SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Meropenem-Rotexmedica 500 mg powder for solution for injection or infusion
Meropenem-Rotexmedica 1 g powder for solution for injection or infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Meropenem-Rotexmedica 500 mg:
Each vial contains Meropenem 3 H_2O equivalent to 500 mg Meropenem.

Other excipients:

Each 500 mg vial contains 104 mg sodium carbonate, equivalent to approximately 2.0 mmol sodium (approximately 45 mg).

Meropenem-Rotexmedica 1g:

Each vial contains Meropenem 3 H_2O equivalent to 1000 mg Meropenem.

Other excipients:

Each 1g vial contains 208 mg sodium carbonate, equivalent to approximately 4.0 mmol sodium (approximately 90 mg).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for preparing injection or infusion solutions

White to light yellow powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Meropenem-Rotexmedica is indicated for the treatment of the following infections in adults and children over 3 months of age (see sections 4.4 and 5.1):

- pneumonia, including community acquired pneumonia and nosocomial pneumonia,
- broncho-pulmonary infections in cystic fibrosis,
- complicated kidney and urinary tract infections,
- complicated intra-abdominal infections,
- intra- and post-partum infections,
- complicated skin and soft tissue infections,
- acute bacterial meningitis.

Meropenem-Rotexmedica may be used in the management of neutropenic patients with fever that is suspected to be due to a bacterial infection.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 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 2 g three times daily in adults and adolescents and a dose of up to 40 mg/kg three times daily in children may be particularly appropriate when treating some types of infections, such as nosocomial infections due to *Pseudomonas aeruginosa* or *Acinetobacter* spp..

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

Adults and adolescents

Infection	Dose to be administered every 8 hours
Pneumonia including community-acquired pneumonia and nosocomial pneumonia.	500 mg or 1 g
Broncho-pulmonary infections in cystic fibrosis	2 g
Complicated kidney and urinary tract infections	500 mg or 1 g
Complicated intra-abdominal infections	500 mg or 1 g
Intra- and post-partum infections	500 mg or 1 g
Complicated skin and soft tissue infections	500 mg or 1 g
Acute bacterial meningitis	2 g
Management of febrile neutropenic patients	1 g

Meropenem is usually given by intravenous infusion over approximately 15 to 30 minutes (see section 6.2, 6.3 and 6.6).

Alternatively, doses up to 1 g can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection.

Renal impairment

When creatine *clearance* is less than 51 ml/min, the dose for adults and adolescents should be adjusted, as shown below. There are limited safety data available to support the administration of a 2 g dose in adults as an intravenous bolus injection.

Creatinine *clearance* (ml/min)	Dose (based on unit dose range of 500 mg or 1 g or 2 g every 8 hours as detailed above)	Dosing frequency
26 – 50	1 unit dose	every 12 hours
10 – 25	½ unit dose	every 12 hours
<10	½ unit dose	every 24 hours

Meropenem is eliminated 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 4.4).

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.

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
Pneumonia including community-acquired pneumonia and nosocomial pneumonia.	10 or 20 mg/kg
Broncho-pulmonary infections in cystic fibrosis	40 mg/kg
Complicated kidney and 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 6.2, 6.3 and 6.6). Alternatively, doses up to 20 mg/kg can be given as an intravenous bolus injection over approximately 5 minutes. There are limited safety data available to support the administration of a 40 mg/kg dose in adults as an intravenous bolus injection.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.
Hypersensitivity to any other carbapenem antibacterial agent.
Severe hypersensitivity (e.g. 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 factors such as the severity of the infection, the prevalence of resistance to other antibacterial agents and the risk of selecting for carbapenem-resistant bacteria.

As with all betalactam 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 betalactam antibiotics may also be hypersensitive to meropenem. Before initiating therapy with meropenem, careful inquiry should be made concerning previous hypersensitivity reactions to betalactam 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-Rotexmedica. They 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 concomitant use of meropenem and valproic acid/sodium valproate is not recommended (see section 4.5).

Meropenem-Rotexmedica contains sodium.

Meropenem-Rotexmedica 500 mg: This medicinal product contains approximately 2.0 mmol of sodium per 500 mg dose which should be taken into consideration for patients on a controlled sodium diet.
Meropenem-Rotexmedica 1 g: This medicinal product contains approximately 4.0 mmol of sodium per 1 g dose which should be taken into consideration for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

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. This is related to 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. This resulted in a 60-100% decrease in valproic acid levels in about 2 days. Due to the rapid onset and the extent of the decrease, co-administration of valproic acid with carbapenem agents is not considered to be manageable and therefore should be avoided (see section 4.4).

Oral anti-coagulants
Concomitant 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. 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.

4.6 Pregnancy and lactation

Pregnancy
There is no or only a limited amount of data for the use of meropenem in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).
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.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

In a review of 4,672 patients with 5,026 meropenem treatment exposures, the 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 3,367 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 parasite 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	Transaminase concentration in serum concentration increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased
	Uncommon	Blood bilirubin increased
Skin and subcutaneous tissue disorders	Common	Rash, pruritus
	Uncommon	Urticaria
	Not known	Toxic epidermal necrolysis, Stevens Johnson syndrome, erythema multiforme Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome)
General disorders and administration site conditions	Common	Inflammation, pain
	Uncommon	Thrombophlebitis
	Not known	Pain at the injection site

<u>Reporting of suspected adverse reactions</u>
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the Federal Institute for Drugs and Medical Devices, Abt pharmacovigilance, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, website:. Display www.bfarm.de.

4.9 Overdose

Relative overdose may be possible in patients with renal impairment if the dose is not adjusted as described in section 4.2. 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. These adverse reactions 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: J01D H02

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 betalactam 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 betalactamases 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 antibacterial agents when the mechanism involved includes impermeability and/or efflux pumps.

Breakpoints

European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints for MIC testing are presented below.

EUCAST clinical MIC breakpoints for meropenem (06 May 2009, 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]	Footnote 3	Footnote 3
Haemophilus influenzae[1] and *Moraxella 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 have not yet been reported. The identification and antimicrobial susceptibility tests on any such isolate must be repeated. If the result is confirmed the isolate is to be sent to a reference laboratory. As long as there is no 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* relate to meningitis only.

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

-- = Susceptibility testing is 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. Therefore local information on resistance is required, 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.

<u>Commonly susceptible species</u>
<u>Gram-positive aerobes</u>
Enterococcus faecialis[$]
Staphylococcus aureus (only methicillin-susceptible strains)[£]
Staphylococcus spp. (only methicillin-susceptible strains), including *Staphylococcus epidermidis*
Streptococcus agalactiae (group B)
Streptococcus milleri group *(S. anginosus, S. constellatus and S. intermedius)*
Streptococcus pneumoniae
Streptococcus pyogenes (group A)

<u>Gram-negative aerobes</u>
Citrobacter freundii
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
Peptococcus- 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 microorganisms
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 half-life is approximately 1 hour; the mean volume of distribution is approximately 0.25 l/kg (11-27 l). The mean plasma-*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 peak plasma concentrations (C_{max}) of approximately 23, 49 and 115 μg/ml respectively, corresponding AUC values were 39.3, 62.3 and 153 μg h/ml. After intravenous infusion over 5 minutes C_{max} values are 52 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 C_{max} and half-life to normal subjects but a greater volume of distribution amounting to 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 betalactam ring generating a microbiologically inactive metabolite. In vitro meropenem shows reduced susceptibility to hydrolysis by human dehydropeptidase-I (DHP-I) compared to imipenem. 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. Meropenem has linear kinetics up to a dose of 1 g.

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 5 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.

Children

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 $t_{1/2}$ 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 cerebrospinal fluid of children with meningitis are approximately 20% of respective 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 patients

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 rodents at doses exceeding 1000 mg/kg.

The intravenous LD_{50} of meropenem in rodents is greater than 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 doses of 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

Sodium carbonate

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

After reconstitution of the solution:
The reconstituted solutions for intravenous injection or infusion should be used immediately.
The period between preparing the reconstituted solution and the end of the intravenous injection or infusion should not be longer than one hour.

6.4 Special precautions for storage

Do not store above 30 °C.
Do not freeze the reconstituted solution.

6.5 Nature and contents of container

Meropenem-Rotexmedica 500 mg
674 mg powder in a 20 ml Type III glass vial with bromobutyl stopper and aluminium cap
Meropenem-Rotexmedica 1g
1348 mg powder in a 20 ml Type III glass vial with bromobutyl stopper and aluminium cap

The medicinal product is supplied in pack sizes of 1 or 10 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Injection

Meropenem to be used for bolus intravenous injection should be constituted with sterile water for injection (concentration: 50 mg/ml).

Infusion

For intravenous infusion meropenem vials may be directly constituted with 0.9% sodium chloride or 5% glucose solutions for infusion (concentration: approx. 5 mg/ml).

Each vial is for single use only.

Standard aseptic techniques should be used for solution preparation and administration.

The solution should be shaken before use.
Before administration, the product should be visually inspected for particles.
Only clear, colourless to light yellow solution may be used.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORIZATION HOLDER

ROTEXMEDICA GmbH Arzneimittelwerk
Bunsenstrasse 4
22946 Trittau
Germany

8. MARKET AUTHORIZATION NUMBER(S)

Meropenem-Rotexmedica 500 mg
Marketing authorization no. 80572.00.00
Meropenem-Rotexmedica 1g
Marketing authorization no. 80573.00.00

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

29.12.2011

10. DATE OF REVISION OF THE TEXT

June 2015

11. LEGAL CATEGORY

POM