120mm

170mm

Ticoplan Injection

(T e i c o p l a n i n)

ٹیکوپلان انجیکشن

(ٹیکوپلانین)

COMPOSITION:
Ticoplan Injection 200mg
Each vial contains:
Teicoplanin powder for reconstitution.....200mg
(Innovator's Specification)
Ticoplan Injection 400mg
Each vial contains:
Teicoplanin powder for reconstitution.....400mg
(Innovator's Specification)

DESCRIPTION:
Teicoplanin is a glycopeptide antibiotic complex isolated from the bacterium Actinoplanes teichomyceticus. Teicoplanin inhibits peptidoglycan polymerization, resulting in inhibition of bacterial cell wall synthesis and cell death. It is active against gram-positive bacteria. It consists of five major components each with a different fatty acid moiety.

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. Peptidoglycan synthesis is blocked by specific binding to D-alanyl-D-alanine residues.

INDICATIONS:
Teicoplanin is indicated in adults and in children from birth for the parenteral treatment of the following infections.

- Complicated skin and soft tissue infections,
- Bone and joint infections,
- Hospital acquired pneumonia,
- Community acquired pneumonia,
- Complicated urinary tract infections,
- Infective endocarditis,
- Peritonitis associated with continuous ambulatory peritoneal dialysis (CAPD),
- Bacteremia that occurs in association with any of the indications listed above.

- Teicoplanin is also indicated as an alternative oral treatment for Clostridium difficile infection-associated diarrhea and colitis.
- Where appropriate, teicoplanin should be administered in combination with other antibacterial agents.
- Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE & ADMINISTRATION:
The dose and duration of treatment should be adjusted according to the underlying type and severity of infection and clinical response of the patient, and patient factors such as age and renal function.

Measurement of serum concentrations:
- Teicoplanin trough serum concentrations should be monitored at steady state after completion of the loading dose regimen in order to ensure that a minimum trough serum concentration has been reached:
- For most Gram-positive infections, teicoplanin trough levels of at least 10 mg/L when measured by High Performance Liquid Chromatography (HPLC), or at least 15 mg/L when measured by Fluorescence Polarization Immunoassay (FPIA) method.
- For endocarditis and other severe infections, teicoplanin trough levels of 15-30 mg/L when measured by HPLC, or 30-40 mg/L when measured by FPIA method.
- During maintenance treatment, teicoplanin trough serum concentrations monitoring may be performed at least once a week to ensure that these concentrations are stable.

Indications	*Loading dose*		*Maintenance dose*	
	Loading dose regimen	*Targeted trough concentrations at day 3 to 5*	*Maintenance dose*	*Targeted trough concentrations during maintenance*
Complicated skin and soft tissue infections, Pneumonia, Complicated urinary tract infections.	6 mg/kg body weight every 12 hours for 3 intravenous or intramuscular administrations	>15 mg/L	6 mg/kg body weight intravenous or intramuscular once a day	>15 mg/L once a week
Bone and joint infections.	12 mg/kg body weight every 12 hours for 3 to 5 intravenous administrations	>20 mg/L	12 mg/kg body weight intravenous or intramuscular once a day	>20 mg/L
Infective endocarditis.	12 mg/kg body weight every 12 hours for 3 to 5 intravenous administrations	30-40 mg/L	12 mg/kg body weight intravenous or intramuscular once a day	>30 mg/L

Adults and elderly patients with normal renal function:
The dose is to be adjusted on bodyweight whatever the weight of the patient.

Duration of treatment:
The duration of treatment should be decided based on the clinical response. For infective endocarditis a minimum of 21 days is usually considered appropriate. Treatment should not exceed 4 months.

Combination therapy:
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.

Elderly population
No dose adjustment is required, unless there is renal impairment.

Adults and elderly patients with impaired renal function
Dose adjustment is not required until the fourth day of treatment, at which time dosing should be adjusted to maintain a serum trough concentration of at least 10 mg/L when measured by HPLC, or at least 15 mg/L when measured by FPIA method.

After the fourth day of treatment:
- In mild and moderate renal insufficiency (creatinine clearance 30-80 mL/min): maintenance 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 30 mL/min) and in haemodialysed patients: dose should be one-third the usual dose, 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 hemodialysis.

Patients in continuous ambulatory peritoneal dialysis (CAPD)
After a single intravenous loading dose of 6 mg/kg bodyweight, 20 mg/L is administered in the bag of the dialysis solution in the first week, 20 mg/L in different bags the second week and then 20 mg/L in the overnight bag in the third week.

Pediatric population
The dose recommendations are the same in adults and children above 12 years of age.

Neonates and infants up to the age of 2 months:

Loading dose
One single dose of 16 mg/kg body weight, administered intravenously by infusion on the first day.

Maintenance dose
One single dose of 8 mg/kg body weight administered intravenously by infusion once a day.

Children (2 months to 12 years):

Loading dose
One single dose of 10 mg/kg body weight administered intravenously every 12 hours, repeated 3 times.

Maintenance dose
One single dose of 6-10 mg/kg body weight administered intravenously once a day.

Method of administration
Teicoplanin should be administered by the intravenous or intramuscular route. The intravenous injection may be administered either as a bolus over 3 to 5 minutes or as a 30-minute infusion.
Only the infusion method should be used in neonates.

Directions for reconstitution
For reconstitution, slowly add 3ml sterile water for injection. The water should be added slowly to the vial which should be rotated until all the powder is dissolved to avoid foaming. If foam is developed, allow the solution to stand for approximately 15 minutes so that the foam disappears. Only clear and yellowish solutions should be used.

PHARMACOKINETICS:

Absorption
Teicoplanin is administered by parenteral route (intravenously or intramuscularly). After intramuscular administration, the bioavailability of teicoplanin (as compared to intravenous administration) is almost complete (90%). After six daily intramuscular administrations of 200 mg the mean (SD) maximum teicoplanin concentration (C_{max}) amounts to 12.1 (0.9) mg/L and occurs at 2 hours after administration.
After a loading dose of 6 mg/kg administered intravenously every 12 hours for 3 to 5 administrations, C_{max} values range from 60 to 70 mg/L and C_{trough} are usually above 10 mg/L. After an intravenous loading dose of 12 mg/kg administered every 12 hours for 3 administrations, mean values of C_{max} and C_{trough} are estimated to be around 100 mg/L and 20 mg/L, respectively.
After a maintenance dose of 6 mg/kg administered once daily C_{max} and C_{trough} values are approximately 70 mg/L and 15 mg/L, respectively. After a maintenance dose of 12 mg/kg once daily C_{trough} values range from 18 to 30 mg/L.

Distribution
The binding to human serum proteins ranges from 87.6 to 90.8% without any variation in function of the teicoplanin concentrations. Teicoplanin is mainly bound to human serum albumin. Teicoplanin is not distributed in red cells.
The volume of distribution at steady-state (Vss) varies from 0.7 to 1.4 L/kg. The highest values of Vss are observed in the recent studies where the sampling period was superior to 8 days.
Teicoplanin distributed mainly in lung, myocardium and bone tissues with tissue/serum ratios superior to 1. In blister fluids, synovial fluid and peritoneal fluid the tissue/serum ratios ranged from 0.5 to 1. Elimination of teicoplanin from peritoneal fluid occurs at the same rate as from serum. In pleural fluid and subcutaneous fat tissue the tissue/serum ratios are comprised between 0.2 and 0.5. Teicoplanin does not readily penetrate into the cerebrospinal fluid (CSF).

Biotransformation
Unchanged form of teicoplanin is the main compound identified in plasma and urine, indicating minimal metabolism. Two metabolites are formed probably by hydroxylation and represents 2 to 3% of the administered dose.
Elimination
Unchanged teicoplanin is mainly excreted by urinary route (80% within 16 days) while 2.7% of the administered dose is recovered in feces (via bile excretion) within 8 days following administration.
Elimination half-life of teicoplanin varies from 100 to 170 hours in the most recent studies where blood sampling duration is about 8 to 35 days.
Teicoplanin has a low total clearance in the range of 10 to 14 mL/h/kg and a renal clearance in the range of 8 to 12 mL/h/kg indicating that teicoplanin is mainly excreted by renal mechanisms.

WARNINGS & PRECAUTIONS:

Hypersensitivity reactions
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.
Teicoplanin must be administered with caution in patients with known hypersensitivity to vancomycin, as crossed hypersensitivity reactions, including fatal anaphylactic shock, may occur.
However, a prior history of "red man syndrome" with vancomycin is not a contraindication to the use of teicoplanin.
Infusion related reactions
In rare cases (even at the first dose), red man syndrome (a complex of symptoms including pruritus, urticaria, erythema, angioneurotic edema, tachycardia, hypotension, dyspnea) has been observed.
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 bullous reactions
Life-threatening or even fatal cutaneous reactions Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) have been reported with the use of teicoplanin. If symptoms or signs of SJS or TEN (e.g. progressive skin rash often with blisters or mucosal lesions) are present teicoplanin treatment should be discontinued immediately.
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 teicoplanin will be used to treat severe infections in patients for whom standard antibacterial activity is considered to be unsuitable.
Loading dose regimen
Since data on safety are limited, patients should be carefully monitored for adverse reactions when teicoplanin doses of 12mg/kg body weight twice a day are administered. Under this regimen blood creatinine values should be monitored in addition to the recommended periodic hematological examination.
Teicoplanin should not be administered by intraventricular route.
Thrombocytopenia
Thrombocytopenia has been reported with teicoplanin. Periodic hematological examinations are recommended during treatment, including complete cell blood count.
Nephrotoxicity
Renal failure has been reported in patients treated with teicoplanin. Patients with renal insufficiency, and/or in those receiving teicoplanin in conjunction with or sequentially with other medicinal products with known nephrotoxic potential (aminoglycosides, colistin, amphotericin B, cyclosporin, and cisplatin) should be carefully monitored, and should include auditory tests.
Since teicoplanin is mainly excreted by the kidney, the dose of teicoplanin must be adapted in patients with renal impairment.
Ototoxicity
As with other glycopeptides, ototoxicity (deafness and tinnitus) has been reported in patients treated with teicoplanin. Patients who develop signs and symptoms of impaired hearing or disorders of the inner ear during treatment with teicoplanin should be carefully evaluated and monitored, especially in case of prolonged treatment and in patients with renal insufficiency. Patients receiving teicoplanin in conjunction with or sequentially with other medicinal products with known neurotoxic/ototoxic potential (aminoglycosides, cyclosporin, cisplatin, furosemide and ethacrynic acid) should be carefully monitored and the benefit of teicoplanin evaluated if hearing deteriorates.
Special precautions must be taken when administering teicoplanin in patients who require concomitant treatment with ototoxic and/or nephrotoxic medicinal products for which it is recommended that regular hematology, liver and kidney function tests are carried out.
Superinfection
As with other antibiotics, the use of teicoplanin, especially if prolonged, may result in overgrowth of non-susceptible organisms. If superinfection occurs during therapy, appropriate measures should be taken.
Pregnancy
There are a limited amount of data from the use of teicoplanin in pregnant women. Studies in animals have shown reproductive toxicity at high doses in rats there was an increased incidence of stillbirths and neonatal mortality. The potential risk for humans is unknown.
Therefore, teicoplanin should not be used during pregnancy unless clearly necessary. A potential risk of inner ear and renal damage to the fetus cannot be excluded.
Breast-feeding
It is unknown whether teicoplanin is excreted in human milk. There is no information on the excretion of teicoplanin in animal milk. 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.
Fertility
Animal reproduction studies have not shown evidence of impairment of fertility.

DRUG INTERACTIONS:

No specific interaction studies have been performed.
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. Teicoplanin should be used with care in conjunction with or sequentially with other medicinal products with known nephrotoxic or ototoxic potential. These include aminoglycosides, colistin, amphotericin B, cyclosporin, cisplatin, furosemide, and ethacrynic acid. However, there is no evidence of synergistic toxicity in combinations with teicoplanin.
In clinical studies, teicoplanin has been administered to many patients already receiving various medications including other antibiotics, anti-hypertensives, anaesthetic agents, cardiac medicinal products and antidiabetic agents without evidence of adverse interaction.

SIDE EFFECTS:

Infections and infestations
Superinfection (overgrowth of non-susceptible organisms), abscess.
Blood and the lymphatic system disorders
Leucopenia, thrombocytopenia, eosinophilia, Agranulocytosis, neutropenia.
Immune system disorders
Anaphylactic reaction (anaphylaxis), drug reaction with eosinophilia and systemic symptoms (DRESS), anaphylactic shock.
Nervous system disorders
Dizziness, headache, Seizures
Ear and Labyrinth disorders
Deafness, hearing loss, tinnitus, vestibular disorder.
Vascular disorders
Phlebitis, thrombophlebitis.
Respiratory, thoracic and mediastinal disorders
Bronchospasm.
Gastro-intestinal disorders
Diarrhea, vomiting, nausea.
Skin and subcutaneous tissue disorders
Rash, erythema, pruritus, red man syndrome (e.g. flushing of the upper part of the body), toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme, angioedema, dermatitis exfoliative, urticaria.
Renal and Urinary disorders
Blood creatinine increased, renal failure (including renal failure acute).
General disorders and administration site conditions
Pain, pyrexia, Injection site abscess, chills (rigors).
Investigations
Transaminases increased (transient abnormality of transaminases), blood alkaline phosphatase increased (transient abnormality of alkaline phosphatase), blood creatinine increased (transient rise of serum creatinine).

CONTRAINDICATIONS:

Hypersensitivity to teicoplanin or to any of the excipients.

STORAGE & INSTRUCTIONS:

Store below 25°C
Protect from heat, sunlight and moisture.
Keep away from the reach of the children.
After reconstitution, the solution is stable for 24 hours when store between 2-8°C.
For single use only.
For Intramuscular & Intravenous use only.
To be sold on the prescription of a registered medical practitioner only.

HOW SUPPLIED

Ticoplan Injection 200mg
1 vial + 3ml sterile water for injection.
Ticoplan Injection 400mg
1 vial + 3ml sterile water for injection.

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
دھوپ، گرمی، نمی سے محفوظ اور بچوں کی پہنچ سے دور رکھیں۔
تیار کردہ محلول ۲-۸ ڈگری سینٹی گریڈ درجہ حرارت پر رکھنے کی صورت میں ۲۴ گھنٹے تک قابل استعمال رہتا ہے۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔ صرف وریدی اور عضلاتی استعمال کے لئے ہے۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate,
Lahore, Pakistan.