Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lidocaine hydrochloride 20 mg/ml, solution for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of solution for injection/infusion contains 20 mg of lidocaine hydrochloride (equivalent to 21.33 mg of lidocaine hydrochloride monohydrate).
Each 50 ml vial of solution for injection/infusion contains 1000 mg of lidocaine hydrochloride (equivalent to 1066.5 mg of lidocaine hydrochloride monohydrate).

Excipients with known effect:
This medicinal product contains sodium.
Each ml of solution for injection contains 2.0 mg of sodium equivalent to 0.09 mmol of sodium.
Each 50-ml vial contains 101 mg of sodium equivalent to 4.4 mmol of sodium.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection/infusion
Clear colourless solution
pH: 5.0 to 7.0
Osmolality: 270-320 mOsm/Kg

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lidocaine hydrochloride is indicated in adult patients for use in infiltration anaesthesia, intravenous regional anaesthesia, nerve blocks and epidural anaesthesia.

4.2 Posology and method of administration

Lidocaine hydrochloride should only be used by, or under the supervision of, doctors with experience of regional anaesthesia and resuscitative skills. Facilities for resuscitation should be available when administering local anaesthetics.

Posology

The lowest possible dose producing the required effect should be given.

The table may serve as a guide for adults having a body weight of about 70 kilograms. The dose should be adjusted according to age, weight and condition of the patient.

Route of administration or procedure	Recommended doses of Lidocaine hydrochloride		
	Concentration (mg/ml)	Volume (ml)	Total dose (mg)
Infiltration anaesthesia:			
Large procedures	20mg/ml	5-10 ml	100-200 mg
Intravenous regional anaesthesia:			
Arm	20mg/ml	5-10 ml	100-200 mg
Leg	20mg/ml	10 ml	200 mg
Nerve blocks	20mg/ml	1-10 ml	20-200 mg

Epidural anaesthesia:			
Lumbar analgesia	20mg/ml	12.5-20 ml	250-400 mg
Thoracic anaesthesia	20mg/ml	10-15 ml	200-300 mg
Sacral surgery analgesia	20mg/ml	20 ml	400 mg
Sacral obstetric analgesia	20mg/ml	10-15 ml	200-300 mg

The dose should be adjusted according to the response of the patient, the site of administration, and the expected duration of the surgical procedure.
It should be considered that usual total dose of lidocaine for anesthesia is 3–5 mg/kg; corresponding to volumes of 1 to 10 mL (at 20 mg/ml).

The average dose to be used in loco-regional anaesthesia is in the range of 20 mg to 30 mg lidocaine hydrochloride per session.
The generally maximum recommended total dose of lidocaine should not exceed 200 mg in adults for infiltration and peripheral nerve block, but depending on the procedure and patient factors, higher maximum doses may be required.
The recommended maximum single dose of lidocaine hydrochloride should not exceed 400 mg.

The volume of the solution used plays a role in the size of the area of spread of anaesthesia.

Special populations

Elderly
For elderly patients, the doses are calculated individually according to the patients' age and body weight. Doses may need adaptation as cardiac output and hepatic blood flow decrease with advanced age indicating a decreased clearance of lidocaine (see section 5.2).

Patients with renal impairment
Patients should be monitored as renal impairment may cause toxic effects due to the accumulation of active metabolites (see section 4.4 and 5.2). The dose may need to be adapted due to reduced clearance and increased half-life of lidocaine.

Patients with hepatic impairment
The dose may need to be reduced up to a half in patients with cardiac or hepatic insufficiency (see section 4.4).

Patients with cardiac insufficiency
The dose may need to be reduced up to a half in patients with cardiac or hepatic insufficiency (see section 4.4).

Other special population
Doses may need to be reduced in patients with poor general condition or in those with reduced protein binding capacity (resulting e.g. from renal insufficiency, liver insufficiency, cancer, pregnancy).

Paediatric population
Lidocaine hydrochloride should not be used for children.

Method of administration

The method of administration of lidocaine varies according to the procedure (infiltration anaesthesia, intravenous regional anaesthesia, i.e. Bier block, nerve block or epidural anaesthesia).
Lidocaine hydrochloride may be administered by intravenous, subcutaneous, infiltration or epidural injection.

4.3 Contraindications

Hypersensitivity to the active substance, to local anaesthetics of the amide type or to any of the excipients listed in section 6.1.
This medicine should not be used for epidural anaesthesia in patients with pronounced hypotension or with cardiogenic or hypovolemic shock.

4.4 Special warnings and precautions for use

Concomitant administration of intravenous lidocaine and local anaesthetics should be avoided. When any use of a local anaesthetic is necessary, the total administrated dose should take into account the amount of intravenous lidocaine administered (see 4.5).

With the exception of the most trivial procedures, regional and local anaesthetic procedures should always be carried out with equipment for resuscitation available. In any large blockade an intravenous cannula should be inserted before the local anaesthetic is injected. As with all local anaesthetic agents, lidocaine can cause acute central nervous and cardiovascular toxic effects when its use causes high concentrations in the blood, particularly after extensive intravascular administration.

Caution should be exercised in the treatment of the following patient categories:

- The elderly and generally debilitated patients.
- Patients with AV block II or III, as local anaesthetic can decrease myocardial conductivity.
- Patients with congestive heart failure, bradycardia or impaired respiratory function.
- Patients with severe hepatic disease or renal impairment.
- Patients with epilepsy.
- Patients with coagulopathy. Treatment with anticoagulants (eg. Heparin), NSAIDs or plasma substitutes causes increased bleeding tendency. Accidental injury of blood vessels may lead to serious bleedings. If necessary bleeding time and activated partial thromboplastin (aPTT), quicktest and platelet count should be checked.
- Third trimester of pregnancy

General and specific precautions for the different local and regional anaesthetic procedures have to be taken into account.

Inadvertent intravascular administration or overdoses may cause high lidocaine blood concentrations responsible for acute central nervous and cardiovascular toxic symptoms.

Caution should also be exercised if the local anaesthetic is to be injected into inflamed (infected) tissue because of increased systemic absorption due to higher blood flow and decreased effect due to the lower pH of infected tissue.

Patients treated with class III antiarrhythmics (e.g. amiodarone) should be kept under careful supervision and ECG monitoring should be considered, as the cardiac effects of lidocaine and class III antiarrhythmics may be additive (see section 4.5).

There have been post-marketing reports of chondrolysis in patients receiving post- operative intra-articular continuous infusion of local anaesthetics. The majority of reported cases of chondrolysis have involved the shoulder joint. Due to multiple contributing factors and inconsistency in the scientific literature regarding mechanism of action, causality has not been established. Intra-articular continuous infusion is not an approved indication for lidocaine.

Epidural anaesthesia may cause severe side effects such as cardiovascular depression, especially in cases of concomitant hypovolaemia. Caution should always be exercised in patients with reduced cardiovascular function.

The main reasons are traumatic nerve injuries and/or local toxic effects on muscles and nerves caused by the injected local anaesthetic. Traumatic nerve injuries and/or local toxic effects on muscles and nerves are mainly caused by the injection of local anaesthetics. The extent of these tissue injuries depends on the size of the trauma, the concentration of the local anaesthetic and the duration of tissue exposure to the local anaesthetic. For this reason, the lowest effective dose should be used.

Accidental intravascular injections in the head and neck areas may cause cerebral symptoms even at low doses.

Retrobulbar injections may rarely reach the cranial subarachnoid space, causing serious/severe reactions including cardiovascular collapse, apnoea, convulsions and temporary blindness.

Retro- and peribulbar injections of local anaesthetics carry a low risk of persistent ocular motor dysfunction. The primary causes include trauma and/or local toxic effects on muscles and/or nerves.

Lidocaine has been shown to be porphyrinogenic in animals and should not be administered to patients with acute porphyria, unless absolutely unavoidable. Strict caution should be exercised in all patients with porphyria.

Epidural anaesthesia may lead to hypotension and bradycardia. This risk can be reduced by intravenous administration of crystalloidal or colloidal solutions.

Hypotension should be treated immediately, with, for example, ephedrine intravenously, repeated as needed.

Paracervical block can sometimes cause foetal bradycardia or tachycardia and careful monitoring of the foetal heart rate is necessary (see section 4.6).

This medicinal product contains sodium.
This medicine contains 4.4 mmol (101 mg) sodium per vial, equivalent to 5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interactions

Pharmacodynamic interactions

Class I antiarrhythmics
Simultaneous administration of lidocaine and other class I antiarrhythmics should be avoided because of the risk that serious cardiac adverse effects occur.

Other anti-arrhythmics
If lidocaine is combined with other anti-arrhythmic medicinal products such as beta receptor blockers or calcium channel blockers, the inhibitory effect on atrioventricular and intraventricular conduction and on contractility may be enhanced.

Combination with other local anaesthetics
Combination of different local anaesthetics may lead to additive effects on the cardiovascular and the central nervous system.

Muscle relaxants
The effect of muscle relaxants (e.g. Suxamethonium) is prolonged by lidocaine.

Sedatives, hypnotics
Lidocaine should be administered with due caution to patients receiving medication with sedatives that also affect the function of the CNS and therefore may alter the toxicity of lidocaine. There may be an additive effect between the local anaesthetic effect and sedatives or hypnotics.

Volatile anaesthetics
If lidocaine and volatile anaesthetics are given simultaneously, the depressive effects of both may be intensified.

Medicinal products that can lower the seizure threshold
As lidocaine itself may reduce the seizure threshold co-administration with other medicinal products lowering the seizure threshold (e.g. tramadol or bupropion) may increase the risk of seizures.

Medicinal products that can raise the seizure threshold
Simultaneously administered diazepam raises the threshold for Lidocaine to produce convulsions. This must be kept in mind when monitoring patients for signs of toxicity of Lidocaine.

Vasoconstrictors:
The local anaesthetic effect is prolonged by combination with a vasoconstrictor, e.g. epinephrine. If lidocaine is given as antiarrhythmic agent, additional medication with epinephrine or norepinephrine may lead to potentiation of the cardiac undesirable effects.

Pharmacokinetic interactions

Lidocaine is mainly metabolized via the cytochrome P 450 isoenzymes CYP 3A4 and CYP 1A2 (see section 5.2). Concomitant administration with active substances that are substrates, inhibitors or inducers of hepatic enzymes, isoenzyme CYP3A4 and CYP1A2, may have an influence on the pharmacokinetics of lidocaine and thus also on its effect.

Inhibitors of CYP 3A4 and/or CYP 1A2

Concurrent administration of lidocaine with inhibitors of CYP3A4 and/or CYP1A2 may lead to accelerated plasma concentrations of lidocaine. Increased plasma levels have been reported for e.g:

- Amiodarone (CYP3A4 inhibitor): Amiodarone decreases hepatic metabolism of lidocaine, thus leading to the risk of increase of lidocaine levels, with subsequent increase of neurological and cardiovascular toxicity. Clinical monitoring, ECG and eventually control of plasma concentration of lidocaine should be performed. If needed dosage of lidocaine should be monitored during and after amiodarone therapy.
- Cimétidine (CYP3A4 and CYP1A2 inhibitor): Cimetidine used at doses equal or higher than 800 mg/day: increase of plasma concentration of lidocaine with subsequent increase of neurological and cardiovascular toxicity. Clinical survey, ECG and eventually control of plasma concentration of lidocaine should be performed. If needed dosage of lidocaine should be monitored during and after cimetidine therapy.
- Fluvoxamine (CYP3A4 and CYP1A2 inhibitor): Increase of lidocaine levels, thus enhancing risk of neurological and cardiovascular toxicity. Clinical monitoring, ECG and eventually control of plasma concentration of lidocaine should be performed. If needed dosage of lidocaine should be monitored during and after the association.
- Betablockers (except esmolol): Lidocaine intravenous: increase of lidocaine levels, with subsequent increase of neurological and cardiovascular toxicity. Clinical monitoring, ECG and eventually control of plasma concentration of lidocaine should be performed. If needed dosage of lidocaine should be monitored during and after betablockers therapy.
- Other known inhibitors of CYP3A4: protease inhibitors (e.g. ritonavir), macrolides antibiotics (e.g. erythromycine), antifungals (e.g. ketoconazole, itraconazole).
- Other known inhibitors of CYP1A2: ciprofloxacin.

Inducers of CYP 3A4 and/or CYP 1A2

Active substances inducing CYP3A4 and/or CYP 1A2 such as barbiturates (mainly phenobarbital), carbamazepine, phenytoin or primidone, accelerate the plasmatic clearance of lidocaine and thus reduce the efficacy of lidocaine.

Other pharmacokinetic interactions

Medicinal products that alter the metabolism, hepatic blood flow, cardiac output or peripheral distribution of lidocaine may influence plasma levels of lidocaine.

Medicinal products that cause hypokalaemia
The electrophysiological effects of lidocaine are highly dependent on the extracellular potassium concentration and can be almost completely blocked by hypokalemia. Concomitant use of medicinal products that can cause severe hypokalemia (e.g. acetazolamide, loop diuretics and thiazides) should therefore be avoided or used under careful monitoring of serum potassium concentration.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate data on treatment in pregnant women.
Lidocaine crosses the placenta (see section 5.2). It is reasonable to assume that lidocaine has been used in a great number of pregnant women and women of fertile age. There is no evidence that lidocaine causes disturbances in the reproductive process such as increased incidence of malformations. The risk to humans has, however, not been completely investigated.
Animal studies have shown reproductive toxicity (see section 5.3).
In short term use during pregnancy and at delivery the benefits should be weighed against the risks. Paracervical blockade or pudendal blockade with lidocaine increases the risk of reactions such as bradycardia/tachycardia in the foetus. The heart rate of the foetus must therefore be carefully monitored (see section 5.2).

Breast-feeding
Lidocaine is excreted in breast milk in small quantities. An effect on the child is unlikely when used at recommended doses. Breast feeding can therefore be continued during treatment with Lidocaine hydrochloride.

Fertility
No human data on the effect of lidocaine on fertility are available.

4.7 Effects on ability to drive and use machines

Lidocaine hydrochloride may have influence on the ability to drive and use machines.
Depending on dose and method of administration, lidocaine can have a temporary effect on motor function and coordination, influencing the ability to drive and use machines. Patients should be advised to avoid these activities until normal function is fully restored.

4.8 Undesirable effects

Summary of the safety profile

The frequency and severity of the undesirable effects of lidocaine depend upon the dose, the method of administration and the patient's individual sensitivity.

The undesirable effects related to local anaesthetics are rare in the absence of an overdose, abnormal rapid systemic absorption or accidental intravascular injection; in such cases, they can be very serious, in particular in terms of cardiac and neurologic function.
Adverse reactions caused by lidocaine may be difficult to distinguish from the physiological effects of the nerve block (e.g. hypotension, bradycardia), events caused directly (e.g. neurological lesions) or indirectly by needle puncture.

Symptoms of local toxicity may occur after the administration of lidocaine. Systemic adverse effects may be expected at plasma concentrations of lidocaine exceeding 5-10 mg/l. They become manifest in the form of both CNS symptoms and cardiovascular symptoms.

The possible undesirable effects after administration of lidocaine are largely the same as those produced by other amide-type local anaesthetics

Tabulated list of adverse reactions

The adverse reactions listed in this section fall in to the following frequency categories: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

The following table list adverse reactions associated with the use of lidocaine.

System Organ Class	Very Common	Common	Uncommon	Rare	Very rare	Frequency Not known
Immune system disorders				allergic reaction*, anaphylactoid reactions, bronchospasm, and in severe cases anaphylactic shock		
Nervous system disorders		Paresthesia, loss of consciousness. Transient neurological symptoms.		Neuropathy, convulsions (overdose) persistent anaesthesia, paresis, headache accompanied by tinnitus and photophobia. Cranial nerve lesions, neurosensory deafness. Regional applications in the thoracic or head/neck region may induce sympathetic blockade resulting in transient symptoms such as Horner's syndrome, Harlequin syndrome.		
Cardiac disorders		bradycardia		Arrhythmia, myocardial depression or possibly cardiac arrest (overdose or inadvertent		

System Organ Class	Very Common	Common	Uncommon	Rare	Very rare	Frequency Not known
				intravascular injection)		
Eye disorders				Double visions		
Respiratory, thoracic and mediastinal disorders				Respiratory depression		
Vascular disorders		hypotension, hypertension				
Gastrointestinal disorders	nausea	vomiting				
Skin and subcutaneous tissue disorders				rash , urticaria, oedema		

* Skin testing for allergy to lidocaine is not considered to be reliable

Paediatric population
Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Other special populations
In elderly patients the incidence of undesirable effects may be increased.

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 national reporting system:
HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

Depending on the individual sensitivity, toxic reactions occur from a concentration of approximately 5 - 10 mg lidocaine per litre upward in venous blood.

The lethal plasma concentration for humans is in the range 6 to 33 mg lidocaine per litre.

An overdose, or an accidental intravascular injection can produce excessive plasma concentrations of lidocaine; this results in signs of acute toxicity, which can lead to very serious undesirable effects. The toxic effects of lidocaine depend on the level of the plasma concentration; the higher the plasma concentration and the more rapid its rise, the more frequent and more serious are the toxic reactions. Such toxic reactions concern the central nervous system and the cardiovascular system.

Symptoms

Low toxic overdoses of lidocaine result in stimulation of the CNS. Gross overdose, producing high toxic plasma concentrations, causes depression of the central functions.
Central nervous system toxicity is a graded response with symptoms and sign of escalating severity.

Initially, symptoms are observed such as: dizziness, vertigo, agitation, hallucination, euphoria, apprehension, yawning, logorrhoea, headaches, nausea, vomiting, labial paresthesia, numbness of the tongue, tinnitus and dysarthria, impaired hearing and vision.

Other subjective central nervous system symptoms include: disorientation, occasional feeling of drowsiness. Tachycardia, hypertension and flushing have also been reported.

These signs of alarm necessitate attentive surveillance : muscular twitching, tremors, shivering, and generalised seizures. Simultaneously administered diazepam raises the threshold for lidocaine to produce convulsions. This must be kept in mind when monitoring patients for signs of toxicity of lidocaine.

In cases of very high dose administered: generalized depression of central nervous system, respiratory depression, coma and respiratory arrest.

Cardiovascular toxicity may be seen in severe cases : cardiac rhythm disorders such as ventricular extrasystole, ventricular fibrillation, unpalpable pulse, pallor, major bradycardia, disorders of atrioventricular conduction, decrease in cardiac contractility, hypotension and cardiac arrest.

Treatment

If signs of acute toxicity occur during administration of the local anaesthetic, administration of the anaesthetic should be stopped immediately. Intravenous fluid should be given in order to prevent hypoxia and acidosis, which potentiate local anaesthetic systemic toxicity (LAST) and exacerbate progression to cardiovascular collapse and seizure.

If convulsions occur, oxygenation should be maintained and circulation should be supported. If required, an anticonvulsant should be administered. Use of intravenous lipid emulsion should be considered.

If cardiovascular depression is evident (hypotension, bradycardia) treatment with intravascular fluid substitution, vasopressoric, chronotropic and/or inotropic drugs should be taken in consideration.

In case of circulatory arrest, immediate cardiopulmonary resuscitation should be initiated. For a successful outcome, prolonged resuscitative efforts may be required.

Patients having manifested signs of LAST should be monitored for at least 12 hours, because cardiovascular depression can persist or recur after treatment.

Centrally acting analeptics are contra-indicated.

There is no specific antidote.

Lidocaine cannot be eliminated by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Local anaesthetics, amides, ATC Code: N01BB02

Lidocaine is a local anaesthetic of the amide type. The mechanism of action is based on a decreased permeability of the membrane of the neuron for sodium ions. As a consequence of this, the depolarization rate is decreased and the threshold of excitation is increased, resulting in a reversible local numbness.

It is used to provide local anaesthesia by nerve blockade at various sites in the body and in the control of dysrhythmias. It acts by inhibiting the ionic refluxes required for the initiation and conduction of impulses, thereby stabilising the neuronal membrane. In addition to blocking conduction in nerve axons in the peripheral nervous system, lidocaine has important effects on the central nervous system and cardiovascular system. After absorption, lidocaine may cause stimulation of the CNS followed by depression and in the cardiovascular system, it acts primarily on the myocardium where it may produce decreases in electrical excitability, conduction rate and force of contraction.

5.2 Pharmacokinetic properties

Absorption and distribution

The rate of absorption will depend on dose, route of administration and perfusion at the injection site. Intercostal blockades lead to the highest plasma concentrations (approx. 1.5 µg/ml per 100 mg injected), whereas subcutaneous injections in the abdominal area lead to lowest plasma concentrations (approx. 0.5 µg/ml per 100 mg injected). The volume of distribution at steady state is 91 litres and binding to plasma proteins, mainly to alpha-1-acid glycoprotein, is 65 %.

Absorption is total and biphasic from the epidural space with half-lives of approximately 9.3 minutes and 82 minutes respectively. The slow absorption is the time-limiting factor in elimination of lidocaine, which explains the slower elimination after epidural injection than after intravenous injection.

Biotransformation and Elimination
Elimination of lidocaine is chiefly through metabolism, mainly by dealkylation to monoethylglycine xylidide (MEGX), which is mediated by both CYP1A2 and CYP3A4. MEGX is metabolised to 2,6-dimethylaniline and glycinexylidide (GX).
2,6-dimethylaniline is further converted by CYP2A6 to 4-hydroxy-2,6- dimethylaniline which is the major urinary metabolite (80%) and is excreted as a conjugate. MEGX has a convulsant activity similar to that of lidocaine whereas GX lacks convulsant activity. MEGX appears to occur in plasma concentrations similar to the mother substance. The speed of elimination of lidocaine and MEGX after an intravenous bolus dose is approx. 1.5-2 hours and 2.5 hours respectively.

Lidocaine crosses the placental barrier and concentration of unbound lidocaine will be the same in both mother and foetus. However, total plasma concentration will be lower in the foetus, due to a lower degree of protein binding.

Special population
Patients with liver impairment
The pharmacokinetics of lidocaine can be influenced by conditions affecting the liver function due to its rapid metabolism. The half-life can be increased by a factor of 2 or more in patients with hepatic dysfunction

Patients with renal impairment
Renal function impairment has no effect on the pharmacokinetics of lidocaine but may lead to the accumulation of its metabolites.

Elderly
Elimination half-life and volume of distribution may appear to be prolonged resp. increased in the elderly due to reduced cardiac output and/or hepatic blood flow.

5.3 Preclinical safety data

In animal studies, the toxicity noted after high doses of lidocaine consisted of effects on the central nervous and cardiovascular systems.
In studies on reproduction toxicity, embryotoxic or fetotoxic effects of lidocaine were detected at doses of 25 mg/kg s.c. in the rabbit. At doses below the maternal toxic range in the rat, lidocaine has no effect on the postnatal development of the offspring. An impairment of the fertility of male or female rats by lidocaine was not observed. Lidocaine crosses the placental barrier by means of simple diffusion.
Lidocaine showed no genotoxic potential in in-vitro and in-vivo genotoxicity tests. However, a metabolite of lidocaine, 2,6-dimethylaniline, showed evidence of genotoxic activity.
Cancer studies have not been performed with lidocaine. 2,6-dimethylaniline has been shown to have carcinogenicity potential in preclinical toxicological studies evaluating chronic exposure. The clinical relevance of these findings is unclear.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years.

Chemical and physical in-use stability has been demonstrated for 2 days at 30°C in a polypropylene syringe. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would not be longer than 24 hours at 2 to 8°C, unless reconstitution /dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
For storage conditions after first opening of the medicinal product, see section 6.3.
Remove any unused material, see section 6.6.

6.5 Nature and contents of container

50 ml clear glass vial with a chlorobutyl rubber stopper and an aluminium flip-off seal.
Box of 1 or 10.
Not all pack sizes may be marketed

6.6 Special precautions for disposal

For single use only.
If only part of a vial is used, discard the remaining solution.
The solution for injection should not be used if particles are present.

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

7 MARKETING AUTHORISATION HOLDER

Laboratoire AGUETTANT
1 Rue Alexander Fleming
69007 LYON
France

8 MARKETING AUTHORISATION NUMBER

PA1968/012/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th November 2020

10 DATE OF REVISION OF THE TEXT