**TICOCIN Injection (Teicoplanin)**

**Composition**

**TICOCIN-200**
Each vial contains:
Teicoplanin .................... 200 mg
As sterile freeze-dried powder for reconstitution with 3 ml sterile water for injection IP.
Each 3 ml of reconstituted injection contains
Teicoplanin......................... 200 mg

**TICOCIN-400**
Each vial contains
Teicoplanin .................... 400 mg
As sterile freeze-dried powder for reconstitution with 3 ml sterile water for injection IP.
Each 3 ml of reconstituted injection contains
Teicoplanin......................... 400 mg

**Dosage Forms**

Powder for reconstitution and I.V. / I.M. use only.

**Pharmacology**

**Pharmacodynamics**

Teicoplanin is a bactericidal; glycopeptide antibiotic produced by fermentation of *Actinoplanes teichomyceticus*.

Species usually sensitive (MIC less than or equal to 16mg/l):
*Staphylococcus aureus* and co agulase negative staphylococci (sensitive or resistant to methicillin)
*Streptococci*
*Enterococci*
*Listeria monocytogenes*
*Micrococci*
*Eikenella corrodens*
group JK corynebacteria
Gram-positive anaerobes including Clostridium difficile, and Peptococci.

Species usually resistant (MIC superior to 16mg/l):
Nocardia asteroids
Lactobacillus spp
Leuconostoc and all Gram-negative bacteria.

Bactericidal synergy has been demonstrated in vitro with aminoglycosides against group D streptococci and staphylococci. In vitro combinations of teicoplanin with rifampicin or fluorinated quinolones show primarily additive effects and sometimes synergy.

One-step resistance to teicoplanin could not be obtained in vitro and multi-step resistance was only reached in vitro after 11-14 passages.

Teicoplanin does not show cross-resistance with other classes of antibiotics.

The use of teicoplanin may result in overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during treatment appropriate measures should be taken.

Pharmacokinetics

Absorption
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 about 3 hours), followed by slow elimination (with a terminal elimination half-life of about 150 hours). At 6mg/kg administered intravenously at 0, 12, 24 hours and every 24 hours thereafter as a 30 minute infusion, a predicted trough serum concentration of 10mg/L would be reached by Day 4.

Distribution
Following injection teicoplanin rapidly penetrates into tissues, including skin, fat and bones and reaches the highest concentrations in the kidney, trachea, lungs and adrenals. Teicoplanin does not readily penetrate into the cerebro-spinal fluid (CSF). The steady state volume of distribution after 3 to 6mg/kg intravenously ranges from 0.94 L/kg to 1.4 L/kg. The volume of distribution in children is not substantially different from that in adults. Approximately 90-95% teicoplanin is bound with weak affinity to plasma proteins. Teicoplanin penetrates readily into blister exudates and into joint fluid; it penetrates neutrophils and enhances their bactericidal activity; it does not penetrate red blood cells.

Metabolism and Excretion
No metabolites of teicoplanin have been identified; more than 97% of the administered teicoplanin is excreted unchanged. The elimination of teicoplanin from the plasma is prolonged with a terminal half-life of elimination in man of about 150 hours. Teicoplanin is excreted mainly in the urine.

Indications

TICOCIN is indicated in potentially serious Gram-positive infections including those which cannot be treated with other antimicrobial drugs, eg. penicillins and cephalosporins.

TICOCIN is useful in the therapy of serious staphylococcal infections in patients who cannot receive
or who have failed to respond to the penicillins and cephalosporins, or who have infections with staphylococci resistant to other antibiotics.

The effectiveness of teicoplanin has been documented in the following infections:
- skin and soft tissue infections,
- urinary tract infections,
- lower respiratory tract infections,
- joint and bone infections,
- septicaemia,
- endocarditis and peritonitis related to continuous ambulatory peritoneal dialysis.

**TICOCIN** may be used for antimicrobial prophylaxis in orthopaedic surgery at risk of Gram-positive infection.

### Dosage And Administration

<table>
<thead>
<tr>
<th>Dosage</th>
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<tbody>
<tr>
<td><strong>Dosage</strong></td>
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<tr>
<td><strong>Adult or elderly patients with normal renal function</strong></td>
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<tr>
<td>Standard doses of 200 and 400 mg equate respectively to mean doses of 3 and 6 mg/kg. In patients weighing more than 85 kg it is recommended to adapt the dosage to the weight following the same therapeutic schedule: moderate infection 3 mg/kg, severe infection 6 mg/kg.</td>
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<tr>
<td>In some clinical situations, such as infected, severely burned patients or <em>Staphylococcus aureus</em> endocarditis, unit maintenance doses of up to 12mg/kg have been administered (intravenously). In endocarditis caused by <em>Staphylococcus aureus</em>, satisfactory results have been achieved with teicoplanin in polytherapy. When serum concentrations are controlled in severe infections, the...</td>
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</table>
trough levels must be 10 times higher than the MIC or, generally, at least 10 mg/l.

In the treatment of antibiotic-associated diarrhoea caused by *Clostridium difficile*: one oral dose of 200 mg twice a day.

**Children (2 months and above)**

*For severe infections and neutropenic patients*

The recommended dose is 10 mg/kg every 12 hours 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 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.

**Neonates**

The recommended dosage regimen for neonates is a loading dose of 16 mg/kg followed by a daily dose of 8 mg/kg.

**In continuous ambulatory peritoneal dialysis**

After a single loading IV dose of 400 mg if the patient is febrile, the recommended dosage is 20 mg/L per bag in the first week, 20 mg/L in alternate bags in the second week and 20 mg/L in the overnight dwell bag only during the third week, feverish patients must also take an I.V. loading dose of 400 mg of teicoplanin, feverish patients must also take an I.V. loading dose of 400 mg of teicoplanin.

Teicoplanin remains stable in solutions for peritoneal dialysis (1.36% or 3.86% dextrose). These solutions must not be kept for more than 24 hours.

**Adults and elderly patients with renal insufficiency**

For patients with impaired renal function, reduction of dosage is not required until the fourth day of TICOCIN treatment. Measurement of the serum concentration of teicoplanin may optimise therapy (See **ADMINISTRATION**).

**From the fourth day of treatment**

*In mild renal insufficiency:*
Creatinine clearance between 40 and 60 mL/min, TICOCIN 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, TICOCIN 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 preparation and administration**

Figure 1: Each vial contains Teicoplanin (200 mg)/(400 mg) depending on the strength of the vial
Figure 2: Each FFS Vial contains 3 ml sterile water for injection

Figure 3: Turn the head to open the FFS Vial

Figure 4: Withdraw all the water from 3 ml FFS Vial with a syringe

Figure 5: Remove coloured plastic vial cap by gently pushing upward
Figure 6: Inject 3 ml of water for injection into the vial containing teicoplanin

Figure 7: DO NOT SHAKE

Shaking this solution causes formation of foam making it difficult to get the expected volume but if teicoplanin has been completely dissolved then the foam does not change the concentration of the solution

Figure 8: Roll vial gently
Gently roll the vial between the hands until the powder is completely dissolved, paying attention to avoid the formation of foam. If the solution becomes foamy then it should be left to stand for 15 minutes. The vial now contains teicoplanin reconstituted solution.

Figure 9: Withdraw the teicoplanin solution slowly from the vial by placing the needle in the central part of the rubber stopper.

ENSURE THAT ALL THE POWDER IS DISSOLVED, EVEN THAT NEAR THE STOPPER.

It is important that the solution is correctly prepared and carefully withdrawn into the syringe; preparations that are not carefully executed can lead to the administration of less than 50% of the dose.

The concentration of a carefully prepared solution will be 100mg in 1.5mL (from the 200 mg vial) and 400mg in 3mL (from 400 mg vial)

The final solution is isotonic with a pH of 7.5.

A calculated excess is included in each vial of TICOCIN so that, when prepared as described above, a full dose of 200mg or 400mg (depending on the strength of the vial) will be obtained if all the reconstituted solution is withdrawn from the vial by a syringe.

The reconstituted solution may be injected directly, or alternatively diluted with: 0.9% Sodium Chloride Injection, Compound Sodium Lactate Injection (Ringer-Lactate Solution, Hartmanns Solution), 5% Dextrose Injection, 0.18% Sodium Chloride and 4% Dextrose Injection; Peritoneal dialysis solution containing 1.36% or 3.86% Dextrose.

Reconstituted Product:
In keeping with good clinical pharmaceutical practise reconstituted vials of TICOCIN should be
used immediately and any unused portion discarded. On the few occasions when changing circumstances make this impractical reconstituted solution should be kept at 4°C and discarded within 24 hours.

Do not store in a syringe.

**Contraindications**

**TICOCIN** is contraindicated in patients who have exhibited previous hypersensitivity to the drug.

**Warnings And Precautions**

**General**

**TICOCIN** 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 for **TICOCIN**.

Thrombocytopenia has been reported with teicoplanin especially at higher doses than those usually recommended. It is advisable for periodic haematological studies to be performed during treatment. Liver and renal function tests are advised during treatment.

Serial renal and auditory function tests should be undertaken in the following circumstances:

i. Prolonged treatment in patients with renal insufficiency.

ii. Concurrent and sequential use of other drugs, which may have neurotoxic, and/or nephrotoxic properties. These include aminoglycosides, colistin, amphotericin B, cyclosporin, cisplatin, frusemide and ethacrynic acid

However, there is no evidence of synergistic toxicity with combinations with teicoplanin.

Superinfection: as with other antibiotics, 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.

**Drug interactions**

**TICOCIN** should be used with care in conjunction with or sequentially with other drugs with known nephrotoxic or ototoxic potential. Of particular concern are streptomycin, neomycin, kanamycin, gentamicin, amikacin, tobramycin, cephaloridine, colistin.

No adverse interactions were noted when teicoplanin was administered to patients already receiving various medications including other antibiotics, antihypertensives, anaesthetic agents, cardiac drugs and antidiabetic agents.

Animal studies have shown lack of interaction with diazepam, thiopental, morphine, neuromuscular
blocking agents or halothane.

Renal impairment

Please refer under **DOSAGE AND ADMINISTRATION**.

Pregnancy

**TICOCIN** should not be used during confirmed or presumed pregnancy unless a physician considers that the potential benefits outweigh the possible risk.

Lactation

There is no information about the excretion of teicoplanin in milk or placental transfer of the drug. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with teicoplanin should be made taking into account the benefit of breast-feeding to the child and the benefit of teicoplanin therapy to the mother.

Undesirable Effects

Although causal relationships have not been established in every case, the following undesirable effects have been reported with the administration of teicoplanin:

<table>
<thead>
<tr>
<th>System organ class</th>
<th>Very common (1/10)</th>
<th>Common (1/100 to &lt;1/10)</th>
<th>Uncommon (1/1,000 to &lt;1/1,000)</th>
<th>Rare (1/10,000 to &lt;1/1,000)</th>
<th>Very rare (&lt;1/10,000)</th>
<th>Frequency not known (cannot be estimated from available data)*</th>
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<tr>
<td>Infections and infestations</td>
<td>Abscess</td>
<td>Injection site abscess, superinfection (overgrowth of non-susceptible organisms)</td>
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<td>Blood and the lymphatic system disorders</td>
<td>Eosinophilia, thrombocytopenia, leucopenia</td>
<td>Agranulocytosis, neutropenia</td>
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<tr>
<td>Immune system disorders</td>
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<td>Nervous system disorders</td>
<td>Dizziness, headache</td>
<td>Seizures with intraventricular use</td>
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<tr>
<td>Category</td>
<td>Adverse Events</td>
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<td>Ear and labyrinth disorders</td>
<td>Deafness (mild hearing loss), tinnitus, vestibular disorder</td>
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<td>Vascular disorders</td>
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<td>Respiratory, thoracic and mediastinal disorders</td>
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<td>Gastrointestinal disorders</td>
<td>Nausea, vomiting, diarrhoea</td>
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<td>Skin and subcutaneous tissue disorders</td>
<td>Erythema (redness), rash (skin rash), pruritus</td>
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<td>Renal and urinary disorders</td>
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<td>General disorders and administration site conditions</td>
<td>Pain, pyrexia (fever), Transaminases abnormal (transient abnormality of transaminases), blood alkaline phosphatase abnormal (transient abnormality of alkaline phosphatase), blood creatinine increased (transient rise of serum creatinine)</td>
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<tr>
<td>Investigations</td>
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*postmarketing experience.

Teicoplanin is generally well tolerated. Side-effects rarely require cessation of therapy and are generally mild and transient: serious side-effects are rare. The following adverse events have been reported:
**Local reactions:** Erythema, local pain, thrombophlebitis, injection site abscess.

**Hypersensitivity:** Rash, pruritis, fever, bronchospasm, anaphylactic reactions, anaphylactic shock, rigans, urticaria, angioedema, rare reports of exfoliative dermatitis, toxic epidermal necrolysis, rare cases of erythema multiforme including Stevens-Johnson Syndrome. In addition, infusion-related events, such as erythema or flushing of the upper body, have been rarely reported in which the events occurred without a history of previous teicoplanin exposure and did not recur on re-exposure when the infusion rate was slowed and/or concentration decreased. These events were not specific to any concentration or rate of infusion.

**Gastric-intestinal:** Nausea, vomiting, diarrhoea.

**Blood:** Eosinophilia, leucopenia, thrombocytopenia, thrombocytosis, neutropenia, rare cases of reversible agranulocytosis.

**Liver function:** Increases in serum transaminases and/or serum alkaline phosphatase.

**Renal function:** Transient elevations of serum creatinine, renal failure.

**Central nervous system:** Dizziness, headache.

**Auditory/vestibular:** Mild hearing loss, tinnitus and vestibular disorder.

**Other:** Superinfection (overgrowth of non-susceptible organisms).

### Overdosage

Teicoplanin is not removed by haemodialysis and only slowly by peritoneal dialysis. Treatment of overdosage should be symptomatic. Despite high plasma concentrations of teicoplanin up to 300mg/ml there were no symptoms or laboratory abnormalities.

### Incompatibility

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

### Storage And Handling Instructions

**Before opening**

Store below 25° C

**After reconstitution**

In keeping with good clinical pharmaceutical practise reconstituted vials of TICOCIN should be
used immediately and any unused portion discarded. On the few occasions when changing circumstances make this impractical reconstituted solution should be kept at 2 - 8°C and discarded within 24 hours.

Do not store in a syringe.

Packaging Information

TICOCIN-200 & TICOCIN-400 mg: Available in vials of 10 mL

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