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Size 100 x 140 mm

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

Rx

TEICOPLANIN INJECTION IP

Tecovan 200
Injection

Composition:
Each vial contains :
Teicoplanin IP 200 mg

As sterile freeze dried powder for reconstitution with sterile water for Injection IP 10ml

PHARMACOLOGICAL CLASSIFICATION:
Broad/Medium Spectrum Antibiotics.

PHARMACOLOGICAL ACTION:
Teicoplanin is a bactericidal, glycopeptide antibiotic, produced by fermentation of Actinoplanes. teicomyceticus. It is active in vitro against both aerobic and anaerobic Gram-positive bacteria. Species usually sensitive: Staphylococcus aureus and coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci, enterococci, Listeria monocytogenes, micrococci, group JK corynebacteria and Gram-positive anaerobes including Clostridium difficile, and peptococci. Species usually resistant: Nocardia asteroides, lactobacillus sp, leuconostoc and all Gram-negative bacteria. Bactericidal synergy has been demonstrated in vitro with aminoglycosides against group D streptococci and staphylococci. In vitro combinations of teicoplanin with rifampicin or fluorinated quinolones show primarily additive effects and sometimes synergy. One-step resistance to teicoplanin could not be obtained in vitro and multi-step resistance was only reached in vitro after 11-14 passages. Teicoplanin does not show cross-resistance with other classes of antibiotics. Following intravenous and intramuscular administration, teicoplanin is widely distributed in body tissues. It is slowly eliminated with a plasma half-life of 70 to 100 hours; the excretory route is renal. Teicoplanin is not absorbed when administered orally. Teicoplanin does not penetrate through the blood-brain barrier.

INDICATIONS: Teicoplanin is indicated in potentially serious Gram-positive infections, including those which cannot be treated with other antimicrobial drugs. The effectiveness of teicoplanin has been documented in the following infections, caused by organisms sensitive to teicoplanin: endocarditis, septicaemia and osteomyelitis, respiratory infections, skin and soft tissue infections, urinary tract infections and peritoniti
sociated with chronic ambulatory peritoneal dialysis (CAPD).

CONTRA-INDICATIONS:
Hypersensitivity to teicoplanin. Safety and efficacy have not been established in children under 3 years of age. Teicoplanin should not be used during pregnancy and lactation as safety has not been shown. It is not known whether teicoplanin passes into breast milk. Teicoplanin must not be injected into the subarachnoid space.

WARNINGS:
Teicoplanin should be administered with caution in patients known to be hypersensitive to vancomycin since cross hypersensitivity may occur. However, a history of "Red Man Syndrome" that can occur with vancomycin is not a contraindication to Teicoplanin. Thrombocytopenia has been reported with teicoplanin, especially at higher doses than those usually recommended. It is advisable for periodic haematological studies to be performed during treatment. Liver and renal function tests are advised during treatment. Serial renal and auditory function tests should be undertaken in the following circumstances: . prolonged treatment in patients with renal insufficiency. . concurrent and sequential use of other drugs which may have neurotoxic and/or nephrotoxic properties. These include aminoglycosides, colistin, amphotericin B, cyclosporin, cisplatin, frusemide and ethacrynic acid. However, there is no evidence of synergistic toxicity with combinations with Teicoplanin.

DOSAGE AND DIRECTIONS FOR USE:
The reconstituted Teicoplanin injection may be administered directly either intravenously or intramuscularly. The intravenous injection may be administered either as a bolus or as a 30 minute infusion. Dosage is usually once daily but, in cases of severe infection, a second injection should be administered on the first day in order to reach more rapidly the required serum concentrations. The majority of patients with infections caused by organisms sensitive to the antibiotic show a therapeutic response within 48-72 hours. The total duration of therapy is determined by the type and severity of the infection and the clinical response of the patient. In endocarditis and osteomyelitis, treatment for three weeks or longer is recommended. Determination of teicoplanin serum concentrations may optimise therapy. In severe infections, trough serum concentrations should not be less than 10 mg/L. Peak concentrations measured one hour after a 400 mg intravenous dose are usually in the range of 20-50 mg/L; peak serum concentrations of up to 250 mg/L have been reported after intravenous doses of 25 mg/kg. A relationship between serum concentration and toxicity has not been established.

Therapeutic dosage:
Adult and elderly patients with normal renal function: Moderate infections:
skin and soft tissue infection, urinary tract infection, lower respiratory tract infection. Loading dose:
one single i.v. injection of 400 mg on the first day. Maintenance dose:
a single i.v. or i.m. injection of 200 mg daily.
Severe infections:
joint and bone infection, septicaemia, endocarditis.
Loading dose:
400 mg i.v. injection every 12 hours for the first three doses. Maintenance dose:
a single i.v. or i.m. injection of 400 mg daily.

In some clinical situations, such as infected, severely burned patients or Staphylococcus aureus endocarditis, unit maintenance doses of up to 12 mg/kg may be required.

NB
Standard doses of 200 and 400 mg equate respectively to mean doses of 3 and 6 mg/kg. In overweight patients it is recommended to adapt the dosage to the weight following the same therapeutic schedule: moderate infection 3 mg/kg, severe infection 6 mg/kg.

Children:
Teicoplanin can be used to treat Gram positive infections in children from the age of 3 years. For severe infections and neutropenic patients the recommended dose is 10 mg/kg every 12 hours by intravenous injection for the first three doses; thereafter a dose of 10 mg/kg should be administered by either intravenous or intramuscular injection as a single dose each day. For moderate infections the recommended dose is 10 mg/kg by intravenous injection every twelve hours for the first three doses: thereafter a dose of 6 mg/kg should be administered by either intravenous or intramuscular injection as a single dose each day.

Adults and elderly patients with renal insufficiency:
For patients with impaired renal function, reduction of dosage is not required until fourth day of Teicoplanin treatment. Measurement of the serum concentration of Teicoplanin may optimise therapy (see section "Administration").

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From the fourth day of treatment
- In mild renal insufficiency: creatinine clearance between 40 and 60 mL/min, Teicoplanin dose should be halved either by administering the initial unit dose every two days, or by administering half this dose once a day.
- In severe renal insufficiency: creatinine clearance less than 40 mL/min, and in haemodialysed patients, Teicoplanin dose should be one third of the normal either by administering the initial unit dose every third day, or by administering one third of this dose once a day. Teicoplanin is not removed by dialysis.
- In continuous ambulatory peritoneal dialysis: after a single loading i.v. dose of 400 mg if the patient is febrile, the recommended dosage is 20 mg/L per bag in the first week, 20 mg/L in alternate bags in the second week, and 20 mg/L in the overnight dwell bag only during the third week.

Monitoring the Plasma Concentrations: If checks are carried out on the teicoplanin serum level in adults and children with severe infections, then the minimum serum level (measured immediately before the next dose) should not be below 10 mg/L.
Dosage Patients with Restricted Kidney Functions: For patients with impaired kidney function, the dose should not be reduced until the fifth dose.
In cases of mild renal insufficiency (creatinine clearance 40-60 mL/min) the daily dose of Teicoplanin from the fifth dose of treatment should be halved or the normal dose given every two days. For patients with severely impaired renal function (creatinine clearance of less than 40 mL/min) and in haemodialysed patients, the daily dose of Teicoplanin should be reduced to a third of the unit dose either by administering the unit dose every third day, or by administering one third of this dose once each day.
Until further clinical experience are available patients with a creatinine clearance lower than/equal to 20 mL/min must be excluded from therapy with teicoplanin - unless measurement of the serum concentrations can be guaranteed to accompany the therapy. Teicoplanin is not removed by haemodialysis. In Gram-positive peritonitis related continuous ambulatory peritoneal dialysis, the recommended dosage is 20 mg/L per bag for the first week, 20 mg/L in alternate bags for the second week and 20 mg/L in the overnight dwell bag in the third week; febrile patients should also receive a loading dose of 400 mg IV Teicoplanin. Teicoplanin is stable in peritoneal dialysis solutions (1,36% or 3,86% dextrose). Do not keep mixed solutions for longer than 24 hours.
Type of Administration and Duration of Use:
a) **Type of Administration**
In order to produce the ready to use solution, all of the Water for Injection contained in the accompanying ampoule is injected slowly into the vial with the dry substance. The vial is then shaken until the dry substance is completely dissolved. Care must be taken to avoid the formulation of foam as far as possible. If foam does nevertheless develop during the preparation of the injection solution, it is recommended that the ready to use solution be left to stand for approximately 15 minutes until the foam has disappeared. Teicoplanin may be administered by either intravenous or intramuscular injection. The intravenous dose may be given by rapid injection over one minute or by short infusion.
Intravenous Injection: Following preparation of the ready to use solution, Teicoplanin is injected directly intravenously and/or, after clamping the infusion tube, injected into the proximal end of the tube.
Teicoplanin can be injected quickly, i.e. within one minute.

Intramuscular Injection: Following preparation of the ready to use solution, Teicoplanin can also be injected intramuscularly. For the purposes of brief infusion, Teicoplanin is dissolved in 20-50 mL within 20-30 minutes

The following infusion solutions are suitable for mixing with Teicoplanin:
- Isotonic saline solution 0.95
- Ringer's solution
- Ringer's lactate solution
- 5% glucose solution
- solutions with 0.18% sodium chloride and 4% glucose

Infusion solutions of Teicoplanin with isotonic saline solution, Ringer's solution, Ringer's lactate solution, 5% glucose solution or solutions with 0.18% sodium chloride and 4% glucose should be used as soon as possible. Otherwise, they may be stored for 24 hours at 4° C.

Solutions of Teicoplanin and aminoglycosides are incompatible and should not be mixed before injection.

b) **Duration of Use**
With infections caused by teicoplanin-sensitive pathogens, a therapeutic result is shown in the majority of cases within 48 to 72 hours.

The duration of treatment is based upon the severity of the infection as well as upon the clinical and bacteriological progress. Basically the treatment should be continued consistently for at least 3 days beyond the fever abating and/or the disappearance of clinical symptoms. In cases of endocarditis or osteomyelitis at least 3 weeks treatment is recommended. Teicoplanin should not be administered for longer than 4 months.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
Side-Effects:- The following side effects have been observed in clinical studies: Occasional hypersensitivity reactions to the active substance, exanthema, erythema, pruritus or fever can occur; bronchospasm or anaphylactic reactions have been observed. As a localised reaction, there can occasionally be pain at the injection site; phlebitis or the formation of an abscess have been observed very occasionally.
In some cases a rise in the transamina has been observed under Teicoplanin therapy. A rise in serum creatinine may occur. Ei hilio, throt p or lp have been described.
In the gastro-intestinal area, Teicoplanin can on rare occasions lead to nausea and vomiting.
Furthermore, headaches or dizziness can be observed . Loss of hearing, tinnitus or vestibular disturbance has been observed in patients treated with teicoplanin in combination with a potentially ototoxic drug such as an aminoglycoside.
and/or alkaline phosphat

Special Precautions:-
In patients with restricted kidney function the therapy should be monitored carefully. Where treatment in such patients is continued for longer than 3 weeks, regular checks are recommended on the serum level as well as on kidney, liver and auditory function. Such tests are also recommended in cases of concurrent and sequential use of other drugs which may have neurotoxic and/or nephrotoxic ies e.g. aminoglyco: in, amphotericin, cyclosporin, cysplatin, frusemide and ethacrynic acid.
Until further clinical experiences are available patients with a creatinine clearance lower than/equal to 20 mL/min must be excluded from therapy with teicoplanin - unless measurement of the serum concentrations can be guaranteed to accompany the therapy. Teicoplanin may not be administered into the subarachnoid space.
Periodic haematological studies plus liver and renal function tests, are advisable during prolonged treatment.
Administer with caution to patients known to be vancomycin-sensitive since cross hypersensitivity may occur. There is no record of any adverse interaction with other medications.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
General symptomatic measures are recommended for the therapy of an overdosage. With regard to overdosage, there is information available on two children with agranulocytosis, to whom several doses of 100 mg/kg/day Teicoplanin each were administered in error. Despite very high serum concentrations of 300 mg/L, no intoxication phenomena appeared. Teicoplanin is not removed by haemodialysis or peritoneal dialysis.

IDENTIFICATION:
Lyophilised product: Spongy, ivory coloured, homogenous mass.
Solvent: Clear, colourless, odourless liquid.
Reconstituted Solution: Clear, yellowish solution.

STORAGE INSTRUCTIONS:
Storage : Store in a cool place. (8°C to 30°C.)

Mfd. by : Protech Telelinks
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