

Data Sheet

Teicoplanin 400 mg lyophilised powder for injection with water for injections ampoule.

PRESENTATION

Teicoplanin lyophilised powder for injections is an off-white, odourless powder contained in a vial of 20 mL (400 mg) together with ampoules of water for injections.

USES

Actions

Teicoplanin is a complex mixture of 6 major components with molecular weights ranging from 1564 - 1894.

Teicoplanin is a glycopeptide antibiotic that has shown *in vitro* bactericidal activity against both anaerobic and aerobic 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 gram-positive anaerobes including *Clostridium difficile*, and peptococci.

Bactericidal synergy has been demonstrated *in vitro* with aminoglycosides against enterococci (group D streptococci) and staphylococci. *In vitro* combinations of teicoplanin with rifampicin, imipenem, 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 produced *in vitro* only after multiple passages.

There have been reports of elevated MICs for teicoplanin in several strains of *Staphylococcus haemolyticus*, but the clinical relevance is not yet known.

Teicoplanin does not show cross-resistance with other classes of antibiotics. Some cross-resistance has been observed between teicoplanin and the glycopeptide vancomycin among enterococci.

Teicoplanin is taken up by leukocytes and macrophages and retains staphylococcal activity within these cells.

Pharmacokinetics

Teicoplanin is administered by parenteral injection. The bioavailability of a single 3-6 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 faeces in a microbiologically active form.

Following intravenous administration of 3-6 mg/kg, the plasma concentration-time profile indicates a biphasic distribution (with a rapid distribution phase having a half-life of about 0.3 hours, followed by a more prolonged distribution phase having a half-life of about 3 hours). The elimination half-life is about 150 hours. This long half-life allows once a day administration; but without a loading dose, a steady-state plasma concentration of 14 mg/L would be attained in 2-3 weeks. With a loading dose of 6 mg/kg every twelve hours, a predicted trough plasma concentration of 10 mg/L, should be attained by the 4th dose. Total plasma clearance is 13.6 mL/h/kg.

The drug distributes readily into skin and blister fluid, myocardium, pulmonary tissue and pleural fluid, bone and synovial fluid but not readily into cerebrospinal (CSF) fluid. It is 90-95% bound with weak affinity to plasma proteins.

Steady-state volume of distribution after 3 - 6 mg/kg IV ranges from 0.94 - 1.4 L/kg.

Metabolic transformation is minor, about 3%; about 80% of administered drug is excreted in the urine. Renal clearance after 3 - 6 mg/kg IV ranges from 10.4 - 12.1 mL/h/kg.

INDICATIONS

Teicoplanin is indicated for the treatment of the following serious infections due to staphylococci or streptococci, which can not be treated satisfactorily with less toxic agents including beta-lactam antibiotics:-

Bone - osteomyelitis

Joint - septic arthritis

Blood - non-cardiac bacteraemia, septicaemia

DOSAGE AND ADMINISTRATION

Teicoplanin can be administered either intravenously or intramuscularly. Intravenous dosing may be by rapid injection over 3-5 minutes, or more slowly over a 30 minute infusion. An intramuscular injection of teicoplanin should not exceed 3 mL (400 mg) at a single site. Dosage is usually once daily following an initial loading dose which is administered as three 12-hourly doses on the first day of therapy.

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. The following periods are often appropriate:

- Uncomplicated bacteraemia 2-4 weeks
- Septic arthritis or osteomyelitis 3-6 weeks

The use of teicoplanin may result in overgrowth of non-susceptible organisms.

Adults

Septicaemia/bacteraemia, acute or chronic osteomyelitis

Treatment should be started with 400 mg (or 6 mg/kg in patients weighing more than 85 kg) by the I.V. route every 12 hours for 3 doses then the daily maintenance dose should be 400 mg (or 6 mg/kg) once daily. Higher doses may be required in some clinical situations.

Septic Arthritis

Patients with septic arthritis should receive 800mg (or (12mg/kg), intravenously, every 12 hours for 3 doses then a daily maintenance dose of 800mg (or 12mg/kg).

Paediatric Patients

Children aged 2 months to 16 years: for severe infections and infections in neutropenic patients, the recommended dose is 10mg/kg intravenously, every 12 hours for the first three doses; thereafter a dose of 10mg/kg should be administered intravenously as a single dose, once daily.

For moderate infections, the recommended dose is 10mg/kg intravenously, every 12 hours for the first three doses; thereafter a dose of 6mg/kg should be administered by either intravenous or intramuscular injection as a single dose, once daily.

Elderly Patients

No dosage adjustment required unless renal function is impaired. The instructions for impaired renal function should then be followed.

Patients with Renal Impairment

For patients with impaired renal function, reduction of dosage is not required until the fourth day of Targocid® treatment. Trough plasma teicoplanin concentrations should be monitored periodically after the first week of therapy and the dosage adjusted to prevent trough concentrations exceeding 30 µg/mL in patients with septic arthritis or 15 µg/mL in other cases, with a minimum of 10 µg/mL.

In mild renal insufficiency (creatinine clearance between 40 and 60 mL/min)

From the fourth day of treatment the Targocid® dose should be halved, either by administering the dose every two days, or by administering half of this dose once a day.

In severe renal insufficiency (creatinine clearance less than 40 mL/min, and in haemodialysed patients)

From the fourth day of treatment the Targocid® dose should be reduced to one third of the normal dose either by administering the dose every third day, or by administering one third of this dose once a day.

Teicoplanin is not appreciably removed by haemodialysis or peritoneal dialysis.

Combination Therapy

Combination with an appropriate bactericidal agent is recommended when mixed infection with a gram-negative pathogen cannot be excluded (e.g. empiric therapy of fever in neutropenic patients).

Preparation of Injection

Note: The powder should be reconstituted strictly in accordance with the instructions below. Errors in reconstitution may result in the formation of a stable foam and delivery of smaller doses.

The entire contents of the accompanying diluent water ampoule should be added **slowly** down the side wall of the vial of Targocid®. The vial should be rolled **gently** between the palms until the powder is completely dissolved, taking care to avoid foam formation. **DO NOT SHAKE.** If the solution does become foamy, allow to stand for 15 minutes for the foam to subside. Withdraw the entire contents from the vial **slowly** into a syringe, trying to recover most of the solution by placing the needle in the central part of the stopper.

The final solution is isotonic with plasma and has a pH of 7.2 -7.8.

The reconstituted solution contains:

For the 400 mg vial: 400 mg/3.0 mL of teicoplanin.

The reconstituted solution may be injected directly, or alternatively diluted with any of the following diluents.

- 0.9 % Sodium Chloride solution
- Compound sodium lactate solution
- 5 % glucose solution
- 0.18 % Sodium Chloride and 4 % glucose solution

As a matter of good pharmaceutical practice, solutions for intravenous infusion should be used immediately after admixing.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Teicoplanin should be administered with caution in patients of known hypersensitivity to vancomycin since cross hypersensitivity may occur.

However, 'Red Man Syndrome', that can occur with vancomycin, is not reported with teicoplanin and a history of 'Red Man Syndrome' from vancomycin is not a contraindication to teicoplanin.

Hearing, haematologic, hepatic and renal toxicities have been reported with teicoplanin. Appropriate periodic haematological studies, auditory, renal and liver function tests should be conducted, particularly during prolonged therapy and when administering teicoplanin to:

- patients with renal insufficiency,
- patients who require concurrent use of drugs which may have ototoxic and/or nephrotoxic properties (aminoglycosides, colistin, amphotericin, cyclosporine, cisplatin, furosemide and ethacrynic acid).

Superinfection: 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.

Use in Pregnancy and During Lactation

Category B3.

Although animal reproduction studies have not shown evidence of impairment of fertility or teratogenic effects, teicoplanin should not be used during confirmed or presumed pregnancy or during lactation unless a physician considers that the potential benefits outweigh any possible risk. Information about the excretion of teicoplanin in milk or placental transfer of the drug is not known.

Effects on ability to drive and use machines

The effect of Targocid on the ability of a patient to drive or to use machines is unclear.

ADVERSE EFFECTS

Teicoplanin is generally well tolerated. Adverse reactions rarely require cessation of therapy and are generally mild and transient: serious side effects are rare. The following have been reported, but a causal effect has not been established in all cases:

Local reactions: erythema, local pain, thrombophlebitis, injection site abscess with I.M. injection

Allergic: rash, pruritus, fever, bronchospasm, anaphylactic reactions, rigors, urticaria, angioedema and rare reports of exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme including Stevens-Johnson syndrome.

Gastrointestinal: nausea, vomiting, diarrhoea.

Blood: eosinophilia, leucopenia, neutropenia, thrombocytopenia and rare cases of reversible agranulocytosis.

Liver function: increases in serum transaminases and/or serum alkaline phosphatase.

Renal function: transient elevations of serum creatinine, renal failure.

Central nervous system: dizziness and headache, seizures with intraventricular use.

Auditory: hearing loss, tinnitus, vertigo and other vestibular disorders.

In addition, infusion-related events such as erythema or flushing of the upper body, have been rarely reported. These events occurred without a history of previous teicoplanin exposure and did not recur on re-exposure when the infusion rate was slowed and/or the concentration was decreased. These events were not specific to any concentration or rate of infusion.

INTERACTIONS

Animal studies have shown lack of interaction with diazepam, thiopentone, morphine, neuromuscular blocking agents or halothane.

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, cyclosporin and frusemide.

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

OVERDOSAGE

Treatment of overdosage should be symptomatic. Haemodialysis does not remove the drug. Overdoses of 100 mg/kg/day have been administered in error to neutropenic paediatric patients. Despite high plasma concentrations of teicoplanin, there were no symptoms or laboratory abnormalities.

PHARMACEUTICAL PRECAUTIONS

Store below 25°C.

MEDICINE CLASSIFICATION

Prescription Medicine.

PACKAGE QUANTITIES

Boxes of 1 vial and 1 ampoule.

FURTHER INFORMATION

Reconstituted solutions should be stored under refrigeration (5°C) and solutions stored for longer than 24 hours should be discarded. After reconstituting solution **do not store in a syringe.**

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