MONEM 500 mg and 1 g
POWDER FOR INJECTION
Antibacterial

FORMULATION
Active ingredient : Meropenem
MONEM 500 mg POWDER FOR INJECTION : Each vial contains Meropenem trihydrate eq. to 500 mg Meropenem
MONEM 1 g POWDER FOR INJECTION : Each vial contains Meropenem trihydrate eq. to 1 g Meropenem
Excipient : Sodium carbonate

DESCRIPTION
Meropenem is sterile, white to off white powder.
Reconstituted solution are clear, colorless to pale yellow solution.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties
Meropenem is a carbapenem antibiotic for parenteral use, that is relatively stable to human dehydropeptidase-1 (DHP-1) and therefore, does not require the addition of an inhibitor of DHP-1.
Meropenem exerts its bactericidal action by interfering with vital bacterial cell wall synthesis.
The ease with which it penetrates bacterial cell walls, its high level of stability to all serine ß- 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.
Meropenem is active in vitro against a wide range of bacteria including:

Gram-positive aerobes:
Bacillus spp., *Corynebacterium diphtheriae, Enterococcus liquifaciens, Enterococcus avium, Listeria monocytogenes, Lactobacillus* spp., *Nocardia asteroides, 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), 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:
Achromobacter xylosoxidans, Acinetobacter anitratus, Acinetobacter lwoffii, Acinetobacter baumannii, Aeromonas hydrophila, Aeromonas sorbria, Aeromonas caviae, Alcaligenes faecalis, Bordetella bronchiseptica, Brucella melitensis, Campylobacter coli, Campylobacter jejuni, Citrobacter freundii, Citrobacter diversus, Citrobacter koseri, Citrobacter amalonaticus, Enterobacter aerogenes, Enterobacter (Pantoea) agglomerans, Enterobacter cloacae, Enterobacter sakazakii, Escherichia coli, Escherichia hermannii, Gardnerella vaginalis, Haemophilus influenzae, (including ß-lactamase positive and ampicillin resistant strains), *Haemophilus parainfluenzae, Haemophilus ducreyi, Helicobacter pyroli, Neisseria meningitidis, Neisseria gonorrhoeae* (including ß-lactamase positive, penicillin resistant and spectinomycin resistant strains), *Hafnia alvei, Klebsiella pneumoniae, Klebsiella aerogenes, Klebsiella ozaenae, Klebsiella oxytoca, Moraxella (Branhamella) catarrhalis, Morganella morganii, Proteus mirabilis, Proteus vulgaris, 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 liquefaciens, Serratia rubidaea, Shigella sonnei, Shigella flexneri, Shigella boydii, Shigella dysenteriae, Vibrio cholerae, Vibrio parahaemolyticus, Vibrio vulnificus, Yersinia enterocolitica.*

Anaerobic 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, Prevotella corporis, 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 asaccharolyticas, Bifidobacterium* spp., *Bilophila wadsworthia, Clostridium perfringens, Clostridium bifermentans, Clostridium ramosum, Clostridium sporogenes, Clostridium cadaveris, Clostridium sordellii, Clostridium 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 anaerobius, Peptostreptococcus micros, Peptostreptococcus saccharolyticus, Peptococcus saccharolyticus, Peptostreptococcus asaccharolyticus, Peptostreptococcus magnus, Peptostreptococcus prevotii, Propionibacterium acnes, Propionibacterium avidum, Propionibacterium granulosum.*
Stenotrophomonas maltophilia, Enterococcus faecium and methicillin-resistant staphylococci have been found to be resistant to meropenem.
Susceptibility test: Meropenem is stable in susceptibility tests and these tests can be performed using normal routine methods. *In vitro* tests show that meropenem acts synergistically with various antibiotics. It has 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. The following susceptibility ranges have been established for meropenem.

Dilution Techniques

	Minimum Inhibitory Concentration (MIC), mg/L
Susceptible	≤ 4
Intermediate	8
Resistant	≥ 16

Diffusion Techniques

	Susceptible Disc Zone size, mm
Susceptible	≥ 14
Intermediate	12-13
Resistant	≤ 11

Pharmacokinetic Properties
A 30 minutes intravenous infusion of a single dose of MONEM 500 mg and 1 g POWDER FOR INJECTION in healthy volunteers results in peak plasma levels of approximately 11 µg/ml for the 250 mg dose, 23 µg/ml for the 500 mg dose and 49 µg/ml for the 1 g dose.
However, there is no absolute pharmacokinetic proportionality with the administered dose both as regards Cmax and AUC. Furthermore, a reduction in plasma clearance from 287 to 205 ml/min for the range of dosage 250 mg to 2 g has been observed.
A 5 minutes intravenous bolus injection of MONEM 500 mg and 1 g POWDER FOR INJECTION in healthy volunteers results in peak plasma levels of approximately 52 µg/ml for the 500 mg dose and 112 µg/ml for the 1 g dose.
Intravenous infusions of 1 g over 2 minutes, 3 minutes and 5 minutes were compared in a three-way crossover trial. These durations of infusion resulted in peak plasma levels of 110, 91 and 94 microgram/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.
In subjects with normal renal function, meropenem's elimination half-life is approximately 1 hour. Plasma protein binding of meropenem is approximately 2%.
Approximately 70% of the 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 µg/ml are maintained for up to 5 hours after the administration of 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.
The only metabolite of meropenem is microbiologically inactive.
Meropenem penetrates well into most body fluids and tissues including cerebrospinal fluid of patients with bacterial meningitis, achieving concentrations in excess of those required to inhibit most bacteria.
Studies in children have shown that the pharmacokinetics of MONEM 500 mg and 1 g POWDER FOR INJECTION in children are similar to those in adults.
The elimination half-life for meropenem was approximately 1.5 to 2.3 hours in children under the age of 2 years and the pharmacokinetics are linear over the dose range of 10 to 40 mg/kg.
Pharmacokinetic studies in patients with renal insufficiency have shown the plasma clearance of meropenem correlates with creatinine clearance. Dosage adjustments are necessary in subjects with renal impairment.
Pharmacokinetic studies in the elderly have shown a reduction in plasma clearance of meropenem which correlated with age-associated reduction in creatinine clearance.
Pharmacokinetic studies in patients with liver disease have shown no effects of liver disease on the pharmacokinetics of meropenem.

INDICATION
Meropenem is indicated for treatment, in adults and children, of the following infections caused by single or multiple bacteria sensitive to meropenem: Pneumonias including hospital acquired pneumonias, Urinary Tract Infection, Intra abdominal Infections, Gynaecological Infections, such as endometritis and pelvic inflammatory disease, Bacterial Meningitis, Septicaemia, and Empiric treatment for presumed infections in patients with febrile neutropenia used as monotherapy or in combination with anti-viral or anti-fungal agents. Meropenem has proved efficacious alone or in combination with other antimicrobial agents in the treatment of polymicrobial infections.

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

Adults
In the treatment of pneumonia, UTI, gynaecological infections, skin and skin structure infections the recommended dosage is 500 mg IV every 8 hours.
In the treatment of nosocomial pneumonias, peritonitis, presumes infections in febrile neutropenic patients, septicaemia the recommended dosage is 1 g every 8 hours.
In the treatment of meningitis the recommended dosage is 2 g every 8 hours.
Caution is recommended in using meropenem as monotherapy in critically ill patients with known or suspected *Pseudomonas aeroginosa* lower respiratory tract infection.

Use in patients with renal insufficiency
Dosage should be reduced in patients with creatinine clearance less than 51 mL/min as scheduled below.

Creatinine Clearance (mL/min)	Dose	Frequency
26-50	recommended dose	Every 12 hours
10-25	one-half recommended dose	Every 12 hours
<10	one-half recommended dose	Every 24 hours

Meropenem is cleared by haemodialysis; it is recommended that the unit dose (based on the type and severity of infection) is administered at the completion of the haemodialysis procedure.
There is no experience with peritoneal dialysis.

Use in patients with hepatic insufficiency
No dosage adjustment is necessary in patients with impaired hepatic function.

Use in the elderly
No dosage adjustment is required for the elderly with creatinine clearance values above 50 mL/min.

Use in children
For children over 3 months and up to 12 years of age the recommended dose is 10-20 mg/kg IV every 8 hours.
In children over 50 kg weight adult dosage should be used.
In meningitis the recommended dose is 40 mg/kg IV every 8 hours.
Febrile episodes in neutropenic patients-the dose should be 20 mg/kg every 8 hours.

Mode of administration
Intravenous bolus injection: Intravenous bolus injection over approximately 5 minutes.
MONEM 500 mg and 1 g POWDER FOR INJECTION to be used for intravenous bolus injection should be constituted with sterile water for injection (5 mL per 250 mg Meropenem). This provides an approximate concentration of 50 mg/mL. Constituted solution are clear, and colorless or pale yellow.
Intravenous infusion: Intravenous infusion over approximately 15 to 30 minutes.
MONEM 500 mg and 1 g POWDER FOR INJECTION for intravenous infusion may be constituted with compatible infusion fluids (5 to 200 mL) (See "Storage" and "Compatibilities").

CONTRAINDICATION
MONEM 500 mg and 1 g POWDER FOR INJECTION (Meropenem) is contraindicated in patients who have hypersensitivity to this drug.

WARNINGS AND PRECAUTIONS
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 MONEM 500 mg and 1 g 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, MONEM 500 mg and 1 g POWDER FOR INJECTION must be discontinued immediately and appropriate alternative therapy instituted.
As with other beta-lactam antibiotics rare hypersensitivity reactions have been reported.
Before therapy with MONEM 500 mg and 1 g POWDER FOR INJECTION is instituted, careful inquiry should be made concerning previous hypersensitivity reaction to beta-lactam antibiotics. If an allergic reaction occurs, the drug should be discontinued.
Use of MONEM 500 mg and 1 g POWDER FOR INJECTION in patients with hepatic disease should be made with careful monitoring of transaminase and bilirubin levels.
Use in infections caused by methicillin resistant staphylococci is not recommended.
Prolonged use may occasionally result in overgrowth of nonsusceptible organisms.
Pseudomembranous colitis has been reported with nearly all antibiotics, including MONEM 500 mg and 1 g POWDER FOR INJECTION, and may range in severity from mild to life-threatening. It is important, therefore, to consider this diagnosis in patients who present with diarrhea subsequent to the administration of any antibiotics. After diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated.
Although studies indicate that a toxin produced by *Clostridium difficile* is one of the main caused of antibiotic-associated colitis, other causes should be considered.
The co-administration of MONEM 500 mg and 1 g POWDER FOR INJECTION with potentially nephrotoxic drugs should be considered with caution (For dosage
see "Dosage and Administration").

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTIONS
Probenecid: Inhibits renal excretion of meropenem thereby increasing its plasma concentrations and prolonging its eliminate half-life. Therefore, the co-administration of probenecid with meropenem is not recommended.
Valproic acid: Meropenem may reduce serum levels of valproic acid to subtherapeutic levels.

PREGNANCY AND LACTATION

Pregnancy
Animal reproduction studies have revealed no evidence of harm to the foetus.
The only adverse effect observed in animal reproductive studies was an increased incidence of abortions in monkeys at 13 times the expected exposure in man. There are no adequate and well controlled studies in pregnant women. Meropenem should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.

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

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES
There is no evidence to suggest that Meropenem may have an effect on a patient's ability to drive or operate machinery.

ADVERSE DRUG REACTIONS
Local reactions: pains, inflammation, thrombophlebitis at the site of injection
Dermatologic reactions: urticaria, rash, pruritus, erythema multiforme, toxic epidermal necrolysis and Stevens-Johnson Syndrome
Gastrointestinal: nausea, vomiting, abdominal pain, diarrhoea, pseudomembranous colitis
Haematology: increase eosinophils, reversible thrombocythaemia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, positive direct or indirect Coomb's test, shortened partial thromboplastin
Hepatic: increased transaminases, alkaline phosphatase, LDH and bilirubin
Central nervous system: paraesthesia, headache, seizures
Systemic allergic reaction: rarely, systemic allergic reaction (hypersensitivity) may occur following administration of meropenem, angioedema and anaphylaxis
Other: oral and vaginal candidosis

OVERDOSAGE
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 and its metabolite

STORAGE CONDITION
Store at temperatures not exceeding 30°C. Protect from light.
It is recommended to use freshly prepared solutions of MONEM 500 mg and 1 g POWDER FOR INJECTION for I.V. injection and infusion.
Reconstituted product, maintains satisfactory potency at room temperature (23-29°C) or under refrigeration (2-8°C) as shown in the following table:

DILUENT	Hours stable	
	at 23-29°C	at 2-8°C
Vial constituted with water for injection for bolus injection	8	48
Solution (10 mg/mL) prepared with :		
- 0.9% sodium chloride	8	48
- 5% glucose	3	10
- 5% glucose and 0.225% Sodium chloride	3	14
- 5% glucose and 0.9% Sodium chloride	3	8
- 5% glucose and 0.15% Potassium chloride	3	12
- 2.5% mannitol intravenous infusion	3	14
- 10% mannitol intravenous infusion	3	14
- 10% glucose	2	4
- 5% glucose and 0.02% sodium bicarbonate intravenous infusion	2	8

COMPATIBILITIES
Meropenem is compatible with the following infusion fluids:
Sterile water for injection
0.9% Sodium chloride
5% or 10% Glucose
5% Glucose with 0.02% Sodium bicarbonate
5% Glucose with 0.9% Sodium chloride
5% Glucose with 0.225% Sodium chloride
5% Glucose with 0.15% Potassium chloride
Mannitol 2.5% or 10%

Instruction for Use/Handling
Refer to "Dosage and Administration" above. Standard aseptic technique should be employed during constitution.
Shake constituted solution before use.
All vials are for single use only.

CAUTION
Keep medicine out of reach of children.
Jauhkan daripada kanak-kanak.

AVAILABILITY
500 mg: 10 Vials (Glass, Type I with butylic rubber stopper and aluminum flip-off cap)
1 g : 10 Vials (Glass, Type I with butylic rubber stopper and aluminum flip-off cap)

SHELF-LIFE : 3 Years

Date of revision : February 2021

Manufactured by:
BIOLAB CO., LTD.
625 Bangpoo Industrial Estate,
Samutprakarn, Thailand

EEI 045/D

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Note :
- Draft Rev.0=เปลี่ยนชื่อใหม่ (03/02/21)
- Draft Rev.1=ลบ IV หลังชื่อยาออก (05/02/21)

◯ ลูกค้าพิจารณาอนุมัติ ◯ ทำเสนอราคา ◯ ส่งพิมพ์
✓ RA ขึ้นทะเบียน ◯ อื่น ๆ .....

Specification
Size 200 x 315 MM. (+/- 3 MM.)
Color พิมพ์ 1 สี คือ สีดำ
Material ใช้กระดาษปอนด์ น้ำหนัก 55 แกรม
Other

Color Guide
Black