SUMMARY OF PRODUCTS CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

MEROPENEM/ANFARM 500 mg
MEROPENEM/ANFARM 1g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Vial for IV injection or infusion	Meropenem/ANFARM	Meropenem/ANFARM
	500mg	1000 mg
Active ingredient:		
Meropenem trihydrate	570 mg	1140 mg
equivalent to anhydrous meropenem	500 mg	1000 mg

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection or infusion

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Meropenem is indicated for treatment in adults and children of the following severe infections caused by single or multiple susceptible bacteria sensitive to meropenem:

- Pneumonias and nosocomial pneumonias.
- Pulmonary infections in patients with cystic fibrosis.
- Urinary tract infections.
- Intra-abdominal infections.
- Gynecological infections such as endometritis and pelvic inflammatory disease.
- Skin and skin structure infections.
- Meningitis
-Septicemia.

Meropenem has proved 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

4.2 Posology and method of administration

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 IV every 8 hours in the treatment of pneumonia, UTI, gynaecological infections such as endometritis, pelvic inflammatory disease, skin and skin structure infections.
- 1 g IV every 8 hours in the treatment of nosocomial pneumonias, peritonitis, presumed infections in neutropenic patients, septicaemia.

In cystic fibrosis, doses up to 2 g every 8 hours have been used; most patients have been treated with 2 g every 8 hours.

In meningitis the recommended dosage is 2 g every 8 hours.

When treating some types of infections such as nosocomial infections suspected to be caused by Pseudomonas aeruginosa a dose of 1g three times daily up to 2 g three times a day in adults and adolescents and a dose of up to 40mg/kg three times daily in children is recommended.

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 and/or Acinetobacter spp. A dose of 1g three times daily up to 2g three times a day in adults and adolescents and a dose of up to 40mg/kg three times daily in children is recommended. Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa* infection.
There are limited safety data available to support the administration of a 2g bolus 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.

Table 1

Creatinine Clearance (ml/min)	**Dose** (based on unit doses of 500 mg, 1 g, 2 g)	**Frequency**
26 to50	one unit dose	every 12 hours
10 to25	one-half unit dose	every 12 hours
<10	one-half unit dose	every 24 hours

Meropenem is cleared by haemodialysis; if continued treatment with Meropenem/ANFARM 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 Meropenem/ANFARM in patients under peritoneal dialysis.

Dosage in Adults with Hepatic Insufficiency

No dosage adjustment is necessary in patients with hepatic insufficiency (see Section 4.4).

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 to 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.
For children aged 4 to 18 years with cystic fibrosis, doses ranging from 25 to 40 mg/kg every 8 hours have been used to treat acute exacerbations of chronic lower respiratory tract infections.
In meningitis the recommended dose is 40 mg/kg every 8 hours.
There is no experience in children with renal impairment.

Method of Administration

Meropenem/ANFARM IV 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 presentations. There is limited safety data available to support the administration of a 40mg/kg bolus dose (in children). There is limited safety data available to support the administration of a 2g bolus dose (in adults).

Meropenem/ANFARM IV 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.
Meropenem/ANFARM IV for intravenous infusion may be constituted with compatible infusion fluids (50 to 200 ml) (see Sections 6.2 and 6.4).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.
Hypersensitivity to any other carbapenem antibacterial agent.
Severe hypersensitivity (eg anaphylactic reaction, severe skin reaction) to any other type of betalactam antibacterial agent (e.g. penicillins or cephalosporins)

4.4 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.

As with all beta-lactam antibiotics, 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. 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 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 4.8). 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 have infrequently been reported during treatment with carbapenems, including meropenem (see section 4.8).

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 4.8).

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 4.2).

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

The co-administration of meropenem with potentially nephrotoxic drugs should be considered with caution.

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

Meropenem/ANFARM contains Sodium.
Meropenem/ANFARM 500mg : This medicinal product contains 41.7 mg of Sodium (1.8 mEq) per 500 mg dose which should be taken into consideration by patients on controlled sodium diet.
Meropenem/ANFARM 1.0 g : This medicinal product contains 83.4 mg of Sodium (3.6 mEq) per 1.0 g dose which should be taken in consideration by patients on controlled sodium, diet.

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid competes with meropenem for active tubular secretion and thus inhibits the renal excretion, 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/ANFARM on the protein binding of other drugs or metabolism has not been studied. The protein binding of Meropenem/ANFARM is low (approximately 2%) and therefore no interactions with other compounds based on displacement from plasma proteins would be expected.

Meropenem/ANFARM may reduce serum valproic acid levels. Subtherapeutic levels may be reached in some patients.
Meropenem/ANFARM has been administered concomitantly with other medications without adverse pharmacological interactions. However, no other specific data regarding potential drug interactions is available (apart from probenecid as mentioned above).
Decrease 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 Meropenem/ANFARM in patients stabilised on valproic acid is not considered to be manageable and therefore should be avoided (see section 4.4).
Oral anti-coagulants
Simultaneous administration of antibiotics with warfarin may augment its anti-coagulant effects. There have been many reports of increases in anti-coagulant effects of orally administered anticoagulant agents, including warfarin in patients who are concomitantly receiving antibacterial agents. The risk may vary with underlying infection, age and general status of the patient so that contribution of 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 anticoagulant agent.

4.6 Pregnancy and lactation

Pregnancy
The safety of Meropenem/ANFARM in human pregnancy has not been evaluated. Animal studies have not shown any adverse effect on the developing 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. Meropenem/ANFARM should not be used in pregnancy unless the potential benefit justifies the potential risk to the foetus.
As a precautionary measure, it is preferable to avoid the use of meropenem during pregnancy.

Lactation
It is unknown whether meropenem is excreted in human milk. Meropenem is detectable at very low concentrations in animal breast milk. Meropenem/ANFARM should not be used in breast-feeding women unless the potential benefit justifies the potential risk to the baby.

4.7 Effects on ability to drive and use machines

No data are available, but it is not anticipated that Meropenem/ANFARM will affect the ability to drive and use machines.
However when driving or operating machines, it should be taken into account that headache, paraesthesia and convulsions have been reported for meropenem.

4.8 Undesirable effects

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 %).

Adverse reactions listed in the table with a frequency of "not known" were not observed in the 2,367 patients who were included in pre-authorisation clinical studies with intravenous and intramuscular meropenem but have been reported during the post-marketing period.

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) and not known (cannot be estimated from the available data). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1

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
	Not known	agranulocytosis, haemolytic anaemia
Immune system disorders	Not known	angioedema, anaphylaxis (see sections 4.3 and 4.4)
Nervous system disorders	Common	headache
	Uncommon	paraesthesiae
	Rare	convulsions (see section 4.4)
Gastrointestinal disorders	Common	diarrhoea, vomiting, nausea, abdominal pain
	Not known	antibiotic-associated colitis (see section 4.4)
Hepatobiliary disorders	Common	transaminases increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, gamma-glutamyltransferase increased.
	Uncommon	blood bilirubin increased

Skin and subcutaneous tissue disorders	Common	rash, pruritis
	Uncommon	urticaria
	Not known	toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme.
Renal and urinary disorders	Uncommon	blood creatinine increased, blood urea increased
General disorders and administration site conditions	Common	inflammation, pain
	Uncommon	thrombophlebitis
	Not known	pain at the injection site

The following adverse reactions have been identified from post-marketing clinical trials and spontaneous reports. Their frequency is presented in the following table. Frequencies of occurrence of undesirable effects are defined as: very common (≥1/10; ≥10%); common (≥1/100 to <1/10; ≥1% to <10%); uncommon (≥1/1,000 to <1/100; ≥0.1% to <1%); rare (≥1/10,000 to <1/1,000; ≥0.01% to <0.1%); very rare (<1/10,000; <0.01%)

Table- Reporting Rate of Adverse Reactions (data derived from a combination of postmarketing clinical trial and spontaneous sources).

System Organ Class	Frequency	Reaction
Blood and lymphatic system disorders	Rare	Agranulocytosis
	Very rare	Haemolytic anaemia
Immune system disorders	Very rare	Angioedema, manifestations of anaphylaxis
Gastrointestinal disorders	Very rare	Pseudomembraneous colitis
Skin and subcutaneous tissue disorders	Very rare	Toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme.

4.9 Overdose

Accidental overdosage could occur during therapy, particularly in patients with renal impairment. Limited post-marketing experience indicates that adverse events following overdosage are consistent with the adverse event 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials for systemic use, carbapenems, ATC code: J01DH02
Mode of action
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).

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 (2009-06-05, v 3.1)		
Organism	Susceptible (S) (mg/l)	Resistant (R)(mg/l)
Enterobacteriaceae	≤2	> 8
Pseudomonas	≤2	> 8
Acinetobacter	≤2	> 8
Streptococcus groups A, B, C, G	≤2	> 2
Streptococcus pneumoniae[1]	≤2	> 2
Other streptococci	2	2
Enterococcus	--	--
Staphylococcus[2]	note 3	note 3
Haemophilus influenzae[1]andMoraxella catarrhalis	≤2	> 2
Neisseria meningitidis[2,4]	≤0.25	> 0.25
Gram-positive anaerobes	≤2	> 8
Gram-negative anaerobes	≤2	> 8
Non-species related breakpoints[5]	≤2	> 8

1 Meropenem breakpoints for Streptococcus pneumoniae and Haemophilus influenzae in meningitis are 0.25/1 mg/L.

2 Strains with MIC values above the S/I breakpoint are 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 above the current resistant breakpoint (in italics) they should be reported as resistant.

3 Susceptibility of staphylococci to meropenem is inferred from the methicillin susceptibility.

4 Meropenem breakpoints in Neisseria meningitidis relates to meningitis only.

5 Non-species related breakpoints have been determined mainly from PK/PD data and are independent of the MIC distributions of specific species. They are for use for species not Mentioned in the table and footnotes.

-- = Susceptibility testing not recommended as the species is a poor target for therapy with the medicinal product.

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

5.2 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 2 g. Doses of 500, 1000 and 2000 mg 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 4.2).

Meropenem is cleared by haemodialysis with clearance during haemodialysis being approximately 4 times higher that 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 4.2).

5.3 Preclinical safety data

Animal studies indicate that meropenem is well tolerated by the kidney. Histological evidence of renal tubular damage was seen in mice and dogs only at doses of 2000 mg/kg and above after a single administration and above and in monkeys at 500 mg/kg in a 7-day study.

Meropenem is generally well tolerated by the central nervous system. Effects were seen in acute toxicity studies in rodent at doses exceeding 1000 mg/kg.

The IV LD_{50} of meropenem in rodents is greater that 2000 mg/kg.

In repeat dose studies of up to 6 months duration only minor effects were seen including a decrease in red cell parameters in dogs.

There was no evidence of mutagenic potential in a conventional test battery and no evidence of reproductive toxicity including teratogenic potential in studies in rats up to 750 mg/kg and in monkeys up to 360 mg/kg.

There was increased evidence of abortions at 500 mg/kg in a preliminary study in monkeys. There was no evidence of increased sensitivity to meropenem in juveniles compared to adult animals. The intravenous formulation was well tolerated in animal studies.

The sole metabolite of meropenem had a similar profile of toxicity in animal studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Meropenem/ANFARM for IV injection and infusion includes the excipient sodium carbonate.

6.2 Incompatibilities

Meropenem/ANFARM should not be mixed with or added to other drugs.
Meropenem/ANFARM is compatible with the following infusion fluids:

- 0.9% Sodium Chloride solution
- 5% or 10% Glucose solution
- 5% Glucose solution with 0.02% Sodium Bicarbonate
- 5% Glucose solution with 0.9% Sodium Chloride
- 5% Glucose with 0.225% Sodium Chloride solution
- 5% Glucose with 0.15% Potassium Chloride solution
- Mannitol 2.5% or 10% solution

6.3 Shelf life

Meropenem/ANFARM has a shelf life of 3 years.
It is recommended to use freshly prepared solutions of Meropenem/ANFARM for IV injection and infusion.

After reconstitution:
Up to 2 hours at 25^0 C when reconstituted in water for injection and up to 4 hours at 25^0 C when reconstituted in saline for infusion.

Intravenous bolus injection administration

A solution for bolus injection is prepared by dissolving the drug product 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 for 2 hours at 25^0 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 drug product in either 0.9% sodium chloride solution for infusion or 5% glucose (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 chloride solution has been demonstrated for 4 hours at 25^0 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.
Reconstituted solution of Meropenem/ANFARM in 5% glucose (dextrose) solution should be used immediately, i.e. within one hour following reconstitution.

6.4 Special precautions for storage
Do not store above 25°C.
Do not freeze.
Protect from light

6.5 Nature and contents of container
Uncoloured glass vials type III having a capacity of 20 ml stoppered with bromobutyl rubber stoppers having a diameter of 20 mm.

Packs for intravenous administration
Pack of 10 vials containing 500 mg or 1 g meropenem.

6.6 Special precautions for disposal and other handling
Refer to Section 4.2 "Posology and method Administration" above. Standard aseptic technique should be employed during constitution. Shake constituted solution before use.
All vials are for single use only.

7. Products' registration numbers:
Meropenem/Anfarm 500mg: 150 53 33675 00
Meropenem/Anfarm 1g : 150 54 33679 00

8. Manufacturer
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