MINISTRY OF HEALTH OF THE REPUBLIC OF BELARUS

PACKAGE LEAFLET

TEICOPLANIN – TF

Powder for preparation of solution for intravenous and intramuscular injections 200 mg, 400 mg

Stamp: APPOVED by the Ministry of Health of the Republic of Belarus
Order of the Ministry of Health of the Republic of Belarus
No. 870 as of 02.09.2015

Trade name Teicoplanin-TF.
International nonproprietary name Teicoplanin.
Dosage form Powder for preparation of solution for intravenous and intramuscular injections 200 mg, 400 mg
Description Amorphous yellowish powder
Composition for 1 vial
Teicoplanin - 200 mg or 400 mg
Pharmacotherapeutic group Glycopeptide-antibiotic
ATX Code JO1XA02
Pharmacological properties
Pharmacodynamics
Teicoplanin is a complex glycopeptide produced by Actinoplanes teichomyceticus. Antibiotic is a complex of six related substances with different antibacterial activity. Antibacterial effect of Teicoplanin-TF is displayed in the result of inhibition of cell-wall biosynthesis. The antibiotic can modify the permeability of the cell membrane of bacteria and to modify RNA synthesis.
Teicoplanin-TF is effective against *gram-positive microorganisms* Enterococcus spp.. Staphylococcus spp., Streptococcus spp., Clostridium spp., Peptostreptococcus spp., Propionibacterium acnes, Corynebacterium jeikeium.
Actinomyces, heterofermentative lactobacilli. Leuconostoc, Nocardia asteroides, Pediococcus, as well as gram-negative aerobes, chlamydiae, mycobacteria, mycoplasmas, Rickettsiae, treponemas are resistant towards Teicoplanin-TF. Teicoplanin-TF is not active against gram-negative bacteria, while the lipid layer of the outer membrane of these bacteria prevent large antibiotic molecules from reaching peptidoglycan layer. The resistance develops slowly, there is no cross-resistance with antibiotics of other groups.
Pharmacokinetic properties
After intravenous or intramuscular injection (3-6 mg/kg) the bioavailability of Teicoplanin-TF amounts to 90% in the blood, the drug substance binds to proteins for 90-95%. Upon internal administration Teicoplanin-TF is poorly soaked from the gastrointestinal tract. Teicoplanin-TF reaches lunges, bones, soft tissues well. It slowly penetrates into cerebrospinal fluid. The elimination half-life of Teicoplanin-TF amounts from 33 to 160 hours. Up to 80% of the antibiotic is excreted with kidneys mostly.
Pharmacokinetic properties in particular medical cases
In case of renal insufficiency therapeutic regimens with Teicoplanin-TF are adjusted taking into account disorders excretory function of the kidneys. In case of moderate renal insufficiency (creatinine clearance amounts to > 21-80 ml/min) the patient is injected with a half of regular dose. Still the level of the medicinal product in blood varies with critically ill patients and often it cannot be predicted on the basis of measurement creatinine clearance. In such cases the dose regimen is determined through constant monitoring of Teicoplanin-TF level in blood.

Indications for use

Infectious inflammatory diseases caused by gram-positive bacteria sensitive towards Teicoplanin, including those resistant towards methicillin: skin and soft tissues infections, bones and joints infections, infections of upper and lower respiratory tract, community-acquired pneumonia and hospital-acquired pneumonia, complicated and noncomplicated urinary tract infections; ENT-organs infections, septicaemia. It is additionally administered with adults with endocarditis or peritonitis associated with permanent peritoneal lavage under outpatient treatment:
for prevention of infectious endocarditis in case of allergy to β-lactam antibiotics; in dentistry and in procedures in upper respiratory tract, when general anesthesia is applied; in case of surgical interference into genitourinary system and gastrointestinal tract.
Teicoplanin-TF is applied in case of allergy to penicillin or β-lactam antibiotics, intolerance or absence of response of other antibiotics, including penicillins or cephalosporins.

Stamp: APPOVED by the Ministry of Health of the Republic of Belarus
Order of the Ministry of Health of the Republic of Belarus

Contraindications

Hypersensitivity to Teicoplanin, pregnancy, lactation period.

Precautions

Special warnings

Prescribed in case of hypersensitivity to Vancomycinum *with caution* (cross allergization is possible).
For patients *with renal deficiency* the dose adjustment is required.
Long-term therapy and treatment with high doses require constant control of liver, kidneys, hematosis function, sense of hearing (especially during the first month of therapy and in case of disorders in the anamnesis).
In case of administration of Teicoplanin-TF ototoxicity, toxic effect upon hematopoietic system, hepatotoxicity and renal toxicity can occur.
Concurrent administration of Teicoplanin-TF with ototoxic, nephrotoxic and neurotoxic medicinal products (aminoglycoside, colistin, amphotericin, cyclosporine, cisplatin, furosemide and ethacrynic acid) *is not recommended*. When administered concurrently with the indicated medicinal products it is necessary to conduct re-examination of renal functions and of those of the sense of hearing.
Presence of “red man syndrome” in the anamnesis caused by Vancomycinum administration is not a contraindication to Teicoplanin application. *Application in pediatrics*
When medicinal product is administered *with children* it is necessary to control Teicoplanin concentration in blood plasma.

Application during pregnancy and lactation

Application of Teicoplanin-TF is necessary only in life-saving cases if potential benefits for mother outweigh potential risks for the fetus. In such case it is necessary to control the hearing function of the newborn because of the ototoxic effect of Teicoplanin-TF.
If the medicinal product is applied *during lactation period*, breast feeding should be stopped.

Effects on ability to drive and use machines

During application of Teicoplanin-TF it is recommended to sustain from driving transport vehicles and from work with complex machines because of the risk of dizziness.

Posology and administration

Posology and administration of Teicoplanin-TF depend on the responsiveness of a causative agent, severity of infection and on the condition of a patient renal functions.

Stamp: APPOVED by the Ministry of Health of the Republic of Belarus
Order of the Ministry of Health of the Republic of Belarus

Teicoplanin-TF should be administered intramuscularly or intravenously (in the form of bolus injection within 3-5 min or in the form of infusion within 15-30 min).
Upper and lower respiratory tract infections, skin and soft tissue infections, urinary tract infections, ENT-organs infections and other moderate severity infections: loading dose for adults and elderly people with normal kidney function amounts to 400 mg intravenously or intramuscularly every 12 hours for first 1-3 injections, then 200 mg intravenously or intramuscularly one time per day.
Septicemia, bones and joints infections, endocarditis, complicated infections of upper respiratory tract and other severe infections: loading dose for adults and elderly people with normal kidney function amounts to 800 mg intravenously every 12 hours for first 3-5 injections; maintenance dose amounts to 12 mg/kg intravenously or intramuscularly one time per day. For prevention of infectious complications in orthopedic or dentofacial surgery during anaesthesia 400 mg is administered intravenously one time.
For maintenance therapy during treatment of septicemia and endocarditis transfer to intravenous administration depends on the clinical progression of a disease.
In particularly severe clinical cases when minimal inhibitory concentrations of teicoplanin are high (4-8 mg/l), considering bacterial loads or when it is difficult to predict pharmacokinetic properties of a medicinal product in blood serum (substantial burns, intensive therapy, etc.) or in conditions of low tissular distribution (bones, heart valve) recommended loading dose – 3-5 injections per 12 mg/kg every 12 hours. If necessary, maintenance doses can be prescribed up to 12 mg/kg and more.
For optimal dose achievement it is necessary to determine antibiotic concentration in blood plasma. When obtaining loading doses it is necessary to monitor residual plasma concentrations to ensure stable residual concentrations in blood plasma within 20-30 mg/l (high performance liquid chromatography) or 30-40 mg/l (enzyme immunoassay), as well as during maintenance therapy so that to ensure stability of these concentrations.
Initial dose for *children in the age from 2 months to 12 years* amounts to 10 mg/kg intravenously every 12 hours 3 times, then *6-10 mg/kg* intravenously 1 time per day; *in the age up to 2 months* – 16 mg/kg (in the form of 30-minute intravenous infusion) in the first day, maintenance dose amounts to 8 mg/kg intravenously 1 time per day. In case of moderate or more severe infection in obtaining loading doses it is necessary to monitor residual plasma concentrations so that to ensure stability of residual concentrations in blood plasma not less than 10mg/l (high performance liquid chromatography) or 15 mg/l (enzyme immunoassay), as well as during maintenance therapy, so that to ensure stability of these concentrations.
In case of *pseudomembranous colitis* Teicoplanin-TF is prescribed 100-200 mg 2 times per day within 7-14 days. Recommended dose of Teicoplanin-TF is administered internally after the dissolution.
With adults and elderly patients with renal function disorders adjustment is commenced from the 4th day so that to maintain Teicoplanin-TF concentration in serum at the level 10 mg/l. If creatinine clearance equals to 30-80 ml/min maintenance dose is decreased by half or administered 1 time per two days.
Patients with creatinine clearance less that 30 ml/min or patients treated with hemodialysis are administered with 1/3 of the dose daily or 1 time per 3 days. Teicoplanin-TF is not excreted through hemodialysis.
With adults and elderly patients with renal function disorders and with secondary peritonitis which resulted from continuous peritoneal lavage, dosage regime per 20 mg for 1 liter of dialysis fluid is recommended; loading dose for such patients equals to 200 mg.
In case of moderate or more severe infection when obtaining loading doses it is necessary to monitor residual plasma concentrations so that to ensure stability of residual concentrations in blood plasma not less than 10 mg/l (high performance liquid chromatography) or 15 mg/l (enzyme immunoassay) or during maintenance therapy so that to ensure stability of these concentrations. In particularly severe clinical cases when minimal inhibiting concentrations of Teicoplanin are high (4-8 mg/l), considering bacterial loads or when it is difficult to predict pharmacokinetic properties of medicinal product in blood serum

(substantial burns, intensive therapy, etc.) or in conditions of low tissular distribution (bones, heart valve) for obtainment of stable residual concentrations in blood plasma within 20-30 mg/l (high performance liquid chromatography) or 30-40 mg/l (enzyme immunoassay), as well as during maintenance therapy so that to ensure stability of these concentrations.

Stamp: APPOVED by the Ministry of Health of the Republic of Belarus
Order of the Ministry of Health of the Republic of Belarus

Rules of solution preparation

200 mg or 400 mg of Teicoplanin-TF is dissolved in 3 ml of one of the following solvents:
0.9% sodium chloride solution, Ringer's lactate solution, 5% glucose solution, 0.18% sodium chloride solution and 4% glucose solution, solution for peritoneal lavage with 1.36% or 3.86% of glucose. The solvent is injected in the vial slowly, carefully wiggling the vial till the complete dissolution of the powder preventing foam formation. If some foam is formed, the vial with solution should be left in vertical position so that to reduce its amount.
The solution obtained can be used for intramuscular administration.
So that to apply the medicinal product in the form of infusions, the solution is reconstituted to 100 ml. For internal administration 200 mg in 400 mg Teicoplanin-TF is dissolved in 10 ml of water.
So that to prevent administration of the dose lower than the required one the medicinal product should be completely dissolved. The solvent is injected into the vial slowly so that to prevent formation of bubbles. In case of foam formation it is necessary to leave the vial in vertical position not less than for 15 minutes. The prepared solution should be thoroughly extracted from the vial.

Side effects

Allergic reactions: rash, itch, erythema, temperature rise, anaphylactic reactions (angioneurotic edema, bronchial spasm, anaphylactic shock), urticaria, exfoliative dermatitis.
Skin and subcutaneous tissues: severe bullous skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, in exceptional cases - erythema multiforme).
Liver: temporary increase of transaminase and/or alkaline phosphatase level.
Blood circulatory and lymphatic system: eosinophilia, leucopenia, thrombocytopenia, neutropenia (rarely-severe form) or agranulocytosis (recurrent after treatment cessation), which often develops in case of high doses administration and during the first month of therapy.
Digestive system: diarrhoea, vomiting, nausea.
Urinary system: temporary increase of creatinine level, renal failure, usually occurring in patients with patients with severe infection course, with presence of main disease and/or with patients treated with other medicinal products with nephrotoxic effect.
Nervous system: dizziness, headache, hearing loss, ringing in the ears, disorders in vestibular system, cases of seizures were reported.
Local reactions: pain in the place of injection, phlebitis, erythema, abscess
Other reactions: superimposed infection (increase of number of insensitive microorganisms).

Overdose

Symptoms: more significant side effects.
Treatment: symptomatic. Teicoplanin-TF is not removed from the organism through hemodialysis.

Interaction with other medicinal products

Concurrent administration of Teicoplanin-TF and aminoglycoside in the form of injections is not allowed. They can be administered in conjunction with one another in the form of solution for dialysis during peritonitis treatment attributed to continuous outpatient peritoneal lavage.
If administered concurrently of Teicoplanin-TF and other potentially with neurotoxic and/or nephrotoxic. and/or ototoxic medicinal products (aminoglycosides, amphotericin B, ciclosporin, furosemide, colistin, cisplatin and ethacrynic acid) synergistic toxicity increase is possible.

Special warning attributed to incompliance of international normalized ratio (INR): many cases of anticoagulant activity rise with patients treated with oral antibiotics were registered. In case of infection or apparent inflammatory process risk factors include the elderly age and severe general condition of a patient.

Storage conditions and shelf life

Protect from light at the temperature at 2 to 8°C.

Keep away from children.

Shelf life is 2 years. Do not use upon expiry of the shelf life indicated on the package.

Prescription status

The medicinal product is dispensed on the doctor's prescription.

Package

200 mg or 400 mg in the vial with the volume 10 ml.

5 vials in a package or 36 vials in a package (package for in-patient hospitals).

Information on the manufacturer

Joint Limited Liability Company "TriplePharm", Minskaya St., house 2B, 223141, the city of Logoisk, Minsk region,
Republic of Belarus,
Phone/fax: (+375) 1774 43 181, e-mail: triplepharm@gmail.com

Stamp: APPOVED by the Ministry of Health of the Republic of Belarus
Order of the Ministry of Health of the Republic of Belarus