120x280mm

Bactiplan
(Teicoplanin)

Highnoon

COMPOSITION:
Bactiplan 200mg IM/IV injection: Each Lyophilized Vial contains: Teicoplanin 200mg Eq. to 200,000 IU (1000 IU/mg)
Bactiplan 400mg IM/IV injection: Each Lyophilized Vial contains: Teicoplanin 400mg Eq. to 400,000 IU (1000 IU/mg)

PHARMACOLOGY:
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.

Mechanism of resistance
Resistance to teicoplanin can be based on the following mechanisms:
Modified target structure; this form of resistance has occurred particularly in *Enterococcus faecium*. The modification is based on the exchange of the terminal D-alanyl-D-alanine function of the amino-acid chain in a murein precursor with D-Ala-D-lactate, thus reducing the affinity to vancomycin. The responsible enzymes are a newly synthesized D-lactate dehydrogenase or ligase.
The reduced sensitivity or resistance of staphylococci to teicoplanin is based on the overproduction of murein precursors to which teicoplanin is bound. Cross-resistance between teicoplanin and the glycoprotein vancomycin may occur. A number of vancomycin-resistant enterococci are sensitive to teicoplanin (Van-B phenotype).

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.

Susceptibility
The prevalence of resistance may vary geographically and over time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

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.

PHARMACOKINETICS:
Teicoplanin is poorly absorbed from the gastrointestinal tract. After 400-mg intravenous dose, peak plasma concentrations 1 hour later are reported to be in the range 20 to 50 micrograms/mL. It is well absorbed on intramuscular injection with a bioavailability of about 90%; after a dose of 3 mg/kg intramuscularly, peak plasma concentrations of 5 to 7 micrograms/mL have been reported after 2 to 4 hours. The pharmacokinetics of teicoplanin are triphasic, with a biphasic distribution and prolonged elimination. Penetration into the CSF is poor. It is taken up into white blood cells, and about 90 to 95 % of teicoplanin in plasma is protein bound. It is excreted almost entirely by glomerular filtration in the urine, as an unchanged drug. The terminal half-life is prolonged, but reported half-lives have ranged from 30 to 190 hours or longer, depending on the sampling time; an effective clinical half-life of about 60 hours has been suggested for use in calculating dosage regimens. Half-life is increased progressively with increasing degrees of renal impairment. Teicoplanin is not removed by hemodialysis. Teicoplanin is a mixture of several components, the pharmacokinetics of which have been shown to vary slightly, depending on their lipophilicity.

INDICATIONS AND USAGE
Bactiplan (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 AND 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.

Adults and elderly patients with normal renal function

Indications	Loading dose		Maintenance dose	
• 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

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.
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 when measured by High Performance Liquid Chromatography (HPLC), or at least 15 mg/L when measured by Fluorescence Polarization Immunoassay (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 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.

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. For *Clostridium difficile* infection-associated diarrhea and colitis, the oral route is to be used.

CONTRA-INDICATIONS
Hypersensitivity to teicoplanin or to any of the excipients.

ADVERSE REACTIONS
The reported adverse events are; rash, erythema, pruritus, pain, pyrexia, leucopenia, thrombocytopenia, eosinophilia, anaphylactic reaction (anaphylaxis), ototoxicity, nephrotoxicity, dizziness, headache, deafness, hearing loss, tinnitus, vestibular disorder, phlebitis, bronchospasm, diarrhea, vomiting, nausea, blood creatinine increase, transaminases increased (transient abnormality of transaminases), blood alkaline phosphatase increased (transient abnormality of alkaline phosphatase), abscess, superinfection (overgrowth of non-susceptible organisms), agranulocytosis, neutropenia, pancytopenia, drug reaction with eosinophilia and systemic symptoms (DRESS), anaphylactic shock, seizures, thrombophlebitis, 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 failure (including renal failure acute), injection site abscess and chills (rigors).

DRUG INTERACTIONS
- 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 and/or neurotoxic/ototoxic potential. These include e.g. aminoglycosides, colistin, amphotericin B, ciclosporin, cisplatin, furosemide, and ethacrynic acid. However, there is no evidence of synergistic toxicity in combinations with teicoplanin.

SPECIAL WARNINGS AND PRECAUTIONS
- Teicoplanin should not be administered by intraventricular route.
- 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.
- In rare cases (even at the first dose), red man syndrome (a complex of symptoms including pruritus, urticaria, erythema, angioneurotic oedema, 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.
- 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.
- 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.
- Thrombocytopenia has been reported with teicoplanin. Periodic hematological examinations, including complete blood count, are recommended during treatment.
- Nephrotoxicity and renal failure has been reported in patients treated with teicoplanin. 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 (e.g. aminoglycosides, colistin, amphotericin B, ciclosporin, and cisplatin) should be carefully monitored, and should get auditory tests. Since teicoplanin is mainly excreted by the kidney, the dose of teicoplanin must be adapted in patients with renal impairment.
- 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 inpatients with renal insufficiency. Patients receiving teicoplanin in conjunction with or sequentially with other medicinal products with known nephrotoxic and/or neurotoxic/ototoxic potential (e.g., aminoglycosides, colistin, amphotericin B, ciclosporin, 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.
- 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.
- 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.

PREGNANCY
Pregnancy Category B
There are a limited amount of data from the use of teicoplanin in pregnant women. 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.

Effects on ability to drive and use machines
Teicoplanin has minor influence on the ability to drive and use machines. Teicoplanin can cause dizziness and headache. The ability to drive or use machines may be affected. Patients experiencing these undesirable effects should not drive or use machines.

Preparation of reconstituted solution
The solution is reconstituted by adding 3 mL of water for injection to the 200 mg or 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.

Incompatibilities
Teicoplanin and aminoglycosides 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 water for injection, 0.9% NaCl infusion, 5% Dextrose and Ringer lactate infusion.

Shelf life of reconstitute solution
Chemical and physical in use stability of the reconstituted solution prepared as recommended has been demonstrated for 2 hours at 25°C to 30°C and 36 hours at 2°C to 8°C. From a microbiological point of view, the medicinal product should be used as soon as after preparation (within 1 hour). If not used immediately, in use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 2 hours at 25°C to 30°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

OVERDOSAGE
Cases of accidental administration of excessive doses to pediatric patients have been reported. Treatment of teicoplanin overdose should be symptomatic. Teicoplanin is not removed by hemodialysis and only slowly by peritoneal dialysis.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 25°C. Keep in a dry place. Protect from light.

PRESENTATION:
Bactiplan 200mg IM/IV injection: 1 vial of 200mg Teicoplanin and 1 ampoule of 5mL sterile water for injection.
Bactiplan 400mg IM/IV injection: 1 vial of 400mg Teicoplanin and 1 ampoule of 5mL sterile water for injection.

بیکٹی پلان
(ٹیکوپلینین)

انجکشن تیار کرنے کا طریقہ:
ڈاکٹر کی ہدایت پر عمل کریں۔
محلول بنانے کیلئے صرف تین ملی لیٹر پانی استعمال کریں۔
تیار کیا ہوا محلول فوراً استعمال کریں۔

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 25° C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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Item Code No. LEF-100592