

INSERT MEROSAN
(29 SEP ‘20) - Exp. Malaysia
Depan

Controlled
Medicine

MEROSAN®

Sterile powder for injection

Meropenem for Injection USP

MEROSAN 0.5 g Sterile powder for injection

Each vial contains:
Meropenem Trihydrate equivalent to 500 mg of An-
hydrous Meropenem

MEROSAN 1 g Sterile powder for injection

Each vial contains:
Meropenem Trihydrate equivalent to 1 g of Anhydrous
Meropenem

Specification: USP

PRODUCT DESCRIPTION

White to pale yellow powder, has characteristic odor; and
clear, colorless to pale yellow solution with characteristic
odor after reconstituted with water for injection.

PHARMACODYNAMICS

Meropenem is a carbapenem antibiotic for parenteral use
which is relatively stable to human dehydropeptidase-1
(DHP-1) and therefore, does not require the addition of an
inhibitor of DHP-1.

Meropenem exerts bactericidal activity by inhibiting cell
wall synthesis by penetrating the cell wall of most Gram-
positive and Gram-negative bacteria to reach penicillin-
binding-protein (PBP) targets. Its strongest affinity is toward
PBPs 2, 3, and 4 of *Escherichia coli* and *Pseudomonas*
aeruginosa, and PBPs 1, 2, and 4 of *Staphylococcus aureus*.
Bactericidal concentrations are typically one to two times
the bacteriostatic concentrations; the exception is *Listeria*
monocytogenes, against which lethal activity has not been
observed. Similar to imipenem, the antibacterial action of
meropenem is related to binding of the drug to penicillin
binding proteins (PBPs) of Gram-positive and Gram-
negative organisms. The high resistance of meropenem to
most bacterial beta-lactamases and good penetration of
the drug through the outer membrane also contribute
significantly to antimicrobial activity. Meropenem may be
less of an inducer of beta-lactamases than imipenem.

PHARMACOKINETICS

Absorption

Peak Concentration: dependent on dose, renal function,
and administration technique. The time to peak
concentration following intravenous administration is
approximately 1 hour (range: 0.5–1.5 hours) after the start
of the infusion.

Distribution

Plasma protein binding of meropenem is approximately
2%. Meropenem achieves concentrations that match or
exceed those required to inhibit most susceptible bacteria
in most body fluids and tissues including cerebrospinal
fluid. Peak concentrations in body fluids were mostly
achieved in 1 hour following intravenous infusion. The
volume of distribution is 12 to 20 L.

Metabolism

Extrarenal, 20% to 25%. Increases up to 50% in patients with
creatinine clearance of less than 20 mL/minute. There is
one metabolite, which is inactive, ICI-213689.

Elimination

Approximately 70% of a meropenem dose administered
intravenously is recovered unchanged in the urine over 12
hours. The clearance of meropenem from plasma
correlates with the creatinine clearance. There is no
accumulation of repeated doses of meropenem 500 mg
every 8 hours or 1 gram every 6 hours in patients with
normal renal function. Dose adjustments are necessary in
patients with renal impairment.

Elimination Half-life

- Adults and children age 2 years and older: 1 hour
- Children age 3 months to 2 years: 1.5 hours
- Preterm neonates (27 to 32 weeks gestational age, 21
days mean postnatal age): 3.4 hours
- Impaired renal function: 3.4 to 20 hours or longer

INDICATIONS

MEROSAN Sterile Powder for Injection is indicated for
treatment, in adults and children, of the following
infections caused by single or multiple bacteria sensitive to
meropenem:

- Pneumonias and Nosocomial pneumonias
- Urinary Tract Infections
- Intra-abdominal infections
- Gynaecological infections, such as endometritis and
pelvic inflammatory disease
- Bacterial meningitis
- Septicaemia
- Empiric treatment, for presumed infections in patients
with febrile neutropenia, used as monotherapy or in
combination with anti-viral or anti-fungal agents.

MEROSAN Sterile Powder for Injection is efficacious alone
or in combination with other antimicrobial agents in the
treatment of polymicrobial infections

CONTRAINDICATIONS

- Anaphylactic reaction to beta-lactam antibiotics.
- Hypersensitivity to meropenem or any component of the
product or other drugs in the same class (carba-
penems).

ADVERSE EFFECTS

- Immunologic Effects: rarely, systemic allergic reactions
(hypersensitivity) which may include angioedema and
manifestations of anaphylaxis.
- Dermatologic Effects: Thrombophlebitis, injection site
pain and inflammation, rash, pruritus, urticaria, ery-
thema multiforme, Stevens-Johnson Syndrome, toxic
epidermal necrolysis.
- Gastro-intestinal Effects: abdominal pain, nausea,
vomiting, diarrhoea.
- Hematologic Effects: reversible thrombocythaemia,
eosinophilia, thrombocytopenia, leucopenia and
neutropenia (including very rare cases of agra-
nulocytosis), haemolytic anaemia, bleeding.
- Hepatic Effects: Increases in serum concentrations of
bilirubin, transaminases, alkaline phosphatase and lactic
dehydrogenase alone or in combination
- Central nervous system Effects: headache, paraes-
thesiae, seizure (convulsions)
- Other: oral and vaginal candidiasis.

OVERDOSE AND TREATMENT

Treatment is symptomatic and supportive. There is no
known antidote.

Rapid renal elimination will occur in patients without renal
impairment.

Haemodialysis will remove meropenem and its metabolite
in patients with renal impairment.

In the event of an overdose, meropenem should be dis-
continued and general supportive treatment given until
renal elimination takes place. Meropenem and its
metabolite are readily dialyzable and effectively removed
by hemodialysis; however, no information is available on
the use of hemodialysis to treat overdose.

WARNING AND PRECAUTIONS

- There is some clinical and laboratory evidence of partial
cross-allergenicity between other carba-penems and
beta-lactam antibiotics, penicillins and cephalosporins.
As with all beta-lactam antibiotics, rare hypersensitivity
reactions have been reported. Before initiating therapy
with meropenem, careful inquiry should be made
concerning previous hyper-sensitivity reactions to beta-
lactam antibiotics. Meropenem should be used with
caution in patients with such a history. If an allergic
reaction to meropenem occurs, the drug should be
discontinued and appropriate measures taken.
- Use of meropenem in patients with hepatic disease
should be made with careful monitoring of trans-aminase
and bilirubin levels.
- As with other antibiotics, overgrowth of non-sus-ceptible
organisms may occur and, therefore, continous
monitoring of each patient is necessary.
- Use in infections caused by methicillin resistant
staphylococci is not recommended.
- Rarely, pseudomembranous colitis has been reported on
meropenem as with practically all antibiotics and may
vary in severity from slight to life-threatening. Therefore,
antibiotics should be prescribed with care for individuals
with a history of gastro-intestinal com-plaints, particularly
colitis.
- It is important to consider the diagnosis of pseudo-
membranous colitis in the case of patients who develop
diarrhoea in association with the use of meropenem.
Although studies indicate that a toxin produced by
Clostridium difficile is one of the main causes of antibiotic-
associated colitis, other causes should be considered.
- The co-administration of meropenem with potentially
nephrotoxic drugs should be considered with caution.
- Meropenem may reduce serum valproic acid levels. Sub-
therapeutic levels may be reached in some patients.
- 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.
There is no experience in children with altered hepatic or
renal function.
- Serious and occasionally fatal hypersensitivity reactions
(including anaphylactoid and severe cutaneous adverse
reactions) have been reported in patients receiving
therapy with beta-lactams. Before initiating therapy with
MEROSAN Sterile Powder for Injection, careful inquiry
should be made concerning previous hypersensitivity
reactions to penicillins, cephalosporins, carbapenems or
other beta-lactam agents. If an allergic reaction occurs,
MEROSAN Sterile Powder for Injection must be
discontinued immediately and appropriate alternative
therapy instituted.

INTERACTIONS WITH OTHER MEDICAMENTS

- Concurrent use of meropenem and valproic acid may
result in decreased valproic acid plasma concen-trations
and loss of anticonvulsant effect.
- Concurrent use of meropenem and probenecid may
result in increased plasma concentrations of mero-
penem.
- Concurrent use of live typhoid vaccine and antibiotics
may result in a decreased immunological response to the
typhoid vaccine.

Country: Malaysia	Packaging: Insert	Dimension: 209 x 193 mm (double side printing)	Material: HVS paper 60 g	Color: BLACK	Scale: 100%
----------------------	----------------------	--	-----------------------------	----------------------------	----------------

INSERT MEROSAN
(29 SEP ‘20) - Exp. Malaysia
Belakang

STATEMENT ON USAGE DURING PREGNANCY AND LACTATION

Pregnancy

The safety of meropenem in human pregnancy has not been evaluated. Animal studies have not shown any adverse effect on the developing foetus. Meropenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus. In every case, it should be used under the direct supervision of the physician.

Lactation

Meropenem is detectable at very low concentrations in animal breast milk. Meropenem should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

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 **MEROSAN**.

RECOMMENDED DOSE

Adults

The dosage and duration of therapy shall be established depending on type and severity of infection and the condition of the patient.

The recommended daily dosage is as follows:

- 500 mg I.V. every 8 hours in the treatment of pneumonia, UTI, gynaecological infections such as endometritis.
- 1 g I.V. every 8 hours in the treatment of hospital acquired pneumonias, peritonitis, presumed infections in febrile neutropenic patients, septicæmia.
- In meningitis the recommended dosage is 2 g every 8 hours.
- A dose of up to 2 g three times daily in adults and adolescents and a dose of up to 40 mg/kg three times daily in children may be particularly appropriate when treating some types of infections, such as nosocomial infections due to *Pseudomonas aeruginosa*.
- Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa* infection.
- There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection.

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. There are limited data to support the application of these dose adjustments for a unit dose of 2 g.

Creatinine clearance (mL/min)	Dose (based on unit doses of 500 mg, 1 g, 2 g)	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

MEROSAN Powder for Injection is cleared by haemodialysis and haemofiltration; if continued treatment with Meropenem I.V. is necessary, it is recommended that the unit dose (based on the type and severity of infection) is administered at the completion of the haemodialysis procedure to restore therapeutically effective plasma concentrations.

There is no experience with the use of **MEROSAN** Powder for Injection in patients under peritoneal dialysis.

Dosage in Adults with Hepatic Insufficiency

No dosage adjustment is necessary in patients with hepatic insufficiency.

Elderly Patients

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

Children

For children over 3 months and up to 12 years of age the recommended dose is 10 - 20 mg/kg every 8 hours depending on type and severity of infection, susceptibility of the pathogen and the condition of the patient. In children over 50 kg weight, adult dosage should be used.

In meningitis the recommended dose is 40 mg/kg every 8 hours.

Febrile episodes in neutropenic patients-the dose should be 20 mg/kg every 8 hours.

There is no experience in children with renal impairment.

There are limited safety data available to support the administration of a 40 mg/kg dose in children as an intravenous bolus injection.

Method of Administration

MEROSAN Powder for Injection can be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 to 30 minutes using the specific available pre-sentations.

MEROSAN Powder for Injection to be used for bolus intravenous injection should be constituted with sterile Water for Injections (5 mL per 250 mg Meropenem). This provides an approximate concentration of 50 mg/mL. Constituted solutions are clear, and colourless or pale yellow.

For intravenous bolus injection administration, this product should be constituted with water for injections as shown in following table:

Vial content	Amount of diluent added (mL)	Approximate withdrawable volume (mL)	Approximate average concentration (mg/mL)
500 mg	10	10	50
1 g	20	20	50

MEROSAN for I.V. infusion may be directly constituted with compatible infusion fluids below:

- 1) Constituted with water for injections
- 2) Solutions (1 - 20 mg/mL) prepared with:

Sodium Chloride 0.9%, Glucose 5%, Glucose 10%, Glucose 5% and Sodium Chloride 0.9%, Glucose 5% and Sodium Chloride 0.45%, Glucose 5% and Sodium Chloride 0.225%, Ringer Lactate and Glucose 5%, Ringer Lactate, Mannitol 2.5%

Alternatively, an injection vial may be constituted, then the resulting solution added to an I.V. container and further diluted with an appropriate infusion fluid in table above.

It is recommended to use freshly prepared solutions of Meropenem for I.V. injection and infusion. Constituted solution are clear and colorless or pale yellow. Shake constituted solution before use.

DOSAGE FORMS AND PACKAGING AVAILABLE

MEROSAN 0.5 g Sterile Powder for Injection

Box of 1 vial @ 0.5 g.
Lic. No. : DKL0722244144A1
MAL No.: MAL16105028AZ

MEROSAN 1 g Sterile Powder for Injection

Box of 1 vial @ 1 g.
Lic. No. : DKL0722244144B1
MAL No.: MAL16105029AZ

SHELF LIFE AND STORAGE CONDITION

Before Reconstitution:

Store dry powder at temperature below 30°C. Do not freeze. The shelf life of **MEROSAN** Sterile Powder for Injection is 24 months.

After Reconstitution:

a. Intravenous bolus injection administration

Reconstituted solution in water for injection is stable for 2 hours at temperature 15° - 25°C or for 12 hours in a refrigerator (2° - 8°C). Discard any unused solutions after these periods.

b. Intravenous infusion administration

Constituted solutions maintain satisfactory potency at 15° - 25°C or under refrigeration (2° - 8°C) as shown in the stability table below. Discard any unused solutions after these periods.

Diluent	Hours stable	
	15° - 25°C	2° - 8°C
Constituted with water for injections	2	12
Solutions (1 - 20 mg/mL) prepared with:		
- Sodium Chloride 0.9%	4	24
- Glucose 5%	1	4
- Glucose 10%	1	2
- Glucose 5% and Sodium Chloride 0.9%	1	2
- Glucose 5% and Sodium Chloride 0.45%	2	4
- Glucose 5% and Sodium Chloride 0.225%	2	4
- Ringer Lactate and Glucose 5%	1	4
- Ringer Lactate	4	12
- Mannitol 2.5%	2	16

Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in the table above.

KEEP OUT OF REACH OF CHILDREN

JAUHI DARIPADA KANAK-KANAK

Name & Address of Manufacturer:

PT SANBE FARMA
Jalan Mahar Martanegara No. 162 (Jl. Leuwigajah No. 162)
RT.01 RW. 12 Kelurahan Baros, Kecamatan Cimahi Tengah,
Kota Cimahi, Indonesia

Name & Address of Product Registration Holder:

Medispec (M) Sdn. Bhd.
55 & 57, Lorong Sempadan 2 (Off Boundary Road),
11400 Ayer Itam, Pulau Pinang, Malaysia

Date of Revision of Package Insert:

07/10/2021

* BF 446 - EMY3

Country:
Malaysia

Packaging:
Insert

Dimension:
209 x 193 mm
(double side printing)

Material:
HVS paper 60 g

Color:
BLACK

Scale:
100%