TICOZID® IM/IV Injection

(TEICOPLANIN)

ٹیکوزڈ انجکشن
(ٹیکوپلانن)

QUALITATIVE AND QUANTITATIVE COMPOSITION
Ticozid 200mg Injection
Each vial contains:
Teicoplanin BP……..200mg
equivalent to 200,000 IU (1000 IU/mg)
(Product Specs: BP)

Ticozid 400mg Injection
Each vial contains:
Teicoplanin BP……..400mg
equivalent to 400,000 IU (1000 IU/mg)
(Product Specs: BP)

PHARMACEUTICAL FORM
Lyophilized powder for Injection

CLINICAL PARTICULARS
Therapeutic indications
Ticozid Injection 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.
- Ticozid Injection is also indicated as an alternative oral treatment for *Clostridium difficile* infection-associated diarrhea and colitis.

Where appropriate, Ticozid injection should be administered in combination with other antibacterial agents.

Posology and method of administration
Posology
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 through 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:
During maintenance treatment, teicoplanin trough serum concentrations monitoring may be performed at least once a week to ensure that these concentrations are stable.

Adults and elderly patients with normal renal function

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	6mg/kg body weight every 12 hours for 3 intravenous or intramuscular administrations	>15mg/L	6mg/kg body weight intravenous or intramuscular once a day	>15mg/L once a week
- Bone and joint infections	12mg/kg body weight every 12 hours for 3 to 5 intravenous administrations	>20mg/L	12mg/kg body weight intravenous or intramuscular once a day	>20mg/L
- Infective endocarditis	12mg/kg body weight every 12 hours for 3 to 5 intravenous administrations	30-40mg/L	12mg/kg body weight intravenous or intramuscular once a day	>30mg/L

The dose is to be adjusted on body weight, 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
It 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.

Clostridium difficile infection-associated diarrhea and colitis
The recommended dose is 100-200 mg administered orally twice a day for 7 to 14 days.

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 .

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 hemodialyzed 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. Ticozid 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
Ticozid 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. This medicinal product is for single use only.

Preparation of reconstituted solution:
The solution is reconstituted by adding water for injection to the 200 mg and 400 mg powder vial. The water is slowly added 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.

Nominal teicoplanin content of vial	200mg	400mg
Volume of powder vial	10mL	20mL
Volume containing nominal teicoplanin	3.0mL	3.0mL

Preparation of the diluted solution before infusion:
Ticozid can be administered in the following infusion solutions:

- Sodium chloride 9 mg/mL (0.9%) solution
- Ringer solution/ Ringer-lactate solution
- 5% dextrose injection/ 10% dextrose injection
- 0.18% sodium chloride and 4% glucose solution
- 0.45% sodium chloride and 5% glucose solution
- Peritoneal dialysis solution containing 1.36% or 3.86% glucose solution.

Any unused product or waste material should be disposed of in accordance with requirements.

Contraindications
Hypersensitivity to teicoplanin

Special warnings and precautions for use
Teicoplanin should not be administered by intraventricular use.

Hypersensitivity reactions: 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.

Infusion related reactions: In rare cases (even at the first dose), red man syndrome 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: 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 will be used to treat severe infections in patients for whom standard antibacterial activity is considered to be unsuitable.

Thrombocytopenia: Thrombocytopenia has been reported with teicoplanin periodic hematological examinations, including complete blood count, are recommended during treatment.

Nephrotoxicity
Patients with renal insufficiency, in those receiving the high dose regimen of teicoplanin, and those receiving teicoplanin in conjunction with or sequentially with other medicinal products with known nephrotoxic potential should be carefully monitored.

Ototoxicity: Special precautions must be taken when administering teicoplanin in patients who require concomitant treatment with ototoxic and/or nephrotoxic medicinal products

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.

Sodium Content: This medicinal product contains 24 mg of sodium chloride per 400mg, corresponding to about 10 mg (0.43 mmol) of sodium, equivalent to 0.012% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Interaction with other medicinal products and other forms of interaction
Teicoplanin should be used with care in conjunction with or sequentially with other medicinal products with known nephrotoxic and/or neurotoxic/ototoxic potential. These include e.g. aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide, and ethacrynic acid.

Fertility, pregnancy and lactation
Pregnancy: 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.

Lactation: It is unknown whether teicoplanin is excreted in human milk. There is no information on the excretion of teicoplanin in animal milk.

Effects on the ability to drive and use machines
Teicoplanin has minor influence on the ability to drive and use machines.

Undesirable effects
Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping,

undesirable effects are presented in order of decreasing seriousness.

System organ class	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)	Rare (≥1/10,000 to <1/1,000)	Not known (cannot be estimated from available data)
Infections and infestations			Abscess	Superinfection (overgrowth of non-susceptible organisms)
Blood and the lymphatic system disorders		Leucopenia, thrombocytopenia, eosinophilia		Agranulocytosis, neutropenia, pancytopenia
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, Acute generalized exanthematous pustulosis, 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)

Overdose
Treatment of teicoplanin overdose should be symptomatic. Teicoplanin is not removed by hemodialysis and only slowly by peritoneal dialysis.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Glycopeptide Antibacterials,
ATC code: J01XA 02.

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.

Susceptibility testing breakpoints
The MICs breakpoints are displayed in the following table:

Microorganism	Susceptible	Resistant
Staphylococcus aureus	≤2 mg/L	>2 mg/L
Coagulase-negative staphylococci	≤4 mg/L	>4 mg/L
Enterococcus spp.	≤2 mg/L	>2 mg/L
Streptococcus groups A, B, C, G	≤2 mg/L	>2 mg/L
Streptococcus pneumoniae	≤2 mg/L	>2 mg/L
Viridans group streptococci	≤2 mg/L	>2 mg/L

Pharmacokinetic/Pharmacodynamic relationship
Teicoplanin antimicrobial activity depends essentially on the duration of time during which the substance level is higher than the minimum inhibitory concentration (MIC) of the pathogen.

Commonly susceptible species
Aerobic Gram-positive bacteria: *Corynebacterium jeikeium, Enterococcus faecalis, Staphylococcus aureus (including methicillin-resistant strains), Streptococcus agalactiae, Streptococcus dysgalactiae subsp. equisimilis (Group C & G streptococci), Streptococcus pneumoniae, Streptococcus pyogenes, Streptococci in the viridans group.*

Anaerobic Gram-positive bacteria: *Clostridium difficile, Peptostreptococcus spp.*

Species for which acquired resistance may be a problem
Aerobic Gram-positive bacteria: *Enterococcus faecium, Staphylococcus epidermidis, Staphylococcus haemolyticus, Staphylococcus hominis.*

Inherently resistant bacteria
All Gram-negative bacteria
Other bacteria: *Chlamydia spp. Chlamydophila spp., Legionella pneumophila, Mycoplasma spp.*

Pharmacokinetic properties
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 (Cmax) amounts to 12.1 (0.9) mg/L and occurs at 2 hours after administration.

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. Teicoplanin distributed mainly in lung, myocardium and bone tissues with tissue/serum In blister fluids, synovial fluid and peritoneal fluid the tissue/serum 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.
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.

Linearity
Teicoplanin exhibited linear pharmacokinetics at dose range of 2 to 25 mg/kg.

Special populations
Renal impairment: As teicoplanin is eliminated by renal route, teicoplanin elimination decreases according to the degree of renal impairment. The total and renal clearances of teicoplanin depends on the creatinine clearance.

Elderly patients:
In the elderly population the teicoplanin pharmacokinetics is not modified unless in case of renal impairment.

Pediatric population
A higher total clearance (15.8 mL/h/kg for neonates, 14.8 mL/h/kg for a mean age 8 years) and a shorter elimination half-life (40 hours neonates; 58 hours for

8 years) are observed compared to adult patients.

PHARMACEUTICAL PROPERTIES
Incompatibilities
Teicoplanin and aminoglycoside are incompatible when mixed directly and must not be mixed before injection. If teicoplanin is administered in combination therapy with other antibiotics, the preparation must be administered separately. This medicinal product must not be mixed with other medicinal products except those mentioned.

Special precautions for storage
Protect from heat, sunlight and moisture. Store below 25°C. Do not freeze.
Keep out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

Presentation:
TICOZID 200mg Injection: Combined pack of one vial providing 200mg Teicoplanin (200,000 IU i.e. 1000 IU/mg) and one ampoule containing Water for Injection 3mL.
TICOZID 400mg Injection: Combined pack of one vial providing 400mg Teicoplanin (400,000 IU i.e. 1000 IU/mg) and one ampoule containing Water for Injection 3mL.

Shelf life:
2 years

REGISTRATION HOLDER / MARKETING AUTHORIZATION HOLDER
Head office:
Bosch Pharmaceuticals (Pvt.) Ltd.,
8, Modern Society, Tipu Sultan Road, Karachi-Pakistan

Manufacturing site:
Bosch Pharmaceuticals (Pvt.) Ltd.,
Plot No. 209, Sector 23, Korangi Industrial area, Karachi-Pakistan

Manufactured for:
Bosch Pharmaceuticals (Pvt.) Ltd.,
Plot No. 221-223, Sector 23, Korangi Industrial area, Karachi-Pakistan

REGISTRATION / MARKETING AUTHORIZATION NUMBER
Ticozid 200mg Injection
050514

Ticozid 400mg Injection
050515

DATE FROM WHICH MARKETING IS AUTHORIZED/RENEWAL OF THE AUTHORIZATION
27.08.2008/26.08.2023

DATE OF REVISION OF THE TEXT.
09.01.2024

ہدایات:۔
دھوپ، گرمی اور نمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
منجمد ہونے سے بچائیں۔ بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

Manufactured by:
Bosch Pharmaceuticals (Pvt) Ltd.
209, Sector 23, Korangi Industrial Area,
Karachi - Pakistan.
For **Bosch Pharmaceuticals (Pvt.) Ltd.**
221-223, Sector 23, K.I.A. Karachi-Pakistan.