APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

DYNA TEICOPLANIN 200 mg (Lyophilised sterile powder for injection)

DYNA TEICOPLANIN 400 mg (Lyophilised sterile powder for injection)

DYNA TEICOPLANIN Solvent (Water for injection)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

DYNA TEICOPLANIN 200 mg contains 200 mg teicoplanin equivalent to 200 000 IU.

DYNA TEICOPLANIN 400 mg contains 400 mg teicoplanin equivalent to 400 000 IU.

DYNA TEICOPLANIN SOLVENT contains 3,2 ml water for injection.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection/infusion or oral solution.

Reconstitute before use.

Lyophilised product: White-yellow freeze-dried powder.

Solvent: Clear, colourless, odourless liquid.

Reconstituted solution: Clear, yellowish solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

DYNA TEICOPLANIN is indicated for the treatment of a wide variety of serious Gram-positive infections, including those Gram-positive infections which cannot be treated with other antimicrobial medicines.

DYNA TEICOPLANIN is indicated for the treatment of the following infections caused by teicoplanin sensitive bacteria:

Blood infections: Septicaemia due to *Staphylococcus aureus, Listeria monocytogenes, Clostridium difficile*, coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci and enterococci.

Respiratory infections caused by methicillin-resistant *Staphylococcus aureus*, streptococci and Gram-positive anaerobes including peptococci.

Cardiac infections: Endocarditis due to *Staphylococcus aureus, Corynebacterium jeikeium, Listeria monocytogene*s, coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci and enterococci.

Skin and soft tissue infections caused by *Staphylococcus aureus*, coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci, micrococci and Gram-positive anaerobes including peptococci.

Urinary tract infections caused by enterococci.

Bone infections: Osteomyelitis due to *staphylococcus aureus*, coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci, enterococci and Gram-positive anaerobes.

Peritonitis associated with chronic ambulatory peritoneal dialysis (CAPD) due to *Staphylococcus aureus* and enterococci.

DYNA TEICOPLANIN may be used as prophylaxis in high risk patients unable to receive penicillin in orthopaedic and vascular surgery at risk of Gram-positive infection.

DYNA TEICOPLANIN 200 may be used orally for the treatment of antibiotic-associated diarrhoea, including pseudomembranous colitis, caused by *Clostridium difficile*.

4.2 Posology and method of administration

The majority of patients, with infections caused by organisms sensitive to DYNA TEICOPLANIN, show a therapeutic response within 2 to 3 days. The duration of therapy is determined by the type and severity of the infection, and the clinical response of the

patient. In endocarditis and osteomyelitis, treatment for three weeks or longer is recommended.

Determination of DYNA TEICOPLANIN serum concentrations may optimise therapy. In severe infections, trough serum concentrations should not be less than 10 mg per litre. Peak concentrations measured one hour after a 400 mg intravenous dose are usually in the range of 20 to 50 mg per litre; peak serum concentrations of up to 250 mg per litre have been reported after intravenous doses of 25 mg/kg.

No relationship has yet been established between plasma concentration and toxicity.

Adults and elderly patients with normal renal function:

Moderate infections:

Skin and soft tissue infections, urinary tract infections, lower respiratory tract infections.

Loading dose: One single IV injection of 400 mg on the first day.

Maintenance dose: A single IV or IM injection of 200 mg daily.

Severe infections:

Joint and bone infections, septicaemia, endocarditis.

Loading dose: 400 mg IV injection every 12 hours for the first three doses.

Maintenance dose: A single IV or IM injection of 400 mg daily.

In some clinical situations, such as infected, severely burned patients or *Staphylococcus aureus* endocarditis, unit maintenance doses of up to 12 mg/kg may be required.

Note:

Standard doses of 200 mg and 400 mg are equivalent to mean doses of 3 mg/kg and 6 mg/kg respectively. In overweight patients it is recommended that the dose be adapted to the weight of the patient as follows: moderate infections 3 mg/kg; severe infections 6 mg/kg.

Prophylaxis in orthopaedic and vascular surgery at risk of Gram-positive infection:

400 mg intravenously as a single dose at induction of anaesthesia.

DYNA TEICOPLANIN 200 mg: Oral treatment of antibiotic-associated diarrhoea, including pseudomembranous colitis, caused by *Clostridium difficile*:

After reconstitution, the contents of the vial may be administered as an oral solution. The DYNA TEICOPLANIN solution is tasteless.

Dosage: 200 mg orally twice a day for 10 days.

Monitoring the plasma concentrations:

If checks are carried out on the DYNA TEICOPLANIN serum level in patients with severe infections, then the minimum serum level should not be below 10 mg per litre (measured just before the following dose).

Special populations

Adults and elderly patients with renal insufficiency:

For patients with impaired renal function, reduction of the dose is not required until the fourth day of treatment.

From the fourth day of treatment:

In mild renal insufficiency:

Creatinine clearance between 40 mL and 60 mL per minute: The dose of DYNA TEICOPLANIN should be halved; either by administering the initial unit dose every two days or by administering half the initial unit dose once a day.

In severe renal insufficiency:

Creatinine clearance less than 40 mL per minute and in haemodialysed patients: The dose of DYNA TEICOPLANIN should be one third of the normal dose; either by administering the initial unit dose every third day, or by administering one third of the unit dose once a day.

DYNA TEICOPLANIN is not removed by dialysis.

Unless measurement of the serum concentrations can be guaranteed to accompany the therapy, patients with a creatinine clearance lower than or equal to 20 mL per minute must be excluded from therapy with DYNA TEICOPLANIN.

In continuous ambulatory peritoneal dialysis:

After a single intravenous loading dose of 400 mg, if the patient is febrile, the recommended dosage is 20 mg per litre, per bag, in the first week; 20 mg per litre in alternate bags in the second week; and 20 mg per litre in the overnight dwell bag only, in the third week.

Do not keep mixed solutions for longer than 24 hours.

Paediatric population

DYNA TEICOPLANIN can be used to treat Gram-positive infections in children and infants older than three years.

For severe infections and neutropenic patients, the recommended dose is 10 mg/kg every 12 hours, by intravenous injection, for the first three doses. Thereafter a dose of 10 mg/kg should be administered by either intravenous or intramuscular injection as a single dose each day.

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

Method of administration

The reconstituted DYNA TEICOPLANIN injection is given intravenously as a bolus or by 30 minute infusion or by intramuscular injection. A once daily dosage regime is usually followed

but, in cases of severe infection, a second injection should be administered on the first day in order to reach the required serum concentrations more rapidly.

Administration:

The entire contents (3,2 mL water for injection) of DYNA TEICOPLANIN SOLVENT in the accompanying ampoule is used to reconstitute the lyophilised teicoplanin to produce the ready-to-use solution by slowly injecting the solvent into the vial with the dry substance. The vial is then rolled, not shaken, until the lyophilised powder is completely dissolved. Care must be taken to avoid the formation of foam. The solution must be left to stand for approximately 15 minutes if foam develops during the preparation of the injection solution, to allow for the foam to disappear.

For intravenous injection, DYNA TEICOPLANIN is injected either directly intravenously; or into the proximal end of a drip line after clamping the line. DYNA TEICOPLANIN can be injected as a bolus within one minute. DYNA TEICOPLANIN can be administered by infusion, it is dissolved in 20 mL to 50 mL of infusion solution and administered over 20 to 30 minutes by the infusion route. DYNA TEICOPLANIN can also be injected intramuscularly.

For the purposes of infusion, the following infusion solutions are suitable for mixing with DYNA TEICOPLANIN:

- 0,9 % sodium chloride solution (saline)
- Ringer's Lactate solution

- Hartman solution
- 5 % glucose solution
- 0,18 % sodium chloride and 4 % dextrose solution.

Reconstituted solutions of DYNA TEICOPLANIN should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not be longer than 24 hours at 2 – 8 °C, unless reconstitution/dilution has taken place under controlled and validated aseptic conditions.

Incompatibilities:

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

Duration of DYNA TEICOPLANIN treatment:

With infections caused by DYNA TEICOPLANIN -sensitive pathogens, a therapeutic result is shown in the majority of cases within 48 to 72 hours.

The duration of treatment with DYNA TEICOPLANIN depends on the severity of the infection as well as upon the bacteriological and clinical progress. DYNA TEICOPLANIN treatment should be continued for at least three days after the disappearance of clinical symptoms and after the patient has become afebrile. In cases of endocarditis or osteomyelitis at least three weeks of DYNA TEICOPLANIN treatment is recommended. DYNA TEICOPLANIN should not be administered for longer than four months.

4.3 Contraindications

- Hypersensitivity to teicoplanin or to any of the ingredients of DYNA TEICOPLANIN (see section 6.1).
- Safety and efficacy have not been established in children less than three years of age.
- Pregnancy and lactation (see section 4.6).
- DYNA TEICOPLANIN must not be injected into the subarachnoid space (see section 4.4).

4.4 Special warnings and precautions for use

- DYNA TEICOPLANIN should be administered with caution in patients known to be hypersensitive to vancomycin since cross hypersensitivity including fatal anaphylactic shock, may occur.
- Infusion related reactions such as red man syndrome (a complex of symptoms including pruritus, urticaria, erythema, angioedema, tachycardia, hypotension, dyspnoea) has been observed with DYNA TEICOPLANIN. 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.
- Life-threatening or even fatal cutaneous reactions Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with the use of DYNA TEICOPLANIN. If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present DYNA TEICOPLANIN,

treatment should be discontinued immediately.

- Since data on safety are limited on loading dose regimen, patients should be carefully monitored for adverse reactions when DYNA TEICOPLANIN doses of 12 mg/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. DYNA TEICOPLANIN should not be administered by intraventricular route, due to the risk of seizure.
- Thrombocytopenia has been reported especially with higher than recommended doses. Periodic haematological examinations are recommended during treatment, including complete cell blood count.
- Renal failure has been reported with DYNA TEICOPLANIN. Patients with renal insufficiency should be carefully monitored by carrying out regular checks on serum level as well as on kidney and auditory function. Dosage adjustments are required in renal impairment.
- DYNA TEICOPLANIN is not recommended in patients with a creatinine clearance lower than or equal to 20 mL per minute.
- Liver function tests are advised during treatment with DYNA TEICOPLANIN.
- Ototoxicity (deafness and tinnitus) has been reported in patients treated with DYNA TEICOPLANIN (see section 4.8). Patients who develop signs and symptoms of impaired hearing or disorders of the inner ear during treatment with DYNA TEICOPLANIN should be carefully evaluated and monitored, especially in case of prolonged treatment and in patients with renal insufficiency.
- The use of DYNA TEICOPLANIN, especially if prolonged, may result in overgrowth

of non-susceptible organisms. Continued evaluation of the patient's condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

In general, periodic blood counts, and renal, liver and auditory function tests are advised in the following cases:

- prolonged treatment in patients with pre-existing renal insufficiency
- in patients receiving other neurotoxic and/or nephrotoxic medicines such as the aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide and ethacrynic acid. However, there is no evidence of synergistic toxicity when DYNA TEICOPLANIN is used in combination with the above medicines
- DYNA TEICOPLANIN may not be administered into the subarachnoid space (see section 4.3).

Spectrum of antibacterial activity

Teicoplanin has a limited spectrum of antibacterial activity (Gram-positive). It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a high suspicion that the most likely pathogen(s) would be suitable for treatment with teicoplanin.

The rational use of teicoplanin should take into account the bacterial spectrum of activity, the safety profile and the suitability of standard antibacterial therapy to treat the individual patient. On this basis it is expected that in most instances DYNA TEICOPLANIN will be

used to treat severe infections in patients for whom standard antibacterial activity is considered to be unsuitable.

4.5 Interaction with other medicines and other forms of interaction

- DYNA TEICOPLANIN and aminoglycoside solutions are incompatible and must not be mixed for injection; however, they are compatible in dialysis fluid and may be freely used in the treatment of CAPD-related peritonitis.
- Concomitant or sequential use of DYNA TEICOPLANIN with medicines known for their ototoxic and/or nephrotoxic properties including aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide and ethacrynic acid, should be used with caution. The required patient monitoring is to be followed (see section 4.4).
- There is no evidence of synergistic toxicity in combinations with DYNA TEICOPLANIN.
- Studies indicate no evidence of adverse interaction in patients administered DYNA TEICOPLANIN who are already receiving various medications, including other antibiotics, antihypertensives, anaesthetics, cardiac medicinal products and antidiabetic medicines.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of DYNA TEICOPLANIN has not been established and it should not be used during pregnancy (see section 4.3).

Breastfeeding

It is not known whether DYNA TEICOPLANIN passes into breast milk.

The safety of DYNA TEICOPLANIN has not been established and it should not be used during lactation (see section 4.3).

Fertility

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

4.7 Effects on ability to drive and use machines

DYNA TEICOPLANIN has minor influence on the ability to drive and use machines.

DYNA TEICOPLANIN can lead to dizziness and patients should be aware how they react to DYNA TEICOPLANIN and exercise caution before driving, operating hazardous machinery or performing hazardous tasks.

4.8 Undesirable effects

Tabulated summary of adverse reactions

System Organ Class	Frequency	Side effects
Infections and Infestations	Less frequent	Abscess, superinfection (overgrowth of non-susceptible organisms)
Blood and lymphatic system disorders	Less frequent	Eosinophilia, thrombocytopenia, neutropenia, leucopoenia, agranulocytosis
Immune system disorders	Frequency unknown	Anaphylactic reactions and anaphylactic shock, angioedema, hypersensitivity reactions
Nervous system disorders	Less frequent Frequency unknown	Headache, dizziness Seizures

Ear and labyrinth disorders	Frequency unknown	Loss of hearing, tinnitus or vestibular disturbances
Vascular disorders	Less frequent Frequency unknown	Phlebitis Thrombophlebitis
Respiratory, thoracic and mediastinal disorders	Less frequent	Bronchospasm
Gastrointestinal disorders	Less frequent	Nausea, vomiting, diarrhoea
Hepatobiliary disorders	Frequency unknown	Rise in the transaminase and/or alkaline phosphatase
Skin and subcutaneous tissue disorders	Frequent Less frequent Frequency unknown	Rash, erythema, pruritus, exanthema Red man syndrome (e.g. flushing of the upper part of the body), toxic epidermal necrolysis Stevens-Johnson syndrome, erythema multiforme, exfoliative dermatitis, urticaria, DRESS syndrome
Renal and urinary disorders	Less frequent Frequency unknown	Renal impairment Renal failure, increased blood creatinine
General disorders and administrative site conditions	Frequent Less frequent	Pain at the injection site, pyrexia Chills (rigors), fever

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 to SAHPRA via the

online service for adverse drug reaction reporting by following the link:

https://www.sahpra.org.za/Publications/Index/8.

An email can be sent directly to the company,

pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

4.9 Overdose

Signs and symptoms:

Available information on two children with agranulocytosis to whom several doses of 100 mg per kg body weight per day were administered in error, shows that despite very high serum concentrations of 300 mg per litre, no intoxication phenomena appeared.

Management of overdose:

General symptomatic and supportive measures are recommended for the management of an overdose.

DYNA TEICOPLANIN is not removed by haemodialysis or peritoneal dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Glycopeptide Antibacterials

ATC code: J01XA 02

Pharmacological classification: A.20.1.1 Broad and medium spectrum antibiotics.

Mechanism of action

Teicoplanin is a bactericidal, glycopeptide antibiotic, active *in vitro* against both aerobic and anaerobic Gram-positive bacteria. Teicoplanin is produced by fermentation and obtained from cultures of *Actinoplanes teicomyceticus*. Teicoplanin is an inhibitor of cell wall synthesis.

In vitro sensitivity does not necessarily imply clinical sensitivity.

Species that are usually resistant include the following:

Nocardia asteroides, Lactobacillus spp., *Leuconostoc* spp. and all Gram-negative bacteria.

Teicoplanin in combination with aminoglycosides has shown bactericidal synergy *in vitro* against group D streptococci and staphylococci. *In vitro* combinations of teicoplanin with rifampicin or fluorinated quinolones show primarily additive effects and sometimes synergy.

Teicoplanin does not show cross-resistance with other classes of antibiotics, but cross resistance with vancomycin has occurred in staphylococci and enterococci.

5.2 Pharmacokinetic properties

Absorption:

Teicoplanin is poorly absorbed from the gastrointestinal tract. After a 400 mg intravenous dose, peak plasma concentrations 1 hour later are reported to be in the range of 20 to 50 micrograms/mL.

Distribution:

The bioavailability of intramuscular teicoplanin injection is approximately 90 %, with peak concentrations being reached between 2 and 4 hours. Teicoplanin is highly bound to by plasma proteins (90-95 %). Teicoplanin does not penetrate through the blood-brain barrier.

Elimination:

Teicoplanin is renally excreted unchanged by glomerular filtration and its half-life is increased in patients with renal impairment.

5.3 Preclinical safety data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Lyophilised product: Store at or below 25 °C. Protect from moisture.

Reconstituted product: If not used immediately, in-use storage times and conditions are the responsibility of the user and would not be longer than 24 hours stored at 2 °C – 8 °C, unless reconstitution/ dilution has taken place under controlled and validated aseptic conditions.

Any unused portion should be discarded in accordance with local requirements.

6.5 Nature and contents of container

DYNA TEICOPLANIN 200 mg: 20 ml clear, colourless, Type I glass vial with grey bromobutyl rubber closure and an aluminium secure cap with a blue plastic removable cover.

DYNA TEICOPLANIN 400 mg: 20 ml clear, colourless, Type I glass vial with grey bromobutyl rubber closure and an aluminium secure cap with a red plastic removable cover.

DYNA TEICOPLANIN SOLVENT: 5 ml clear, colourless, Type I glass ampoules.

One vial and one ampoule are presented in an outer carton, for single use only.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd

1st Floor, Grapevine House, Steenberg Office Park

Silverwood Close

Westlake, Cape Town

7945, South Africa

8. REGISTRATION NUMBER(S)

DYNA TEICOPLANIN 200 mg: A43/20.1.1/0573

DYNA TEICOPLANIN 400 mg: A43/20.1.1/0575

DYNA TEICOPLANIN SOLVENT: A43/32.4/0574

9. DATE OF FIRST AUTHORISATION

Date of registration: 10 October 2013

10. DATE OF REVISION OF THE TEXT

13 April 2023

NAMIBIA

DYNA TEICOPLANIN 200 mg: 15/20.1.1/0167

DYNA TEICOPLANIN 400 mg: 15/20.1.1/0166

DYNA TEICOPLANIN SOLVENT: 16/34/0028