AUSTRALIAN PRODUCT INFORMATION – TARGOCID (TEICOPLANIN)

1 NAME OF THE MEDICINE

Teicoplanin

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains lyophilised teicoplanin 460 mg* and sodium chloride 24.8 mg with an accompanying ampoule containing Water for injections 3.14 mL*.

* An overage is included to allow withdrawal of the correct dose.

The reconstituted solution contains:

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

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Powder for injection.

Sterile, pyrogen-free ivory white powder for reconstitution with water for injections. It is freely soluble in water and on reconstitution gives a clear solution.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Targocid 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 β-lactam antibiotics:

Bone - osteomyelitis

Joints - septic arthritis

Blood - non-cardiac bacteraemia, septicaemia

4.2 DOSE AND METHOD OF ADMINISTRATION

Note: Special instructions apply for reconstitution. See below.

The reconstituted Targocid 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.

The dose is to be adjusted on bodyweight whatever the weight of the patient.

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

Targocid should not be administered by intraventricular route, due to risk of seizure.

Adults:

Septicaemia/bacteraemia, acute or chronic osteomyelitis:

Treatment should be started with 6-12 mg/kg by the I.V. route every 12 hours for 3 doses then the daily maintenance dose should be 6 mg/kg.

Septic arthritis

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

Elderly Patients:

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

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 2-4 weeks

Septic arthritis or osteomyelitis 3-6 weeks

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.

From the fourth day of treatment:

in mild renal insufficiency:

creatinine clearance between 40 and 60 mL/min, Targocid dose should be halved, either by administering the initial unit 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, Targocid 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.**

Method of administration

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.

Satisfactory potency of the reconstituted injection is retained for 48 hours at 25°C and for 7 days at 4°C. As a matter of good pharmaceutical practice, it is recommended that reconstituted solutions be stored under refrigeration (4°C) and solutions stored longer than 24 hours be discarded. When storing reconstituted solution **do not store in a syringe**.

The reconstituted solution contains:

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

Dilution of reconstituted solution:

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

If necessary, solutions with the above diluents may be stored at 4°C for up to 7 days. Solutions left at room temperature for longer than 24 hours should be discarded.

5% glucose solution

0.18% Sodium Chloride and 4% glucose solution

Solutions containing the above diluents (which contain glucose) should be stored at 4°C and should be used within 24 hours; solutions kept longer than 24 hours should be discarded.

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

4.3 CONTRAINDICATIONS

Targocid is contraindicated in patients with known hypersensitivity to the drug.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypersensitivity reactions and anaphylaxis

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

Hypersensitivity to vancomycin

Targocid should be administered with caution in patients known to be hypersensitive to vancomycin since cross-hypersensitivity reactions, including fatal anaphylactic shock, may occur. However, a history of the "Red Man Syndrome" that can occur with vancomycin is not a contraindication to Targocid.

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 cutaneous adverse reactions (SCARS)

Life-threatening and fatal cutaneous reactions, including Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of Targocid. Acute generalised exanthematous pustulosis (AGEP) has also been reported. Patients should be informed about the signs and symptoms of serious skin manifestations and monitored closely. If symptoms or signs of SJS, or TEN, DRESS or AGEP (eg progressive skin rash often with blisters or mucosal lesion or pustular rash, or any other sign of skin hypersensitivity) are present, Targocid treatment should be discontinued immediately.

Nephrotoxicity

Nephrotoxicity and renal failure have been reported in patients treated with Targocid (see Section 4.8 Adverse effects (Undesirable Effects)). Patients with renal insufficiency, or with risk factors for development of nephrotoxicity, patients receiving the high loading dose regimen of teicoplanin, and/or patients receiving Targocid in conjunction with or sequentially with other medicinal products with known nephrotoxic potential (e.g. aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide and ethacrynic acid) should be carefully monitored.

Ototoxicity

Hearing impairment has been reported with use of Targocid (see Section 4.8 Adverse effects (undesirable effects)). Periodic auditory function tests are advised especially in cases of prolonged treatment, patients with renal insufficiency and/or patients receiving teicoplanin in conjunction with or sequentially with other medicinal products with known nephrotoxic and/or neurotoxic/ototoxic potential (e.g. aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide and ethacrynic acid). These patients should be carefully monitored and the benefit of teicoplanin evaluated if hearing deteriorates.

Hepatic toxicity

Hepatic toxicities have been reported with use of Targocid (see Section 4.8 Adverse effects (undesirable effects)). Periodic liver function tests are recommended for prolonged treatment.

Haematologic toxicity

Haematologic toxicities have been reported with the use of Targocid (see Section 4.8 Adverse effects (undesirable effects)). Periodic haematological studies are advised during prolonged treatment.

Loading dose regimen

Safety data show increased rates of nephrotoxicity when high Targocid loading doses such as 12 mg/kg body weight twice a day are administered (see Section 4.8 Adverse Effects (Undesirable Effects)). For patients given high loading dose regimens, blood creatinine values should be closely monitored for nephrotoxicity in addition to haematological examinations.

Intraventricular use

Targocid should not be administered by intraventricular route, due to the risk of seizure.

Superinfection

The use of Targocid 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.

The safety and efficacy of Targocid by the intrathecal route has not been studied.

Use in hepatic impairment

No data available.

Use in renal impairment

See Section 4.2 Dose and method of administration - Patients with Renal Impairment and Section 4.4 Special warnings and precautions for use – Loading dose regimen, Ototoxicity and Nephrotoxicity

Use in the elderly

See Section 4.2 Dose and method of administration - Elderly Patients

Paediatric use

No data available.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy - 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 ≥ 100 mg/kg/day. Pup weight was reduced at all doses tested (SC doses ≥ 10 mg/kg/day). It is not known if teicoplanin is excreted in breast milk during lactation.

Targocid should not be used during confirmed or presumed pregnancy unless the potential benefits outweigh possible risks.

Use in lactation

Targocid should not be used during lactation unless the potential benefits outweigh possible risks.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Targocid can cause dizziness and headache. The ability to drive or operate machinery may be affected. Patients experiencing these undesirable effects should not drive or operate machinery.

4.8 ADVERSE EFFECTS (UNDESIRABLE 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, Acute generalised exanthematous pustulosis (see Section 4.4 Special Warnings and Precautions for Use – Severe cutaneous adverse reactions (SCARS))

Hepatic: increased transaminases and/or alkaline phosphatase

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

Renal and urinary disorders including: rise in serum creatinine, blood urea, renal failure. Based on literature reports, the estimated rate of nephrotoxicity in patients receiving low loading dose regimen of average 6 mg/kg twice a day, followed by a maintenance dose of average 6 mg/kg once daily, is around 2%. In an observational post-authorisation safety study which enrolled 300 patients with a mean age of 63 years (treated for bone and joint infection, endocarditis or other severe infections) who received the high loading dose regimen of 12 mg/kg twice a day (receiving 5 loading doses as a median) followed by a maintenance dose of 12 mg/kg once daily, the observed rate of confirmed nephrotoxicity was 11.0% (95% CI = [7.4%; 15.5%]) over the first 10 days. The cumulative rate of nephrotoxicity from the start of treatment up to 60 days after the last dose was 20.6% (95% CI = [16.0%; 25.8%]). In patients receiving more than 5 high loading doses of 12 mg/kg twice a day, followed by a maintenance dose of 12 mg/kg once daily, the observed cumulative rate of nephrotoxicity from the start of treatment up to 60 days after the last administration was 27% (95% CI = [20.7%; 35.3%]).

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).

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 Targocid 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.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

In an observational post-authorisation safety study, patients receiving more than 5 high loading doses of 12 mg/kg twice a day, followed by a maintenance dose of 12 mg/kg once daily, had an observed cumulative rate of nephrotoxicity from the start of treatment up to 60 days after the last administration of 27% (95% CI = [20.7%; 35.3%]).

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 400 mg I.V. (95 mg/kg). In the other cases, there were no symptoms or laboratory abnormalities associated with teicoplanin.

Treatment of overdosage should be symptomatic. Teicoplanin is not removed by haemodialysis or peritoneal dialysis.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antiinfectives for systemic use, Glycopeptide antibacterials, ATC code: J01XA02

Mechanism of action

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 β-lactams. Teicoplanin is therefore effective against staphylococci (including those resistant to methicillin and other β-lactam antibiotics) and streptococci.

Some cross-resistance is observed between teicoplanin and the glycopeptide vancomycin.

Teicoplanin has shown no cross-resistance to β-lactam antibiotics, macrolides, aminoglycosides, tetracycline, rifampicin or chloramphenicol.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Following intramuscular injection bioavailability is 100%; average peak plasma levels of 7.1 µg/mL are achieved in 3-4 hours following a dose of 3 mg/kg.

Distribution

In man, 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 3 mg/kg dose.

The apparent volume of distribution at steady state is similar to total body water, i.e. 0.6 L/kg.

Approximately 90-95 % 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%.

Excretion

The elimination half-life is 70-100 hours. About 80% of administered drug is excreted in the urine over a 16 day collection period.

5.3 PRECLINICAL SAFETY DATA

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.

Carcinogenicity

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

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Vial

Sodium chloride

Ampoule

Water for injections

6.2 INCOMPATIBILITIES

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

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

See Section 4.2 Dose and method of administration, for the shelf life of the reconstituted and diluted solutions.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C

See Section 4.2 Dose and method of administration, for the shelf life of the reconstituted and diluted solutions.

6.5 NATURE AND CONTENTS OF CONTAINER

One 25 mL glass vial containing teicoplanin powder for injection.

One ampoule containing diluent.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Teicoplanin is a glycopeptide-antibiotic produced by *Actinoplanes teichomyceticus*.

Chemical structure

No data available.

CAS number

61036-62-2

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription Only Medicine (Schedule 4)

8 SPONSOR

sanofi-aventis australia pty ltd

International Tower 3, Level 23

300 Barangaroo Avenue

Sydney NSW 2000

Freecall: 1800 818 806

Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

19 October 1994

10 DATE OF REVISION

7 May 2026

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
8	Updated sponsor details