CARPOREM P1537924

CARPOREM P1537924

Professional Information for Medicines for Human Use

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINAL PRODUCT

CARPOREM 500 mg (powder for injection)

CARPOREM 1000 mg (powder for injection)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CARPOREM 500 mg:

Each vial contains meropenem trihydrate equivalent to 500 mg anhydrous meropenem.

CARPOREM 1000 mg:

Each vial contains meropenem trihydrate equivalent to 1000 mg anhydrous meropenem.

Sugar free

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

CARPOREM 500 mg:

Powder:

White to pale yellow crystalline powder filled in clear glass vial stoppered with grey rubber stopper and sealed with an aluminium seal having a taxim blue colour PP disc.

Reconstituted solution:

Clear colourless to yellow colour solution.

CARPOREM 1000 mg:

Powder:

White to pale yellow crystalline powder filled in clear glass vial stoppered with grey rubber stopper and sealed with an aluminium seal having a white colour PP disc.

Reconstituted solution:

Clear colourless to yellow colour solution.

pH of the product after reconstitution is 7,3 to 8,3.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

CARPOREM is indicated for treatment of the following infections, caused by single or multiple susceptible bacteria and as empiric therapy prior to the identification of the causative organisms.

Acute exacerbation of chronic bronchitis and pneumonia due to:

*Staphylococcus aureus (*methicillin-susceptible strains only*), Streptococcus pneumoniae, Streptococcus* spp., *Escherichia coli, Haemophilus influenzae, Haemophilus parainfluenzae, Pseudomonas aeruginosa, Moraxella (Branhamella) catarrhalis, Klebsiella* spp., *Enterobacter cloacae, Enterobacter* spp., *Acinetobacter* spp.

Pneumonia in children due to:

Staphylococcus aureus (methicillin-susceptible strains only), *Streptococcus pneumoniae, Haemophilus influenzae, Pseudomonas aeruginosa insert* .

Urinary tract infections in adults and children, including complicating infections due to:

Enterobacter cloacae, Escherichia coli, Morganella morganii, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens, Citrobacter freundii insert .

Pelvic Inflammatory Disease (including tubo-ovarian abscess) and endometritis due to:

Enterococcus faecalis, Staphylococcus aureus (methicillin-susceptible strains only), coagulase-negative Staphylococcus spp. (methicillin-susceptible strains only), *Streptococcus agalactiae* (Group B), *Streptococcus viridans, Streptococcus* spp., *Escherichia coli, Neisseria gonorrhoeae, Klebsiella pneumoniae, Enterobacter aerogenes, Enterobacter cloacae, Proteus mirabilis, Acinetobacter anitratus, Acinetobacter Iwoffii, Gardnerella vaginalis, Bacteroides fragilis* group, *Peptostreptococcus anaerobius, Peptostreptococcus asaccharolyticus, Peptostreptococcus magnus insert* .

Skin and skin structure infections in adults due to:

Staphylococcus aureus (methicillin-susceptible strains only), coagulase-negative *Staphylococcus* spp. (methicillin-susceptible strains only), *Streptococcus pyogenes* (Group A), *Streptococcus agalactiae, Streptococcus viridans, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Bacteroides fragilis, Peptostreptococcus* spp.

Meningitis in adults and children due to:

Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis insert .

Septicaemia in adults and children due to:

Streptococcus pneumoniae, Escherichia coli, Klebsiella pneumoniae.

Empiric treatment, including initial monotherapy, for presumed bacterial infections in host-compromised neutropenic patients due to:

Streptococcus epidermidis, Streptococcus mitis, Streptococcus sanguinis, Escherichia coli

Intra-abdominal abscess and peritonitis due to:

Streptococcus milleri, Enterococcus faecalis, Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Pseudomonas aeruginosa, Bacteroides fragilis group *(*including *Bacteroides distasonis, Bacteroides fragilis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides vulgatus), Clostridium perfringens, Streptococcus mitior insert* .

Polymicrobial infections insert .

4.2 Posology and method of administration

Posology

Intravenous administration:

Adults:

Usual dose:

500 mg to 1000 mg by intravenous administration every 8 hours depending on the type and severity of infection, the known or suspected susceptibility of the pathogen(s), and the condition of the patient. See section 4.1 for types of infections and *in vivo* susceptible organisms.

Instruction for inserting the needle into the rubber stopper:
In order to avoid a coring phenomenon of the plug, when inserting the needle into the rubber stopper, it is recommended to use a needle with a 21-gauge or smaller diameter needle for the reconstitution of the product. The needle should be inserted only at the center of the rubber stopper and in a vertical direction.

Exceptions:

(1) Febrile episodes in neutropenic patients - the dose should be 1000 mg every 8 hours.

(2) Meningitis - the dose should be 2000 mg every 8 hours.

Caution may be required in using beta-lactam antibiotics in critically ill patients with known or suspected *Pseudomonas aeruginosa* lower respiratory tract infections. Concomitant use of an aminoglycoside is recommended.

Regular sensitivity testing is recommended when treating *Pseudomonas aeruginosa*.

CARPOREM should be given as an intravenous bolus injection over approximately 5 minutes or by intravenous infusion over approximately 15 - 30 minutes (see "*Constitution, compatibility, and stability*" section for constitution details).

Dosage schedule for adults with impaired renal function:

Dosage should be reduced in patients with creatinine clearance less than 51 mL/minute, as scheduled below.

Creatinine clearance (mL/min)	Dose (based on "unit" dose range of 500 mg to 2000 mg every 8 hours - see above)	Frequency
26 - 50	one unit dose	every 12 hours
10 - 25	one-half unit dose	every 12 hours
< 10	one-half unit dose	every 24 hours

CARPOREM is cleared by haemodialysis, if continued treatment with **CARPOREM** is necessary, the unit dose based on the infection type and severity is recommended at the completion of the haemodialysis procedure to re-institute effective treatment.

There is no experience with peritoneal dialysis.

Use in adults with hepatic insufficiency:

No dosage adjustment is necessary in patients with impaired hepatic metabolism.

Elderly:

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

Paediatric population:

Children under 3 months of age

Safety and efficacy in babies under 3 months have not been established.

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

For infants and children over 3 months and up to 12 years of age the IV dose is 10 - 40 mg/kg every 8 hours depending on type and severity of infection, the known or suspected susceptibility of the pathogen(s), and the condition of the patient.

Children over 50 kg body weight

The adult dosage should be used.

There is no experience in children with renal impairment.

Exceptions:

Meningitis - the dose should be 40 mg/kg every 8 hours.

CARPOREM should be given as an IV bolus over approximately 5 minutes or by intravenous infusion over approximately 15 - 30 minutes (see "*Constitution, compatibility, and stability*" section for constitution details).

Constitution, compatibility and stability:

CARPOREM to be used for bolus intravenous injection should be constituted with sterile water for injection (5 mL/250 mg; 10 mL/500 mg and 20 mL/1000 mg). This provides an approximate available concentration of 50 mg/mL. Constituted solutions are clear colourless to a yellow colour solution.

For intravenous infusion **CARPOREM** vials may be directly constituted with a compatible infusion fluid (as listed below) and then further diluted with the compatible infusion fluid, as needed.

Freshly prepared solutions of **CARPOREM** should be used whenever possible. However, constituted solutions of **CARPOREM**, as supplied in injection and infusion vials, and constituted as noted above maintain satisfactory potency at room temperature (15 - 25 °C) or under refrigeration (2 - 8 °C) as shown in the following table:

CARPOREM should not be mixed with or physically added to solutions containing other medicines.

Diluent	Hours stable at 15 - 25 °C	Hours stable at 2 - 8 °C
Vials constituted with water for injection for bolus injection	3	4
Infusions (1 - 20 mg/ml) prepared with: 0,9 % sodium chloride	3	24
5 % dextrose	1	1

Solutions of **CARPOREM** should not be frozen.

Method of Administration

For intravenous use only.

4.3 Contraindications

CARPOREM is contra-indicated in:

- Patients who have demonstrated hypersensitivity to meropenem or to any of the excipients listed in section 6.1.
- Patients who have a history of hypersensitivity to carbapenems, penicillins, cephalosporins or other beta-lactam antibiotics, may also be hypersensitive to **CARPOREM** and is contra-indicated in patients.

4.4 Special warnings and precautions for use

Prescribers must adhere to the principles of antibiotic stewardship.

The selection of **CARPOREM** 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 world. Prescribers are advised to take into account the local prevalence of resistance in these bacteria to penems.

Hypersensitivity reactions

Serious and occasionally fatal hypersensitivity reactions have been reported with meropenem (see sections 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

Antibiotic-associated colitis and pseudomembranous colitis have been reported with nearly all antibacterial 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 **CARPOREM**, (see section 4.8). Discontinuation of therapy with **CARPOREM**, and the administration of specific treatment for *Clostridium difficile* should be considered. Medicinal products that inhibit peristalsis should not be given.

Skin reactions

Severe Cutaneous Adverse Reactions (SCAR), such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Acute Generalised Exanthematous Pustulosis (AGEP) have been reported in patients taking beta-lactam antibiotics. When SCAR is suspected beta-lactam antibiotics should be discontinued.

Seizures

Seizures have infrequently been reported during treatment with carbapenems, including meropenem (see section 4.8).

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 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).

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 **CARPOREM** and valproic acid/sodium valproate/valpromide is not recommended (see section 4.5).

Paediatric population

Efficacy and tolerability in infants under 3 months of age have not been established, therefore, **CARPOREM**, may only be used in children over 3 months of age.

Contains sodium

CARPOREM contains 104 mg and 208 mg sodium per dose in the 500 mg and 1000 mg respectively, equivalent to 5.2 % and 10.4 % respectively of the WHO recommended maximum daily intake for sodium.

Meropenem is considered high in sodium. This should be particularly taken into account for those on a low salt 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 **CARPOREM** 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 **CARPOREM**. Caution is required if probenecid is co-administered with **CARPOREM**.

The potential effect of **CARPOREM** 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 4.4).

Oral anti-coagulants

Simultaneous administration of **CARPOREM** 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 normalized ratio) is difficult to assess. It is recommended that the INR should be monitored frequently during and shortly after coadministration of antibiotics with an oral anti-coagulant agent.

Paediatric population

Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

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

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3).

The safety in pregnant women has not been established. **CARPOREM** should therefore not be used during pregnancy.

Breastfeeding

Small amounts of **CARPOREM** have been reported to be excreted in human milk. **CARPOREM** should not be used in breastfeeding women unless the potential benefit for the mother justifies the potential risk to the baby.

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

CARPOREM 500 mg (Meropenem powder for injection)
CARPOREM 1000 mg (Meropenem powder for injection)
Sugar free

Read all of this leaflet carefully before you are given CARPOREM.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **CARPOREM** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What **CARPOREM** is and what it is used for
2. What you need to know before you take **CARPOREM**
3. How to take **CARPOREM**
4. Possible side effects
5. How to store **CARPOREM**
6. Contents of the pack and other information

1. WHAT CARPOREM IS AND WHAT IS USED FOR

CARPOREM contains the active substance meropenem and belongs to a group of medicines called carbapenem antibiotics.

CARPOREM is indicated for single or multiple susceptible bacterial infections. **CARPOREM** is majorly used prior to determine the causative organisms of several infections.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE CARPOREM

Do not take CARPOREM:

- If you have ever had an allergic reaction to **CARPOREM** or any ingredients of **CARPOREM**.
- If you are hypersensitive to any beta-lactam antibiotics, carbapenems, penicillins or cephalosporins.
- If you are already taking probenecid (used to treat gout) because **CARPOREM** and probenecid are contraindicated.
- Oral anti-coagulant agent (used to treat or prevent blood clots).
- If you are taking valproates (used to treat epilepsy).
- If your baby's age is below 3 months.
- If you are breastfeeding your baby.

Warnings and precautions

Tell your doctor or health care provider before being given the injection of **CARPOREM**:

- If you are suffering from kidney or liver problems.
- If you have previously had severe diarrhoea after taking other antibiotics.
- If you have any disorders like epilepsy (seizures).
- If you have a condition which requires you to monitor your sodium intake, please inform your doctor or nurse.

Other medicines with CARPOREM:

CARPOREM may have an effect on other medicines or other medicines may have an effect on **CARPOREM**.

Always tell your healthcare professional if you are taking any other medicine.

Pregnancy and breastfeeding:

CARPOREM is not recommended during pregnancy or breastfeeding.

If your pregnant or breastfeeding your baby, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before receiving **CARPOREM**.

Driving and using machinery:

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, tingling or pricing skin (paraesthesia) and convulsions that are usually accompanied with a loss of consciousness, and any of these could affect your ability to drive or operate machines.

CARPOREM contains sodium:

This medicinal product contains 104 mg and 208 mg sodium per dose in the 500 mg and 1000 mg respectively, equivalent to 5.2 % and 10.4 % respectively of the recommended maximum daily intake of 2 g sodium for an adult. If you have a condition which requires you to monitor your sodium intake please inform your doctor or healthcare professional.

HOW TO BE GIVEN CARPOREM

You will not be expected to give yourself CARPOREM. It will be given to you by a person who is qualified to do so.

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 (milligram). 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 **CARPOREM** 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.

3. How to use CARPOREM

- **CARPOREM** will be given to you as an injection or infusion into a large vein.
- Your doctor or nurse will normally give **CARPOREM** to you.

Your doctor will tell you how long your treatment with **CARPOREM** will last. Do not stop treatment early because this may reoccurrence of your condition. If you have the impression that the effect of **CARPOREM** is too strong or too weak, tell your doctor or pharmacist.

If you take more CARPOREM than you should:

Since a healthcare provider will administer **CARPOREM,** he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you forget to take CARPOREM:

Since a healthcare provider will administer **CARPOREM,** it is unlikely that the dose will be missed

4. POSSIBILE SIDE EFFECTS

CARPOREM can have side effects:

If any of the following happens, stop taking **CARPOREM** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Inflammation at site of injection,
- Skin rash and itching or hives on the skin,
- Shortness of breath, wheezing or trouble breathing.

These all are very serious side effects. If you have them, you may have had a serious allergic reaction to **CARPOREM**. You may need urgent medical attention or hospitalization.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Swelling of the face, lips, tongue or other parts of the body (angioedema).

These all are serious side effects. You may need urgent medical attention.

The following side effects occur frequently:

- Anemia (deficiency of red blood cells),
- gastrointestinal disturbances,
- pain.

The following side effects occur less frequently:

- Sepsis (presence of pus-forming bacteria or their toxins in the blood or tissues),
- thrombophlebitis (conjunction with the formation of a blood clot in the vein),
- bleeding events,
- hemoperitoneum (presence of blood in the peritoneal cavity),
- hypoglycaemia (abnormally low blood sugar),
- pruritus (an intense itching sensation),
- skin discolouration,
- skin ulceration.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **CARPOREM**. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

The following side effects occur frequently:

- Thrombocytopenia (abnormally small number of platelets in the blood),
- headache,
- diarrhoea (frequent and watery bowel movements) moderate or severe,
- vomiting,
- nausea,
- rash,
- pain,
- itching skin,
- inflammation of the skin,
- Increased blood alkaline phosphate,
- hives,
- a condition called Stevens Johnson Syndrome or Toxic Epidermal Necrolysis,

The following side effects occur less frequently:

- Lymphopenia (an abnormally small number of lymphocytes in the circulating blood),
- neutropenia (decrease is primarily in number of neutrophils),
- oral fungal infection,
- paresthesia (abnormal skin sensations),
- phlebitis (inflammation of a vein (usually in the legs)),
- infection,
- hyperbilirubinemia (high amounts of bile pigment (bilirubin) in the blood),
- blood creatinine and urea levels increased,
- thrombophlebitis (conjunction with the formation of a blood clot).

The following side effects frequency cannot be determined:

- Eosinophilia (increase in number of eosinophils-type of white blood cells),
- seizures.

Not all side effects reported for **CARPOREM** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **CARPOREM**, please consult your doctor, pharmacist or other healthcare professional for advice.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **"6.04 Adverse Drug Reaction Reporting Form"**, found online under SAHPRA's publications: http:///www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **CARPOREM.**

5. HOW TO STORE CARPOREM

Store at or below 25 °C.

Keep the vial in the carton until required for use.

Store the vials out of reach of children.

Do not use **CARPOREM** if you observe any discolouration upon storage.

Do not freeze the reconstituted solution.

Do not use **CARPOREM** after the expiry date which is stated on the container. The expiry date refers to the last day of that month.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What CARPOREM contains

The other ingredients of **CARPOREM** are sodium carbonate as a solubilizer and buffering agent.

What CARPOREM looks like and contents of the pack

CARPOREM 500 mg:

Powder for injection is filled in 30 mL clear glass tubular vial type-I stoppered with grey rubber stoppers and sealed with aluminium seal having taxim blue colour PP disc.

CARPOREM 1000 mg:

Powder for injection is filled in 40 mL clear glass tubular vial type-I stoppered with grey rubber stoppers and sealed with aluminium seal having white colour PP disc.

Pack sizes:

1. Single vial packed in a printed carton with package insert.
2. 10 vials packed in a printed carton with partition and package insert.

Holder of Registration

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53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

Registration numbers

CARPOREM 500 mg: 49/20.1.1/1224
CARPOREM 1000 mg: 49/20.1.1/1225

This leaflet was revised In
23 November 2023

4.7 Effects on ability to drive and use machines

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

Summary of the safety profile

In a review of patients treated with meropenem, the most frequently reported meropenem related adverse reactions were diarrhoea, nausea/vomiting and injection site inflammation. The most commonly reported meropenem related laboratory adverse events were thrombocytosis and increased hepatic enzymes.

Tabulated risk of adverse reactions

In the table below all adverse reactions are listed by system organ class and frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

System Organ Class	Frequency	Event
Infections and infestations	Less frequent	Oral and vaginal candidiasis
Blood and lymphatic system disorders	Frequent	Thrombocythaemia
	Less frequent	Eosinophilia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, haemolytic anaemia
Immune system disorders	Less frequent	Angioedema, anaphylaxis (see sections 4.3 and 4.4)
Nervous system disorders	Frequent	Headache
	Less frequent	Paraesthesiae, convulsions (see section 4.4)
Gastrointestinal disorders	Frequent	Diarrhoea, vomiting, nausea, abdominal pain
	Less frequent	Antibiotic-associated colitis (see section 4.4)
Hepatobiliary disorders	Less frequent	Transaminases increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, blood bilirubin increased
Skin and subcutaneous tissue disorders	Frequent	Rash, pruritis
	Less frequent	Urticaria, toxic epidermal necrolysis, Stevens Johnson Syndrome, erythema multiforme.
	Frequency unknown	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome), Acute Generalized Exanthematous Pustulosis (AGEP),Toxic Epidermal Necrolysis (TEN)
Renal and urinary disorders	Less frequent	Blood creatinine increased, blood urea increased
General disorders and administration site conditions	Frequent	Inflammation, pain
	Less frequent	Thrombophlebitis, pain at the injection site

Paediatric population

CARPOREM may be used in 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

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. Treatment symptomatic and supportive.

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

Category and class: A 20.1.1 Broad and medium spectrum antibiotics

Pharmacotherapeutic group: Antibacterials for systemic use, carbapenems, ATC code: J01DH02

Mechanism 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).

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).

Isolates may be reported as R (Resistant) 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 list of pathogens listed is derived from clinical experience and therapeutic guidelines.

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 pneumonia

All methicillin-resistant staphylococci are resistant to meropenem. Resistance rate ≥ 50 % in one or more EU countries.

5.2 Pharmacokinetic properties

Absorption

Meropenem is not absorbed orally; the formulation is administered by intravenous infusion.

A 30-minute intravenous infusion of a single dose of 500 mg and 1000 mg meropenem in normal volunteers results in peak plasma levels of approximately 11 µg/mL for the 250 mg dose, 23 µg/mL for the 500 mg dose, 49 µg/mL for the 1000 mg dose, and 115 µg/mL following the 2000 mg dose.

A 5-minute intravenous bolus injection of meropenem in normal volunteers resulted in peak plasma levels of approximately 52 µg/mL for 500 mg dose and 112 µg/mL for the 1000 mg dose respectively Intravenous infusions of 1000 mg of meropenem over 2 minutes, 3 minutes and 5 minutes resulted in peak plasma levels of 110,91 and 94 µg/mL, respectively.

After an intravenous dose of 500 mg, plasma levels of meropenem decline to values of 1 µg/mL or less 6 hours after administration.

When multiple doses are administered at 8 hourly intervals to subjects with normal renal function accumulation of meropenem does not occur.

In subjects with normal renal function, meropenem's elimination half-life is approximately 1 hour. Plasma protein binding of meropenem is approximately 2 %.

70 % of the IV administered dose is recovered as unchanged meropenem in the urine, over 12 hours, after which little further urinary excretion is detectable. Urinary concentrations of meropenem in excess of 10 µg/mL are maintained for up to 5 hours at the 500 mg dose. No accumulation of rneropenem in plasma or urine was observed with regimen's using 500 mg administered every 8 hours or 1000 mg administered every 6 hours in volunteers with normal renal function.

When multiple doses are administered at 8 hourly intervals, the concentrations at steady-state are approximately 20 % higher than after a single dose.

Distribution

Meropenem penetrates well into most body fluids and tissues including cerebro-spinal fluid (CSF) of patients with bacterial meningitis, achieving concentrations in excess of those required to inhibit most bacteria.

The plasma protein binding of meropenem is approximately 2 %.

Biotransformation

There is one metabolite which is microbiologically inactive.

Elimination

Meropenem is mostly excreted unchanged by the kidneys. The elimination half-life is approximately 1 hour in patients with normal renal function. The pharmacokinetics are linear over the dose range of 10 to 40 mg/kg.

Specific patient groups

Renal Insufficiency:

The plasma clearance of meropenem correlates with the creatinine clearance. Dose adjustment is required for patients with moderate to severely impaired renal function.

Hepatic insufficiency:

Hepatic impairment does not seem to affect the pharmacokinetics of meropenem in patients with impaired liver function.

Elderly:

Elderly patients with age-related reduction in creatinine clearance, requires a reduction of dosage.

Paediatric population:

The pharmacokinetics of meropenem in children are essentially similar to those in adults. The elimination half-life for meropenem is approximately 1,5 hours in children under the age of 2 years. The pharmacokinetics are linear over the dose range of 10 - 40 mg/kg.

5.3 Preclinical safety data

There was no evidence reproductive toxicity including teratogenic potential in studies in rats up to 750 mg/kg and in monkeys up to 360 mg/kg.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The other ingredients of **CARPOREM** are sodium carbonate as a solubilizer and buffering agent.

6.2 Incompatibilities

CARPOREM is to be administered either by intravenous bolus or intravenous infusion.

For intravenous bolus administration, the **CARPOREM** must be constituted with Sterile Water for Injection which gives a final concentration of 50 mg/mL. The reconstituted solution may be stored for 3 hours at room temperature (15 - 25 °C) and for 4 hours at 2 - 8 °C.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 °C and protect from light.

Keep the vial in the carton until required for use.

Do not use **CARPOREM** if you observe any discoloration upon storage.

6.5 Nature and contents of container

CARPOREM 500 mg:

Powder for injection is filled in 30 mL clear glass tubular vial type-I stoppered with grey rubber stoppers and sealed with aluminium seal having taxim blue colour PP disc.

CARPOREM 1000 mg:

Powder for injection is filled in 40 mL clear glass tubular vial type-I stoppered with grey rubber stoppers and sealed with aluminium seal having white colour PP disc.

Pack sizes:

1. Single vial packed in a printed carton with package insert.
2. 10 vials packed in a printed carton with partition and package insert.

6.6 Special precautions for disposal and other handling

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

7. HOLDER OF CERTIFICATE OF REGISTRATION

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12
Johannesburg
South Africa

8. REGISTRATION NUMBER

CARPOREM 500 mg: 49/20.1.1/1224

CARPOREM 1000 mg: 49/20.1.1/1225

9. DATE OF FIRST AUTHORISATION

10 August 2021

10. DATE OF REVISION OF THE TEXT

23 November 2023

P1537924

PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS: S4

CARPOREM 500 mg (meropenem poeier vir inspuiting)

CARPOREM 1000 mg (meropenem poeier vir inspuiting)

Suikervry

Lees hierdie hele blad noukeurig deur voordat CARPOREM aan u gegee word.
- Hou hierdie blad. Dit mag nodig wees dat u dit weer moet lees.
- As u nog vrae het, vra asseblief vir u dokter of u apteker.
- **CARPOREM** is vir u persoonlik voorgeskryf en u moet nie u medisyne vir ander mense gee nie. Dit kan hulle skaad, selfs al is hulle simptome dieselfde as u s'n.

Wat in hierdie blad is

1. Wat **CARPOREM** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **CARPOREM** kry
3. Hoe om **CARPOREM** te gebruik
4. Moontlike newe-effekte
5. Hoe om **CARPOREM** te bêre
6. Inhoud van die pak en ander inligting

1. WAT CARPOREM IS EN WAARVOOR DIT GEBRUIK WORD

CARPOREM bevat die aktiewe stof meropenem wat aan 'n groep medisyne genaamd karbapenemantibiotika behoort.

CARPOREM is aangedui vir enkele of meervoudige vatbare bakteriële infeksies. **CARPOREM** word hoofsaaklik gebruik voordat die oorsaaklike organismes van verskeie infeksies bepaal word.

2. WAT U MOET WEET VOORDAT U CARPOREM KRY

Moenie **CARPOREM** gebruik nie:
- As u ooit 'n allergiese reaksie op **CARPOREM** of enige bestanddeel van **CARPOREM** gehad het.
- As u hipersensitief vir enige beta-laktaamantibiotikum, karbapenems, penisilliene of sefalosporiene is.
- As u reeds probenesied gebruik (om jig te behandel) omdat **CARPOREM** en probenesied teenaangedui is.
- Orale teenstolmiddel (om bloedklonte te behandel of te voorkom).
- As u valproate (vir epilepsie).
- As u baba onder 3 maande oud is.
- As u u baba borsvoed.

Waarskuwings en voorsorgmaatreëls

Sê voordat u die inspuiting van **CARPOREM** kry vir u dokter of gesondheidsorgverskaffer as:
- As u nier- of lewerprobleme het.
- As u voorheen na gebruik van ander antibiotika erge diarree gekry het.
- As u enige versteurings soos epilepsie (aanvalle) het.
- As u 'n toestand het waarvoor u u natriuminname moet monitor, moet u asseblief vir u dokter of verpleegkundige daarvan sê.

Ander medisyne saam met CARPOREM:

CARPOREM kan 'n effek op ander medisyne hê, of ander medisyne kan 'n effek op **CARPOREM** hê.

Sê altyd vir u gesondheidspraktisyn as u enige ander medisyne gebruik.

Swangerskap en borsvoeding:

CARPOREM word nie tydens swangerskap aanbeveel nie.

As u swanger is of u baba borsvoed, dink dat u dalk swanger kan wees of beplan om 'n baba te hê, moet u u dokter, apteker of ander gesondheidspraktisyn asseblief om advies raadpleeg voordat u **CARPOREM** drink.

Motorbestuur en gebruik van masjinerie:

Geen studies van die effek op die vermoë om 'n voertuig te bestuur of masjiene te gebruik is gedoen nie. As 'n voertuig bestuur of masjiene hanteer word, moet in ag geneem word dat hoofpyn, tinteling of prikkeling op die vel (parestesie) en stuiptrekkings wat gewoonlik met 'n verlies van bewussyn gepaardgaan, u vermoë om te bestuur of om masjiene te hanteer kan beïnvloed.

CARPOREM bevat natrium:

Hierdie medisinale produk bevat 104 mg en 208 mg natrium in onderskeidelik die 500 mg- en 1000 mg-dosisse, gelykstaande aan onderskeidelik 5,2 % en 10,4 % van die aanbevole maksimum daaglikse inname van 2 g natrium vir 'n volwassene. As u 'n toestand het waarvoor u u natriuminname moet monitor, moet u asseblief vir u dokter of gesondheidskundige daarvan sê.

HOE OM CARPOREM TE KRY

Dit sal nie van u verwag word om CARPOREM aan uself te gee nie. Dit sal aan u gegee word deur 'n persoon wat bevoeg is om dit te doen.

Gebruik deur volwassenes
- Die dosis hang af van die tipe infeksie wat u het, waar die infeksie in die liggaam is en hoe ernstig die infeksie is. U dokter sal besluit oor die dosis wat u nodig het.
- Die dosis vir volwassenes is gewoonlik tussen 500 mg en 2000 mg. U sal gewoonlik elke 8 uur 'n dosis kry.

U kan egter minder dikwels 'n dosis kry as u niere nie baie goed werk nie.

Gebruik deur kinders en adolessente
- Die dosis vir kinders ouer as 3 maande en tot 12 jaar word deur die ouderdom en gewig van die kind bepaal. Die gewone dosis is tussen 10 mg en 40 mg **CARPOREM** vir elke kilogram (kg) wat die kind weeg. 'n Dosis word gewoonlik elke 8 uur gegee. Kinders wat meer as 50 kg weeg, sal die volwasse dosis kry.

3. Hoe om CARPOREM te gebruik
- **CARPOREM** sal as 'n inspuiting of infusie in 'n groot aar aan u gegee word.
- U dokter of 'n verpleegkundige sal **CARPOREM** gewoonlik aan u gee.

U dokter sal vir u sê hoe lank u behandeling met **CARPOREM** sal duur. Moenie die behandeling vroeg stop nie, want dit kan maak dat u toestand weer terugkeer. Sê vir u dokter of apteker as u die indruk het dat die effek van **CARPOREM** te sterk of te swak is.

As u meer CARPOREM gekry het as wat u moes:

Omdat 'n gesondheidsorgverskaffer **CARPOREM** sal gee, sal hy/sy die dosis beheer. In geval van oordosering, sal u dokter die oordosering egter bestuur.

As u vergeet om CARPOREM te kry:

Aangesien 'n gesondheidsorgverskaffer **CARPOREM** sal toedien, is dit onwaarskynlik dat 'n dosis oorgeslaan sal word.

4. MOONTLIKE NEWE-EFFEKTE

CARPOREM kan newe-effekte veroorsaak.

Indien enige van die volgende voorkom, moet u ophou om **CARPOREM** te gebruik en onmiddellik vir u dokter sê of na die ongevalle-afdeling van u naaste hospitaal gaan:
- Ontsteking op die plek van inspuiting,
- veluitslag, jeuk of galbulte op die vel,
- kortasemheid of moeilike asemhaling.

Hierdie is almal baie ernstige newe-effekte. As u dit ervaar, kan dit wees dat u 'n ernstige allergiese reaksie op **CARPOREM** gehad het. Jy mag dringende mediese aandag of hospitalisasie nodig hê.

Sê dadelik vir u dokter of gaan na die ongevalle-afdeling van u naaste hospitaal as u enige van die volgende opmerk:
- Swelling van die gesig, lippe, tong of ander dele van die liggaam (angioedeem).

Hierdie is almal ernstige newe-effekte. Dit mag wees dat u dringende mediese aandag nodig het.

Die volgende newe-effekte kom dikwels voor:
- Anemie (tekort aan roobloedselle),
- gastro-intestinale versteurings,
- pyn.

Die volgende newe-effekte kom minder dikwels voor:
- Sepsis (ettervormende bakterieë of hul gifstowwe in die bloed of weefsel),
- tromboflebitis (saam met die vorming van 'n bloedklont in die aar),
- bloedings,
- hemoperitoneum (bloed in die buikvliesholte),
- hipoglisemie (abnormale lae bloedsuikervlakke),
- pruritus ('n intense jeuksensasie),
- verkleuring van die vel,
- sere op die vel.

Hierdie is almal baie ernstige newe-effekte. As u dit ervaar, kan dit wees dat u 'n ernstige allergiese reaksie op **CARPOREM** gehad het. Dit mag wees dat u dringende mediese aandag of hospitalisasie nodig het.

Sê vir u dokter as u enige van die volgende opmerk:

Die volgende newe-effekte kom dikwels voor:
- Trombositopenie (abnormaal min bloedplaatjies in die bloed),
- hoofpyn,
- matige of erge diarree (los of waterige stoelgang),
- braking,
- naarheid,
- veluitslag,
- pyn,
- jeukende vel,
- inflammasie van die vel,
- hoër vlakke alkaliese fosfatase in die bloed,
- galbulte,
- 'n toestand wat die Stevens-Johnsonsindroom of toksiese epidermale nekrolise genoem word.

Die volgende newe-effekte kom minder dikwels voor:
- Limfopenie ('n abnormaal klein aantal limfosiete in die sirkulerende bloed),
- neutropenie (afname in hoofsaaklik die aantal neutrofiele),
- orale fungusinfeksie,
- parestesie (abnormale velsensasies),
- flebitis (ontsteking van 'n aar, gewoonlik in die bene),
- infeksie,
- hiperbilirubinemie [groot hoeveelhede galpigment (bilirubien) in die bloed],
- hoër vlakke kreatinien en ureum in die bloed,
- tromboflebitis (saam met die vorming van 'n bloedklont).

Die frekwensie van die volgende newe-effekte kan nie bepaal word nie:
- Eosinofilie. (toename in die aantal eosinofiele - 'n soort witbloedsel),
- toevalle.

Nie al die newe-effekte wat vir **CARPOREM** aangemeld is, is in hierdie blad opgeneem nie. As u algemene gesondheidstoestand vererger of as u newe-effekte ervaar terwyl jy **CARPOREM** ontvang, moet u u dokter, apteker of ander gesondheidspraktisyn om advies raadpleeg.

Aanmeld van newe-effekte

Praat met u dokter, apteker of verpleegkundige as u enige newe-effekte kry. Dit sluit alle moontlike newe-effekte in wat nie in hierdie blad gelys word nie. U kan newe-effekte ook by SAHPRA aanmeld *via* die vorm "6.04 Adverse Drug Reaction Reporting Form" wat aanlyn onder SAHPRA se publikasies gekry kan word: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van **CARPOREM** te gee.

5. HOE OM CARPOREM TE BÊRE

Bêre by of onder 25 ºC.

Hou die flessie in die karton totdat dit benodig word.

Hou die flessie buite bereik van kinders.

Moenie **CARPOREM** gebruik as u 'n verkleuring tydens berging opmerk nie.

Die aangemaakte oplossing moet nie gevries word nie.

CARPOREM moet nie na die vervaldatum op die houer gebruik word nie. Die vervaldatum verwys na die laaste dag van daardie maand.

HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS.

Gee alle ongebruikte medisyne terug aan u apteker.
Ongebruikte medisyne moet nie in dreinering- of rioolstelsels (bv. toilette) gegooi word nie.

6. INHOUD VAN DIE PAK EN ANDER INLIGTING

Wat CARPOREM bevat

Die ander bestanddele van **CARPOREM** is natriumkarbonaat as 'n oplosbevorderaar en buffer.

Hoe CARPOREM lyk en die inhoud van die pakkie

CARPOREM 500 mg:

Die poeier vir inspuiting is in 'n helder buisvormige flessie van 30 mL van tipe I glas met 'n grys rubberprop en verseël met aluminiumseël met 'n taximblou PP-skyf.

CARPOREM 1000 mg:

Die poeier vir inspuiting is in 'n helder buisvormige flessie van 40 mL van tipe I glas met 'n grys rubberprop en verseël met 'n aluminiumseël met 'n wit PP-skyf.

Pakgrootte:

1. 'n Enkel flessie in n voorafgedrukte kartondosie met n voubiljet.
2. 10 flessies verpak in n voorafgedrukte kartondosie met afskorting en n voubiljet.

Registrasiehouer

Aurogen South Africa (Edms) Bpk
Woodhillkantoorpark, Gebou 1, Eerste vloer
53 Phillip Engelbrechtlaan 53
Meyersdal Uitbr. 12, 1448
Johannesburg
Suid-Afrika

Registrasienommers

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Hierdie blad is hersien op

23 November 2023

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