

- ▶ With parenteral use Granulocytopenia · leucocytosis · leucopenia · nerve disorders · thrombocytopenia · urine abnormalities · vertigo

SIDE-EFFECTS, FURTHER INFORMATION Manufacturer advises to monitor serum-tobramycin concentration in patients with known or suspected signs of auditory dysfunction; if ototoxicity develops — discontinue treatment until serum concentration falls below 2 mg/litre.

● RENAL IMPAIRMENT

- ▶ When used by inhalation Manufacturer advises monitor serum-tobramycin concentration; if nephrotoxicity develops—discontinue treatment until serum concentration falls below 2 mg/litre.

● MONITORING REQUIREMENTS

- ▶ With intravenous use in neonates *Extended interval dose regimen in neonates*: pre-dose ('trough') concentration should be less than 2 mg/litre.
- ▶ With intravenous use *Once daily dose regimen*: pre-dose ('trough') concentration should be less than 1 mg/litre. *Multiple daily dose regimen*: one-hour ('peak') serum concentration should not exceed 10 mg/litre (8–12 mg/litre in cystic fibrosis); pre-dose ('trough') concentration should be less than 2 mg/litre.
- ▶ When used by inhalation Measure lung function before and after initial dose of tobramycin and monitor for bronchospasm; if bronchospasm occurs in a patient not using a bronchodilator, repeat test using bronchodilator. Manufacturer advises monitor renal function before treatment and then annually.

● DIRECTIONS FOR ADMINISTRATION

- ▶ With intravenous use For *intravenous infusion*, dilute with Glucose 5% or Sodium Chloride 0.9%; give over 20–60 minutes.
- ▶ When used by inhalation Other inhaled drugs should be administered before tobramycin.

● PRESCRIBING AND DISPENSING INFORMATION

- ▶ With intravenous use or when used by inhalation Local guidelines may vary in dosing advice provided.

● PATIENT AND CARER ADVICE

- ▶ When used by inhalation Patient counselling is advised for Tobramycin dry powder for inhalation (administration).

VANTOBRA[®] NEBULISER SOLUTION

Missed doses ▶ When used by inhalation Manufacturer advises if a dose is more than 6 hours late, the missed dose should not be taken and the next dose should be taken at the normal time.

● NATIONAL FUNDING/ACCESS DECISIONS

NICE decisions

- ▶ Tobramycin by dry powder inhalation for pseudomonal lung infection in cystic fibrosis (March 2013) NICE TA276
- ▶ When used by inhalation Tobramycin dry powder for inhalation is recommended for chronic pulmonary infection caused by *Pseudomonas aeruginosa* in patients with cystic fibrosis only if there is an inadequate response to colistimethate sodium, or if colistimethate sodium cannot be used because of contra-indications or intolerance. The manufacturer must provide tobramycin dry powder for inhalation at the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS. Patients currently receiving tobramycin dry powder for inhalation can continue treatment until they and their clinician consider it appropriate to stop.

www.nice.org.uk/TA276

- **MEDICINAL FORMS** There can be variation in the licensing of different medicines containing the same drug. Forms available from special-order manufacturers include: oral solution

Solution for injection

▶ Tobramycin (Non-proprietary)

Tobramycin 40 mg per 1 ml Tobramycin 80mg/2ml solution for injection vials | 5 vial [PoM] £20.80 DT = £20.80
Tobramycin 240mg/6ml solution for injection vials | 1 vial [PoM] £19.20 DT = £19.20

▶ Nebcin (Flynn Pharma Ltd)

Tobramycin 40 mg per 1 ml Nebcin 80mg/2ml solution for injection vials | 1 vial [PoM] £5.37 DT = £5.37

Inhalation powder

▶ Tob Podhaler (Novartis Pharmaceuticals UK Ltd)

Tobramycin 28 mg Tob Podhaler 28mg inhalation powder capsules with device | 224 capsule [PoM] £1,790.00 DT = £1,790.00

Nebuliser liquid

▶ Tobramycin (Non-proprietary)

Tobramycin 60 mg per 1 ml Tobramycin 300mg/5ml nebuliser liquid ampoules | 56 ampoule [PoM] £1,187.00 DT = £780.00

▶ Bramitob (Chiesi Ltd)

Tobramycin 75 mg per 1 ml Bramitob 300mg/4ml nebuliser solution 4ml ampoules | 56 ampoule [PoM] £1,187.00 DT = £1,187.00

▶ TOBI (Novartis Pharmaceuticals UK Ltd)

Tobramycin 60 mg per 1 ml Tob 300mg/5ml nebuliser solution 5ml ampoules | 56 ampoule [PoM] £1,305.92 DT = £780.00

▶ Tymbrineb (Teva UK Ltd)

Tobramycin 60 mg per 1 ml Tymbrineb 300mg/5ml nebuliser solution 5ml ampoules | 56 ampoule [PoM] £780.00 DT = £780.00

▶ Vantobra (Pari Medical Ltd)

Tobramycin 100 mg per 1 ml Vantobra 170mg/1.7ml nebuliser solution 1.7ml ampoules | 56 ampoule [PoM] £1,305.00

ANTIBACTERIALS > CARBAPENEMS

Carbapenems

Overview

The carbapenems are beta-lactam antibacterials with a broad-spectrum of activity which includes many Gram-positive and Gram-negative bacteria, and anaerobes; **imipenem** (imipenem with cilastatin p. 325) and meropenem p. 326 have good activity against *Pseudomonas aeruginosa*. The carbapenems are not active against meticillin-resistant *Staphylococcus aureus* and *Enterococcus faecium*.

Imipenem (imipenem with cilastatin) and meropenem are used for the treatment of severe hospital-acquired infections and polymicrobial infections caused by multiple-antibacterial resistant organisms (including septicaemia, hospital-acquired pneumonia, intra-abdominal infections, skin and soft-tissue infections, and complicated urinary-tract infections).

Ertapenem p. 325 is licensed for treating abdominal and gynaecological infections and for community-acquired pneumonia, but it is not active against atypical respiratory pathogens and it has limited activity against penicillin-resistant pneumococci. Unlike the other carbapenems, ertapenem is not active against *Pseudomonas* or against *Acinetobacter* spp.

Imipenem is partially inactivated in the kidney by enzymatic activity and is therefore administered in combination with **cilastatin** (imipenem with cilastatin), a specific enzyme inhibitor, which blocks its renal metabolism. Meropenem and ertapenem are stable to the renal enzyme which inactivates imipenem and therefore can be given without cilastatin.

Side-effects of imipenem with cilastatin are similar to those of other beta-lactam antibiotics. Meropenem has less seizure-inducing potential and can be used to treat central nervous system infection.