NEW ZEALAND DATA SHEET
TEICOPLANIN MEDSURGE POWDER FOR INJECTION

1 PRODUCT NAME

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

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 400mg teicoplanin equivalent to not less than 400,000 IU.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

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

The final solution is isotonic with plasma and has a pH of 7.2 -7.8. See section 6.6.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Teicoplanin is indicated in adults and in children from 2 months 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

Joint - septic arthritis

Blood - non-cardiac bacteraemia, septicaemia

4.2 DOSE AND METHOD OF ADMINISTRATION

Teicoplanin Medsurge 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. For instructions on reconstitution of the medicine before administration see Section 6.6.

Dosage is usually once daily following an initial loading dose which is administered as three 12hourly doses on the first day of therapy. The dose is to be adjusted on body weight whatever

the weight of the patient.

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.

Teicoplanin 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 mg/kg by the I.V. route every 12 hours for 3 doses then the daily maintenance dose should be 6 mg/kg once daily. Higher doses may be required in some clinical situations.

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.

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 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 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 (creatine clearance between 40 and 60 mL/min)

From the fourth day of treatment the Teicoplanin 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 Teicoplanin® 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).

4.3 CONTRAINDICATIONS

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Hypersensitivity reactions and anaphylaxis

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.

Hypersensitivity to vancomycin

Teicoplanin must be administered with caution in patients of known hypersensitivity to vancomycin since cross hypersensitivity reactions, including fatal anaphylactic shock, may occur.

However, a history of 'Red Man Syndrome' with vancomycin is not a contraindication to teicoplanin.

Infusion related reactions

“Red man syndrome” (a complex of symptoms including pruritus, urticaria, 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 teicoplanin. 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, 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, teicoplanin treatment should be discontinued immediately.

Nephrotoxicity

Nephrotoxicity and renal failure have been reported in patients treated with Teicoplanin (see Section 4.8). 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 teicoplanin 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 Teicoplanin (see Section 4.8). 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 Teicoplanin (see Section 4.8). Periodic liver function tests are recommended for prolonged treatment.

Haematologic toxicity

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

Loading dose regimen

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

Intraventricular use

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

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.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

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, ciclosporin and furosemide (frusemide).

Solutions of teicoplanin and aminoglycosides are incompatible and should not be mixed before injection. See section 6.2.

4.6 FERTILITY, PREGNANCY AND 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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Teicoplanin 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 UNDESIRABLE 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:

Infections and Infestations: superinfection (overgrowth of non-susceptible organisms)

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

Not known: **pancytopenia**

Immune system disorders: rash, pruritus, fever, bronchospasm, anaphylactic reactions, anaphylactic shock, rigors, urticaria, angioedema and rare reports of exfoliative dermatitis, DRESS syndrome (drug reaction with eosinophilia and systemic symptoms), toxic epidermal necrolysis, erythema multiforme including Stevens-Johnson syndrome, acute generalised exanthematous pustulosis (see Section 4.4)

Nervous system disorders: dizziness and headache, seizures with intraventricular use.

Ear and labyrinth disorders: hearing loss/deafness, tinnitus, vertigo and other vestibular disorders.

Gastrointestinal disorders: nausea, vomiting, diarrhoea.

Hepatobiliary disorders: increases in serum transaminases and/or serum alkaline phosphatase.

Renal and urinary disorders: transient elevations of serum creatinine, 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%]).

General disorders and administration site conditions: erythema, local pain, thrombophlebitis, injection site abscess with I.M. injection

In addition, infusion-related events called “red man syndrome” such as erythema or flushing of the upper body, have been rarely reported (see section 4.4). 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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

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

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.

Contact the Poisons Information Centre on 0800 POISON or 0800 764 766 for advice on management of overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Glycopeptide Antibacterials, ATC code: J01XA 02

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.

Mechanism of action

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.

Mechanism of resistance

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 crossresistance 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.

5.2 PHARMACOKINETIC PROPERTIES

Teicoplanin is administered by parenteral injection. The bioavailability of a single 3-6 mg/kg intramuscular injection is over 90%.

Absorption

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.

Distribution

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.

Biotransformation

Metabolic transformation is minor, about 3%;

Elimination

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

5.3 PRECLINICAL SAFETY DATA

No further relevant information other than that which is included in the other sections of the Data Sheet.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Vial
Sodium chloride
Sodium hydroxide (for pH adjustment)

Ampoule
Water for Injection

6.2 INCOMPATIBILITIES

Solutions of teicoplanin and aminoglycosides are incompatible and should not be mixed before injection. See section 4.5

This medicine must not be mixed with other medicines except those mentioned in Section 6.6.

6.3 SHELF LIFE

Shelf life of powder as packaged for sale: 24 months

Reconstituted solutions should be stored at 2-8°C (refrigerate, do not freeze) and solutions stored for longer than 24 hours should be discarded. After reconstituting solution **do not store in a syringe.**

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store at or below 30°C.

For storage conditions after reconstitution of the medicine see Section 6.3.

6.5 NATURE AND CONTENTS OF CONTAINER

Primary Packaging:

Glass vial (Teicoplanin Medsurge powder for injection)

Glass ampoule (diluent)

Pack sizes:

1 x 400mg powder vial and diluent water for injection

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

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 Teicoplanin Medsurge. 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.

7 MEDICINE SCHEDULE

Prescription Medicine.

8 SPONSOR

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27 May 2024

10 DATE OF REVISION OF THE TEXT

Not applicable

SUMMARY TABLE OF CHANGES

New data sheet