MEROSAN®

Meropenem for Injection USP
Sterile powder for Injection

What is in this leaflet

This leaflet includes the information needed to use **MEROSAN®** safely and effectively.

What MEROSAN® is used for

MEROSAN® is indicated for treatment, in adult 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
- Skin and skin structure infection
- Meningitis
- Septicemia
- Empiric treatment, for presumed infections in adult patients with febrile neutropenia, used as monotherapy or in combination with anti-viral or anti-fungal agents.

MEROSAN® is efficacious alone or in combination with other antimicrobial agents in the treatment of polymicrobial infections.
There is no experience in pediatric patients with neutropenia or primary or secondary immunodeficiency.

How MEROSAN® works

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 it's bactericidal action by interfering with vital bacterial cell wall synthesis. These ease with which it penetrates bacterial cell walls. Its high level of stability to all serine β-lactamases and its marked affinity for the Penicillin Binding Proteins (PBPs) explain the potent bactericidal action of Meropenem against a broad spectrum of aerobic and anaerobic bacteria.
Minimum bactericidal concentration (MBC) are commonly the same as the minimum inhibitory concentration (MIC). For 76% of bacteria tested, the MBC : MIC ratios were 2 or less.
Meropenem is stable in susceptibility tests and these tests can be performed using the normal routine methods.
In vitro tests show that Meropenem acts synergistically with various antibiotics. It has been demonstrated both in vitro and in vivo that Meropenem has a post antibiotic effect.
A single set of Meropenem susceptibility criteria are recommended based on pharmacokinetics and correlation of clinical and microbiological outcomes with zone diameter and minimum inhibitory concentration (MIC) of the infecting organisms.

Categorization	Method of Assessment	
	Zone Diameter (mm)	MIC Breakpoint (mg/l)
Susceptible	≥ 14	≤ 14
Intermediate	12 – 13	8
Resistant	≤ 11	≥ 11

The in vitro antibacterial spectrum of Meropenem includes the majority of clinically significant Gram-positive and Gram-negative, aerobic and anaerobic strains of bacteria, as shown below:

Gram-Positive Aerobes:
Bacillus spp., Corynebacterium diphteriage, Enterococcus liquifaciens, Enterococcus avium, Listeria monocytogenes, Lactobacillus spp., Nocardia asteroids, Staphylococcus aureus (penicillinase-negative and –positive), *Staphylococci coagulase-negative* including *Staphylococcus saprophyticus, Staphylococcus capitis, Staphylococcus cohnii, Staphylococcus xylosus, Staphylococcus warneri, Staphylococcus hominis, Staphylococcus simulans, Staphylococcus intermedius, Staphylococcus sciuri, Staphylococcus lugdunensis, Streptococcus pneumoniae* (penicillin susceptible and resistant strains), *Streptococcus agalactiae, Streptococcus pyogenes, Streptococcus equi, Streptococcus bovis, Streptococcus mitis, Streptococcus mitior, Streptococcus milleri, Streptococcus sanguis, Streptococcus viridans, Streptococcus salivarius, Streptococcus morbillorum, Streptococcus Group G, Streptococcus Group F, Rhodococcus equi.*

Gram-Negative Aerobes Bacteria:
Achromobacter xylosoxidans, Acinetobacter anitratus, Acinetobacter lwofii, Acinetobacter baumannii, Aeromonas hydrophila, Aeromonas sorbria, Aeromonas caviae, Alcaligenes faecalis, Bordetella bronchiseptica, Brucalia melitensis, Campylobacter

coli, Campylobacter jejuni, Citrobacter freundii, Citrobacter diversus, Citrobacter koseri, Citrobacter amalonaticus, Enterobacter aerogenes, Enterobacter (Pantoea) agglomerans, Enterobacter cloacae, Anterobacter sakazakii, Escherichia coli, Escherichia hermannii, Gardinerella vaginalis, Haemophilus influenzae (including β-lactamase positive and ampicillin resistant strains), *Haemophilus parainfluenzae, Haemophilus ducreyl, Helicobacter pylori, Neisseria meningiditis, Neisseria gonorrhoeae* (including β-lactamase positive, penicillin resistant and spectinomycin resistant strains), *Hafnia alvei, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella azaenae, Klebsiella oxytoca, Moraxella (Branhamelia) catarrhalis, Marganelia morganii, Proteus penneri, Providencia rettgeri, Providencia stuartii, Providencia alcalifaciens, Pasteurella multocida, Plesiomonas shigelloides, Pseudomonas aeruginosa, Pseudomonas putida, Pseudomonas alcaligenes, Burkholderia (Pseudomonas) cepacia, Pseudomonas fluorescens, Pseudomonas stutzeri, Pseudomonas pseudomallei, Pseudomonas acidovorans, Salmonella spp. (*including *Salmonella enteritidis/typhi), Serratia marcescens, Serratia liquifaciens, Serratia rubidaea, Shigella sonnei, Shigella flexneri, Shigella boydii, Shigella dysenteriae, Vibrio cholerae, Vibrio para haemolyticus, Vibrio vulnificus, Yersinia enterocolitica*

Anaerobes Bacteria:
Actinomyces odontolyticus, Actinomyces meyeri, Bacteroides-Prevotella Porphyromonas spp., Bacteroides fragilis, Bacteroides vulgatus, Bacteroides variabilis, Bacteroides pneumosintes, Bacteroides coagulans, Bacteroides uniformis, Bacteroides distasonis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides eggerthii, Bacteroides capsillosis, Prevotella buccalis, Bacteroides gracilis, Prevotella melaninogenica, Prevotella intermedia, Prevotella bivia, Prevotella splanchnicus, Prevotella oralis, Prevotella disiens, Prevotella rumenicola, Bacteroides ureolyticus, Prevotella oris, Prevotella buccae, Prevotella denticola, Bacteroides levii, Porphyromonas asaccharolytica, Bifidobacterium spp., Bilophila wadsworthia, Clostridium perfringens, Clostridium bifermentans, Clostridium ramosum, Clostridium sporogenes, Clostridium cadaveris, Clostridium sordellii, Clostridum butyricum, Clostridium clostridiiformis, Clostridium innocuum, Clostridium subterminale, Clostridium tertium, Eubacterium lentum, Eubacterium aerofaciens, Fusobacterium mortiferum, Fusobacterium necrophorum, Fusobacterium nucleatum, Fusobacterium varium, Mobiluncus curtisii, Mobiluncus mulieris, Peptostreptococcus micros, Peptostreptococcus magnus, Peptostreptococcus prevotii, Propionibacterium acnes, Propionibacterium avidum, Propionibacterium granulosum.

Streptophomonas maltophilia, Enterococcus faecium, and methicilin-resistant Staphylococci have been found to be resistant to Meropenem.

Before you use MEROSAN®

When you must not take it

MEROSAN® must not be taken when there is known hypersensitivity to Meropenem, other carbapenems, or any ingredient in the formulation.

Before you start to take it

- **MEROSAN®** to be used for bolus I.V. injection should be constituted with water for injections as shown in following table:

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

- It is recommended that freshly prepared solutions of Meropenem are used whenever possible.
- Constituted solution is clear, colorless or pale yellow.
- Shake constituted solution before use.
- **MEROSAN®** for I.V infusion may be directly constituted with compatible infusion fluids (50-200 ml) as shown in stability table below.
- Constituted solutions maintain satisfactory potency at room temperature (up to 25°C) or under refrigeration (2°-8°C) as shown in these following stability table:

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

- Constituted solution should not be frozen.

Taking other medicines

- The co-administration of probenecid with **MEROSAN®** is not recommended.
- The potential effect of **MEROSAN®** on the protein-binding of other drugs or metabolism has not been studied. The protein-binding of **MEROSAN®** is low (approximately 2%) and therefore no interactions with other compounds based on displacement from plasma proteins would be expected.
- **MEROSAN®** should not be mixed or added to other drugs, unless with several infusion fluids (see stability table).

How to take MEROSAN®

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

How much to take

Adults

- 500 mg I.V. every 8 hours in the treatment of pneumonia, urinary tract infections, gynaecological infections e.g, endometritis, skin and skin structure infections.
- 1 g I.V. every 8 hours in the treatment of nosocomial pneumonias, peritonitis, presumed infections in neutropenic patients and septicaemia.
- In meningitis the recommended dosage is 2 g every 8 hours.
- As with other antibiotics, particular caution is recommended in using Meropenem as monotherapy in critically ill patients with known or suspected *Pseudomonas aeruginosa* lower respiratory tract infection.
  Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa* infection.

Adults with impaired renal function

Dosage should be reduced in patients with creatinine clearance < 51 mL/minute, as scheduled as follows:

Creatinine clearance (mL/min)	Dose (Based on unit doses of 500 mg, 1 g)	Frequency
26 – 50	1 unit dose	Every 12 hours
10 – 25	½ unit dose	Every 12 hours
< 10	½ unit dose	Every 12 hours

Meropenem is cleared by haemodialysis, if continued treatment with **MEROSAN®** is necessary; it is recommended that the unit dose (based on type and severity of infection) be administered at the completion of the haemodialysis procedure to restore therapeutically effective plasma concentrations.
There is no experience in the use of **MEROSAN®** in patients under peritoneal dialysis.

Adults with hepatic insufficiency

No dosage adjustment is necessary in patients with hepatic insufficiency (see precautions).

Elderly

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

Children

For pediatric patients ≥ 3 months, the recommended dose is 20-40 mg/kg every 8 hours, (maximum dose is 2 g every 8 hours) depending on the type of infection (intra-abdominal or meningitis). As shown in dosing table below:

Type of infection	Dose (mg/kg)	Dosing Interval
Intra-abdominal	20	Every 8 hours
Meningitis	40	Every 8 hours

Pediatric patients weighing over 50 kg should be administered at dose of 1 g every 8 hours for intra-abdominal infections and 2 g every 8 hours for meningitis.
MEROSAN® should be given as intravenous infusion over approximately 15 to 30 minutes or as intravenous bolus injection (5-20 mL) over approximately 3-5 minutes. There is no experience in pediatric patients with renal impairment.

When to take it

To reduce the development of drug-resistant bacteria and maintain the effectiveness of **MEROSAN®** and other antibacterial drugs, **MEROSAN®** should only be used to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

How long to take it

IV injections of **MEROSAN®** should be given over a 3- to 5- minute period.
IV infusions of **MEROSAN®** should be given over approximately 15-30 minutes.

If you take too much (overdose)

Accidental overdose could occur during therapy, particularly in patients with renal impairment. Treatment of overdose should be sympatomimetic. In normal individuals rapid renal elimination will occur, in subjects with renal impairment haemodialysis will remove Meropenem and its metabolite.

While you are using MEROSAN®

Things you must do

- Advice patients that antibacterials (including **MEROSAN®**) should only be used to treat bacterial infections and not used to treat viral infections (e.g., the common cold).
- Importance of completing full course of therapy, even if feeling better after a few days.
- Importance of informing clinicians of existing of other medical conditions, including history of seizures.
- Importance of discontinuing therapy and informing clinician if an allergic or hypersensitivity reaction occurs.
- Importance of informing clinicians of existing or contemplated concomitant therapy, including prescription and OTC drugs, and any concomitant illnesses.
- Importance of women informing clinicians if they are or plan to become pregnant or plan to breast-feed.
- Importance of informing patients of other important precautionary information.

Things you must not do

- **MEROSAN®** should not be mixed with or added to other drugs.
- Using **MEROSAN®** without monitoring from your clinicians
- Skipping doses or not completing the full course of therapy. It may decrease effectiveness and increase the likelihood that bacteria will develop resistance and will not be treatable with **MEROSAN®** or other antibacterials in the future.

Things to be careful of

- Caution in patients with history of hypersensitivity reaction to β-lactam antibiotics, if an allergic reaction occur, the drug should be discontinued.
- Monitoring of transaminase and bilirubin levels should be made carefully in patients with hepatic disease.
- Use in infections caused by methicillin-resistant staphylococci is not recommended.
- It is important to consider the diagnosis of pseudomembranous colitis in the case of patients who develop diarrhea in association with the use of **MEROSAN®**. 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.
- Caution in co-administration with potentially nephritic drugs.
- No data are available, but it is not anticipated that **MEROSAN®** will affect the ability to drive and use machines.
- Use in children:
  Efficacy and tolerability in infants < 3 months have not been established; therefore **MEROSAN®** is not recommended for use below this age. There is no experience in children with altered hepatic or renal function.
- Use in pregnant and lactating women:
  The safety of **MEROSAN®** in pregnancy has not been evaluated. **MEROSAN®** should not be used in pregnant and lactating women unless the potential benefit justifies the potential risk to the foetus or baby. In every case, it should be used under the direct supervision of the physician.

Side effects

- Local intravenous injection site reaction: inflammation, thrombophlebitis and pain at the site of injection.
- Allergic reaction: rarely, systemic allergic reaction (hypersensitivity) may occur following administration of Meropenem. These reaction may include angioedema and manifestation of anaphylaxis.
- Skin: rash, pruritus and urticaria. Rarely severe skin reactions eg, erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been observed.
- Gastrointestinal: abdominal pain, nausea, vomiting, and diarrhea. Pseudomembranous colitis has been reported.
- Blood: reversible thrombocythaemia, eosinophilia, thrombocytopenia, leucopenia and neutropenia (including very rare cases of agranulocytosis).
- Liver: increases in serum concentrations of bilirubin, transaminases, alkaline phosphatase and lactic dehydrogenase alone or in combination have been reported.
- Central nervous system: headache, paraesthesiae, convulsion.
- Other: oral and vaginal candidiasis.

After using MEROSAN®

Storage

Store dry powder at temperature below 30°C. Do not freeze.
Reconstituted solution in w.f.i is stable for 2 hours at temperature 15° – 25°C or for 12 hours in a refrigerator (2° – 8°C).

Keep out of reach of children

Disposal

Discard any unused solutions after these periods.

Product description

What it looks like?

MEROSAN® is white to pale yellow powder, has specific odor; and is clear, colorless solution after reconstituted.

Ingredients

Each vial contains:
Meropenem Trihydrate USP equivalent to 0.5 g/1 g Anhydrous Meropenem USP

Manufacturer

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