Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Metronidazole 5 mg/mL solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

100 mL of solution for infusion contain 500 mg of Metronidazole.
Each mL of solution for infusion contains 5mg metronidazole.

Excipient with known effect: this medicinal product contains 13.51 mmoles (or 310.58 mg) sodium per 100 mL.
Each mL of solution for infusion contains 0.14 mmoles (3.11 mg) of sodium. To be taken into consideration by patients on a controlled sodium diet.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

A clear, free of visible particles, almost colourless to pale yellow solution.

pH: 4.5-6.0
Osmolality: 270 – 310 mOsm/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Metronidazole 5 mg/mL solution for infusion is indicated in adults and children for the prophylaxis and treatment of infections in which susceptible anaerobic microorganisms have been identified or are suspected to be the cause (see sections 4.4 and 5.1).

- The prophylaxis of post-operative infections where anaerobic bacteria are expected to be causative pathogens (gynaecologic and intra-abdominal operations)
- The treatment of peritonitis, brain abscess, necrotising pneumonia, osteomyelitis, puerperal sepsis, pelvic abscess, and post-operative wound infections from which pathogenic anaerobes have been isolated.

Treatment of patients with bacteraemia that occurs in association with any of the infections listed above.

In a mixed aerobic and anaerobic infection, antibiotics appropriate for the treatment of the aerobic infection should be used in addition to Metronidazole.

A prophylactic use is always indicated prior to operations with a high risk of anaerobic infections (gynaecologic and intra-abdominal operations).

- Severe intestinal and hepatic amoebiasis

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration

<u>Posology</u>

The dosage is adjusted according to the patient's individual response to therapy, her/his age and body weight and according to nature and severity of the disease.

The following dosage guidelines should be followed:

Adults and adolescents:

Amoebiasis
1.50 g per day (500 mg three times daily, intravenous infusions).
In hepatic amoebiasis, at the abscess stage, the abscess must be evacuated concomitantly with metronidazole treatment.

Duration of treatment: 5-10 days

Treatment of anaerobic infections
500 mg (100 mL) every 8 hours. Alternatively 1000 mg – 1500 mg may be given daily as a single dose.
The duration of therapy is dependent on the effect of the treatment. In most cases a treatment course of 7 days will be sufficient. If clinically indicated, treatment may be continued beyond this time although a duration of 10 days should not normally be exceeded. (See also section 4.4.)

Prophylaxis against post-operative infection caused by anaerobic bacteria:
500 mg, with administration completed approximately one hour before surgery. The dose is repeated after 8 and 16 hours.

The Elderly:
Caution is advised in the elderly, particularly at high doses, although there is limited information available on modification of dosage.

Paediatric population:

Amoebiasis
35 to 50 mg/kg/day intravenously, divided into 3 doses for 5 to 10 days. A maximum of 2400 mg/day must not be exceeded.
In hepatic amoebiasis, at the abscess stage, the abscess must be evacuated concomitantly with metronidazole treatment.

Treatment of anaerobic infections

- Children > 8 weeks to 12 years of age:

The usual daily dose is 20 – 30 mg per kg BW per day as a single dose or divided into 7.5 mg per kg BW every 8 hours. The daily dose may be increased to 40 mg per kg BW, depending on the severity of the infection.

- Neonates and infants < 8 weeks of age:

15 mg per kg BW as a single dose daily or divided into 7.5 mg per kg BW every 12 hours.

- In newborns with a gestational age < 40 weeks, accumulation of metronidazole can occur during the first week of life; therefore the concentrations of metronidazole in serum should preferably be monitored after a few days therapy.

Duration of treatment is usually 7 days.

Prophylaxis against postoperative infections caused by anaerobic bacteria

- Children < 12 years:

20 – 30 mg/kg BW as a single dose given 1 – 2 hours before surgery

- Newborns with a gestation age < 40 weeks:

10 mg/kg BW as a single dose before surgery

Patients with renal insufficiency
Limited data are available in this population. These data do not indicate the need for dose reduction (see section 5.2.)
In patients undergoing haemodialysis the conventional dose of metronidazole should be scheduled after haemodialysis on dialysis days to compensate the removal of metronidazole during the procedure.
No routine dose adjustment is necessary in patients with renal failure undergoing intermittent peritoneal dialysis (IDP) or continuous ambulatory peritoneal dialysis (CAPD).

Patients with hepatic insufficiency
As serum half-life is prolonged and plasma clearance is delayed in severe hepatic insufficiency, patients with severe liver disease will require lower doses (see section 5.2).

In patients with hepatic encephalopathy, the daily dosage should be reduced to one third and may be administered once daily (see section 4.4).

Method of administration

Intravenous use.
The contents of one bottle are to be infused slowly intravenously, i.e. 100 mL max. over not less than 20 minutes, but normally over one hour.

Concurrently prescribed antibiotics are to be administered separately.

4.3 Contraindications

Hypersensitivity to metronidazole or other nitroimidazole derivatives or any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Regular clinical and laboratory monitoring (including full blood count) are advised in cases of high-dose or prolonged treatment, in case of antecedents of blood dyscrasia, in case of severe infection and in severe hepatic insufficiency.

In patients with severe liver damage or impaired haematopoiesis (e.g. granulocytopenia) metronidazole should only be used if its expected benefits clearly outweigh potential hazards.

Metronidazole is mainly metabolised by hepatic oxidation. Substantial impairment of metronidazole clearance may occur in the presence of advanced hepatic insufficiency. Significant cumulation may occur in patients with hepatic encephalopathy and the resulting high plasma concentrations of metronidazole may contribute to the symptoms of the encephalopathy. Metronidazole should therefore be administered with caution to patients with hepatic encephalopathy (see section 4.2).

Due to the risk of aggravation, metronidazole should also be used in patients with active or chronic severe peripheral and central nervous system diseases only if its expected benefits clearly outweigh potential hazards.

Convulsive seizures, myoclonus and peripheral neuropathy, the latter mainly characterized by numbness or paresthesia of an extremity, have been reported in patients treated with metronidazole. The appearance of abnormal neurological signs demands the prompt evaluation of the benefit/risk ratio of the continuation of therapy (see section 4.8).

In the case of severe hypersensitivity reactions (e.g. anaphylactic shock; see also section 4.8), treatment with Metronidazole 5 mg/mL Solution for Infusion must be discontinued immediately and established emergency treatment must be initiated by qualified healthcare professionals.

Severe persistent diarrhoea occurring during treatment or during the subsequent weeks may be due to pseudomembranous colitis (in most cases caused by Clostridioides difficile), see section 4.8. This intestinal disease, precipitated by the antibiotic

treatment, may be life-threatening and requires immediate appropriate treatment. Anti-peristaltic medicinal products must not be given.

The duration of therapy with metronidazole or drugs containing other nitroimidazoles should not exceed 10 days. Only in specific elective cases and if definitely needed, the treatment period may be extended, accompanied by appropriate clinical and laboratory monitoring. Repeat therapy should be restricted as much as possible and to specific elective cases only. These restrictions must be observed strictly because the possibility of metronidazole developing mutagenic activity cannot be safely excluded and because in animal experiments an increase of the incidence of certain tumours has been noted.

Prolonged therapy with metronidazole may be associated with bone marrow depression, leading to an impairment of haematopoiesis. For manifestations see section 4.8. Blood cell counts should be carefully monitored during prolonged therapy.

This medicinal product contains 310.58 mg sodium per 100 mL, equivalent to 15.5% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Interference with laboratory tests
Metronidazole interferes with the enzymatic-spectrophotometric determination of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), triglycerides and glucose hexokinase resulting in decreased values (possibly down to zero).

Metronidazole has a high absorbance at the wavelength at which nicotinamideadenine dinucleotide (NADH) is determined. Therefore elevated liver enzyme concentrations may be masked by metronidazole when measured by continuous-flow methods based on endpoint decrease in reduced NADH. Unusually low liver enzyme concentrations, including zero values, have been reported.

Patients should be warned that Metronidazole may darken urine.

Hepatotoxicity in patients with Cockayne Syndrome
Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should not be used unless the benefit is considered to outweigh the risk and if no alternative treatment is available. Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued. Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with other medicinal products

Amiodarone
QT interval prolongation and torsade de pointes have been reported with the co-administration of metronidazole and amiodarone. It may be appropriate to monitor QT interval on the ECG if amiodarone is used in combination with metronidazole. Patients treated on an outpatient basis should be advised to seek medical attention if they experience symptoms that could indicate the occurrence of torsade de pointes such as dizziness, palpitations, or syncope.

Barbiturates
Phenobarbital may increase the hepatic metabolism of metronidazole, reducing its plasma half-life to 3 hours.

Busulfan
Co-administration with metronidazole may significantly increase the plasma concentrations of busulfan. The mechanism of interaction has not been described. Due to the potential for severe toxicity and mortality associated with elevated busulfan plasma levels, concomitant use with metronidazole should be avoided.

Carbamazepine
Metronidazole may inhibit the metabolism of carbamazepine and raise the plasma concentrations as a consequence.

Cimetidine

Concurrently administered cimetidine may reduce the elimination of metronidazole in isolated cases and subsequently lead to increased metronidazole concentrations in serum.

Contraceptive drugs
Some antibiotics can, in some exceptional cases, decrease the effect of contraceptive pills by interfering with the bacterial hydrolysis of steroid conjugates in the intestine and hereby reduce the re-absorption of unconjugated steroid. Therefore the plasma levels of the active steroid decrease. This unusual interaction can occur in women with a high excretion of steroid conjugates through the bile. There are case reports of oral contraceptive failure in association with different antibiotics, e.g. ampicillin, amoxicillin, tetracyclines and also metronidazole.

Coumarin derivatives
Concomitant treatment with metronidazole may potentiate the anticoagulant effect of these and increase the risk for bleeding as a consequence of decreased hepatic degradation. Dose adjustment of the anticoagulant can be necessary.

Cyclosporine
During simultaneous therapy with cyclosporine and metronidazole there is a risk for increased serum concentrations of cyclosporine. Frequent monitoring of cyclosporine and creatinine is required.

Disulfiram
Simultaneous administration of disulfiram may cause states of confusion or even psychotic reactions. Combination of both agents must be avoided.

Fluorouracil
Metronidazole inhibits the metabolism of concurrently administered fluorouracil, i.e. the plasma concentration of fluorouracil is increased.

Lithium
Caution is to be exercised when metronidazole is administered simultaneously with lithium salts, because under metronidazole therapy raised serum concentrations of lithium have been observed. Lithium treatment should be tapered or withdrawn before administering metronidazole. Plasma concentrations of lithium, creatinine and electrolytes should be monitored in patients under treatment with lithium while they receive metronidazole.

Mycophenolate mofetil
Substances that alter the gastrointestinal flora (e.g., antibiotics) may reduce the oral bioavailability of mycophenolic acid products. Close clinical and laboratory monitoring for evidence of diminished immunosuppressive effect of mycophenolic acid is recommended during concomitant therapy with anti-infective agents.

Phenytoin
Metronidazole inhibits the metabolism of concurrently administered phenytoin, i.e. the plasma concentration of phenytoin is increased. On the other hand, the efficacy of metronidazole is reduced when phenytoin is administered concurrently.

Tacrolimus
Co-administration with metronidazole may increase the blood concentrations of tacrolimus. The proposed mechanism is inhibition of hepatic tacrolimus metabolism via CYP 3A4. Tacrolimus blood levels and renal function should be checked frequently and the dosage adjusted accordingly, particularly following initiation or discontinuation of metronidazole therapy in patients who are stabilized on their tacrolimus regimen.

Other forms of interaction
Alcohol
Intake of alcoholic beverages must be avoided during metronidazole therapy since adverse reactions such as dizziness and vomiting may occur (disulfiram-like effect).

4.6 Fertility, pregnancy and lactation

Contraception in males and females
See section 4.5 "Contraceptive drugs"

Pregnancy

The safety of the use of metronidazole during pregnancy has not sufficiently been demonstrated. In particular, reports on the use during early pregnancy are contradictory. Some studies indicated an increased rate of malformations. In animal studies with metronidazole no teratogenicity was observed (see section 5.3).
During the first trimester, Metronidazole 5 mg/mL solution for infusion should only be used to treat severe life-threatening infections, if there is no safer alternative. During the second and third trimester, Metronidazole 5 mg/mL solution for infusion may also be used to treat other infections if its expected benefits clearly outweigh any possible risk.

Breastfeeding
Since metronidazole is secreted into breast milk, nursing should be stopped during therapy. Also after the end of the therapy with metronidazole, nursing should not be resumed before another 2 – 3 days because of the prolonged half-life period of metronidazole.

Fertility
Animal studies only indicate a potential negative influence of metronidazole on the male reproductive system if high doses lying well above the maximum recommended dose for humans were administered.

4.7 Effects on ability to drive and use machines

Although the conditions of administration are incompatible with driving vehicles and using machines, patients should be warned of the potential risk of dizziness, confusion, hallucinations, convulsions or visual disturbances and be advised not to drive or use machines in case of occurrence of such problems.

4.8 Undesirable effects

Undesirable effects are mainly associated with prolonged use or high doses. The most commonly observed effects include nausea, abnormal taste sensations and the risk of neuropathy in case of long term treatment.
In the following listing, for the description of the frequencies of undesirable effects the following terms are used:
- 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 (Frequency cannot be estimated from the available data)

System Organ Class (MedDRA)	**Common (≥ 1/100 to < 1/10)**	**Rare (≥ 1/10,000 to < 1/1,000)**	**Very Rare (< 1/10,000)**	**Not Known (Frequency cannot be estimated from the available data)**
Infections and infestations	Superinfections with candida (e.g. genital infections)	Pseudomembranous colitis, which may occur during or after therapy, manifesting as severe persistent diarrhea. For details regarding emergency treatment (see section 4.4)		
Blood and lymphatic system disorders			Granulocytopenia, Agranulocytosis, thrombocytopenia, pancytopenia. See section 4.4	Leucopenia, aplastic anaemia
Immune system disorders		Severe acute systemic hypersensitivity reactions: anaphylaxis, up to anaphylactic shock (see section		Mild to moderate hypersensitivity reactions, e. g. skin reactions (see "Skin and subcutaneous disorders" below) Angiodema

		4.4).		
Metabolism and nutrition disorders				Anorexia
Psychiatric disorders			Psychotic disorders, including states confusion, hallucination	Depression
Nervous system disorders			Encephalopathy, fever, headache, disturbances in sight and movement, ataxia, dysathria, vertigo drowsiness, dizziness, convulsions	• Somnolence or insomnia, myoclonus, seizures, peripheral neuropathy manifesting as paraesthesia, pain, furry sensation, and tingling in the extremities, aseptic meningitis • If seizures or signs of peripheral neuropathy or encephalopathy appear, the attending doctor should be informed immediately. See section 4.4
Eye disorders			Disturbance of vision, e.g.diplopia, myopia	Oculogyric crisis, Optic neuropathy/ neuritis (isolated cases)
Cardiac disorders		ECG changes like flattening of the T-wave		
Gastrointestinal disorders				Vomiting, nausea, diarrhoea, glossitis and stomatitis, eructation with taste, epigastric pressure, metallic taste, furred tongue Dysphagia (caused by central nervous effects of metronidazole)
Hepatobiliary disorders			• Abnormal values of hepatic enzymes and bilirubin • Hepatitis, jaundice, pancreatitis	
Skin and subcutaneous tissue disorders			Allergic skin reactions, e. g. pruritus, urticaria Stevens-Johnson syndrome	Toxic epidermal necrolysis Erythema multiforme
Musculoskeletal and connective tissue disorders			Myalgia, arthralgia	
Renal and urinary disorders			Dark coloured urine (due to metronidazole metabolite)	
General disorders and administration site conditions				Vein irritations (up to thrombophlebitis) after IV infusion states of weakness, fever

Cases of severe irreversible hepatotoxicity/acute liver failure, including cases with fatal outcomes with very rapid onset after initiation of systemic use of metronidazole, have been reported in patients with Cockayne Syndrome (see section 4.4).

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

Reporting possible side effects
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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Symptoms
As signs and symptoms of overdose the undesirable effects described under section 4.8 may appear. Single doses of metronidazole, up to 12 g have been reported in suicide attempts and accidental overdoses.
The symptoms were limited to vomiting, ataxia and slight disorientation.

Treatment
There is no specific treatment or antidote that can be applied in the case of gross overdose of metronidazole. If required, metronidazole can be effectively eliminated by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, imidazol derivatives
ATC code: J01XD01

Mechanism of action
Metronidazole itself is ineffective. It is a stable compound able to penetrate into microorganisms.
Under anaerobic conditions nitroso radicals acting on DNA are formed from metronidazole by the microbial pyruvate-ferredoxin-oxidoreductase, with oxidation of ferredoxin and flavodoxin. Nitroso radicals form adducts with base pairs of the DNA, thus leading to breaking of the DNA chain and consecutively to cell death.

PK/PD relationship
Metronidazole acts in a concentration dependent manner. The efficacy of metronidazole mainly depends on the quotient of the maximum serum concentration (c_{max}) and the minimum inhibitory concentration (MIC) relevant for the microorganism concerned.

Breakpoints
For the testing of metronidazole usual dilution series are applied. The following minimum inhibitory concentration has been established to distinguish susceptible from resistant microorganisms:

EUCAST *(European Committee on Antimicrobial Susceptibility Testing, Version 13.1, June 2023)* breakpoints separating susceptible (S) from resistant organisms (R) are as follows:

Organism	Susceptible	Resistant
Bacteroides spp.	≤ 4 mg/L	> 4 mg/L
Prevotella spp.	≤ 4 mg/L	> 4 mg/L
Fusobacterium necrophorum	≤ 0.5 mg/L	> 0.5 mg/L
Clostridium perfringens	≤ 4 mg/L	> 4 mg/L
Clostridioides difficile[1]	≤ 2 mg/L	> 2 mg/L
Helicobacter pylori	≤ 8 mg/L	> 8 mg/L

[1] The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.

List of susceptible and resistant organisms.

Commonly susceptible species
Anaerobes
Clostridioides difficile°
Clostridium perfringens°$^{\Delta}$
Fusobacterium spp.°
Peptoniphilus spp.°
Peptostreptococcus spp.°
Porphyromonas spp.°
Prevotella spp.
Veillonella spp.°
Bacteroides fragilis
Other micro-organisms
Entamoeba histolytica°
Gardnerella vaginalis°
Giardia lamblia°
Trichomonas vaginalis°

Species for which acquired resistance may be a problem
Gram-negative aerobes
Helicobacter pylori
Anaerobes

Inherently resistant organisms
All obligate aerobes
Gram-positive micro-organisms
Enterococcus spp.
Staphylococcus spp.
Streptococcus spp.
Gram-negative micro-organisms
Enterobacteriaceae
Haemophilus spp.

° At the time of publication of these tables, no up-to-date data were available. In primary literature, standard reference books and therapy recommendations susceptibility of the respective strains is assumed.
$^{\Delta}$ Only to be used in patients with allergy to penicillin

Mechanisms of resistance to metronidazole
The mechanisms of metronidazole resistance are still understood only in part. Strains of *Bacteroides* being resistant to metronidazole possess genes encoding nitroimidazole reductases converting nitroimidazoles to aminoimidazoles. Therefore the formation of the antibacterially effective nitroso radicals is inhibited.
There is full cross resistance between metronidazole and the other nitroimidazole derivatives (tinidazole, ornidazole, nimorazole). The prevalence of acquired resistance of individual species may vary, depending on region and time. Therefore especially for the adequate treatment of severe infections specific local information regarding resistance should be available. If there is doubt about the efficacy of metronidazole due to the local resistance situation, expert advice should be sought. Especially in the case of severe infections or failure of treatment, microbiological diagnosis including determination of species of the microorganism and its susceptibility to metronidazole is required.

5.2 Pharmacokinetic properties

Absorption
Metronidazole is readily absorbed from the gastrointestinal tract and the oral bioavailability is > 90%. Consequently, the same mg dose will result in similar exposure (AUC) when switching between intravenous and oral dosing.
Since Metronidazole5 mg/mL solution for infusion is infused intravenously the bioavailability is 100%.

Distribution

- The intravenous injection of 500 mg of metronidazole results, after a single infusion, at a mean peak of 18 mcg per mL at the end of a 20-minute infusion.
- Repeated intake every 8 hours results in an identical mean peak.
- Intake every 12 hours results in a mean peak of 13 mcg per mL.
- The plasma half-life is 8 to 10 hours.
- The plasma protein binding is low: less than 10 percent.

- Diffusion is rapid and extensive in the: lungs, kidneys, liver, skin, bile, CSF, saliva, seminal fluid, vaginal secretions.

Metronidazole crosses the placental barrier and is excreted in breast milk.

Biotransformation
It produces two non-conjugated metabolites which exhibit antibacterial activity (10 to 30 percent).
Metronidazole is metabolised in the liver by side-chain oxidation and glucuronide formation. Its metabolites include an acid oxidation product, a hydroxy derivative and glucuronide. The major metabolite in the serum is the hydroxylated metabolite, the major metabolite in the urine is the acid metabolite. The metabolism occurs predominantly via microsomal cytochrome P450 oxidases in the liver.

Elimination
Approximately 80% of the substance is excreted in urine with less than 10% in the form of the unchanged drug substance. Small quantities are excreted via the liver. Elimination half-life is 8 (6-10) hours.

Characteristics in special patient groups:
Renal insufficiency delays excretion only to an unimportant degree. The elimination half-life of metronidazole remains unchanged in the presence of renal failure, however such patients retain the metabolites of metronidazole. The clinical significance of this is not known at present.

Delayed plasma clearance and prolonged serum half-life (up to 30 h) is to be expected in severe liver disease.

5.3 Preclinical safety data

Repeated dose toxicity
Following repeated administration ataxia and tremor were observed in the dog and a dose-dependent increase in hepatocellular degeneration was observed in the monkey during a 12 month study.

Mutagenic and tumorigenic potential
Metronidazole was mutagenic in bacteria after nitroreduction, however it was not mutagenic in mammalian cells in vitro and in vivo. In addition, DNA damage was not observed in the lymphocytes of patients treated with metronidazole.
There is evidence to suggest that metronidazole is tumorigenic in the mouse and rat. There was an increase in the incidence of lung tumours in mice (after the oral administration of 3.1-fold the maximum recommended human dose of metronidazole of 1,500 mg/d), however, this does not seem to be due to a genotoxic mechanism as no changes in the mutation rates were observed in various organs of transgenic mice following high doses of metronidazole.

Reproduction toxicity
No teratogenicity or embryotoxicity was observed in the rat or rabbit.
Following repeated administration for 26-80 weeks to rats, testicular and prostatic dystrophy were observed at high doses (14.2 to 28.5-fold the maximum recommended human dose of metronidazole of 1,500 mg/d).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate dodecahydrate
citric acid monohydrate
sodium chloride
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

36 months.
Use immediately after first opening.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless 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.

6.5 Nature and contents of container

Blow-fill-sealed 100 mL polypropylene bottle over sealed with a molded plastic cap with a rubber gasket and a pull ring or with a plastic cap with embedded elastomers (twin ports).

Pack sizes of 10, 20 or 24 bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For single use only. Discard any remaining solution. Not to be used if container is found leaking or solution is not clear.

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

7 MARKETING AUTHORISATION HOLDER

Noridem Enterprises Limited
Evagorou & Makariou,
Mitsi Building 3, Office 115,
1065 Nicosia
Cyprus

8 MARKETING AUTHORISATION NUMBER

PA1122/041/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 6th December 2024

10 DATE OF REVISION OF THE TEXT