolonged-release tablets

Alfuzosin hydrochloride

Text box

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See Section 4.

What is in this leaflet

1. WHAT Xatral LP 10 mg prolonged-release tablets ARE AND WHAT THEY ARE USED FOR

Pharmacotherapeutic group - ALPHA-BLOCKERS - ATC code: G04CA01 - G: genito-urinary system and sex hormones

Xatral contains alfuzosin. This medicine belongs to a group of medicines called alpha-blockers. It has an effect on the bladder, the tube which takes urine outside of the body (the urethra) and the prostate.

Xatral is used when your prostate increases in size (benign prostatic hyperplasia):

- to make it easier to urinate,
- or in addition to the urine being drained using a catheter in your bladder, when it is impossible to urinate.

This medicine is for use in men only.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE Xatral LP 10 mg prolonged-release tablets

Do not take Xatral LP 10 mg prolonged-release tablets:

- if you are allergic to alfuzosin or any of the other ingredients of this medicine (listed in section 6).
- if you have postural hypotension (drop in blood pressure when standing up, possibly with dizziness and/or fainting);
- if you have a serious liver disease (liver failure) or a serious kidney disease (severe kidney failure);
- if you are taking certain medicines used to treat HIV (e.g. a protease inhibitor in combination with ritonavir or cobicistat), or used to treat hepatitis C (e.g. telaprevir, boceprevir, ombitasvir and paritaprevir), or used to treat certain fungal infections (e.g. ketoconazole, itraconazole, posaconazole), or used in certain bacterial infections (e.g. clarithromycin, erythromycin, telithromycin) (see section **"**Other medicines and **Xatral LP** 10 mg prolonged-release tablets**"**).

Warnings and precautions

Talk to your doctor or pharmacist before taking **Xatral LP** 10 mg prolonged-release tablets.

Before beginning treatment, inform your doctor if you have heart disease (particularly if you have angina pectoris, acute heart failure or heart rhythm problems) or if you have ever experienced a significant drop in blood pressure with another medicine from the same group of medicines as Xatral (alpha-blockers).

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During treatment

Postural hypotension (drop in blood pressure when standing up) may develop in the first few hours after taking the medicine and be accompanied by dizziness, tiredness or sweating.

If this effect occurs, lie down until these symptoms, which are temporary, completely wear off, and contact your doctor.

This effect is seen particularly in elderly patients or patients who are also taking medicine to treat high blood pressure or nitrate derivatives (medicines used for angina pectoris).

This medicine must be used with caution in patients with blood flow problems in the brain, particularly in elderly patients.

Contact your doctor immediately if you experience painful prolonged erection.

You should avoid using this medicine in combination with medicines used to treat high blood pressure (antihypertensives such as doxazosin, prazosin and urapidil) (see section "Other medicines and **Xatral LP** 10 mg prolonged-release tablets").

If you are going to have eye surgery (on a cataract) tell your ophthalmologist before the operation if you have recently been or are currently being treated with Xatral. This medicine can have an effect on the pupil (intraoperative floppy iris syndrome) that may lead to complications during surgery.

However, if the surgeon is warned in advance, he or she will take the necessary precautions.

This medicine contains castor oil, which can cause digestive disorders (mild laxative effect, diarrhea).

Other medicines and Xatral LP 10 mg prolonged-release tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You must not take this medicine in combination with certain medicines used to treat HIV (e.g. a protease inhibitor in combination with ritonavir or cobicistat), or used to treat hepatitis C (e.g. telaprevir, boceprevir, ombitasvir and paritaprevir), or used to treat certain fungal infections (e.g. ketoconazole, itraconazole, posaconazole), or used in certain bacterial infections (e.g. clarithromycin, erythromycin, telithromycin) (see section "Do not take **Xatral LP** 10 mg").

You should avoid taking this medicine in combination with certain medicines used to treat high blood pressure (antihypertensives such as doxazosin, prazosin and urapidil) (see section "Warnings and precautions").

Xatral LP 10 mg prolonged-release tablets with food and drink

Not applicable.

Pregnancy, breast-feeding and fertility

This medicine is not intended for use in women.

Driving and using machines

You must take care if you drive a vehicle or use machines.

This medicine can cause a significant drop in blood pressure when standing up, along with dizziness, tiredness or vision disorders, especially at the start of treatment.

Xatral LP 10 mg prolonged-release tablets contain castor oil.

3. HOW TO TAKE Xatral LP 10 mg prolonged-release tablets

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Dosage

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

Your doctor will tell you how long you should take the medicine for.

If you use a vesical catheter, take this medicine from the first day the catheter is inserted.

Method of administration

This medicine must be swallowed whole with a glass of water. These are prolonged-release tablets, i.e. the active ingredient diffuses slowly inside your body.

For the tablets to retain all their properties, you must not crunch, chew, crush or grind them into a powder.

Use in children

Xatral must not be taken by children aged between 2 and 16 years.

If you take more Xatral LP 10 mg prolonged-release tablets than you should:

Consult your doctor or go to the emergency room immediately.

If you forget to take Xatral LP 10 mg prolonged-release tablets:

Do not take a double dose to make up for a forgotten dose.

If you stop taking Xatral LP 10 mg prolonged-release tablets:

Not applicable.

4. POSSIBLE SIDE EFFECTS

Like all medicines, **Xatral LP** 10 mg prolonged-release tablets can cause side effects, although not everybody gets them.

Common effects:

- Lightheadedness, dizzy spells, fainting, headache;
- Digestive disorders such as nausea, stomach pain;
- Tiredness.

Uncommon effects:

- Dizziness, drowsiness, syncope (sudden loss of consciousness);
- Drop in blood pressure when standing up from a lying position (see section **"**Warnings and precautions**"**);
- Accelerated heart rate, palpitations,
- Diarrhea;
- Vomiting,
- Dry mouth;
- Nasal congestion or runny nose (rhinitis);
- Outbreak of spots on the skin or itching;
- Swelling, chest pain;
- Redness of the face.

Very rare effects:

- Angina pectoris in patients with a history of coronary artery disorders (see section **"**Warnings and precautions**"**);
- Hives, sudden swelling of an organ, the face and/or the neck that can make it difficult to breathe and be life-threatening to the patient (angioedema).;

Effects of unknown frequency:

- Liver disease (hepatitis), particularly due to biliary tract obstruction;
- Painful, prolonged erection;
- Floppy pupil during cataract surgery (see section **"**Warnings and precautions**"**);
- Irregular heartbeat (atrial fibrillation);
- Decreased number of white blood cells (neutropenia);
- Decreased number of platelets (thrombocytopenia);
- Stroke (not enough blood flow to the brain).

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system, i.e. *Agence Nationale de Sécurité du Médicament et des Produits de Santé* (ANSM) under "*Réseau des*

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Centres Régionaux de Pharmacovigilance" (network of Regional Pharmacovigilance Centers) - Website: www.ansm.sante.fr

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE Xatral LP 10 mg prolonged-release tablets

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the box.

No special precautions for storage.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Xatral LP 10 mg prolonged-release tablets contain

- The active substance is:
  Alfuzosin hydrochloride..... 10 mg

  For one prolonged-release tablet.
- The other ingredients are: hypromellose, hydrogenated castor oil, ethylcellulose, yellow iron oxide, colloidal hydrated silica, magnesium stearate, mannitol, povidone, microcrystalline cellulose.

What Xatral LP 10 mg prolonged-release tablets look like and contents of the pack

This medicine is supplied as prolonged-release tablets.

Box of 28, 30, 50, 90 or 100 tablets.

Marketing Authorization Holder

Sanofi-Aventis France
82 avenue Raspail
94250 Gentilly, France

Operating Company

Sanofi-Aventis France
82 avenue Raspail
94250 Gentilly, France

Manufacturer

Sanofi Winthrop Industrie
30-36 avenue Gustave Eiffel
37000 Tours, France

or

Sanofi Synthelabo Limited
Edgefield Avenue
Fawdon, Newcastle on Tyne
Tyne & Wear NE3 3TT
United Kingdom

Names of the medicinal product in the Member States of the European Economic Area

Not applicable.

This leaflet was last revised in:

[To be filled in subsequently by the Marketing Authorization holder]

Other

Detailed information about this medicine is available on the ANSM website (France).

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