NAME OF THE MEDICINE

*Generic name:* Teicoplanin

*Chemical structure:*  
![Teicoplanin molecular structure](image)

Teicoplanin is a factorial mixture of glycopeptides, comprised of at least 80% of the teicoplanin A2 group, not more than 20% of the teicoplanin A3 group, and not more than 5% of other components.

*CAS:* 61036-62-2

DESCRIPTION

Teicoplanin is a glycopeptide antibiotic produced by *Actinoplanes teichomyceticus*. It is presented as a sterile, lyophilised white to light yellow powder for reconstitution with water for injections. It is freely soluble in water and on reconstitution gives a clear solution.

In addition to teicoplanin, each vial of Teicoplanin Sandoz powder for injection also contains 24mg sodium chloride.
PHARMACOLOGY

Pharmacodynamics

Microbiology
Teicoplanin is bactericidal or bacteriostatic on growing populations of susceptible Gram positive organisms, depending on the sensitivity of the organism and antibiotic concentration.

Teicoplanin inhibits the growth of susceptible organisms by interfering with cell wall biosynthesis at a different site from that affected by beta-lactams. Teicoplanin is therefore effective against Staphylococci (including those resistant to methicillin and other beta-lactam antibiotics) and Streptococci.

Some cross resistance is observed between teicoplanin and the glycopeptide vancomycin. Teicoplanin has shown no cross resistance to beta-lactam antibiotics, macrolides, aminoglycosides, tetracycline, rifampicin or chloramphenicol.

Pharmacokinetics

Distribution
In humans, the plasma level profile after intravenous administration 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 3 hours). At the end of the distribution phase, plasma levels and the subsequent time concentration curves, are identical following intramuscular or intravenous administration of a 3mg/kg dose. Following intramuscular injection bioavailability is 100%; average peak plasma levels of 7.1microgram/mL are achieved in 3 to 4 hours following a dose of 3mg/kg.

The elimination half-life is 70 to 100 hours. The apparent volume of distribution at steady state is similar to total body water, i.e. 0.6L/kg.

Approximately 90 to 95% of teicoplanin is bound to plasma proteins. Teicoplanin penetrates into blister exudates and bone where it achieves peak concentrations comparable to those in serum after intramuscular injection. Peak levels in joint fluid are approximately 60% of peak serum concentrations. Teicoplanin penetrates very poorly into cerebrospinal fluid (CSF) and red blood cells.

Metabolism
Metabolic transformation is minor (about 3%); about 80% of administered drug is excreted in the urine over a 16 day collection period.

INDICATIONS

Teicoplanin Sandoz is indicated for the treatment of the following serious infections due to Staphylococci or Streptococci, which cannot be treated satisfactorily with less toxic agents, including beta-lactam antibiotics: bone (osteomyelitis); joints (septic arthritis); blood (non-cardiac bacteraemia, septicaemia).
CONTRAINDICATIONS

Teicoplanin Sandoz is contraindicated in patients with known hypersensitivity to teicoplanin or any excipients associated with this product.

PRECAUTIONS

Use with caution in the following circumstances:

_Hypersensitivity to vancomycin_
Serious, life-threatening hypersensitivity reactions, sometimes fatal, have been reported with teicoplanin (e.g. anaphylactic shock). If an allergic reaction to teicoplanin occurs, treatment should be discontinued immediately and appropriate emergency measures should be initiated.

Teicoplanin Sandoz should be administered with caution in patients known to be hypersensitive to vancomycin since cross hypersensitivity may occur. However, a history of the 'red man syndrome', that can occur with vancomycin, is not a contraindication to Teicoplanin Sandoz.

_Infusion related reactions_
“Red man syndrome” (a complex of symptoms including pruritus, urticarial, erythema, angioneurotic oedema, tachycardia, hypotension, dyspnoea), has been rarely observed (even at the first dose). Stopping or slowing the infusion may result in cessation of these reactions. Infusion related reactions can be limited if the daily dose is not given via bolus injection but infused over a 30-minute period.

_Severe bullous reactions_
Life-threatening or even fatal cutaneous reactions such as Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with the use of Teicoplanin Sandoz. If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesion) are present, Teicoplanin Sandoz treatment should be discontinued immediately.

_Monitoring_
Hearing, haematologic, hepatic and renal toxicities have been reported with Teicoplanin Sandoz.
Periodic haematological studies, and renal and liver function tests are advised during prolonged treatment. Serial renal and auditory function tests should be undertaken in the following circumstances:
- In patients receiving prolonged therapy.
- In patients with renal insufficiency.
- During concurrent and sequential use of other drugs which may have ototoxic or nephrotoxic properties. These include aminoglycosides, amphotericin, cyclosporin, cisplatin, frusemide and ethacrynic acid. However, there are no toxicity data on the concurrent use of these drugs with Teicoplanin Sandoz.
Loading dose regimen
Patients should be carefully monitored for adverse reactions when Teicoplanin Sandoz loading doses of 12mg/kg body weight twice a day are administered. Under this regimen blood creatinine values should be monitored in addition to the recommended periodic haematological examination. Teicoplanin Sandoz should not be administered by intraventricular route, due to the risk of seizure.

Prolonged treatment
Periodic haematological studies, and renal and liver function tests are advised during prolonged treatment.

Renal and auditory function
Serial renal and auditory function tests should be undertaken in the following circumstances: in patients receiving prolonged therapy; in patients with renal insufficiency; during concurrent and sequential use of other drugs which may have ototoxic or nephrotoxic properties. These include aminoglycosides, amphotericin, cyclosporin, cisplatin, frusemide and ethacrynic acid. However there are no toxicity data on the concurrent use of these drugs with teicoplanin.

Superinfection
The use of teicoplanin may result in overgrowth of non-susceptible organisms. Repeated evaluation of the patient's condition is essential. If new infections due to bacteria or fungi appear during treatment, appropriate measures should be taken.

Intrathecal use
The safety and efficacy of teicoplanin by the intrathecal route has not been studied.

Fertility
Animal reproduction studies have not shown evidence of impairment of fertility.

Solutions of Teicoplanin Sandoz and aminoglycosides are incompatible when mixed directly and therefore should not be mixed before injection.

Use in pregnancy (Category B3)
Reproductive studies in rats and rabbits with subcutaneous doses up to 200 mg/kg/day and 15 mg/kg/day respectively did not reveal teratogenic effects. Teicoplanin was associated with an increase in the number of stillborn pups when rats were treated with subcutaneous doses greater than or equal to 100 mg/kg/day. Pup weight was reduced at all doses tested (subcutaneous doses greater than or equal to 10 mg/kg/day).

Teicoplanin Sandoz should not be used during confirmed or presumed pregnancy unless the potential benefits outweigh possible risks.
Use in lactation
It is not known if teicoplanin is excreted in breast milk during lactation. Teicoplanin Sandoz should not be used during lactation unless the potential benefits outweigh possible risks.

Paediatric population
Interaction studies have only been performed in adults.

Carcinogenicity
Long-term studies in animals to evaluate the carcinogenic potential of teicoplanin have not been performed.

Genotoxicity
Teicoplanin was negative in assays evaluating the potential to cause gene mutations, but assays to evaluate the potential to cause chromosome damage have not been performed.

Effects on ability to drive and use machines
Teicoplanin has minor influence on the ability to drive and use machines.

Teicoplanin can cause dizziness and headache. The ability to drive or use machines may be affected. Patients experiencing these undesirable effects should not drive or use machines.

INTERACTIONS WITH OTHER MEDICINES
Due to the potential for increased adverse effects, Teicoplanin Sandoz should be administered with caution in patients receiving concurrent nephrotoxic or ototoxic drugs, such as aminoglycosides, amphotericin B, cyclosporin and frusemide and ethacrynic acid.

ADVERSE EFFECTS
In an open clinical trial involving patients with bone or joint infections, teicoplanin was associated with adverse reactions in 32% of the patients. However, treatment was discontinued because of adverse reactions in 17% of patients only. A clear cause-effect relationship was not established in these patients. The most frequent adverse reactions were fever, rashes, nausea, vomiting, rigors, pruritus and diarrhoea.

The following adverse effects have been reported:

Local reactions
Pain, phlebitis, redness, abscess, thrombophlebitis.

Hypersensitivity
Skin rash, erythema, pruritus, rigor, fever, bronchospasm, anaphylaxis, urticaria, angioedema, DRESS syndrome (drug reaction with eosinophilia and systemic
symptoms), toxic epidermal necrolysis, erythema multiforme including Stevens-Johnson syndrome and rare reports of exfoliative dermatitis.

**Hepatic**
Increased transaminases and/or alkaline phosphatase.

**Haematological**
Eosinophilia, thrombocytopenia, leucopenia, neutropenia and rare cases of reversible agranulocytosis.

**Renal**
Rise in serum creatinine, blood urea, acute renal failure.

**Gastrointestinal**
Nausea or vomiting, diarrhoea.

**Nervous system**
Dizziness, headache, seizures with intraventricular use.

**Auditory**
Hearing loss, tinnitus, vertigo, other vestibular disorders.

**Infections and infestations**
Superinfection (overgrowth of non-susceptible organisms)

**Infusion related events**
Infusion related events, such as red man syndrome (a complex of symptoms including pruritus, urticaria, erythema, angioneurotic oedema, tachycardia, hypotension, dyspnoea), 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.

**DOSAGE AND ADMINISTRATION**

The reconstituted Teicoplanin Sandoz injection should be administered intravenously or intramuscularly. Intravenous dosing may be by slow injection over 5 minutes or by infusion over 30 minutes.

Maintenance dosage is once daily; however, initially a loading dose regimen of three doses at 12 hourly intervals is recommended for rapid attainment of steady state plasma levels.

An intramuscular injection of Teicoplanin Sandoz should not exceed 3mL (400mg) at a single site.

**Adults**
*Septicaemia/bacteraemia, acute or chronic osteomyelitis*
Treatment should be started with 6 to 12mg/kg by the intravenous route every 12 hours for 3 doses, then the daily maintenance dose should be 6mg/kg.

Septic arthritis
Patients with septic arthritis should receive 12mg/kg intravenously every 12 hours for 3 doses then a daily maintenance dose of 12mg/kg.

Duration of treatment
While the total duration of therapy is determined by the type and severity of infection and by the clinical response of the patient, the following periods are often appropriate. Uncomplicated bacteraemia: two to four weeks; septic arthritis or osteomyelitis: three to six weeks.

Use in the elderly
As for adults. If renal function is impaired, the instructions for impaired renal function should be followed.

Use in patients with renal impairment
Reduction of dosage in patients with impaired renal function is not required until the fourth day of teicoplanin treatment. Trough plasma teicoplanin concentrations should be monitored periodically after the first week of therapy and the dosage adjusted to prevent trough concentrations exceeding 30microgram/mL in patients with septic arthritis or 15microgram/mL in other cases. From the fourth day of treatment, dose adjustments should be made as follows.

Mild renal insufficiency
If the creatinine clearance is between 40 and 60mL/minute, the dose should be halved, either by administering the initial unit dose every two days, or by administering half of this dose once a day.

Severe renal insufficiency
If the creatinine clearance is less than 40mL/minute and in haemodialysed patients, the dose should be one-third of the normal dose. This is achieved 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.

Preparation of Teicoplanin Sandoz injection
The powder should be reconstituted strictly in accordance with the instructions that follow. Errors in reconstitution may result in the formation of a stable foam and delivery of smaller doses.

Withdraw 3.0mL from the accompanying water for injections ampoule and add it slowly down the side wall of the vial of Teicoplanin Sandoz. 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.
To reduce microbiological hazard, use as soon as practicable after reconstitution/dilution. If storage is necessary, hold at 2°C-8°C for not more than 24 hours. When storing the reconstituted solution, do not store it in a syringe. The reconstituted solution contains teicoplanin 400mg/3.0mL.

Dilution of reconstituted solution

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

Sodium chloride solution 0.9% and Hartmann’s solution: if necessary, diluted solutions may be stored between 2°C and 8°C for up to 24 hours. Solutions left for longer than 24 hours should be discarded.

Glucose 5% solution, sodium chloride 0.18% and glucose 4% solution: solutions containing these diluents can be stored between 2°C and 8°C and should be used within 24 hours; solutions kept longer than 24 hours should be discarded.

Ringer’s solution: the diluted solution can be stored between 2°C and 8°C for up to 24 hours only.

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

Compatibility

Solutions of Teicoplanin Sandoz and aminoglycosides are incompatible when mixed directly and therefore should not be mixed before injection.

Teicoplanin Sandoz injection is for single use in one patient only. Discard any residue.

OVERDOSAGE

Contact the Poisons Information Centre on 13 11 26 for advice on management of overdose.

Cases of excessive doses administered in error to paediatric patients have been reported. In one report, agitation occurred in a 29 day-old newborn given 400mg I.V. (95mg/kg). In the other cases, there were no symptoms or laboratory abnormalities associated with teicoplanin.

Treatment

In case of overdose treatment should be supportive and symptomatic. Teicoplanin is not removed by haemodialysis or peritoneal dialysis.
PRESENTATION AND STORAGE CONDITIONS

Teicoplanin Sandoz 400mg injection – 25mL clear glass vial with rubber stopper and flip-off aluminium crimp, containing a white to pale yellow, sterile lyophilised powder, equivalent to 400mg teicoplanin. Each pack also contains an accompanying diluent containing 3.2mL sterile water for injections in a glass ampoule.

Available in a single pack containing one vial of teicoplanin powder for injection and one ampoule of water for injections diluent.

Store below 25°C.

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

Schedule 4 – Prescription Only Medicine

Date of first inclusion in the Australian Register of Therapeutic Goods (the ARTG): 11/08/2010

Date of most recent amendment: 15/05/2017