**PROPOSED AMENDED PACKAGE INSERT FOR**

**CIPLA-TEICOPLANIN 200 / 400**

**SCHEDULING STATUS:**

S4

**PROPRIETARY NAME** (AND DOSAGE FORM):

**CIPLA-TEICOPLANIN 200** (**Lyophilised** Powder for Solution for Infusion)

**CIPLA-TEICOPLANIN 400** (**Lyophilised** Powder for Solution for Infusion)

**COMPOSITION:**

| | |
|---|---|
| **CIPLA-TEICOPLANIN 200:** | Each 10 ml vial contains teicoplanin 200 mg as teicoplanin sodium in a lyophilised solid powder or cake. |
| **CIPLA-TEICOPLANIN 400:** | Each 10 ml vial contains teicoplanin 400 mg as teicoplanin sodium in a lyophilised solid powder or cake. |

The inactive ingredient in the formulations is sodium chloride.

CIPLA-TEICOPLANIN needs to be reconstituted before use with 3 ml of water for injection.

**PHARMACOLOGICAL CLASSIFICATION:**

A 20.1.1 Broad and medium spectrum antibiotics.

## PHARMACOLOGICAL ACTION:

### Pharmacodynamics:

**CIPLA-TEICOPLANIN** is a glycopeptide antibiotic.

Teicoplanin inhibits cell wall synthesis and is active only against gram-positive bacteria. It is bactericidal against susceptible strains, except for enterococci. It is active against methicillin-susceptible and methicillin-resistant staphylococci.

**Species usually resistant:**

All gram-negative bacteria, *Nocardia asteroids, Lactobacillus* spp*., Leuconostoc* bacteria.

**Species usually sensitive:**

Gram-positive anaerobes including *Clostridium difficile* and peptococci, *Staphylococcus aureus* and coagulase negative staphylococci (sensitive or resistant to methicillin), streptococci, enterococci, *Listeria monocytogenes,* micrococci, group JK *Corynebacteria*.

### Pharmacokinetics:

Following intravenous and intramuscular administration, teicoplanin is widely distributed in body tissues. It is slowly eliminated with a plasma half-life of 70 to 100 hours; the excretory route is renal. Teicoplanin is not absorbed when administered orally. Teicoplanin does not penetrate through the blood-brain barrier.

## INDICATIONS:

**CIPLA-TEICOPLANIN** is indicated in the following:

- Potentially serious Gram-positive infections, including those which cannot be treated with other antimicrobial agents.
- Endocarditis.
- Septicaemia and osteomyelitis.
- Skin and soft tissue infections.
- Urinary tract infections and peritonitis associated with chronic ambulatory peritoneal dialysis (CAPD).
- May be used as prophylaxis in orthopaedic and vascular surgery at risk of Gram-positive infection.

## CONTRA-INDICATIONS:

**CIPLA-TEICOPLANIN** is contra-indicated in the following:

- Hypersensitivity to teicoplanin or any component of this medicine.
- Pregnancy and lactation: safety has not been established (see **"PREGNANCY AND LACTATION"**).
- Children under three years of age: safety and efficacy have not been established.
- Subarachnoid space: do not inject into the subarachnoid space.

## WARNINGS:

Since cross-hypersensitivity may occur, **CIPLA-TEICOPLANIN** should be administered with caution in patients known to be hypersensitive to vancomycin.

Thrombocytopenia has been reported with **CIPLA-TEICOPLANIN**, especially in high dosages.

**Renal and auditory function tests should be undertaken in the following:**

- Prolonged therapy in patients with pre-existing renal impairment.
- In patients receiving other ototoxic or nephrotoxic medicines. These include medicines, such as aminoglycosides, colistin, amphotericin B, cyclosporine, cisplatin, furosamide and ethacrynic acid.

There is no evidence of synergistic toxicity when **CIPLA-TEICOPLANIN** is used in combination with the above medicines.

Periodic blood counts and liver and renal function tests are advised during treatment.

A history of “Red Man Syndrome”, which may occur with vancomycin, is not a contra-indication to **CIPLA-TEICOPLANIN**.

## INTERACTIONS:

Concurrent and sequential use of other medicines which may have neurotoxic and/or nephrotoxic properties may lead to neurotoxicity or nephrotoxicity. These include aminoglycosides, colistin, amphotericin B, cyclosporine, cisplatin, furosemide and ethacrynic acid.

## PREGNANCY AND LACTATION;

**Use during pregnancy and lactation:**

The use of **CIPLA-TEICOPLANIN** in pregnancy and lactation is not recommended as safety and efficacy have not been established.

## DOSAGE AND DIRECTION FOR USE:

The reconstituted **CIPLA-TEICOPLANIN** is given intravenously, as a bolus dose or by infusion over 30 minutes, or by intramuscular injection.

The duration of therapy is determined by the type and severity of the infection, and the clinical response of the patient. The majority of patients, with infections caused by organisms sensitive to the antibiotic, show therapeutic response within 48 to 72 hours. Treatment for three weeks or longer is recommended in patients with endocarditis and osteomyelitis.

Dosage is usually once daily but, in cases of severe infection, a second injection should be administered on the first day in order to reach the required serum concentration more rapidly.

### Dosage in elderly patients and adults with normal renal function:

**Moderate infections:**

Urinary tract infections, skin and soft tissue infections.

*Loading dose:*

Single i.v injection of 400 mg on the first day.

*Maintenance dose:*

Single i.v or i.m injection of 200 mg daily.

**Severe infections:**

Endocarditis, septicaemia, joint and bone infections.

*Loading dose:*

For the first three doses 400 mg i.v every 12 hours.

*Maintenance dose:*

Single i.v or i.m injection of 400 mg daily.

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

**Note:**

Mean doses of 3 mg/kg is equivalent to 200 mg and mean doses of 6 mg/kg is equivalent to 400 mg. In patients who are overweight, it is recommended that the dose be adjusted according to the weight of the patient as follows:

- Moderate infections 3 mg/kg.
- Severe infections 6 mg/kg.

**For prophylaxis in orthopaedic and vascular surgery at risk of Gram-positive infection:**

At induction of anaesthesia a single dose of 400 mg intravenously may be given.

**Dosage in children:**

**CIPLA-TEICOPLANIN** can be used in children from the age of three years to treat Gram-positive infections.

The dose for **severe infections** is 10 mg/kg intravenously every 12 hours for three doses followed by 10 mg/kg either intravenously or intramuscularly daily as a single dose.

The recommended dose for **moderate infections** is 10 mg/kg intravenously every 12 hours for the first three dose followed by 6 mg/kg either intravenously or intramuscularly daily as a single dose.

**Administration in adults and patients with renal impairment:**

Reduction of the dose of **CIPLA-TEICOPLANIN** in patients with renal impairment is not required until the fourth day of treatment. **CIPLA-TEICOPLANIN** should be given in usual doses for the first three days of therapy, thereafter the dose is adjusted accordingly to creatinine clearance:

- **In mild renal insufficiency:**

  **CIPLA-TEICOPLANIN** dose should be halved either by administering the initial unit dose every two days, or by administering half the initial unit dose once a day for patients with creatinine clearance of between 40 ml and 60 ml per minute.

- **In severe renal insufficiency:**

  **CIPLA-TEICOPLANIN** dose 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 for patients with creatinine clearance of less than 40 ml per minute and in haemodialysed patients. **CIPLA-TEICOPLANIN** is not removed by dialysis.

  **CIPLA-TEICOPLANIN** therapy must be excluded in patients with a creatinine clearance lower than or equal to 20 ml per minute, unless measurement of the serum concentrations can be guaranteed to accompany the therapy.

- **In continuous ambulatory peritoneal dialysis:**

**CIPLA-TEICOPLANIN** is stable in peritoneal dialysis solutions (1,36 % dextrose).

**Do not keep mixed solutions for longer than 24 hours.**

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.

Monitoring the plasma concentrations: If checks are carried out on the 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).

**Types of administration and duration of use:**

**1. Type of administration:**

To reconstitute **CIPLA-TEICOPLANIN**, **3 ml of** water for injection is injected slowly into the vial with the dry substance. The vial is then rolled until the dry substance is completely dissolved. **Do not shake the vial.** Foam is likely to form when the vial is shaken. If foam does develop during the preparation of the injection solution, it is recommended that the solution be left to stand for approximately 15 minutes until the foam has disappeared. **CIPLA-TEICOPLANIN** may be administered intravenously or intramuscularly. The intravenous dose may be given by rapid injection over one minute or by short infusion.

Once the preparation is ready, **CIPLA-TEICOPLANIN** is injected directly intravenously or into the proximal end of a dripline after clamping the line. **CIPLA-TEICOPLANIN**

can be injected quickly, i.e. within one minute. **CIPLA-TEICOPLANIN** can also be injected intramuscularly.

The following infusion solutions are suitable for mixing with **CIPLA-TEICOPLANIN:**

- 0,9 % sodium chloride solution.
- Ringer's solution.
- Ringer's lactate solution.
- 5 % dextrose solution. For infusion purposes, **CIPLA-TEICOPLANIN** is dissolved in 20 to 50 ml of infusion solution and administered over 20 to 30 minutes.

**CIPLA-TEICOPLANIN** and aminoglycosides are incompatible and should not be mixed in the same solution.

**Reconstituted solutions of CIPLA-TEICOPLANIN should be used immediately and any remaining solution must be discarded.**

**2. Duration of use:**

**CIPLA-TEICOPLANIN** should not be used for longer than four months. In cases of endocarditis or osteomyelitis, at least three weeks treatment is recommended.

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

The duration of the treatment depends on the severity of the infection as well as on the clinical and bacteriological progress. Treatment should be continued for at least three days after the patient has become afebrile and after the disappearance of clinical symptoms.

## SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

### Side-effects:

The following side-effects may occur:

**Gastrointestinal system disorders:**

*Less frequent*: Nausea, vomiting, diarrhoea and stomach pain.

**Skin and subcutaneous tissue disorders:**

*Less frequent:* Skin rash and pruritus.

*The following side-effects have been reported and frequencies are unknown:*

Exfoliative dermatitis, erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis.

**Respiratory system disorders:**

*Less frequent:* Bronchospasm.

**Special organ system disorders:**

*Less frequent:* Loss of hearing, tinnitus or vestibular disturbances.

**Renal system disorders:**

*Less frequent:* Renal impairment.

**General disorders:**

*Less frequent:* Fever, anaphylaxis, tissue necrosis, rigors, angioedema, dizziness, headache, thrombocytopenia, leucopenia, neutropenia, eosinophilia, disturbances in liver enzyme values, and pain, erythema and thrombophlebitis or abscess at the injection site, flushing of the upper body.

***"RED-MAN SYNDROME"***- Chills or fever, fainting, fast heartbeat, hives, itching, low blood pressure, rash or redness of the face, base of neck, upper body, back and arms.

Superinfection.

**Haematological system disorders:**

*Less frequent:* Agranulocytosis.

**Special Precautions:**

Patients with renal impairment should be monitored carefully during therapy with **CIPLA-TEICOPLANIN**. In general, periodic blood counts, liver, renal and auditory function tests are advised during prolonged treatment.

Auditory functions should be tested in those patients receiving other ototoxic or nephrotoxic medicines, which may have neurotoxic and/or nephrotoxic properties e.g. aminoglycosides, colistin, amphotericin, cyclosporine, cisplatin, furosamide and ethacrynic acid.

**CIPLA-TEICOPLANIN** may not be administered into the subarachnoid space.

The use of **CIPLA-TEICOPLANIN**, especially if prolonged, may result in overgrowth of non-susceptible organisms. If superinfections occur during therapy, appropriate measures should be taken. Repeated evaluation of the patient's condition is essential.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**

**CIPLA-TEICOPLANIN** is not removed by haemodialysis or peritoneal dialysis. General symptomatic measures are recommended for the management of an overdose.

**IDENTIFICATION:**

**Lyophilised product:**

**CIPLA-TEICOPLANIN 200:** White to off-white powder/cake.

**CIPLA-TEICOPLANIN 400:** White to off-white powder/cake.

**PRESENTATION:**

**CIPLA-TEICOPLANIN 200:** Pack of 1 x 10 ml transparent glass vials each with a grey rubber stopper and red aluminium flip-off seal containing 200 mg teicoplanin.

**CIPLA-TEICOPLANIN 400:** Pack of 1 x 10 ml transparent glass vials each with a grey rubber stopper and green aluminium flip-off seal containing 400 mg teicoplanin.

**CIPLA-TEICOPLANIN needs to be reconstituted with 3 ml water for injection prior to use.**

**STORAGE INSTRUCTIONS:**

Lyophilised product: Store at or below 30 °C.

**Reconstituted product must be used immediately and any remaining solution must be discarded.**

**STORE THIS MEDICINE OUT OF REACH OF CHILDREN.**

**REGISTRATION NUMBERS:**

CIPLA-TEICOPLANIN 200: **43/20.1.1/0610**

CIPLA-TEICOPLANIN 400: **43/20.1.1/0611**

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:**

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**DATE OF PUBLICATION OF THIS PACKAGE INSERT:**

06 August 2015