COMPOSITION

One vial contains Benzypenicillin G Potassium (Sodium) of 0.600 g, equivalent respectively to 1,000,000 UI, Benzylpenicillin.

The content of sodium (potassium) is approx. 64.5 mg/g (104.9 mg/g).

PROPERTIES AND ANTIMICROBIAL SPECTRUM

Penicillin G is a beta-lactam antibiotic with bactericidal type of action against large number of gram-positive and gram-negative microorganisms.

The drug inhibits the bacterial cell wall synthesis during the stage of active multiplication of the microorganisms. This effect is suppressed by the penicillinase enzyme and other beta-lactamases, produced by gram-positive and gram-negative microorganisms.

The antibacterial spectrum of Penicillin G includes:

- **Gram-positive aerobes and anaerobes**: Staphylococcus (non-penicillinase producing), Streptococcus (Gr. A, C, G, H, L and M), Bacillus anthracis, Clostridium sp. (except for Clostridium difficile), Corynebacterium diphtheriae, Erysipelothrix rhusiopathiae, Listeria monocytogenes.

- **Gram-negative aerobes and anaerobes**: Neisseria meningitidis, Neisseria gonorrhoeae, Pasteurella multocida, Streptobacillus moniliformis, Spirillum
minus, Haemophilus sp., Bacteroides sp. (except for Bacteroides fragilis) and Fusobacterium sp.

Certain gram-negative strains are susceptible to high Penicillin G concentrations, attained after intravenous application (all strains of Proteus mirabilis, Salmonella and Shigella, Aerobacter aerogenes and Alcaligenes faecalis).

- **Other microorganisms** - susceptible to Penicillin G are Actinomyces, Borrelia sp., Leptospira sp., Treponema sp. (Treponema pallidum is extremely sensitive to Penicillin G).

**PHARMACOKINETICS**

Penicillin G is rapidly absorbed following intramuscular administration. Maximum serum concentrations are attained within 15-30 min after the injection. Benzylpenicillin penetrates the body tissues and fluids to a different extent. It penetrates in the pleural, pericardial, peritoneal, synovial, intestinal and ascite fluids.

The drug attains minimal concentrations in purulent exudates (abscess, empyema), in the eyes, middle ear, cerebrospinal fluid and prostate. Penicillin G crosses the placental barrier. It passess in small quantities (5-10%) into the breast milk. The absorption after intramuscular administration of the drug is impeded by diabetes.

The plasma half-life ($T_{1/2}$) is approximately 30 min and could be prolonged in neonates and infants due to immaturity of the renal function. The serum half-life of Penicillin G becomes prolonged (to approximately 10 hours) in the presence of
impaired renal function. Penicillin G has a serum protein - binding rate of approximately 60%.

The antibiotic is partially metabolised and quickly excreted in the urine primarily by glomerular filtration and active tubular secretion. About 60-90% of the intramuscularly injected Penicillin G is excreted in the urine within 1 h.

In patients with normal renal function only small quantities are excreted in the bile and faeces.

The tubular excretion of Penicillin G is impeded by probenicid, the combination results in elevation of the plasma Penicillin G concentrations.

**INDICATIONS**

Penicillin G is indicated for the treatment of infections, caused by penicillin-susceptible microorganisms: abscesses, anthrax, actinomycosis, leptospiroses, Lyme disease, skin infections incl. erysipelas, wound infections; gas gangrene, tetanus, prostatitis, gonorrhea, syphilis, frambesia, pinta, diphtheria, croupous pneumonia, scarlatina, rheumatism, tonsillitis, certain types of subacute bacterial endocarditis, meningitis, otitis media, acute and chronic osteomyelitis.

It is administered for prophylaxis before dental procedures and surgical interventions, in patients particularly at risk of endocarditis, as well as a preventive treatment against eventual recurrence of rheumatic fever.

**CONTRAINDICATIONS**

Hypersensitivity to Penicillin G found in the past or immediately before the treatment.
ADVERSE EFFECTS

Penicillin is a substance of low toxicity, but it does possess a significant index of sensitization.

The most common adverse effects, connected with the Penicillin G administration are allergic reactions and rashes.

Administration to hypersensitive patients may cause an anaphylactic shock. Angioedema or bronchospasm are also possible to occur. General reaction of hypersensitivity may be observed from several hours to weeks after the beginning of Penicillin G treatment, the symptoms being urticaria, fever, headache or eosinophilia. Other possible allergic reactions include exfoliative dermatitis, interstitial nephritis, vasculites. Haemolitic anaemia, leucopenia or trombocytopenia occur rarely, particularly after intravenous administration of high doses. Convulsions or other CNS toxicity symptoms may occur with high-dose intravenous administration, as well as in renal failure patients. Intrathecal administration of Penicillin G could bring about encephalopathia. Disturbance of the plasma electrolytic balance has been reported with the administration of high doses of Penicillin G potassium or sodium salt. In the therapy of some infections (syphilis, pertussis) could be released large quantities of endotoxins, causing shock reactions (endotoxic shock).

PRECAUTIONS

The low toxicity of the Penicillin G preparations enables the treatment of infections during pregnancy. Due to its excretion in the breast milk rashes may occur in the breast-fed infant as a result of sensitization.

Administration to patients with a history of clinically significant hypersensitivity to Penicillin G is contraindicated!
At the beginning of every new course of Penicillin G treatment, the patient must be tested for hypersensitivity and in case allergic anamnesis is absent, a skin scarification test is necessary to perform - dilution 60 mg/ml (100 000 UI/ml). If the anamnesis indicates allergic reaction: first, an epicutaneous test (with the same dilution) is to be made, if negative, the second step is the scarification test.

Adrenaline must be available in case of anaphylactic shock, usually the treatment is carried out with 0.1 mg - 0.3 mg - 0.5 mg adrenaline, injected hypodermically, intravenous infusion of corticosteroids, antihistaminic preparation (parenteral), novphyllin and selective beta-adrenomimetics in case of bronchospasm. In treatment regimens, requiring high Penicillin G doses, Penicillin G sodium should be used to avoid hyperkalemia with neurological and cardiovascular symptoms.

Intrathecal administration of Penicillin G should be avoided!

**DRUG INTERACTIONS**

Probenecid prolongs the plasma half-life of Penicillin G.

The combination of Penicillin G and gentamicin is synergistic against some gram-positive and gram-negative aerobes, including lactobacilli and certain streptococci.

An additive effect or restricted synergism has been observed in combination of Penicillin G and tetracycline or erythromycin against Chlamydia trachomatis.

Antagonism occurs with the co-administration of amikacin against enterococci or chloroamphenicol against the causatives of pneumococcal meningitis and infections, caused by group A - streptococci, as well as with the combination of Penicillin G and erythromycin against streptococcal infection.
In the treatment of infections, caused by beta-lactamase producing microorganisms, the effect of Penicillin G is enhanced by combining with beta-lactamase inhibitors, such as sulbactam, clavulanic acid and etc.

Combinations with cephalosporins should be avoided!

**DOSAGE AND MODE OF ADMINISTRATION**

Penicillin G is administered parenterally as a sodium or potassium salt. An obligatory test for tolerance and hypersensitivity is prior to the administration.

In adults, depending on the severity of the infection, the dosage varies from 0.6 g (1 000 000 UI) to 2.4 g (4 000 000 UI), divided in two or four doses, administered intramuscularly or intravenously.

Dosage from 3.0 g (5 000 000 UI) up to 12 g (20 000 000 UI) are administered intravenously (microjet or drip infusion) most often in endocarditis or meningitis. Higher Penicillin G doses are possible to administer - up to 24 g (40 000 000 UI) daily.

The treatment of subacute bacterial endocarditis and osteomyelitis should continue at least 4 to 6 weeks.

Penicillin G potassium (sodium salt) for i.m. injection is dissolved in sterile water for injection.

Doses of 0.300 g (500 000 UI) are dissolved in 1 ml of solvent, higher doses - in 2-3 ml.

A single dose of 0.6 -1.2 g (1 000 000 UI - 2 000 000 UI) Penicillin G for intravenous microjet infusion should be dissolved in 5-10 ml of sterile saline or water for injection. Infusion time - 3-5 min.
Penicillin G for intravenous drip in doses of 1.2 - 3.0 g (2 000 000 UI - 5 000 000 UI) should be dissolved in 100 - 200 ml of sterile isotonic sodium chloride solution or in 5-10 % glucose solution. Dripping rate - 30 -40 drops / min.

In children, aged 1 month - 12 years, the daily dosage of 10-20 mg (16 700 - 33 400 UI)/kg is fractionated in 4 doses.

The dosage could be raised to 40 mg (66 800 UI)/kg daily in the treatment of meningitis.

In new-borns the dosage is 30 mg (50 100 UI)/kg daily, but may be raised up to 90 mg (150 300 UI)/kg daily in case of meningitis.

Intrathecal injections should be avoided, but for compelling reasons, Penicillin G is applied in adults at a dose of 6 mg (10 000 UI)/kg. Daily dosage exceeding 12 mg (20 000 UI/kg) is not recommended. For babies and children the intrathecal Penicillin G dose is 0.1 mg (167 UI)/kg.

The duration of treatment and the intervals between the applications are prescribed by the physician.

PACKAGE

Vials of 0.600 g (1 000 000 UI); boxes of 10,50 or 100 vials.

STORAGE

In dry places, protected from sunlight at temperature not exceeding 25°C.

SHELF LIFE

Four years.

MANUFACTURED BY: Balkanpharma - Razgrad, Bulgaria.