TARGOPLANIN®

Teicoplanin

ACTION

Targoplanin is a glycopeptide antibiotic obtained from the fermentation of *Actinoplanes teichomyceticus*. Its activity is predominantly bactericidal. It can be administered intravenously or intramuscularly.

The active principle in Targoplanin is teicoplanin; and it is active against both aerobic and anaerobic Gram-positive bacteria. In-vitro tests have confirmed that Targoplanin is active against *Staphylococci* (including strains resistant to methicillin and other betalactams), *Streptococci, Enterococci, Listeria, Diphtheroids* and *Clostridia* (including *Clostridium difficile*).

Targoplanin has not induced the development of bacterial resistance in-vitro, and does not display cross-resistance with other classes of antibiotics (penicillin and cephalosporins, macrolides, tetracycline and chloramphenicol, aminoglycosides and rifampicin).

Targoplanin is not absorbed when administered by mouth. Following i.v. or i.m. administration it is distributed among the tissues and exudates of the body. Targoplanin is slowly eliminated, with a serum half-life of 70-100 hours. Its excretion predominantly occurs via the kidneys.

INDICATIONS

Severe infections caused by susceptible Gram-positive bacteria, especially *Staphylococcus aureus* (methicillin and cephalosporin - resistant). As prophylaxis against Gram-positive endocarditis in dental surgery to high risk heart patients, particularly in the event of allergy to betalactams.

Intraperitoneal administration to treat peritonitis in patients undergoing chronic ambulatory peritoneal dialysis.

CONTRAINDICATIONS

Targoplanin should not be prescribed for patients with known hypersensitivity to glycopeptide antibiotics.

DOSAGE AND ADMINISTRATION

Targoplanin can be administered intravenously (bolus or infusion), intramuscularly or intraperitoneally in a single daily dose following one or more loading doses.

Mode of use

Withdraw 3 ml of water for injection with a syringe and inject slowly down the side of the vial containing the active product.

Gently roll the vial between the hands until all the powder has dissolved completely, taking care to avoid forming any foam. The resulting isotonic solution contains approximately 66.7 mg Targoplanin/ml, pH 7.5 and can be stored for 48 hours at room temperature.

Adults with normal renal function

The dose of Targoplanin should be adjusted according to the severity of the infection:

- 6 mg/kg (approximately 400 mg) - is recommended on the first day. Subsequently, either 6 mg/kg (approximately 400 mg) i.v. or 3 mg/kg (approximately 200 mg) i.v. or i.m. can be given once a day. The higher dose and i.v. route are recommended in more severe infections.
- In severe and life-threatening infections, an initial loading dose of 6 mg/kg (approximately 400 mg) administered twice daily for 1-4 days should be followed by a maintenance dose of 6 mg/kg/day thereafter intravenously.

Targoplanin should be combined with another suitable bactericidal drug to treat infections requiring maximum bactericidal activity (such as *staphylococcal endocarditis*) or in situations where the presence of a Gram-negative component cannot be excluded (empirical treatment of febrile episodes in neutropenic patients).

Most patients obtain benefit from treatment within 48-72 hours. The total duration of treatment is, however, determined by the type and severity of infection treated and the patient's individual response. Targoplanin should be administered for at least 3 weeks in the case of endocarditis or osteomyelitis.

Adults and elderly patients with renal impairment

The dose should be adjusted starting from the 4th day of treatment as shown below:

- ***Moderate impairment***

(Creatinine clearance of 40-60 ml/min): the daily dose of Targoplanin should be halved or administered every other day.

- ***Severe impairment:***

(Creatinine clearance less than 40 ml/min) and patients undergoing haemodialysis: The daily dose of Targoplanin should be reduced to 1/3 initial level or administered every 3 days. Patients with creatinine clearance equal to or less than 20 ml/min can only receive Targoplanin if monitoring of serum concentrations of the drug is guaranteed. Teicoplanin is not removed from the circulation by dialysis. Serum concentrations of teicoplanin can be determined in order to optimize treatment. In severe infections, minimum serum concentrations should not fall below 10 mg/l.

Prophylaxis against endocarditis during dental surgery

400 mg i.v. at the time of general anaesthesia induction.

Patients with valve prostheses must receive a combination of Targoplanin and aminoglycosides.

Intraperitoneal administration

For patients with renal impairment and with peritonitis secondary to continuous ambulatory peritoneal dialysis, the recommended dose is 20 mg teicoplanin per litre of dialysis fluid, preceded by a loading dose of 400 mg i.v. if the patient is febrile. It is permissible to continue treatment for more than 7 days provided that the endoperitoneal dose is halved during the second week (20 mg/l. in every other dialysis pack) and reduced to 1/4 the initial level during the third week (20 mg/l. in the nocturnal pack).

Targoplanin is stable in peritoneal dialysis solutions (1.36 % or 3.86 % dextrose) for up to 24 hours if stored at 4°C. Solutions should not be used after 24 hours.

Children

Children with normal renal function: The dose and duration of treatment should be defined according to the type and severity of the infection and taking into account the patient response.

Treatment should be started at a dose of 10 mg/kg every 12 hours for a total of 3 doses and continued at a dose of 6-10 mg/kg/day, reserving the higher dosage for the most severe infections or for neutropenic children. In neonates, treatment should be started at a dose of 16 mg/kg on the first day, followed by maintenance doses of 8 mg/kg/day by slow intravenous infusion (about 30 minutes).

Children with renal impairment: It is recommended to adjust the doses as for adults (see above).

WARNINGS AND PRECAUTIONS

Although animal reproduction studies have not shown evidence of impairment of fertility or teratogenic effects, Targoplanin should not be used during confirmed or presumed pregnancy unless the physician considers that the potential benefits outweigh any possible risk. As a precautionary measure in the absence of data about the excretion of teicoplanin in breast-milk, Targoplanin should not be administered to nursing mothers.

Where prolonged treatment is indicated it is desirable to carry out periodic blood analyses and tests of renal and hepatic function.

In the presence of concomitant renal impairment or hypoacusis and during prolonged treatment, it is advisable to monitor serum Targoplanin levels as well as renal and otovestibular function. Similar monitoring is also recommended in patients requiring concomitant treatment with neurotoxic or nephrotoxic drugs such as aminoglycosides, cefaloridine, polymyxin B, colistin, amphotericin, cyclosporin, cisplatin, frusemide and ethacrynic acid.

Targoplanin has been administered to many patients in combination with other classes of drugs including antibiotics, antihypertensives, cardioactive and antidiabetic drugs, etc, during clinical trials without evident interaction.

In the event of an overdose, symptomatic treatment should be administered. Targoplanin cannot be extracted from the circulation by haemodialysis.

Bacterial sensitivity should be determined using a standard type of antibiogram to ensure the correct use of antibiotics.

Since the use of a selective antibiotic can promote the growth of non-susceptible microrganisms, appropriate complementary treatment is required to treat any superinfection that might develop.

SIDE EFFECTS

While Targoplanin is generally well tolerated, local reactions to the antibiotic have been reported on rare occasions (pain, phlebitis and subcutaneous abscess) in addition to hypersensitivity reactions (skin rash, erythema, pruritis, fever, bronchospasm and anaphylaxis). Elevated transaminases and/or alkaline phosphatase and transient increases in serum creatinine, eosinophilia thrombocytopenia, leucopenia and presence of anti- factor VIII antibodies accompanied by bleeding have also been reported.

Nausea, vomiting, diarrhoea, vertigo, headache, asthenia, oedema, chest discomfort, tachycardia and increased serum levels of uric acid and amylases have occasionally been reported. Audiometric, tests performed on several subjects before and after treatment have not revealed any changes, with the sole exception of a single case of high frequency hearing loss in a patient suffering from Down's syndrome. Isolated cases of vestibular and auditory changes have been noted in patients concomitantly receiving gentamycin and frusemide.

OVERDOSAGE

Targoplanin is not removed from the circulation by haemodialysis. Symptomatic treatment should be administered in the event overdose.

Several 100 mg/kg/day doses have accidentally been administered to 2 neutropenic children aged 4 and 8 years; in spite of the high serum concentrations of teicoplanin detected (up to 300 mg/l.), no signs of intoxication or laboratory abnormalities were detected.

STORAGE

Store below 25°C.

PRESENTATIONS

Vials:

TARGOPLANIN 200 mg: Teicoplanin as lyophilized product 200 mg

Excipients: Sodium chloride.

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by Hikma Italy, SpA, Italy
for Hikma Pharmaceuticals, Amman-Jordan

Keep medicament out of the reach of children

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duplication