Professional Prescribing Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

MERCIDE 500 (Injection)

MERCIDE 1 g (Injection)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MERCIDE 500

Each vial contains:

Meropenem (sterile) equivalent to anhydrous meropenem 500 mg.

Sugar free

MERCIDE 1 g

Each vial contains:

Meropenem (sterile) equivalent to anhydrous meropenem 1g.

Sugar Free

3. PHARMACEUTICAL FORM

White to pale yellow crystalline powder in clear glass vial. After reconstitution a clear, colourless to pale yellow coloured solution is formed.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

MERCIDE is indicated for treatment of the following infections caused by single or multiple susceptible bacteria and as empiric therapy prior to the identification of the causative organisms:

Acute exacerbation of chronic bronchitis and pneumonia due to:

Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus spp, Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Pseudomonas aeruginosa,

Branhamella catarrhalis, Klebsiella pneumoniae, Klebsiella spp, Enterobacter cloacae, Enterobacter spp., Acinetobacter.

Pneumonia in children due to:

Staphylococcus aureus, Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas aeruginosa.

Urinary tract infections in adults and children, including complicating infections due to:

Escherichia coli, Haemophilus influenzae, Pseudomonas aeruginosa, Enterobacter cloacae, Morganella morganii, Proteus mirabilis, Serratia marcescens, Citrobacter freundii.

Pelvic inflammatory Disease (including tubo-ovarian abscess) and endometritis due to:

Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus haemolyticus, Staphylococcus spp., Staphylococcus spp. (coagulase negative), Streptococcus agalactiae Group B, *Pseudomonas aeruginosa, Streptococcus beta-haemolytic, Streptococcus faecalis, Streptoccocus gamma haemolyticus,* Group D *Streptoccocus (enterococcus and non-enterococcus), Streptococcus viridans, Acinetobacter anitratus, Acinetobacter Iwoffii, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Gardnerella vaginalis, Klebsiella pneumoniae, Neisseria gonorrhoeae, Proteus mirabilis.*

Skin and Skin Structure Infections in adults due to:

Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Coagulase negative staphylococcus, Streptococcus agalactiae, Streptococcus faecalis, Group A *Streptococcus, Streptococcus viridans, Bacteroides fragilis, Peptostreptococcus spp.*

Meningitis in adults and children due to:

Streptococcus pneumoniae, Haemophilus influenzae , Neisseria meningitidis

Septicaemia in adults and children due to:

Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae.

Empiric treatment, including initial monotherapy, for presumed bacterial infections in host-compromised neutropenic patients due to:

Staphylococcus aureus, Micrococcus spp., Streptococcus sanguis, Escherichia coli, Pseudomonas aeruginosa

Intra-abdominal abscess and peritonitis due to:

Streptococcus milleri, Streptococcus mitior, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacteroides fragilis, Bacteroides ovatus, Bacteroides distasonis, Klebsiella oxytoca, Clostridium perfinges.

Polymicrobial infections

In the treatment of infections caused by *Pseudomonas aeruginosa*, an aminoglycoside should be administered concomitantly.

4.2 Posology and method of administration

Intravenous administration:

Adults:

Usual dose:

500 mg to 1 g by intravenous administration every 8 hours depending on the type and severity of infection, the known or expected susceptibility of the pathogen(s), and the condition of the patient.

Exceptions:

- Febrile episodes in neutropenic patients – the dose should be 1 g every 8 hours.
- Meningitis – the dose should be 2 g every 8 hours.

Caution may be required in using beta-lactam antibiotics such as **MERCIDE** in critically ill patients with known or suspected *Pseudomonas aeruginosa* lower respiratory tract infections. Concomitant use of an aminoglycoside is recommended.

Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa.*

MERCIDE should be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes (see Constitution, compatibility and stability below)

Dosage schedule for adults with impaired renal function:

Dosage should be reduced in patients with creatinine clearance less than 51 ml/min, as scheduled below:

Creatinine Clearance (ml/min)	**Dose (based on "unit" dose range of 500 mg to 2 g every 8 hours)**	**Frequency**
26-50	One unit dose	Every 12 hours
10-25	One-half unit dose	Every 12 hours
<10	One-half unit dose	Every 24 hours

MERCIDE is cleared by haemodialysis. If continued treatment with **MERCIDE** is necessary, the unit dose based on the infection type and severity is recommended at the completion of the haemodialysis procedure to re-institute effective treatment.

There is no experience with peritoneal dialysis.

Use in adults with hepatic insufficiency:

No dosage adjustment is necessary in patients with impaired hepatic metabolism.

Elderly:

No dosage adjustment is required for the elderly with normal renal function or creatinine clearance values above 50 ml/min.

Children:

For infants and children over 3 months and up to 12 years of age the IV dose is 10 to 40 mg/kg every 8 hours depending on type and severity of infection, the known or suspected susceptibility of the pathogen(s) and the condition of the patient. In children over 50 kg weight, adult dosage should be used.

Exceptions:

Meningitis - the dose should be 40 mg/kg every 8 hours.

MERCIDE should be given as an IV bolus over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes.

There is no experience in children with renal impairment.

Constitution, compatibility and stability:

MERCIDE to be used for bolus intravenous injection should be constituted with sterile water for injection (10 ml/500 mg and 20 ml/1 g). This provides an approximate available concentration of 50 mg/ml. For intravenous infusion **MERCIDE** IV vials may be directly constituted with a compatible infusion fluid (as listed below) and then further diluted with the compatible infusion fluid as needed.

Freshly prepared solutions of **MERCIDE** IV should be used whenever possible, however, constituted solutions of **MERCIDE** IV, as supplied in injection and infusion vials, and constituted as noted above maintain satisfactory potency at room temperature (up to 25 °C) or under refrigeration (4 °C) as shown in the following table:

MERCIDE should not be mixed with or physically added to solutions containing other medicines.

Diluent	Hours stable up to 25 °C	Hours stable up to 4 °C
Vials constituted with water for injection for bolus injection	**7**	**48**
Infusions (1-20 mg/ml) prepared with 0,9 % sodium chloride	**8**	**48**
5,0 % dextrose **5,0 % dextrose and 0,2 % sodium chloride** **5,0 % dextrose and 0,9 % sodium chloride** **5,0 % dextrose and 0,15 % potassium chloride** **2,5 % or 10 % mannitol** **Normosol-M in 5 % glucose**	**3**	**14**
10 % dextrose **5 % dextrose and 0,02% sodium bicarbonate solution**	**2**	**8**

Solutions of **MERCIDE** should not be frozen.

4.3 Contraindications

- **MERCIDE** is contra-indicated in patients who have demonstrated hypersensitivity to this product.
- Patients who have a history of hypersensitivity to carbapenems, penicillins or other beta-lactam antibiotics may also be hypersensitive to **MERCIDE**. As with all beta-lactam antibiotics hypersensitivity reactions have been reported.
- Pregnancy and breastfeeding.

4.4 Special warnings and precautions for use

The selection of meropenem to treat an individual patient should take into account the appropriateness of using a carbapenem antibacterial agent based on factors such as

severity of the infection, the prevalence of resistance to other suitable antibacterial agents and the risk of selecting for carbapenem-resistant bacteria.

Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter spp. resistance

Prescribers are advised to take into account the local prevalence of resistance in these bacteria to penems.

Hypersensitivity reactions

As with all beta-lactam antibiotics, serious and occasionally fatal hypersensitivity reactions have been reported (see sections 4.3 and 4.8).

Patients who have a history of hypersensitivity to carbapenems, penicillins or other beta-lactam antibiotics may also be hypersensitive to meropenem. Before initiating therapy with meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics.

If a severe allergic reaction occurs, the medicinal product should be discontinued and appropriate measures taken.

Severe cutaneous adverse reactions (SCAR), such as Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme (EM) and acute generalised exanthematous pustulosis (AGEP) have been reported in patients receiving meropenem (see section 4.8). If signs and symptoms suggestive of these reactions appear, meropenem should be withdrawn immediately and an alternative treatment should be considered.

Antibiotic-associated colitis

Antibiotic-associated colitis and pseudomembranous colitis have been reported with nearly all anti-bacterial agents, including meropenem, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of meropenem

(see section 4.8). Discontinuation of therapy with meropenem and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Seizures

Seizures have infrequently been reported during treatment with carbapenems, including meropenem (see section 4.8).

Hepatic function monitoring

Hepatic function should be closely monitored during treatment with meropenem due to the risk of hepatic toxicity (hepatic dysfunction with cholestasis and cytolysis) (see section 4.8).

Use in patients with liver disease: patients with pre-existing liver disorders should have liver function monitored during treatment with meropenem. There is no dose adjustment necessary (see section 4.2).

Renal Insufficiency

Pharmacokinetic studies in patients with renal insufficiency have shown that the plasma clearance of meropenem correlates with creatinine clearance

Dosage adjustments are necessary in subjects with renal impairment (see section 5.2).

Direct antiglobulin test (Coombs test) seroconversion

A positive direct or indirect Coombs test may develop during treatment with meropenem.

Concomitant use with valproic acid/sodium valproate/valpromide

The concomitant use of meropenem and valproic acid/sodium valproate/valpromide is not recommended (see section 4.5).

MERCIDE contains sodium.

MERCIDE 500: This medicinal product contains 104 mg sodium per 500 mg vial, equivalent to 5,2 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

MERCIDE 1 g: This medicinal product contains 208 mg sodium per 1 g vial, equivalent to 10,4 % of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Paediatric use:

Efficacy and tolerability in infants under 3 months old have not been established. Therefore, meropenem is not recommended for use below this age.

Overgrowth of non-susceptible organisms may occur and repeated evaluation of each patient is necessary. Infrequently, *pseudomembranous colitis* has been reported on **MERCIDE**. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea in association with **MERCIDE** use.

4.5 Interaction with other medicines and other forms of interaction

Probenecid competes with meropenem for active tubular secretion and thus inhibits the renal excretion of meropenem with the effect of increasing the elimination half-life and plasma concentration of meropenem. As the potency and duration of action of meropenem dosed without probenecid are adequate, the co-administration of probenecid with meropenem is not recommended. The potential effect of meropenem

on the protein binding of other drugs or metabolism has not been studied. However, the protein binding is so low that no interactions with other compounds would be expected.

Meropenem has been administered concomitantly with many other medications without apparent adverse interactions.

Decreases in blood levels of valproic acid have been reported when it is co-administered with carbapenem agents resulting in a 60-100 % decrease in valproic acid levels in about two days. Due to the rapid onset and the extent of the decrease, co-administration of valproic acid/sodium valproate/valpromide with carbapenem agents is not considered to be manageable and therefore should be avoided (see section 4.4). Meropenem may reduce serum valproic acid levels. Sub therapeutic levels may be reached in some patients.

Oral anti-coagulants

Simultaneous administration of antibiotics with warfarin may augment its anti-coagulant effects. There have been many reports of increases in the anti-coagulant effects of orally administered anti-coagulant agents, including warfarin inpatients who are concomitantly receiving antibacterial agents. The risk may vary with the underlying infection, age and general status of the patient so that the contribution of the antibiotic to the increase in INR (international normalised ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after co-administration of antibiotics with an oral anti-coagulant agent.

Paediatric population

Interaction studies have only been performed in adults.

However, no specific data regarding other potential drug interactions are available.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of meropenem in human pregnancy has not been established.

Breast-feeding

Meropenem is detectable at very low concentrations in animal breast milk. Meropenem should not be used in breast-feeding women. (See section 4.3).

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed. However, when driving or operating machines, it should be taken into account that headache, paraesthesia and convulsions have been reported for meropenem.

4.8 Undesirable effects

System Organ Class	**Frequent**	**Less frequent**	**Frequency Unknown**
Blood and the lymphatic system disorders	Thrombocythaemia	Thrombocytopenia, leukopenia, neutropenia, agranulocytosis, haemolytic anaemia, Eosinophilia	A positive direct or indirect Coomb's test may develop.
Immune system disorders		Systemic allergic reactions (hypersensitivity) including angioedema and manifestations of anaphylaxis.	
Psychiatric disorders		Delirium	

Nervous system disorders	Headache	Paraesthesia, Convulsions (See section 4.4)	
Gastro-intestinal disorders	Nausea, vomiting, diarrhoea, constipation, Abdominal pain	Pseudomembranous colitis.	Antibiotic-associated colitis (see section 4.4)
Hepato-biliary disorders	Increases in serum transaminases, increase blood alkaline phosphatases, increased lactic dehydrogenase	Blood bilirubin increased	
Skin and subcutaneous tissue disorders	Rash, pruritus	Urticaria, Severe skin reactions, such as erythema multiforme (see section 4.4), Stevens-Johnson Syndrome and toxic epidermal necrolysis.	Drug reaction with eosinophilia and systemic symptoms, acute generalised exanthematous pustulosis (see section4.4)
Renal and urinary disorders			Blood creatinine increased, blood urea increased
General disorders and administration site conditions	Inflammation, pain	Thrombophlebitis, oral and vaginal candidiasis	

Paediatric population

MERCIDE is registered for children over 3 months of age. There is no reported evidence of an increased risk of any adverse drug reaction in children. All reported reactions were consistent with events observed in adult population.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Treatment of over dosage/accidental or deliberate poisoning:

The pharmacological properties and mode of administration make it unlikely that intentional overdose will occur. Accidental overdosage could occur during therapy particularly in patients with renal impairment. Treatment of overdosage should be symptomatic. In normal individuals rapid renal elimination will occur. In subjects with renal impairment haemodialysis will remove meropenem such as in **MERCIDE** and its metabolite.

5.PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A.20.1.1 Broad and medium spectrum antibiotics.

Pharmacotherapeutic group: antibacterials for systemic use, carbapenems, ATC code: J01DH02

Mechanism of action

Meropenem is a carbapenem antibiotic for parenteral use.

Meropenem exerts its bactericidal action by interfering with vital bacterial cell wall synthesis. Bactericidal concentrations are commonly the same as the minimum inhibitory concentrations (MIC's).

Meropenem has a high degree of stability to almost all beta-lactamase produced by Gram-positive and Gram-negative bacteria. Meropenem is stable in susceptibility test systems. Susceptibility tests can be performed using routine methods. In vitro, meropenem can act synergistically with various antibiotics. A post-antibiotic effect has been demonstrated in-vitro and in-vivo.

Pharmacokinetic/Pharmacodynamic (PK/PD) relationship

Similar to other beta-lactam antibacterial agents, the time that meropenem concentrations exceed the MIC (T>MIC) has been shown to best correlate with efficacy. In reported preclinical models meropenem demonstrated activity when plasma concentrations exceeded the MIC of the infecting organisms for approximately 40 % of the dosing interval. This target has not been established clinically.

Mechanism of resistance

Bacterial resistance to meropenem may result from: (1) decreased permeability of the outer membrane of Gram-negative bacteria (due to diminished production of porins) (2) reduced affinity of the target penicillin-binding proteins (PBPs) (3) increased expression of efflux pump components, and (4) production of beta-lactamases that can hydrolyse carbapenems.

There is no target-based cross-resistance between meropenem and agents of the quinolone, aminoglycoside, macrolide and tetracycline classes. However, bacteria may exhibit resistance to more than one class of antibacterial agents when the mechanism involved include impermeability and/or an efflux pump(s).

5.2 Pharmacokinetic properties

A 30 minute intravenous infusion of a single dose of meropenem in normal volunteers results in peak plasma levels of approximately 11 µg/ml for the 250 mg dose, 23 µg/ml for the 500 mg dose, 49 µg/ml for the 1 g dose and 115 µg/ml following the 2 g dose.
A 5 minute intravenous bolus injection of meropenem in normal volunteers results in peak plasma levels of approximately 52 µg/ml for a 500 mg dose and 112 µg/ml for the 1 g dose. Intravenous infusions of 1 g of meropenem over 2 minutes, 3 minutes and 5 minutes resulted in peak plasma levels of 110, 91 and 94 µg/ml respectively.
After an IV dose of 500 mg, plasma levels of meropenem decline to values of 1 µg/ml or less, 6 hours after administration. When multiple doses are administered at 8 hourly intervals to subjects with normal renal function, accumulation of meropenem does not occur.

Distribution

Plasma protein binding of meropenem is approximately 2 %. After rapid administration (5 minutes or less) the pharmacokinetics are biexponential but this is much less evident after 30 minutes infusion. Meropenem has been shown to penetrate well into several body fluids and tissues: including lung, bronchial secretions, bile, cerebrospinal fluid, gynaecological tissues, skin, fascia, muscle, and peritoneal exudates, achieving concentrations in excess of those required to inhibit most bacteria.
When multiple doses are administered at 8 hourly intervals to patients the concentrations at steady state are approximately 20 % higher than after a single dose.

Biotransformation

Meropenem is metabolised by hydrolysis of the beta-lactam ring generating a microbiologically inactive metabolite.

In vitro meropenem shows reduced susceptibility to hydrolysis by human dehydropeptidase-I (DHP-I) compared toimipenem and there is no requirement to co-administer a DHP-I inhibitor.

Elimination

Approximately 70 % of the IV administered dose is recovered as unchanged meropenem in the urine over 12 hours, after which little further urinary excretion is detectable. Urinary concentrations of meropenem in excess of 10 microgram/ml are maintained for up to 5 hours after a 500 mg dose.

No accumulation of meropenem in plasma or urine was observed with regimens using 500 mg administered every 8 hours or 1 g administered every 6 hours in volunteers with normal renal function. In subjects with normal renal function, meropenem's half-life is approximately 1 hour.

There is one metabolite which is microbiologically inactive.

Faecal elimination represents only approximately 2 % of the dose. The measured renal clearance and the effect of probenecid show that meropenem undergoes both filtration and tubular secretion.

The elimination half-life for meropenem was approximately 1,5 hours in children under the age of 2 years. The pharmacokinetics are linear over the dose range from 10 to 40 mg/kg.

Renal insufficiency

Pharmacokinetic studies in patients with renal insufficiency have shown that the plasma clearance of meropenem correlates with creatinine clearance. Renal impairment results in higher plasma AUC and longer half-life for meropenem. There were AUC increases of 2,4 fold in patients with moderate impairment (CrCL 33-74 ml/min), 5 fold in severe impairment (CrCL 4-23 ml/min) and 10 fold in haemodialysis patients (CrCL < 2 ml/min) when compared to healthy subjects (CrCL > 80 ml/min). The AUC of the

microbiologically inactive ring opened metabolite was also considerably increased in patients with renal impairment.
Dosage adjustments are necessary in subjects with renal impairment.

Meropenem is cleared by haemodialysis with clearance during haemodialysis being approximately 4 times higher than in anuric patients.

Hepatic insufficiency

Pharmacokinetic studies in patients with liver disease have shown no effects of liver disease in the pharmacokinetics of meropenem.

Adult patients

Pharmacokinetic studies report patients have not shown significant pharmacokinetic differences versus healthy subjects with equivalent renal function. A population model developed from data in 79 patients with intra-abdominal infection or pneumonia, showed a dependence of the central volume on weight and the clearance on creatinine clearance and age.

Paediatric population

Studies in children have shown that the pharmacokinetics of meropenem in children are essentially similar to those in adults.The pharmacokinetics in infants and children with infection at doses of 10, 20 and 40 mg/kg showed Cmax values approximating to those in adults following 500, 1000 and 2000 mg doses, respectively. Comparison showed consistent pharmacokinetics between the doses and half-lives similar to those observed in adults in all but the youngest subjects (<6 months t1/2 1,6 hours). The mean meropenem clearance values were 5,8 ml/min/kg (6-12 years), 6,2 ml/min/kg (2-

5years), 5,3 ml/min/kg (6-23 months) and 4,3 ml/min/kg (2-5 months). Approximately 60 % of the dose is excreted in urine over 12 hours as meropenem with a further 12 % as metabolite. Meropenem concentrations in the CSF of children with meningitis are approximately 20 % of concurrent plasma levels although there is significant inter-individual variability.

The pharmacokinetics of meropenem in neonates requiring anti-infective treatment showed greater clearance in neonates with higher chronological or gestational age with an overall average half-life of 2,9 hours. Monte Carlo simulation based on a population PK model showed that a dose regimen of 20 mg/kg 8 hourly achieved 60 % T>MIC for *P. aeruginosa* in 95 % of pre-term and 91 % of full term neonates.

Elderly

Pharmacokinetic studies in the elderly have shown a reduction in plasma clearance of meropenem which correlated with age-associated reduction in creatinine clearance. No dose adjustment is required in elderly patients, except in cases of moderate to severe renal impairment (see section 4.2).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Carbonate Sterile

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Before reconstitution the dry powder should be stored at or below 25 ^{0}C. The vial must be stored in the carton until required for use. For storage and stability of reconstituted solution, see under **Posology and Method of Administration.**

Diluent	Hours stable up to 25 °C	Hours stable up to 4 °C
Vials constituted with water for injection for bolus injection	**7**	**48**
Infusions (1-20 mg/ml) prepared with 0,9 % sodium chloride	**8**	**48**
5,0 % dextrose **5,0 % dextrose and 0,2 % sodium chloride** **5,0 % dextrose and 0,9 % sodium chloride** **5,0 % dextrose and 0,15 % potassium chloride** **2,5 % or 10 % mannitol** **Normosol-M in 5 % glucose**	**3**	**14**
10 % dextrose **5 % dextrose and 0,02% sodium bicarbonate solution**	**2**	**8**

The container must be stored in the carton until required for use. The product is for single use only and any unused portion must be discarded. After reconstitution do not freeze.

6.5 Nature and contents of container MERCIDE 500

30 ml clear glass tubular vial with light grey Bromo-Butyl rubber plug and sealed with a tear-off seal having a blue coloured polypropylene flip off disc.

MERCIDE 1 g

40 ml clear glass tubular vial with light grey Bromo-Butyl rubber plug and sealed with a tear-off seal having a red coloured polypropylene flip off disc.

6.6 Special precautions for disposal and other handling

Injection

Meropenem to be used for bolus intravenous injection should be constituted with sterile water for injection.

Infusion

For intravenous infusion meropenem vials may be directly constituted with 0,9 or 0,2 % sodium chloride or 5 or 10 % dextrose, 0,15 % potassium chloride, 2,5 % or 10 % mannitol, Normosol-M in 5 % glucose or 0,02 % sodium bicarbonate solution solutions for infusion.

Each vial is for single use only. Standard aseptic techniques should be used for solution preparation and administration. The solution should be shaken before use.

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

Return all unused or expired medicines to your pharmacist for safe disposal. Do not dispose of unused medicines in drains or sewerage systems (e.g. toilets).

7. HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICALS (PTY) LTD

14 LAUTRE ROAD

STORMILL

EXT.1

ROODEPOORT

1724

SOUTH AFRICA

8. REGISTRATION NUMBERS

South Africa

MERCIDE 500: 43/20.1.1/0769

MERCIDE 1 g: 43/20.1.1/0770

Namibia

MERCIDE 500: NS2 Reg. No.: 10/20.1.1/0461

MERCIDE 1 g: NS2 Reg. No.: 10/20.1.1/0462

9. DATE OF FIRST AUTHORISATION

01 October 2010

10. DATE OF REVISION OF THE TEXT

06 July 2021