

Name of Medicine

BENPEN INJECTION

Benzylpenicillin Sodium 600mg, 1.2g and 3g/vial

Presentation

White powder in vial nominally containing 600mg, 1.2g or 3g of Benzylpenicillin Sodium. These presentations contain no other excipients.

Uses

Actions

Benzylpenicillin is bactericidal and is active against most Gram-positive organisms e.g. pneumococci, streptococci, non-beta-lactamase-producing staphylococci, clostridia and some Gram-negative organisms, eg. gonococci and meningococci. It is also active against spirochetes such as *Treponema pallidum*

Pharmacokinetics

Benzylpenicillin appears rapidly in the blood after intramuscular injection, maximum concentrations being reached in 20 to 30 minutes. The concentration with a particular dose varies in different patients and in the same patient on different occasions. Serum concentrations of penicillin have been reported to range from 1.2 to 12 µg per mL, 3 to 6 hours after the intramuscular injection of 60 to 600 mg. The minimum effective serum-penicillin concentration is about 0.02 µg per mL for sensitive organisms, but higher levels (0.03 to 0.06 µg per mL) are required in the treatment of sub-acute bacterial endocarditis or infections due to relatively less sensitive organisms. The half-life of benzylpenicillin when given intramuscularly is 30 minutes.

Benzylpenicillin diffuses across the placenta into the foetal circulation and small amounts may appear in the milk of nursing mothers. However, very little passes into the cerebrospinal fluids except when the meninges are inflamed. Small amounts are excreted in the bile. It is rapidly excreted by the renal tubules, causing a steep decline in serum-penicillin concentrations; up to 60% of a single intramuscular dose may appear in the urine within 1 hour of administration and 95% within 4 hours. The renal tubular excretion of penicillin can be partly blocked by probenecid, but the latter is not often used with benzylpenicillin clinically since adequate serum concentrations can be attained by simply increasing the dose. In patients with renal impairment, the serum half-life of penicillin may be prolonged, but normal doses of benzylpenicillin can be given except when there is severe impairment.

Indications

Treatment of infections due to Gram-positive organisms. It may also be used for prevention of wound infections and sepsis in surgical procedures where the likely pathogens are streptococci. Benzylpenicillin is also active against some spirochetes.

Dosage and Administration

There is no need to monitor the rate of injection with the sodium salt of benzylpenicillin, but with intravenous doses of the potassium salt greater than 900 mg, the rate of administration should not be more than 300 mg per minute. To achieve a particular concentration, Water for Injections BP should be added to the penicillin according to the table on the carton.

Intramuscular Administration

For intramuscular administration doses up to 300 mg should be dissolved in 1 mL of Water for Injections BP and larger doses in the volume of Water for Injections BP indicated in the table on the carton to give 300 mg per mL.

The minimum dosage should be:

300 mg 6 hourly for adults and children over 10 years of age.
150 to 300 mg 6 hourly for children 3 to 10 years of age.
60 mg 6 hourly for children under 3 years of age.
30 to 60 mg 12 hourly for premature babies and neonates.

For severe infections or where more resistant organisms are involved, the dose may be increased in amount and frequency of administration.

Intravenous Administration

Intravenous administration may be by bolus injection or intermittent addition to the drip chamber. For some severe infections, from 4 to 24 g may need to be given daily.

Antimicrobial Prophylaxis for Surgery: Where the likely pathogens are streptococci, 600 mg benzylpenicillin should be given intravenously immediately prior to surgery. For prolonged operations, the same dose may be given 4 to 8 hourly for the duration of the procedure. Post operative administration is usually unnecessary and may be harmful. In the case of a lower limb amputation, especially of an ischaemic limb, there is a risk of clostridial infection and benzylpenicillin 1.2 g should be given IV 6 hourly for 48 hours.

Intrathecal: Intrathecal administration of benzylpenicillin is undesirable and unnecessary because therapeutic levels can be attained in the theca by using large parenteral doses at frequent intervals e.g. 900 mg every 2 to 3 hours.

Subacute Bacterial Endocarditis: Prolonged treatment is required with not less than 1.2 g daily in divided doses. Up to 24 g daily may be needed when the infecting organism is relatively resistant. Treatment must be continued for 4 to 6 weeks.

Meningeal Infections: The initial dose of benzylpenicillin for children in the treatment of meningococcal meningitis is 600 mg followed by 300 mg intramuscularly every 4 to 6 hours; for pneumococcal meningitis at least 300 mg should be given every 4 hours for 14 days and then every 6 hours for 7 days.

Renal Failure: In patients with severe renal damage up to 6 g daily should be well tolerated, but massive doses e.g. 20 g or more given intravenously may lead to convulsions and coma. If it is desired to give large doses to these patients, it is necessary to assess the daily maintenance dose of benzylpenicillin to achieve the desired serum-penicillin concentration. A suitable method of assessment is based on the endogenous creatinine clearance as follows: Clearance of benzylpenicillin (mL/min) = $35.5 + 3.35 \times \text{creatinine clearance (mL/min)}$ and the maintenance dose of benzylpenicillin in gram/24 hours is given by the product: penicillin clearance (mL/min) x desired serum-penicillin concentration ($\mu\text{g/mL}$) x 0.00138. This is equally applicable to continuous and intermittent intravenous infusion.

Contraindications

Benzylpenicillin is contraindicated in patients who are known to be allergic to penicillin.

Warnings and Precautions

Care is necessary if large doses, 5 g per dose, are given to patients with impaired renal function or congestive cardiac failure. Benzylpenicillin has been taken by a large number of pregnant women and women of child bearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

Adverse Effects

Mild urticaria may occur in a small proportion of patients treated but clears rapidly on discontinuing the drug. Severe allergic reactions are uncommon after its use.

At very high doses of benzylpenicillin, convulsions and other signs of toxicity to the central nervous system may occur. Disturbances of blood electrolytes may also follow the administration of large doses and with prolonged high doses coagulation disorders, neutropenia and other blood disorders may occur. The potential for supra-infection including *Pseudomonas* and *Candida* exists.

Interactions

Intravenous solutions of benzylpenicillin are physically incompatible with many other substances including certain antihistamines, some other antibiotics, metaraminol tartrate, noradrenaline acid tartrate, thiopentone sodium and phenytoin sodium. Probenecid prolongs the half life of benzylpenicillin. Benzylpenicillin may interfere with dipstick tests for glycosuria and the Guthrie test.

Overdosage

At very high doses of benzylpenicillin, convulsions and other signs of toxicity to the central nervous system may occur. Also, disturbances of blood electrolytes may follow the administration of large doses. Haemolytic anaemia and leucopenia have been reported usually following high intravenous doses of benzylpenicillin.

Pharmaceutical Precautions

Store below 25°C protected from light and moisture. After reconstitution, benzylpenicillin injection should be administered immediately. Any unused portion should be discarded.

Medicine Classification

Prescription Medicine.

Package Quantities

All strengths are presented in a carton containing a single vial.

Further Information

Nil

Name and Address

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