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

This package insert is continually updated: Please read carefully before using a new pack.

Teicoplanin

Targocid® I.M. / I.V.

Composition

Targocid® 200mg - Each vial contains (as lyophilisate) Teicoplanin I.P. 200mg
Targocid® 400mg - Each vial contains (as lyophilisate) Teicoplanin I.P. 400mg.

Indications

In serious gram +ve infections, serious staphylococcal infections in patients sensitive or unresponsive to penicillins and cephalosporins, CAPD related peritonitis, prophylaxis in orthopaedic surgery at risk of gram +ve infections.

Dosage and Administration

Adults:

For most gram-positive infections: loading regimen of three 12-hourly doses of 400 mg IV, followed by a maintenance dose of 400 mg IV or IM once daily. The standard dose of 400 mg equates to approximately 6 mg/kg. In patients weighing more than 85 kg, a dose of 6 mg/kg should be used.

Higher doses may be required in some clinical situations.

Surgical Prophylaxis: 400 mg (or 6 mg/kg if >85 kg) IV single dose at time of anesthesia induction.

Pediatrics:

>2 months to 16 years: For most gram-positive infections: loading regimen of three 12-hourly doses of 10 mg/kg IV, followed by a maintenance dose of 6 mg/kg IV or IM once daily.

Severe infections and infections in the neutropenic patient: Loading regimen of three 12-hourly doses of 10 mg/kg IV, followed by 10 mg/kg IV once daily.

<2 months: A single loading dose of 16 mg/kg IV the first day, followed by 8 mg/kg IV once daily. The IV dose should be infused over 30 minutes.

Elderly:

No dose adjustment required, unless there is renal impairment (see below).

Special Populations:

Renal Insufficiency: Dose adjustment is not required until the fourth day of treatment, at which time dosing should be adjusted to maintain a serum trough concentration of at least 10 mg/L
After the 4th day of treatment:

- mild renal insufficiency (Cr Cl between 40 to 60 mL/min): maintenance dose should be halved, either by administering the usual recommended dose every 2 days, or administering one-half the dose daily.
- severe renal insufficiency (Cr Cl <40 mL/min) and in hemodialyzed patients: maintenance dose should be one-third the usual recommended dose, either by administering the dose every third day, or administering one-third of the dose daily. Teicoplanin is not removed by hemodialysis.

Continuous ambulatory peritoneal dialysis for peritonitis: After a single loading dose of 400 mg IV, 20 mg/L is administered per bag in the first week, 20 mg/L in alternate bags in the second week, then 20 mg/L in the overnight dwell bag during the 3rd week.

Administration:

Teicoplanin may be given IV or IM. The IV dose may be administered as a rapid injection over 3 to 5 minutes or as an infusion over 30 minutes. Only the infusion method should be used in neonates Severity of illness and infection site need to be considered in selecting teicoplanin doses.

Preparation and handling

SLOWLY inject the prescribed amount of sterile water down the side of the vial.

GENTLY roll the vial between the hands until the powder is completely dissolved, paying attention to avoid the formation of foam. IT IS IMPORTANT TO ENSURE THAT ALL THE POWDER IS DISSOLVED, EVEN THAT NEAR THE STOPPER.

Shaking this solution will cause the formation of foam which will make it difficult to recover the required volume. Nevertheless, if teicoplanin has been completely dissolved the foam does not change the concentration of the solution which will remain 100 mg in each 1.5 mL, 200 mg in 3.0 mL (from the 100 mg and 200 mg vials) or 400 mg in 3.0 mL (from the 400 mg vial). If the solution does become foamy, then it should be left to stand for about 15 minutes.

Withdraw the teicoplanin solution slowly from the vial, trying to recover most of it by placing the needle in the central part of the rubber stopper.
The reconstituted solutions will contain 100 mg of teicoplanin in 1.5 mL, 200 mg in 3.0 mL (from the 100 mg and 200 mg vials), and 400 mg in 3.0 mL (from the 400 mg vial).
It is important that the solution is correctly prepared and carefully withdrawn into the syringe; preparations that are not carefully executed can lead to the administration of less than the full dose.

The final solution is isotonic with plasma and has a pH of 7.2-7.8.
The reconstituted solution may be injected directly or alternatively further diluted.
As a matter of good pharmaceutical practice, these solutions should be used immediately after admixing.

Incompatibilities/ Compatibilities
Solutions of teicoplanin and aminoglycosides are incompatible when mixed directly and should not be mixed before injection.

Storage conditions and shelf life
Teicoplanin powder is stable for 3 years when stored at room temperature. The vials should be protected from heat.
Reconstituted solutions should be stored under refrigeration (5°C) and solutions stored for longer than 24 hours be discarded.

Contraindications
Teicoplanin is contraindicated in patients who have exhibited previous hypersensitivity to teicoplanin.

Warnings
Teicoplanin should be administered with caution in patients of known hypersensitivity to vancomycin since cross hypersensitivity may occur.
Hearing, hematologic, hepatic, and renal toxicities have been reported with teicoplanin. Appropriate monitoring of hearing, hematologic, liver, and renalfunction should be done, particularly in patients with renal insufficiency, patients receiving prolonged therapy, or patients who receive concurrent ototoxic or nephrotoxic drugs.

Precautions
Superinfection: As with other antibiotics, the use of teicoplanin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Driving a Vehicle or Performing Other Hazardous Tasks
None

Interactions

Due to the potential for increased adverse effects, teicoplanin should be administered with caution in patients receiving concurrent nephrotoxic or ototoxic drugs, such as aminoglycosides, amphotericin B, ciclosporin, and furosemide.

Pregnancy
Teicoplanin should not be used during confirmed or presumed pregnancy unless a physician considers that the potential benefits outweigh any possible risk.
Animal reproduction studies have not shown evidence of teratogenic effects.

Lactation
Information about the excretion of teicoplanin in human breast milk is not known.
Therefore, teicoplanin should not be used during lactation unless a physician considers that the potential benefits outweigh any possible risk.

Adverse Reactions
Hypersensitivity: rash, pruritus, fever, rigors, bronchospasm, anaphylactic reactions, anaphylactic shock urticaria, angioedema, and rare reports of exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme including Stevens-Johnson syndrome.
In addition, infusion-related events, such as erythema or flushing of the upper body, have been rarely reported in which the events occurred without a history of previous teicoplanin exposure and did not recur on reexposure when the infusion rate was slowed and/or the concentration decreased. These events were not specific to any concentration or rate of infusion.
Gastrointestinal: nausea, vomiting, diarrhea.
Blood: rare cases of reversible agranulocytosis, leucopenia, neutropenia, thrombocytopenia, eosinophilia
Liver function: increases in serum transaminases and/or serum alkaline, phosphatase.
Renal function: elevations of serum creatinine, renal failure.
Central nervous system: dizziness, headache, seizures with intraventricular use.
Auditory/vestibular: hearing loss, tinnitus, vestibular disorder.
Other: superinfection (overgrowth of non-susceptible organisms).

Overdosage
Human Experience:
Cases of excessive doses administered in error to pediatric patients have been reported. In one report, agitation occurred in a 29-day-old newborn given 400 mg I.V. (95 mg/kg). In the other cases, there were no symptoms or laboratory abnormalities associated with teicoplanin. In these cases, the ages ranged from 1 month to 8 years. When reported, teicoplanin doses ranging from 35.7 mg/kg to 104 mg/kg were administered in error.

Management: Treatment of overdosage should be symptomatic. Hemodialysis does not remove the drug.

Pharmacodynamics and antimicrobial spectrum
Teicoplanin is a glycopeptide antibiotic that has shown in vitro bactericidal activity against both aerobic and anaerobic gram-positive organisms. Teicoplanin inhibits the growth of susceptible organisms by interfering with cell-wall biosynthesis at a site different from that affected by beta-lactams. It is active against staphylococci (including those resistant to methicillin and other beta-lactam antibiotics), streptococci, enterococci, Listeria monocytogenes, micrococci, group J/K corynebacteria, and grampositive anaerobes including Clostridium difficile, and peptococci.
Bactericidal synergy has been demonstrated in vitro with teicoplanin when combined with aminoglycosides against Staphylococcus aureus ; synergism has also been demonstrated with imipenem against these organisms . The in vitro combination of teicoplanin and rifampin has shown additive and synergistic effects against Staphylococcus aureus . In vitro synergy with ciprofloxacin against Staphylococcus epidermidis has also been observed.

One-step resistance to teicoplanin could not be obtained in vitro and multi-step resistance was produced *in vitro* only after multiple passages.
There have been reports of elevated MICs for teicoplanin in several strains of Staphylococcus haemolyticus.
Teicoplanin does not show cross-resistance with other classes of antibiotics. Some cross-resistance is observed between teicoplanin and the glycopeptide vancomycin among enterococci.
Teicoplanin is taken up by leukocytes, and macrophages , and retains antistaphylococcal activity within these cells.

Pharmacokinetics
Teicoplanin is administered by parenteral injection. The bioavailability of a single 3 to 6 mg/kg intramuscular injection is over 90% .
Following oral administration, teicoplanin is not systemically absorbed from the normal gastrointestinal tract; 40% of the administered dose is present in the feces in a microbiologically active form.
Following intravenous administration of 3 to 6 mg/kg, the plasma concentration declines with a terminal elimination half-life of about 150 hours; total plasma clearance ranges from 11.9 mL/hr/kg to 14.7 mL/hr/kg. This long half-life

allows once a day administration. At 6 mg/kg administered intravenously at 0, 12, 24 hours and every 24 hours thereafter as a 30-minute infusion, a predicted trough serum concentration of 10 mg/L would be reached by Day 4 . Predicted steady state peak and trough serum concentrations of approximately 64 mg/L and 19 mg/L, respectively, would be attained by Day 28 .The drug distributes readily into skin (subcutaneous fat) and blister fluid, myocardium , pulmonary tissue [134] and pleural fluid , bone and synovial fluid but not readily into cerebrospinal (CSF) fluid . It is 90% to 95% bound with weak affinity to plasma proteins . Steady-state volume of distribution after 3 to 6 mg/kg intravenously ranges from 0.94 L/kg to 1.4 L/kg. When administered parenterally, the metabolic transformation is minor, about 3%about 80% of administered drug is excreted in the urine Renal clearance after 3 to 6 mg/kg intravenously ranges from 10.4 to 12.1 mL/hr/kg .

Non-clinical safety data

Animal reproduction studies have not shown evidence of teratogenic effects.
Animal reproduction studies have not shown evidence of impairment of fertility.

Manufactured by:

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