PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

1 NAME OF THE MEDICINE

MEROBAX™ 500, powder for solution for injection or infusion

MEROBAX™ 1 000, powder for solution for injection or infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

MEROBAX 500: Each vial contains meropenem trihydrate equivalent to 500 mg meropenem anhydrous.

MEROBAX 1 000: Each vial contains meropenem trihydrate equivalent to 1 000 mg meropenem anhydrous.

Excipients with known effect:

MEROBAX contains sodium which should be taken into consideration by patients on a controlled sodium diet.

MEROBAX 500: 45 mg sodium per vial

MEROBAX 1 000: 90 mg of sodium per vial

MEROBAX is sugar free.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

A white to light yellow, crystalline powder for solution for injection or infusion.

The reconstituted solution is a clear colourless solution practically free from particulate matter.

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4 CLINICAL PARTICULARS

4.1 Therapeutic indications

MEROBAX 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 (methicillin susceptible strains only), *Streptococcus pneumoniae, Streptococcus* spp., *Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae*, *Pseudomonas aeruginosa, Moraxella (Branhamella) catarrhalis, Klebsiella* spp, *Enterobacter cloacae, Enterobacter* spp., *Acinetobacter* spp.

Pneumonia in children due to:

Staphylococcus aureus (methicillin susceptible strains only), *Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas aeruginosa*.

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

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

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

Enterococcus faecalis, Staphylococcus aureus (methicillin susceptible strains only), coagulase-negative *Staphylococcus* spp. (methicillin susceptible strains only), *Streptococcus agalactiae* (Group B), *Streptococcus viridans, Streptococcus* spp., *Escherichia coli, Neisseria gonorrhoeae, Klebsiella pneumoniae, Enterobacter aerogenes, Enterobacter cloacae, Proteus mirabili*s, *Acinetobacter anitratus, Acinetobacter lwoffii, Gardnerella vaginalis, Bacteroides fragilis* group, *Peptostreptococcus anaerobius, Peptostreptococcus asaccharolyticus, Peptostreptococcus magnus.*

Skin and skin structure infections in adults due to:

Staphylococcus aureus (methicillin susceptible strains only), coagulase-negative *Staphylococcus* spp (methicillin susceptible stains only), *Streptococcus pyogenes (*Group A), *Streptococcus agalactiae, Streptococcus viridans, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, 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 pneumonia.

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

Streptococcus epidermidis, Streptococcus mitis, Streptococcus sanguinis, Escherichia coli.

Intra-abdominal abscess and peritonitis due to:

Streptococcus milleri, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Pseudomonas aeruginosa, Bacteroides fragilis group (including *Bacteroides distasonis, Bacteroides fragilis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides vulgatus), Clostridium perfringens*, *Streptococcus mitior.*

Polymicrobial infections

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

4.2 Posology and method of administration

Posology

Adults:

Usual dose: 500 mg to 1 000 mg is administered by intravenous infusion every 8 hours, depending on the type or severity of the infection, the known or suspected susceptibility of the pathogen(s) and the condition of the patient.

Dose exceptions:

1. Febrile episodes in neutropenic patients – the dose should be 1 000 mg every 8 hours.
2. Meningitis – the dose should be 2 000 mg every 8 hours.

Caution may be required in using beta-lactam antibiotics 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.*

Special populations

Dosage schedule for adults with impaired renal function

The dosage should be reduced in patients with creatinine clearance less than 51 ml/minute, as scheduled below.

Creatinine clearance (ml per minute)	**Dose (based on "unit" dose range of 500 mg to 2 000 mg every 8 hours – see above)**	**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

Dosage for the treatment of adults on haemodialysis:

MEROBAX is cleared from the circulation by haemodialysis. If continued treatment with MEROBAX is necessary, the required dose should be used at completion of the haemodialysis cycle to re-institute effective treatment.

There is no experience with peritoneal dialysis.

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/minute.

Paediatric population

Safety and efficacy in babies under 3 months have not been established.

For infants and children over 3 months and up to 12 years of age:

The intravenous dose is 10 – 40 mg/kg every 8 hours, depending on the type and severity of the infection, the known or suspected susceptibility of the pathogen(s) and the condition of the patient.

For children > 50 kg: The dosage as indicated for adults should be used.

Dose exceptions*:*

Meningitis: The dose should be 40 mg/kg every 8 hours.

There is no experience in children with renal impairment.

Method of administration

MEROBAX should be given as an intravenous bolus injection* over approximately 5 minutes or by intravenous infusion** over approximately 15-30 minutes.

* For instructions on reconstitution of MEROBAX before administration, see section 6.6.

** For further dilution for infusion, see section 6.6. See instructions for compatibility and stability in sections 6.2, 6.3 and 6.6.

In the treatment of beta-haemolytic streptococcal infections, a therapeutic dose should be administered for at least 10 days.

4.3 Contraindications

MEROBAX is contraindicated in:

- Patients with hypersensitivity to meropenem or any of the other ingredients of MEROBAX (see section 6.1).
- Patients hypersensitive to carbapenems, penicillins or other beta-lactam antibacterials (e.g., cephalosporins, imipenem) may be hypersensitive to meropenem as in MEROBAX.
- Pregnancy and lactation (see section 4.6).

4.4 Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship.

The selection of meropenem to treat an individual patient should take into account the appropriateness of using a carbapenem antibacterial medicine based on factors such as severity of the infection, the prevalence of resistance to other suitable antibacterial medicines and the risk of selecting for carbapenem-resistant bacteria.

***Enterobacteriaceae, Pseudomonas aeruginosa* and *Acinetobacter* spp. resistance:**

Prescribers are advised to consider the local prevalence of resistance in these bacteria to penem antibiotics.

Paediatric use:

Efficacy and tolerability in infants under 3 months of age have not been established and MEROBAX is only approved for children over 3 months of age (see section 4.2).

Hypersensitivity reactions

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 (see section 4.3). Before initiating therapy with MEROBAX, careful inquiry should be made concerning previous hypersensitivity reactions to beta-lactam antibiotics.

If a severe allergic reaction occurs, MEROBAX 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, MEROBAX 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 antibacterial medicines, including meropenem, and may range in severity from mild to life-threatening. Therefore, it is

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important to consider this diagnosis in patients who present with diarrhoea during or subsequent to the administration of MEROBAX (see section 4.8). Discontinuation of therapy with MEROBAX and the administration of specific treatment for *Clostridium difficile* should be considered. Medicines that inhibit peristalsis should not be given.

Seizures

Seizures have infrequently been reported during treatment with carbapenems, including meropenem as in MEROBAX. Special care is necessary in patients with central nervous system (CNS) disorders such as epilepsy (see section 4.8).

Hepatic function monitoring

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

Patients with pre-existing liver disorders should have liver function monitored during treatment with MEROBAX. There is no dose adjustment necessary (see section 4.2).

Direct antiglobulin test (Coombs test) seroconversion

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

Concomitant use with valproic acid/sodium valproate/valpromide

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

MEROBAX contains sodium

MEROBAX 500 contains 45 mg sodium per 500 mg vial, equivalent to 2,3 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. This should be taken into consideration by patients on a controlled sodium diet.

MEROBAX 1 000 contains 90 mg sodium per 1 000 mg vial, equivalent to 4,5 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. This should be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicines and other forms of interaction

No specific interaction studies other than probenecid were conducted.

Probenecid

Probenecid inhibits the renal excretion of MEROBAX thereby increasing its plasma concentrations and prolonging the elimination half-life. As the potency and duration of action of MEROBAX dosed without probenecid are adequate, the co-administration of probenecid with MEROBAX is not recommended.

The potential effect of meropenem on the protein binding of other medicines or metabolism has not been studied. However, the protein binding is so low that no interactions with other compounds would be expected on the basis of this mechanism.

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Valproate/valproic acid

Valproic acid plasma levels may be reduced by meropenem when it is co-administered with carbapenem medicines, 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 medicines is not considered to be manageable and therefore should be avoided (see section 4.4).

Oral anti-coagulants

Simultaneous administration of MEROBAX 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 medicines, including warfarin, in patients who are concomitantly receiving antibacterial medicines. 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.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety in pregnant women has not been established. MEROBAX should therefore not be used during pregnancy (see section 4.3).

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Breastfeeding

Meropenem is detectable at very low concentrations in animal breast milk. Small amounts of meropenem have been reported to be excreted in human milk. MEROBAX should not be used in breastfeeding mothers, or mothers should not breastfeed their babies if treatment with MEROBAX is deemed essential for them.

Fertility

There is no data on fertility and the use of MEROBAX.

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 considered that headache, paraesthesia and convulsions have been reported for meropenem.

4.8 Undesirable effects

Summary of the safety profile

Meropenem-related adverse reactions most frequently reported were diarrhoea, rash, nausea/vomiting, injection site inflammation, thrombocytosis and increased hepatic enzymes.

Tabulated summary of adverse reactions

In the table below all adverse reactions are listed by system organ class and frequency: frequent; less frequent; and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	Event
Infections and infestations	Less frequent	Oral and vaginal candidiasis, pharyngitis
Blood and the lymphatic system disorders	Frequent Less frequent	Thrombocythaemia Agranulocytosis, haemolytic anaemia, thrombocytopenia, neutropenia, leukopenia, eosinophilia, lymphadenopathy, positive direct or indirect antiglobulin test may develop
Immune system disorders	Less frequent	Anaphylaxis (see sections 4.3 and 4.4), angioedema
Metabolism and nutrition disorders	Less frequent	Hypoglycaemia
Psychiatric disorders	Less frequent	Delirium
Nervous system disorders	Frequent Less frequent	Headache Paraesthesia, convulsions (see section 4.4)
Vascular disorders	Frequency unknow	Peripheral vascular disorder

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Respiratory, thoracic, and mediastinal disorders	Less frequent	Epistaxis, apnoea
Gastrointestinal disorders	Frequent	Diarrhoea, abdominal pain, vomiting, nausea, constipation
	Less frequent	Pseudomembranous colitis, antibiotic-associated colitis (see section 4.4)
Hepatobiliary disorders	Frequent	Increases in serum transaminases, bilirubin, alkaline phosphatase, lactic dehydrogenase
Skin and subcutaneous tissue disorders	Frequent	Rash, pruritus
	Less frequent	Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme (see section 4.4), urticaria
	Frequency unknown	Drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP) (see section 4.4)

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Renal and urinary disorders	Less frequent	Blood creatinine increased, blood urea increased
General disorders and administration site conditions	Frequent	Inflammation, pain, thrombophlebitis
	Less frequent	Pain at the injection site

Paediatric population

Meropenem as in MEROBAX is approved for children over 3 months of age. There is no evidence of an increased risk of adverse reactions in children based on the limited available data. All reports were consistent with events observed in the 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. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

In patients with renal impairment relative overdosage is possible if the dose is not adjusted as described in section 4.2.

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Treatment is symptomatic and supportive. In normal individuals, rapid renal elimination will occur.

In patients with renal impairment, haemodialysis will remove MEROBAX and its metabolite.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other beta-lactam antibacterials, Carbapenems

ATC code: J01DH02

Category and class: A 20.1.1 Broad and medium spectrum antibiotics

Mechanism of action

Meropenem is a carbapenem antibiotic for intravenous administration that is stable to human dehydropeptidase-1 (DHP-1). It is structurally similar to imipenem.

Meropenem exerts its bactericidal activity by inhibiting bacterial cell wall synthesis through binding to penicillin-binding proteins (PBPs).

Meropenem has a high degree of stability to hydrolysis by almost all beta-lactamases produced by Gram-positive and Gram-negative bacteria.

In vitro, meropenem can act synergistically with various antibiotics.

A post-antibiotic effect has been demonstrated *in vitro* and *in vivo.*

Meropenem may be active *in vitro* against imipenem-resistant strains of Pseudomonas aeruginosa. *In vitro* sensitivity does not necessarily imply clinical sensitivity. For *in vivo* efficacy information, refer to section 4.1.

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Pharmacokinetic/Pharmacodynamic (PK/PD) relationship

Similar to other beta-lactam antibacterial medicines, 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 medicines when the mechanism involved include impermeability and/or an efflux pump(s).

Inherently resistant organisms

Gram-negative aerobes:

Stenotrophomonas maltophilia, Legionella species

Other micro-organisms:

Chlamydophila pneumoniae, Chlamydophila psittaci, Coxiella burnetiid

Mycoplasma pneumoniae

5.2 Pharmacokinetic properties

Absorption

A 30-minute intravenous infusion of a single dose of meropenem as in MEROBAX in normal volunteers results in peak plasma levels of approximately 23 micrograms/ml for the 500 mg dose, 49 micrograms/ml for the 1 000 mg dose, and 115 micrograms/ml following a dose of 2 g.

A 5-minute intravenous bolus injection of meropenem in normal volunteers results in peak plasma concentrations of approximately 52 micrograms/ml for the 500 mg dose and 112 micrograms/ml for the 1 000 mg dose.

Intravenous infusions of 1 000 mg meropenem over 2 minutes, 3 minutes, and 5 minutes resulted in peak plasma concentrations of 110, 91 and 94 micrograms/ml, respectively.

After an IV dose of 500 mg, plasma levels of meropenem decline to 1 microgram/ml or less, 6 hours after administration.

When multiple doses are administered at 8 hourly intervals to patients with normal renal function, accumulation of meropenem does not occur.

Distribution

Meropenem is well distributed in most body fluids and tissues with a low (2 %) protein binding.

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,

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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 to imipenem and there is no requirement to co-administer a DHP-I inhibitor.

Elimination

Approximately 70 % of an administered dose is recovered in the urine as unchanged meropenem over 12 hours. A further 28 % is recovered as the microbiologically inactive metabolite. 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.

Urinary concentrations of meropenem in excess of 10 microgram/ml are maintained for up to 5 hours at the 500 mg dose.

The plasma elimination half-life of meropenem may be prolonged in patients with renal impairment.

Meropenem is primarily excreted unchanged, with one inactive metabolite having been identified.

Specific patient groups

Renal insufficiency:

The plasma clearance of meropenem correlates with the creatinine clearance. Dose adjustments are required for patients with moderate to severely impaired renal function (see section 4.2).

Hepatic insufficiency:

Hepatic impairment does not seem to affect the pharmacokinetics of meropenem in patients with impaired liver function.

Paediatric patients:

The pharmacokinetics of meropenem in children are essentially similar to those in adults. The elimination half-life of meropenem was approximately 1,5 hours in children under the age of 2 years. The pharmacokinetics are linear over the dose range of 10-40 mg/kg (see section 4.2).

Elderly patients:

Elderly patients with age-related reduction in creatinine clearance have shown a reduction in plasma clearance of meropenem. No dosage adjustment is required in the elderly, except in the case of moderate to severe renal impairment (see section 4.2).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

MEROBAX 500: sodium carbonate.

MEROBAX 1 000: sodium carbonate.

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6.2 Incompatibilities

MEROBAX must not be mixed with or physically added to other medicines except those mentioned in section 6.6.

6.3 Shelf life

Dry powder in vial or bottle: 36 months

After reconstitution:

Intravenous bolus injection administration

A solution for bolus injection is prepared by dissolving the MEROBAX in water for injection to a final concentration of 50 mg/ml. Chemical and physical in-use stability for a prepared solution for bolus injection has been demonstrated that reconstituted solution of the product in water for injection should be used immediately at up to 25 °C or 30 minutes under refrigerated conditions (2 – 8 °C).

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Intravenous infusion administration

A solution for infusion is prepared by dissolving the MEROBAX in either 0,9 % sodium chloride solution for infusion or 5 % dextrose solution for infusion to a final concentration of 1 to 20 mg/ml. Chemical and physical in-use stability for a prepared solution for infusion using 0,9 % sodium

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chloride solution has been demonstrated for 1 hour at up to 25 °C or 5 hours under refrigerated conditions (2 °C to 8 °C).

MEROBAX infusion solutions with 5 % dextrose at 1 to 20 mg/ml should be used immediately at up to 25 °C or 2 hours at refrigerated conditions (2 °C to 8 °C).

From a microbiological point of view, unless the method of opening/reconstitution/dilution precludes the risk of microbiological contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Dry powder

Store the dry powder at or below 25 °C and protect from light. Do not freeze. Keep the vial in the outer container until required for use.

Reconstituted solution

For storage conditions after reconstitution, see section 6.3.

The product must be used immediately after first opening.

Do not freeze the reconstituted solution.

6.5 Nature and contents of container

MEROBAX 500: 20 ml Type I colourless glass vials with grey bromobutyl rubber stoppers and aluminium-plastic caps, available in pack sizes of 1 or 10 vials.

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MEROBAX 1 000: 30 ml Type I colourless glass vials with grey bromobutyl rubber stoppers and aluminium-plastic cap, available in pack sizes of 1 or 10 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Injection

MEROBAX, used as bolus intravenous injection, should be constituted with sterile water for injection, 10 ml per 500 mg and 20 ml per 1 000 mg of meropenem. This provides an approximate concentration of 50 mg/ml. Prepared solutions are clear or pale yellow, without visible particles.

Infusion

For intravenous infusion MEROBAX vials may be directly reconstituted with 0,9 % sodium chloride or 5 % dextrose solutions for infusion to a final volume of 50 – 200 ml. Do not mix MEROBAX with other medicines.

Standard aseptic techniques should be used for solution preparation and administration.

Shake the solution before use and inspect visually for clarity and absence of particles. Freshly prepared solutions should be used whenever possible (see section 6.3).

Each vial is for single use only.

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

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7 HOLDER OF CERTIFICATE OF REGISTRATION

Abex Pharmaceutica (Pty) Ltd

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617 Rubenstein Drive

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South Africa

8 REGISTRATION NUMBERS

MEROBAX 500: 57/20.1.1/0512

MEROBAX 1 000: 57/20.1.1/0513

9 DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 August 2025.

Date of latest renewal: Not applicable.

10 DATE OF REVISION OF THE TEXT

Not applicable.

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