SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINE

Clopixol Depot 200 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Zuclopenthixol decanoate 200 mg/ml.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Injectable solution

Clear, light yellow oily solution, practically free of particles.

4. CLINICAL DATA

4.1 Therapeutic indications

Indicated for the maintenance treatment of schizophrenia and other psychotic disorders with primarily symptoms of hallucinations, delusions and thought disorders accompanied by agitation, impatience, hostility and aggression.

Clopixol Depot is indicated for use in adults.

4.2 Dosage and method of administration

Dosage

Adults:
The dose to be used and the interval between injections will be adapted by the attending physician to the clinical condition of the individual patient, in order to obtain maximum suppression of psychotic symptoms with a minimum of adverse effects.

The maintenance dose normally ranges from 200 to 400 mg (1 to 2 ml) administered every 2 to 4 weeks. Occasionally, some patients require a higher dose or a shorter interval between injections.
Injection volumes exceeding 2 ml should be divided between two injection sites.

To switch from oral zuclopenthixol or intramuscular zuclopenthixol acetate treatment to zuclopenthixol decanoate maintenance treatment, the following guidelines apply:

1) Switching from oral zuclopenthixol to zuclopenthixol decanoate:
x mg orally per day corresponds to 8x mg decanoate every 2 weeks.
x mg orally per day corresponds to 16x mg decanoate every 4 weeks.

During the first week after the first injection, treatment should be continued orally, however at a reduced dose.

2) Switching from zuclopenthixol acetate to zuclopenthixol decanoate:
In conjunction with the last zuclopenthixol acetate (100 mg) injection, an intramuscular injection of 200 mg–400 mg (1 ml–2 ml) of zuclopenthixol decanoate should be administered and repeated every 2 weeks. Higher doses and shorter intervals between injections may be necessary.
Zuclopenthixol acetate and zuclopenthixol decanoate can be mixed in a syringe for administration in a single injection (co-injection).

Patients who are to switch from other depot preparations to zuclopenthixol decanoate should receive a dose of 200 mg of zuclopenthixol decanoate which is equivalent to 25 mg of flufenazine decanoate, 40 mg of cis(Z)flupentixol decanoate or 50 mg of haldol decanoate.

The subsequent doses of zuclopenthixol decanoate and the intervals between injections will be determined based on the patient's response.

Elderly patients
receive the lowest effective dose possible.

Children:
The use of Clopixol Depot in children is not recommended due to a lack of clinical data.

Renal insufficiency:
Clopixol Depot can be administered to patients with renal insufficiency at the usual dosage.

Liver failure
: Dosage with caution and, if possible, blood level measurement is advised.

Method of administration

Clopixol Depot is administered as an intramuscular injection in the upper lateral quadrant of the gluteus maximus. Injection volumes exceeding 2 ml should be divided between two injection sites. Local tolerance is good.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Circulatory collapse, decreased consciousness of any cause (e.g. due to alcohol, barbiturate or opiate intoxication), coma.

4.4 Special warnings and precautions for use

As with any neuroleptic, there is a risk of developing **neuroleptic malignant syndrome** , the symptoms of which include hyperthermia, rigidity, unstable consciousness, and unstable autonomic nervous system function. However, the risk is higher with more potent neuroleptics. Patients with pre-existing organic brain syndrome, intellectual disability, and opiate and alcohol abuse are overrepresented among fatal cases.
Treatment involves discontinuing the neuroleptic and providing general supportive care. The administration of dantrolene and bromocriptine may be helpful.

Symptoms may continue for more than a week after stopping oral neuroleptic use and sometimes even longer in the case of the depot form.

Extrapyramidal effects may occur, particularly during the first few days after injection and at the start of treatment. In most cases, these adverse effects can be satisfactorily controlled by reducing the dosage and/or administering antiparkinsonian drugs. The use of antiparkinsonian drugs is not recommended for routine prophylaxis. Antiparkinsonian drugs do not alleviate tardive dyskinesia and may worsen it. It is recommended to reduce the dosage or, when possible, discontinue treatment with zuclopenthixol. In cases of persistent akathisia, a benzodiazepine or propranolol may be helpful.

Dysphagia can occur secondary to extrapyramidal symptoms, as well as sialorrhea, sedation, or neuroleptic malignant syndrome, and can lead to life-threatening complications such as aspiration pneumonia and suffocation.

Like any other neuroleptic, zuclopenthixol will be used with **caution** in patients with **organic cerebral syndrome, seizures, diabetes, or advanced liver or kidney disease** .

As has been described for other psychotropic drugs, zuclopenthixol decanoate can alter **blood levels of insulin and glucose** ; consequently, antidiabetic therapy must be adapted in diabetics.

In cases of prolonged treatment, especially at high doses, close monitoring of the patient is advised with a view to reducing the maintenance dose.

Great caution is also required in patients suffering from **angle-closure glaucoma or benign prostatic hyperplasia (BPH**).

Hyperprolactinemia induced by taking Clopixol Depot can negatively affect the prognosis of pre-existing breast cancer. Therefore, the drug should be administered with caution in such circumstances **.**

As with other drugs in the antipsychotic class, zuclopenthixol decanoate can cause QT interval prolongation. Continued **QT interval** prolongation may increase the risk of malignant arrhythmias. For this reason, zuclopenthixol decanoate should be used with caution in individuals at risk (hypokalemia, hypomagnesemia, or genetic predisposition) and in patients with a history of cardiovascular disorders, e.g., QT prolongation, significant bradycardia (<50 beats/min), recent acute myocardial infarction, uncompensated heart failure, or cardiac arrhythmias. Furthermore, zuclopenthixol should be used with caution in patients with a family history of QT interval prolongation.
Concomitant treatment with other antipsychotics should be avoided. (See section 4.5)

Cases of venous thromboembolism (**VTE**) have been reported with antipsychotic medications. Since patients treated with antipsychotics often have acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Clopixol Depot, and preventive measures should be taken.

Leukopenia, neutropenia, and agranulocytosis have been reported with antipsychotics, including zuclopentixol decanoate.
Long-acting depot neuroleptics should be used with caution in combination with other drugs known to have myelosuppressive potential, as they cannot be rapidly withdrawn from the body when necessary.

elderly patients

Cerebrovascular:
In randomized, placebo-controlled clinical trials with certain atypical antipsychotics, approximately three times the risk of **cerebrovascular adverse events** was observed in patients **with dementia** . The mechanism for this increased risk is unknown. A high risk cannot be excluded for other antipsychotics or for other patient groups. Clopixol Depot should be used with caution in patients who exhibit risk factors for a cerebrovascular event.

Increased Mortality in Older Adults with Dementia:
Data from two large-scale observational studies have shown that older adults with dementia who are treated with antipsychotics have a slightly increased risk of death compared to those who are not treated. There is insufficient data to provide a definitive estimate of the precise magnitude of the risk, and the cause of the increased risk is unknown.

Clopixol Depot is not authorized for the treatment of behavioral disorders related to dementia.

4.5 Interactions with other medicinal products and other forms of interaction

Combinations requiring precautions for use

Zuclopenthixol decanoate may enhance the sedative effect of alcohol, barbiturates, and other drugs that cause central nervous system depression.

Neuroleptics can either enhance or counteract the hypotensive effect of antihypertensive drugs.

Simultaneous use with lithium increases the risk of neurotoxic effects.

Neuroleptics lower the seizure threshold; therefore, caution is required when used concomitantly with other drugs that could cause seizures, e.g. tramadol.

Tricyclic antidepressants and neuroleptics can mutually inhibit their metabolism.

Zuclopenthixol decanoate may decrease the effect of levodopa and adrenergic drugs, including dopamine agonists.

Combining zuclopenthixol decanoate with metoclopramide or piperazine may increase the risk of extrapyramidal symptoms.

Since zuclopenthixol is partially metabolized by CYP2D6, the concomitant use of drugs that inhibit this enzyme may decrease the plasma clearance of zuclopenthixol.

Regarding antipsychotic treatment, QT interval prolongation may be exacerbated by the concomitant administration of other drugs known to significantly prolong the QT interval, as well as with drugs that disrupt electrolyte balance (hypokalemia, hypomagnesemia) and with drugs that cause bradycardia. Concomitant administration of these drugs should be avoided.
The classes of drugs concerned include, but are not limited to:

- Class Ia and III antiarrhythmics (e.g., quinidine, amiodarone, sotalol)
- Some antipsychotics (e.g., thioridazide)
- Some macrolides (e.g., erythromycin)
- Some antihistamines (e.g., terfenadine)
- Some antibiotics in the quinolone group (e.g., moxifloxacin)

This list is not exhaustive and other specific drugs that are known to significantly prolong the QT interval (e.g. lithium) should be avoided.

Zuclopenthixol should be used with caution with drugs known to disrupt fluid/electrolyte balance, such as thiazide diuretics (hypokalemia), or known to increase plasma concentrations of zuclopenthixol, as this may increase the risk of QT prolongation and malignant arrhythmias. (see section 4.4)

4.6 Fertility, pregnancy and breastfeeding

Pregnancy:
Zuclopenthixol decanoate should only be used during pregnancy if the therapeutic benefit outweighs the risk to the fetus.
Newborns who have been exposed to antipsychotics (including Clopixol Depot) during the third trimester of pregnancy are at risk of adverse effects, including extrapyramidal effects and/or withdrawal symptoms after delivery, which may vary in severity and duration. The following effects have been reported: agitation, hypertonia, hypotonia, tremors, drowsiness, respiratory disturbances, or feeding difficulties. Therefore, newborns should be closely monitored.

Newborns of mothers treated with neuroleptics at the end of pregnancy or during delivery may exhibit signs of intoxication such as lethargy, tremors, hyperexcitability, and a low Apgar score.

Animal studies have shown reproductive toxicity (see section 5.3).

Breastfeeding:
Given the low concentrations of zuclopenthixol found in breast milk, it is unlikely that a therapeutic dose would have any effect on the infant. The dose ingested by the newborn is less than 1% of the mother's daily dose per unit of weight (mg/kg). When the clinical benefit outweighs the risks, breastfeeding can be continued during treatment with zuclopenthixol decanoate, but monitoring of the newborn, especially during the first 4 weeks after birth, is advised.

Fertility:
There are no clinical study data available on the effect of the active substance zuclopenthixol on fertility.

Side effects such as hyperprolactinemia, galactorrhea, amenorrhea, erectile dysfunction, and ejaculation disorders have been reported (see section 4.8). These side effects may negatively impact sexual function and fertility in women and/or men.

In the event of clinically significant hyperprolactinemia, galactorrhea, amenorrhea, or sexual dysfunction, a dose reduction (if possible) or discontinuation of treatment should be considered. Side effects are reversible upon discontinuation of treatment.

Animal studies have shown an adverse effect on fertility (see section 5.3).

4.7 Effects on the ability to drive vehicles and use machinery

Clopixol Depot has a sedative effect, which has a minor to moderate influence on the ability to drive and operate machinery. Patients taking this psychotropic medication may experience mild problems with attention and concentration. For this reason, caution is advised when driving and operating machinery.

4.8 Side effects

Summary of the safety profile.
Most adverse reactions are dose-dependent. The frequency and intensity of adverse reactions most often occur during the initial phase of treatment and subside during treatment.

List of adverse effects presented in tabular form.
The reported frequencies were taken from the literature and also from spontaneous reports. Frequencies are defined as follows:
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), not known (cannot be estimated from the available data).

Organ system classes	Frequency	Preferred term
Hematological and lymphatic system disorders	Rare	Thrombocytopenia, neutropenia, leukopenia, agranulocytosis
Immune system disorders	Rare	Hypersensitivity, anaphylactic reaction
Endocrine disorders	Rare	Hyperprolactinemia

Metabolism and nutrition disorders	Frequent	Increased appetite, weight gain
	Uncommon	Decreased appetite, weight loss
	Rare	Hyperglycemia, impaired glucose tolerance, hyperlipidemia
Psychiatric disorders	Frequent	Insomnia, depression, anxiety, nervousness, abnormal dreams, agitation, decreased libido,
	Uncommon	Apathy, nightmares, increased libido, confusion
Disorders of the nervous system	Very common	Drowsiness, akathisia, hyperkinesia, hypokinesia, extrapyramidal symptoms (see section 4.4)
	Frequent	Tremors, dystonia, hypertonia, dizziness, headache, paresthesia, difficulty concentrating, amnesia, gait disturbances
	Uncommon	Tardive dyskinesia, hyperreflexia, dyskinesia, parkinsonism, syncope, ataxia, speech disorder, hypotonia, seizures, migraine
	Very rare	Neuroleptic malignant syndrome
Eye conditions	Frequent	Accommodation disorder, visual disturbances
	Uncommon	Oculogyric crisis, mydriasis
Ear and labyrinth disorders	Frequent	Vertigo
	Uncommon	Hyperacusis, ringing in the ears
Heart conditions	Frequent	Tachycardia, palpitations
	Rare	Electrocardiogram: QT interval prolongation
Vascular disorders	Frequent	Hypotension, orthostatic hypotension
	Uncommon	Hot flashes
	Very rare	Venous thromboembolism
Respiratory, thoracic and mediastinal disorders	Frequent	Nasal congestion, dyspnea
Gastrointestinal disorders	Very common	Dry mouth
	Frequent	Hypersalivation, constipation, vomiting, dyspepsia, diarrhea
	Uncommon	Abdominal pain, nausea, flatulence
	Rare	Dysphagia* (see section 4.4)
Hepatobiliary disorders	Uncommon	Abnormal liver function tests
	Very rare	Cholestatic hepatitis, jaundice
Skin and subcutaneous tissue disorders	Frequent	Hyperhidrosis, itching
	Uncommon	Rash, photosensitivity reaction, pigmentation disorder, seborrhea, dermatitis, purpura
Musculoskeletal and systemic disorders	Frequent	Myalgia
	Uncommon	Muscle rigidity, trismus, torticollis
Kidney and urinary tract disorders	Frequent	Urinary problems, urinary retention, polyuria
Pregnancy, puerperal and perinatal conditions	Frequency not known	Neonatal withdrawal syndrome (see section 4.6)

Diseases of the reproductive organs and breast	Uncommon	Ejaculation disorder, erectile dysfunction, female orgasmic disorder, vulvovaginal dryness
	Rare	Gynecomastia, galactorrhea, amenorrhea, priapism
General disorders and administration site abnormalities	Frequent	Asthenia, fatigue, malaise, pain
	Uncommon	Thirst, injection site reaction, hypothermia, fever

Dysphagia *can occur following extrapyramidal symptoms, as well as sialorrhea, sedation or neuroleptic malignant syndrome and can lead to life-threatening complications such as aspiration pneumonia and suffocation.*

Description of selected adverse reactions
As with other drugs belonging to the therapeutic class of antipsychotics, rare cases of QT prolongation, ventricular arrhythmia, ventricular fibrillation, ventricular tachycardia, Torsades de Pointes, cardiac arrest and sudden death have been reported with zuclopenthixol decanoate (see section 4.4).

Abrupt discontinuation of zuclopenthixol decanoate may be accompanied by withdrawal symptoms. The most common symptoms are nausea, vomiting, anorexia, diarrhea, rhinorrhea, sweating, myalgia, paresthesia, insomnia, restlessness, anxiety, and agitation. Patients may also experience dizziness, alternating hot and cold flashes, and tremors. Generally, symptoms appear on days 1 to 4 after stopping treatment and subside after 7 to 14 days.

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 national reporting systems.

In Belgium:
Federal Agency for Medicines and Health Products
www.afmps.be
Vigilance Division:
Website: www.notifieruneffetindesirable.be
Email: adr@fagg-afmps.be

In Luxembourg:
Regional Pharmacovigilance Centre of Nancy or Pharmacy and Medicines Division of the Directorate of Health.
Website: www.guichet.lu/pharmacovigilance

4.9 Overdose

Given the method of administration, symptoms of overdose are unlikely to occur.

Symptoms:
Drowsiness, coma, movement disorders, seizures, shock, hyper- or hypothermia.
In case of overdose with drugs known to affect the heart, ECG changes, QT interval prolongation, Torsades de Pointes, cardiac arrest, and ventricular arrhythmias have been observed.

Treatment
will be symptomatic and supportive. Measures should be taken to support the respiratory and cardiovascular systems. Epinephrine (adrenaline) will not be used, as it may exacerbate a drop in blood pressure. Seizures may be treated with diazepam, and extrapyramidal symptoms with biperiden.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic class: Neuroleptics (antipsychotic), ATC code: N05AF05.

Mechanism of action:
Zuclopenthixol is a neuroleptic belonging to the thioxanthene group. The antipsychotic effect of neuroleptics is linked to their antagonistic effect on dopaminergic receptors, but blockade of the 5-HT (5-hydroxytryptamine) receptor likely also plays a role. *In vitro* , zuclopenthixol has a high affinity for both D1 and D2 dopaminergic receptors, as well as for α1-adrenergic and 5- HT2 receptors , but no affinity for muscarinic cholinergic receptors. It possesses only weak antihistamine properties and does not block □2 - adrenergic receptors .

In vivo, affinity for D2 binding sites dominates over affinity for D1 receptors . Zuclopenthixol has demonstrated potent neuroleptic activity in all behavioral studies (dopamine receptor blockade). A correlation was found between *in vivo* test models , affinity for dopamine D2 binding sites in *vitro* , and average daily oral doses of the antipsychotic.

Like most neuroleptics, zuclopenthixol increases plasma prolactin levels.

Pharmacological studies have clearly demonstrated a pronounced neuroleptic effect after parenteral injection of zuclopenthixol decanoate oily solution; the amount of drug required to maintain a certain effect over a prolonged period is significantly lower with depot preparations than with daily oral administration of zuclopenthixol. Regarding clinical use, study results may indicate that a prolonged neurological effect can be achieved without significant sedation using the depot preparation.

Clinical efficacy and safety:
In clinical use, zuclopenthixol decanoate is intended for the maintenance treatment of patients with acute psychosis. Positive results have also been obtained in controlling hyperactivity and aggression in mentally disabled patients.

Zuclopenthixol decanoate induces dose-dependent but transient sedation. However, if the patient switches from oral zuclopenthixol or zuclopenthixol acetate to maintenance therapy with zuclopenthixol decanoate, sedation will not be a problem. Tolerance to this non-specific sedative effect develops rapidly.

Zuclopenthixol decanoate is especially useful for treating agitated, disturbed, hostile, or aggressive patients.

Zuclopenthixol decanoate allows for uninterrupted treatment, especially for patients who are not adherent to their prescribed oral medication. Zuclopenthixol decanoate thus prevents frequent relapses in patients who are not compliant with oral treatment.

Pediatric population:
No data available.

5.2 Pharmacokinetic properties

Absorption
: Esterification of zuclopenthixol by decanoic acid transforms zuclopenthixol into a more lipophilic substance: zuclopenthixol decanoate. Solubilized in vegetable oil and injected intramuscularly, this substance diffuses slowly into the interstitial fluid, where it undergoes rapid enzymatic hydrolysis, releasing the active ingredient: zuclopenthixol.

Peak serum concentration is reached within 3–7 days after intramuscular injection. The mean serum elimination half-life (which reflects the release of the oily phase) is estimated at 3 weeks. Steady-state conditions after repeated administration are reached after approximately 3 months.

Distribution
The apparent volume of distribution (Vd) β is ± 20 l/kg. Binding to serum proteins is approximately 98–99%.

Biotransformation:
Zuclopenthixol is metabolized via three main pathways: sulfoxidation, N-dealkylation of the side chain, and glucuronidation. The metabolites have no pharmacological activity. In the brain and other tissues, the concentration of zuclopenthixol is higher than that of its metabolites.

Elimination:
The elimination half-life (T _{1/2β}) of zuclopenthixol is approximately 20 hours and the mean blood clearance (CL _s) is approximately 0.86 L/min.
Zuclopenthixol is primarily excreted in the feces and to a lesser extent (10%) in the urine.

Only about 0.1% of the dose is excreted unchanged in the urine, indicating that the influence of the drug on the kidneys is negligible.

Zuclopenthixol is secreted in small amounts into breast milk in breastfeeding mothers. The steady-state milk/serum concentration ratio was approximately 0.29 after oral administration (or administration of the depot form) in women.

Linearity/non-linearity
The kinetics are linear. The mean steady-state plasma levels of injectable zuclopenthixol, corresponding to a dose of 200 mg of zuclopenthixol decanoate every 2 weeks, are approximately 10 ng/l (25 nmol/ml).

Elderly patients:
Pharmacokinetic parameters are largely independent of patient age.

Decreased renal function
Based on the elimination characteristics described above, it can be reasonably estimated that a decrease in renal function should not significantly influence plasma levels of the parent substance.

Decreased liver function:
No data available

Polymorphism
An *in vivo* study showed that metabolism is partly subject to genetic polymorphism of sparteine/debrisoquine oxidation (CYP2D6).

Pharmacokinetic/pharmacodynamic relationship:
A plasma concentration (measured before injection) of 2.8–12 ng/ml (7–30 nmol/l) and a maximum/minimum fluctuation < 2.5 is recommended as a guideline for maintenance treatment of patients with mild to moderate schizophrenia. From a pharmacokinetic perspective, a dose of 200 mg every 2 weeks or 400 mg every 4 weeks of zuclopenthixol decanoate is equivalent to a daily oral dose of 25 mg zuclopenthixol.

Pediatric population:
No data available.

5.3 Preclinical safety data

Chronic toxicity:
In chronic toxicity studies, there were no worrying results regarding the therapeutic use of zuclopenthixol.

Reproductive toxicity:
In a three-generation rat study, delayed mating was observed. After mating, there was no effect on fertility. In a study where zuclopenthixol was administered via food, impaired mating ability and a decreased chance of conception were observed.

Animal reproduction studies have shown no embryotoxic or teratogenic effects. In peri- or postnatal studies in rats, doses of 5 and 15 mg/kg/day resulted in increased stillbirths, decreased pups survival, and delayed development in offspring. The relevance of these findings is unclear, and it is possible that the effect on the pups was due to neglect by the dam, who was exposed to toxic doses during gestation.

Mutagenicity and Carcinogenicity:
Zuclopenthixol has neither mutagenic nor carcinogenic potential.
An oncogenicity study in rats at a dose of 30 mg/kg/day (the highest dose) for 2 years resulted in a small increase in the incidence of mammary adenocarcinoma of the pancreatic islets, carcinomas in females, and parafollicular thyroid carcinomas; these results are not statistically proven. The small increase in the incidence of these tumors is the general result for D2 antagonists $_{\text{that}}$ increase prolactin secretion when administered to rats. Physiological differences between rats and humans with respect to prolactin make the clinical relevance of these results unclear; however, it is presumed that this is not a predictor of oncogenic risk for the patient.

Local toxicity:
Local muscle damage has been observed following injection of neuroleptics solubilized in aqueous solutions, including zuclopenthixol. Muscle damage is progressively more pronounced with aqueous solutions of neuroleptics than with oily solutions of zuclopenthixol acetate and zuclopenthixol decanoate.

6. PHARMACEUTICAL DATA

6.1 List of excipients

Medium-chain saturated triglycerides

6.2 Incompatibilities

Zuclopenthixol decanoate can only be mixed with zuclopenthixol acetate for which the solvent is also medium-chain saturated triglycerides.

Zuclopenthixol decanoate cannot be mixed with other preparations containing sesame oil, as this may permanently alter the pharmacokinetic properties of the preparations concerned.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original outer packaging, away from light.

6.5 Nature and contents of the outer packaging

Colorless ampoules (type I glass) of 1 ml.
Cardboard boxes containing 1 x 1 ml, 10 x 1 ml

Not all presentations may be commercially available.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

7. MARKETING AUTHORISATION HOLDER

Lundbeck sa
Stephanie Square Centre
Avenue Louise 65/11
1050 Brussels

8. MARKETING AUTHORISATION NUMBER

BE: BE104736
LU: 2005068794

- 0023179: 1 x 1 ampoule, 1 ml
- 0023182: 1 x 10 ampoules, 1 ml

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION

Date of first authorization: June 1, 1976
Date of last renewal: June 17, 2016

10. TEXT UPDATE DATE

Date of text approval: 01/2026
Date of text update: 01/2026