150 mm

For the use only of Registered Medical Practitioner or a Hospital or a Laboratory

℞ Meropenem Injection IP 1000 mg

WINPENOM™ 1000

FOR IV USE ONLY

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient(s)

Each combipack contains:
(A) Each vial contains:
Meropenem (Sterile) IP
Eq. to anhydrous Meropenem .. 1000 mg
Sodium Carbonate IP
Eq. to Sodium .... 90.20 mg
(A Sterile mixture of Meropenem IP &
Sodium carbonate IP)
(B) Sterile Water for Injections IP 20 ml

Excipients with known effect

Not Applicable
(For a full list of excipients, see Active ingredient(s))

DOSAGE FORM AND STRENGTH

Injection 1000 mg

CLINICAL PARTICULARS

Therapeutic indication

For treatment of pneumonia, nonocomial pneumonia, UTI, intra-abdominal infection, gynaecological infection, skin & soft tissue infection, meningitis, septicaemia & empiric treatment of presumed infection in adult patients with febrile neutropenia.

For Treatment, in 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 Endometriatis and Pelvic Inflammatory Disease, Skin and Skin Structure Infections, Meningitis, Septicaemia. Meropenem has been Proved Efficacious alone or in Combination with other Antimicrobial agents in the Treatment of Polymicrobial Infections.

Posology and method of administration

The tables below provide general recommendations for dosing.

The dose of meropenem administered and the duration of treatment should take into account the type of infection to be treated, including its severity, and the clinical response.

A dose of up to 2000 mg 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 infections due to less susceptible bacterial species (e.g. Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter spp.), or very severe infections.

Additional considerations for dosing are needed when treating patients with renal insufficiency (see further below).

Adults and adolescents

Infections	Dose to be administered every 8 hours
Severe pneumonia including hospital and ventilator-associated pneumonia.	500 mg or 1000 mg
Broncho-pulmonary infections in cystic fibrosis	2000 mg
Complicated urinary tract infections	500 mg or 1000 mg
Complicated intra-abdominal infections	500 mg or 1000 mg
Intra- and post-partum infections	500 mg or 1000 mg
Complicated skin and soft tissue infections	500 mg or 1000 mg
Acute bacterial meningitis	2000 mg
Management of febrile neutropenic patients	1000 mg

Meropenem is usually given by intravenous infusion over approximately 15 to 30 minutes (see sections Incompatibilities, Shelf life and Special precautions for disposal and other handling)

Alternatively, doses up to 1000 mg can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 2000 mg dose in adults as an intravenous bolus injection.

Renal Impairment

The dose for adults and adolescents should be adjusted when creatinine clearance is less than 51 ml/min, as shown below. There are limited data to support the application of these dose adjustments for a unit dose of 2000 mg.

Creatinine clearance (ml/min)	Dose (based on "unit" dose range of 500 mg or 1000 mg or 2000 mg, see table above	Frequency
26-50	one unit dose	every 12 hours
10-25	half of one unit dose	every 12 hours
<10	half of one unit dose	every 24 hours

Meropenem is cleared by haemodialysis and haemofiltration. The required dose should be administered after completion of the haemodialysis cycle.

There are no established dose recommendations for patients receiving peritoneal dialysis.

Hepatic impairment

No dose adjustment is necessary in patients with hepatic impairment (see section special warning and precautions).

Dose in elderly patients

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

Paediatric population

Children under 3 months of age

The safety and efficacy of meropenem in children under 3 months of age have not been established and the optimal dose regimen has not been identified. However, limited pharmacokinetic data suggest that 20 mg/kg every 8 hours may be an appropriate regimen (see section Pharmacokinetic properties).

Children from 3 months to 11 years of age and up to 50 kg body weight

The recommended dose regimens are shown in the table below:

Infection	Dose to be administered every 8 hours
Severe pneumonia including hospital and ventilator-associated pneumonia.	10 or 20 mg/kg
Broncho-pulnonary infections in cystic fibrosis	40 mg/kg
Complicated urinary tract infections	10 or 20 mg/kg
Complicated intra-abdominal infections	10 or 20 mg/kg
Complicated skin and soft tissue infections	10 or 20 mg/kg
Acute bacterial meningitis	40 mg/kg
Management of febrile neutropenic patients	20 mg/kg

Children over 50 kg body weight

The adult dose should be administered

There is no experience in children with renal impairment.

Meropenem is usually given by intravenous infusion over approximately 15 to 30 minutes (see section sections Incompatibilities, Shelf life and Special precautions for disposal and other handling). Alternatively, meropenem doses of up to 20 mg/kg may be given as an intravenous bolus over approximately 5 minutes. There are limited safety data available to support the administration of a 40 mg/kg dose in children as an intravenous bolus injection.

Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section list of excipients.

Hypersensitivity to any other carbapenem antibacterial agent.

Severe hypersensitivity (e.g anaphylactic reaction, severe skin reaction) to any other type of beta-lactam antibacterial agent (e.g. penicillins or cephalosporins).

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

Resistance to penems of Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter spp. varies across the European Union. 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 hyper-sensitivity reactions have been reported (see sections Contraindications and Undesirable effects).

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.

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 Undesirable effects). 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 Undesirable effects).

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 Undesirable effects).

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 Posology and method of administration).

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 Drug interactions).

Paediatric population

Meropenem is licensed for children over 3 months of age. There is no evidence of an increased risk of any adverse drug reaction in children based on the limited available data. All reports received were consistent with events observed in the adult population.

Meropenem contains sodium.

Meropenem 500 mg: This medicinal product contains approximately 2.0 mEq of sodium per 500 mg dose which should be taken into consideration by patients on a controlled sodium diet.

Meropenem 1000 mg: This medicinal product contains approximately 4.0 mEq of sodium per 1000 mg dose which should be taken into consideration by patients on a controlled sodium diet.

Drugs interactions

No specific medicinal product interaction studies other than probenecid were conducted. 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. Caution is required if probenecid is co-administered with meropenem.

The potential effect of meropenem on the protein binding of other medicinal products 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.

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 special warning and precautions).

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 in patients 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.

Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no or limited amount of data from the use of meropenem in pregnant women.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section Non clinical properties)

As a precautionary measure, it is preferable to avoid the use of meropenem during pregnancy.

Lactation

Small amounts of meropenem have been reported to be excreted in human milk. Meropenem should not be used in breast-feeding women unless the potential benefit for the mother 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, paraesthesiae and convulsions have been reported for meropenem.

Undesirable effects

Summary of the safety profile

In a review of 4,872 patients with 5,026 meropenem treatment exposures, meropenem-related adverse reactions most frequently reported were diarrhoea (2.3 %), rash (1.4 %), nausea/vomiting (1.4 %) and injection site inflammation (1.1 %). The most commonly reported meropenem-related laboratory adverse events were thrombocytosis (1.6 %) and increased hepatic enzymes (1.5-4.3 %).

Tabulated risk of adverse reactions

In the table below all adverse reactions are listed by system organ class and frequency: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1,000 to <1/100); rare (≥ 1/10,000 to <1/1,000); very rare (< 1/10,000) Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	Event
Infections and infestations	Uncommon	oral and vaginal candidiasis
Blood and lymphatic system disorders	Common	thrombocythaemia
	Uncommon	eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, haemolytic anaemia.
Immune system disorders	Uncommon	angioedema, anaphylaxis (see sections Contraindications and Special warnings and precautions for use)
Nervous system disorders	Common	headache
	Uncommon	paraesthesiae
	Rare	convulsions (see section Special warnings and precautions for use)
Gastrointestinal disorders	Common	diarrhoea, vomiting, nausea, abdominal pain
	Uncommon	antibiotic-associated colitis (see section Special warnings and precautions for use)
Hepato-biliary disorders	Common	transaminases increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased.
	Uncommon	blood bilirubin increased
Skin and subcutaneous tissue disorders	Common	rash, pruritis
	Uncommon	urticaria toxic epidermal necrolysis, Stevens Johnson syndrome, erythema, multiforme
	Unknown	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome)
Renal and urinary disorders	Uncommon	blood creatinine increased, blood urea increased
General disorders and administration site conditions	Common	inflammation, pain
	Uncommon	thrombophlebitis pain at the injection site

Paediatric population

Meropenem is licensed for children over 3 months of age. There is no evidence of an increased risk of any adverse drug reaction in children based on the limited available data. All reports received were consistent with events observed in the adult population.

Overdose

Relative overdose may be possible in patients with renal impairment if the dose is not adjusted as described in section posology. Limited post-marketing experience indicates that if adverse reactions occur following overdose, they are consistent with the adverse reaction profile described in section undesirable effects, are generally mild in severity and resolve on withdrawal or dose reduction. Symptomatic treatments should be considered.

In individuals with normal renal function, rapid renal elimination will occur.

Haemodialysis will remove meropenem and its metabolite.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action

Pharmacotherapeutic group: antibacterials for systemic use, carbapenems.

ATC code: J01DH02

Meropenem exerts its bactericidal activity by inhibiting bacterial cell wall synthesis in Gram-positive and Gram-negative bacteria through binding to penicillin-binding proteins (PBPs).

Pharmacodynamic properties

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 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 PBPs (3) increased expression of efflux pump components, and (4) production of beta-lactamases that can hydrolyse carbapenems.

Localised clusters of infections due to carbapenem-resistant bacteria have been reported in the European Union.

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 antibacterials agents when the mechanism involved include impermeability and/or an efflux pump(s).

Breakpoints

European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints for MIC testing are presented below. **EUCAST clinical MIC breakpoints for meropenem (2013-02-11, v 3.1)**

Organism	Susceptible (S) (mg/l)	Resistant (R) (mg/l)
Enterobacteriaceae	≤2	>8
Pseudomonas spp.	≤2	>8
Acinetobacter spp.	≤2	>8
Streptococcus groups A, B, C and G	note 6	note 6
Streptococcus pneumoniae[1]	≤2	>2
Viridans group streptococci[2]	≤2	>2
Enterococcus spp	--	--
Staphylococcus spp	note 3	note 3
Haemophilus influenzae[1, 2] and *Moraxella catarrhalis*[2]	≤ 2	> 2
Neisseria meningitidis[2,4]	≤ 0.25	> 0.25
Gram-positive anaerobes except Clostridium difficile	≤ 2	> 8
Gram-negative anaerobes	≤ 2	> 8
Listeria monocytogenes	≤ 0.25	> 0.25
Non-species related breakpoints[5]	≤ 2	> 8

1 Meropenem breakpoints for *Streptococcus pneumoniae* and *Haemophilus influenzae* in meningitis are 0.25 mg (Susceptible) and 1 mg/l (Resistant).

2 Isolates with MIC values above the susceptible breakpoint are very rare or not yet reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated and if the result is confirmed the isolate sent to a reference laboratory. Until there is evidence regarding clinical response for confirmed isolates with MIC values above the current resistant breakpoint they should be reported as resistant.

3 Susceptibility of staphylococci to Carbepenem is inferred from the cefoxitinsusceptibility.

4 Breakpoints relate to meningitis only.

5 Non-species related breakpoints have been determined using PK/PD data and are independent of MIC distributions of specific species. They are for use only for organisms that do not have specific breakpoints. Non species related breakpoints are based on the following dosages: EUCAST breakpoints apply to meropenem 1000 mg x 3 daily administered intravenously over 30 minutes as the lowest dose. 2000 mg x 3 daily was taken into consideration for severe infections and in setting the I/R breakpoint.

6 The beta-lactam susceptibility of streptococcus groups A, B, C and G is inferred from the penicillin susceptibility.

– = Susceptibility testing not recommended as the species is a poor target for therapy with the drug. Isolates may be reported as R without prior testing.

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

The following table of pathogens listed is derived from clinical experience and therapeutic guidelines.

Commonly susceptible species

Gram-positive aerobes

Enterococcus faecalis[$]

Staphylococcus aureus (methicillin-susceptible)[£]

Staphylococcus species (methicillin-susceptible) including *Staphylococcus epidermidis*

Streptococcus agalactiae (Group B)

Streptococcus milleri group (*S. anginosus, S. constellatus, and S. intermedius*)

Streptococcus pneumoniae Streptococcus pyogenes (Group A)

Gram-negative aerobes

Citrobacter freudii

Citrobacter koseri

Enterobacter aerogenes

Enterobacter cloacae

Escherichia coli

Haemophilus influenzae

Klebsiella oxytoca

Klebsiella pneumoniae

Morganella morganii

Neisseria meningitidis

Proteus mirabilis

Proteus vulgaris

Serratia marcescens

Gram-positive anaerobes

Clostridium perfringens

Peptoniphilus asaccharolyticus

Peptostreptococcus species (including P. micros, P anaerobius, P. magnus)

Gram-negative anaerobes

Bacteroides caccae

Bacteroides fragilis group *Prevotella bivia*

Prevotella disiens

Species for which acquired resistance may be a problem

Gram-positive aerobes

Enterococcus faecium[$†]

Gram-negative aerobes

Acinetobacter species

Burkholderia cepacia

Pseudomonas aeruginosa

Inherently resistant organisms

Gram-negative aerobes

Stenotrophomonas maltophilia

Legionella species

Other micro-organisms

Chlamydophila pneumoniae

Chlamydophila psittaci

Coxiella burnetii

Mycoplasma pneumoniae

[$] Species that show natural intermediate susceptibility

[£] All methicillin-resistant staphylococci are resistant to meropenem

†Resistance rate ≥ 50% in one or more EU countries.

Glanders and melioidosis: Use of meropenem in humans is based on *in vitro B.mallei* and *B. pseudomallei* susceptibility data and on limited human data. Treating physicians should refer to national and/or international consensus documents regarding the treatment of glanders and melioidosis.

Pharmacokinetic properties

In healthy subjects the mean plasma half-life is approximately 1 hour; the mean volume of distribution is approximately 0.25 l/kg (11-27 l) and the mean clearance is 287 ml/min at 250 mg falling to 205 ml/min at 2000 mg. Doses of 500, 1000 and 2000 mg doses infused over 30 minutes give mean Cmax values of approximately 23, 49 and 115 μg/ml respectively, corresponding AUC values were 39.3, 62.3 and 153 μg.h/ml. After infusion over 5 minutes Cmax values are 52 and 112 μg/ml after 500 and 1000 mg doses respectively. When multiple doses are administered 8-hourly to subjects with normal renal function, accumulation of meropenem does not occur.

A study of 12 patients administered meropenem 1000 mg 8 hourly post-surgically for intra-abdominal infections showed a comparable Cmax and half-life to normal subjects but a greater volume of distribution 27 l.

Distribution

The average plasma protein binding of meropenem was approximately 2 % and was independent of concentration. 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.

Metabolism

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

Meropenem is primarily excreted unchanged by the kidneys; approximately 70 % (50 –75 %) of the dose is excreted unchanged within 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.

Renal insufficiency

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. Dose adjustment is recommended for patients with moderate and severe renal impairment (see section Posology and method of administration).

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

Hepatic insufficiency

A study in patients with alcoholic cirrhosis shows no effect of liver disease on the pharmacokinetics of meropenem after repeated doses.

Adult patients

Pharmacokinetic studies performed in 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.

Paediatrics

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 (2-5 years), 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 healthy elderly subjects (65-80 years) have shown a reduction in plasma clearance, which correlated with age-associated reduction in creatinine clearance, and a smaller reduction in non-renal clearance. No dose adjustment is required in elderly patients, except in cases of moderate to severe renal impairment (see section Posology and method of administration).

NONCLINICAL PROPERTIES

Animal Toxicology and/or Pharmacology

Relative overdose may be possible in patients with renal impairment if the dose is not adjusted as described in section Posology and method of administration. Limited post-marketing experience indicates that if adverse reactions occur following overdose, they are consistent with the adverse reaction profile described in section 4.8, are generally mild in severity and resolve on withdrawal or dose reduction. Symptomatic treatments should be considered.

In individuals with normal renal function, rapid renal elimination will occur.

Haemodialysis will remove meropenem and its metabolite.

DESCRIPTION

A white or almost white powder filled in 20 ml clear and colorless glass vials

PHARMACEUTICAL PARTICULARS

Incompatibilities

Not Applicable

Shelf-life

24 Months

Packaging information

20 ml glass vials

Storage and handing instructions

Storage : Store below 30°C. Protect from moisture.

List of excipients

Refer section Active ingredient(s)

PATIENT COUNSELING INFORMATION

1. What Meropenem is and what it is used for

Meropenem belongs to a group of medicines called carbapenem antibiotics. It works by killing bacteria, which can cause serious infections. Meropenem is used to treat the following in adults and children aged 3 months and older: • Infection affecting the lungs (pneumonia). • Lung and bronchial infections in patients suffering from cystic fibrosis. • Complicated urinary tract infections. • Complicated infections in the abdomen. • Infections that you can catch during or after the delivery. • Complicated skin and soft tissues infections. • Acute bacterial infection of the brain (meningitis). Meropenem may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection. Meropenem may be used to treat bacterial infection of the blood which might be associated with a type of infection mentioned above.

2. What you need to know before you take Meropenem

Do not take Meropenem

- If you are allergic to meropenem or any of the other ingredients of this medicine
- If you are allergic to other antibiotics such as penicillins, cephalosporins or carbapenems as you may also be allergic to meropenem.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Meropenem.

- If you have health problems, such as liver or kidney problems.
- If you have had severe diarrhoea after taking other antibiotics.

You may develop a positive test (Coombs test) which indicates the presence of antibodies that may destroy red blood cells. Your doctor will discuss this with you.

You may develop signs and symptoms of severe skin reactions. If this happens talk to your doctor or nurse immediately so that they can treat the symptoms.

- If you are not sure if any of the above applies to you, talk to your doctor or nurse before using Meropenem.

Other medicines and Meropenem Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines. This is because Meropenem can affect the way some medicines work and some medicines can have an effect on Meropenem. In particular, tell your doctor or nurse if you are taking any of the following medicines: • Probenecid (used to treat gout). • Valproic acid/sodium valproate/ valpromide (used to treat epilepsy). Meropenem should not be used because it may decrease the effect of sodium valproate. • Oral anti-coagulant agent (used to treat or prevent blood clots).

Pregnancy, breast-feeding and fertility

• If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is preferable to avoid the use of meropenem during pregnancy. Your doctor will decide whether you should use meropenem. It is important that you tell your doctor if you are breast-feeding or if you intend to breastfeed before receiving meropenem. Small amounts of this medicine may pass into the breast milk. Therefore, your doctor will decide whether you should use meropenem while breastfeeding.

3. How to take Meropenem

Always use this medicine exactly as your doctor or nurse has told you. Check with your doctor or nurse if you are not sure.

Use in Adults

- The dose depends on the type of infection that you have, where the infection is in the body and how serious the infection is. Your doctor will decide on the dose that you need.
- The dose for adults is usually between 500 mg (milligrams) and 2000 mg (milligrams). You will usually receive a dose every 8 hours. However you may receive a dose less often if your kidneys do not work very well.

Use in children and adolescents

- The dose for children over 3 months old and up to 12 years of age is decided using the age and weight of the child. The usual dose is between 10 mg and 40 mg of Meropenem for each kilogram (kg) that the child weighs. A dose is usually given every 8 hours. Children who weigh over 50 kg will be given an adult dose.

How to use Meropenem

- Meropenem will be given to you as an injection or infusion into a large vein.
- Your doctor or nurse will normally give Meropenem to you.
- However, some patients, parents and carers are trained to give Meropenem at home. Instructions for doing this are provided in this leaflet (in the section called 'Instructions forgiving Meropenem to yourself or someone else at home').

Always use Meropenem exactly as your doctor has told you. You should check with your doctor if you are not sure.

- Your injection should not be mixed with or added to solutions that contain other medicines.
- The injection may take about 5 minutes or between 15 and 30 minutes. Your doctor will tell you how to give Meropenem.
- You should normally have your injections at the same times each day.

If you take more Meropenem than you should

If you accidentally use more than your prescribed dose, contact your doctor or nearest hospital straight away. If you forget to take Meropenem If you miss an injection, you should have it as soon as possible. However, if it is almost time for your next injection, skip the missed injection. Do not take a double dose (two injections at the same time) to make up for a forgotten dose.

If you stop taking Meropenem

Do not stop having Meropenem until your doctor tells you to. If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Severe allergic reactions

If you have a severe allergic reaction, stop having Meropenem and see a doctor straight away. You may need urgent medical treatment.

The signs may include a sudden onset of:

- Severe rash, itching or hives on the skin.
- Swelling of the face, lips, tongue or other parts of the body.
- Shortness of breath, wheezing or trouble breathing.
- Serious skin reactions which include
  - Serious hypersensitivity reactions involving fever, skin rash, and changes in the blood tests that check how the liver is working (increased levels of liver enzymes) and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes. These may be signs of a multi-organ sensitivity disorder known as DRESS syndrome.
  - Severe red scaly rash, skin bumps that contain pus, blisters or peeling of skin, which may be associated with a high fever and joint pain.
  - Severe skin rashes that can appear as reddish circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome) or a more severe form (toxic epidermal necrolysis).

Damage to red blood cells (not known)

The signs include:

- Being breathless when you do not expect it.
- Red or brown urine.

If you notice any of the above, see a doctor straight away.

Other possible side effects: Common (may affect up to 1 in 10 people)

- Abdominal (stomach) pain.
- Feeling sick (nausea).
- Being sick (vomiting).
- Diarrhoea.
- Headache.
- Skin rash, itchy skin.
- Pain and inflammation.
- Increased numbers of platelets in your blood (shown in a blood test).
- Changes in blood tests, including tests that show how well your liver is working. Uncommon (may affect up to 1 in 100 people)
- Changes in your blood.

These include reduced numbers of platelets (which may make you bruise more easily), increased numbers of some white blood cells, decreased numbers of other white cells and increased amounts of a substance called 'bilirubin'. Your doctor may do blood tests from time to time.

- Changes in blood tests, including tests that show how well your kidneys are working.
- A tingling feeling (pins and needles).
- Infections of the mouth or the vagina that are caused by a fungus (thrush). Inflammation of the bowel with diarrhea.
- Sore veins where Meropenem is injected.
- Other changes in your blood.

The symptoms include frequent infections, high temperature and sore throat. Your doctor may do blood tests from time to time.

Rare (may affect up to 1 in 1,000 people)

- Fits (convulsions).
- Acute disorientation and confusion

5. How to store Meropenem

Keep this medicine out of the sight and reach of children. Do not use this medicine after the expiry date which is stated on vial label and carton after EXP. The expiry date refers to the last day of that month. The medicinal product does not require any special storage

DETAILS OF MANUFACTURER

Manufactured by :
Protech Telelinks
(A WHO-GMP Certified Co.)
Mauza Ogli, Suketi Road, Kala Amb,
Distt. Sirmaur-173030 (H.P.), India.

windlas

Marketed in India by :
Windlas Biotech Limited
(A WHO GMP Certified Company)
40/1, Mohabewala Industrial Area,
Dehradun- 248110 (Uttarakhand)
TM-Trardemark Under Registration

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