Product Information

Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

Benzylpenicillin sodium for injection 1.0 Mega/vial

2. Qualitative and quantitative composition

Components	Unit dose	Function
Benzylpenicillin Sodium	Benzylpenicillin sodium 1.0 Mega	Active ingredient

3. Pharmaceutical form

Powder for injection

4. Clinical particulars

Therapeutic indications

Aqueous penicillin G (parenteral) is indicated in the therapy of severe infections caused by penicillin G-susceptible microorganisms when rapid and high penicilin levels are required in the conditions listed below. Therapy should be guided by bacteriological studies (including susceptibility tests) and by clinical response.

Posology and method of administration

Severe infections due to Susceptible Strains of Streptococci, Pneumococci, and Staphylococcl: bacteremia, pheumonia, endocarditis, pericarditis, empyema, meningitis and other severe infections- a minimum of 5 million units daily.

Syphilis: Aqueous penicillin G may be used in the treatment of acquired and congenital syphilis but because of the necessity of frequent dosage, hospitalization is recommended. Dosage and duration of therapy will be determined by age of patient and stage of the disease.

Gonorrheal endocarditis: a minimum of 5 million units daily.

Meningococcic meningitis: 1-2 million units intramuscularly every 2 hours, or continuous IV drip of 20- 30 million units/day.

Actinomycosis: 1-6 million units/day for cervicofacial cases, 10-20 million units/day for thoracic and abdominal disease.

Clostridial infections: 20 million units/day penicillin is adjunctive therapy to antitoxin,

Fusospirochetal infections: severe infections of oropharynx, lower respiratory tract, and genital area 5-10 million units/day.

Rat-bite fever (Spirillum minus or Streptobacillus moniliformis): 12-15 million unit/day for 3-4 weeks.

Listeria infections (Listeria monocytogenes): Neonates- 500,000 to 1 million units/day.

Adults with meningitis- 1 5 -20 million units/day for 2 weeks.

Adults with endocarditis -15-20 million units/day for 4 weeks.

Pasteurella infections (Pasteurella multocida):

Bacteremia and meningitis- 4-6 million units/day for 2 weeks .

Erysipeloid (Erysipelothrix insidiosa) Endocarditis: 2-20 milion units/day for 4-6 weeks.

Gram-negative bacillary infections (E. coli , Enterobacter aerogenes, A. faecalis, Salmonella,Shigella and Proteus mirabilis):

Bacteremia- 20-80 million units/day.

Diphtheria: carrier state- 300,000- -400,000 units of penicillin/day in divided doses for 10-12 days.

Anthrax: A minimum of 5 million units of penicillin/day in divided doses until cure is effected.

THE 20,000,000 UNIT DOSAGE MAY BE ADMINISTERED BY INTRAVENOUS INFUSION ONLY.

(1) Intramuscular Injection: Keep total volume of injection small. The intramuscular route is the preferred route or administration. Solutions containing up to 1 00,000 units of penicillin per mL of diluent may be used with a minimum of discomfort. Greater concentration of penicillin G per mL is physically possible and may be employed where therapy demands. When large dosages are required,it may be advisable to administer aqueous solutions of penicillin by means of continuous intravenous drip.

(2) Continuous Intravenous Drip: Determine the volume of fluid and rate of its administration required by the patient in a 24 hour period in the usual manner for fluid therapy and add the appropriate daily dosage of penicillin to this fluid. For example, if an adult patient requires 2 liters of fluid in 24 hours and a daily dosage of 10 million units of penicillin, add 5 million units to 1 liter and adjust the rate of flow so the liter will be infused in 12 hours.

(3) Intrapleural or Other Local Infusion: If fluid is aspirated, give infusion in a volume equal to 1/4 or 1/2 the amount of fluid aspirated, otherwise, prepare as for intramuscular injection.

(4) Intrathecal Use: The intrathecal use of penicillin in meningitis must be highly individualized. It should be employed only with full consideration of the possible irritating effects of penicillin when used by this route. The preferred route of therapy in bacterial meningitis is intravenous, supplemented by intramuscular injection.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Sterile solution may be left in refrigerator for one week without significant loss of potency.

Contraindications

Allergy to penicillins. Hypersensitivity to any ingredient of the preparation.

Cross allergy to other beta-lactams such as cephalosporins should be taken into account.

Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillin, cephalosporins, or other allergens.If an allergic reaction occurs, the drug should be discontinued and the appropriate therapy instituted.Serious anaphylactoid reactions require immediate emergency treatment with epinephrine. Oxygen,intravenous steroids, and airway management including intubation, should also be administered as indicated.

General: Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.

Intramuscular Therapy: Care should be taken to avoid intravenous or accidental intra-arterial administration or injection into or near major peripheral nerves or blood vessels, since such injections may produce neurovascular damage. Particular care should be taken with IV administration because of the possibility of thrombophlebitis.

In streptococcal infections, therapy must be sufficient to eliminate the organism (10 days minimum),otherwise the sequelae of streptococcal disease may occur.

Cultures should be taken following the completion of treatment to determine whether streptococci have been eradicated.

Whenever allergic reactions occur, penicillin should be withdrawn unless in the opinion of the physician, the condition being treated is life threatening and amenable only to penicillin therapy.

Interaction with other medicinal products and other forms of interaction

Concurrent administration of bacteriostatic antibiotics (e.g., erythromycin, tetracycline) may diminish the bactericidal effects of penicillins by slowing the rate of bacterial growth.

Bactericidal agents work most effectively against the immature cell wall of rapidly proliferating microorganisms.

Penicillin blood levels may be prolonged by concurrent administration of probenecid which blocks the renal tubular secretion of penicillins.

Displacement of penicillin from plasma protein binding sites will elevate the level of free penicillin in the serum.

Pregnancy and lactation

Teratogenic Effects: Reproduction studies performed in the mouse, rat, and rabbit have revealed no evidence of impaired fertility or harm to the fetus due to penicillin G. Human experience with the penicillins during pregnancy has not shown any positive evidence of adverse effects on the fetus. This drug should be used during pregnancy only if clearly needed.

Penicillins are excreted in human milk. Caution should be exercised when penicillin G is administered to a nursing woman.

Effects on ability to drive and use machines

Not applicable.

Undesirable effects

Penicillin is a substance of low toxicity but does have a significant index of sensitization. The following hypersensitivity reactions have been reported: skin rashes ranging from maculopapular eruptions to exfoliative dermatitis; urticaria; and reactions resembling serum sickness, including chills, fever,edema, arthralgia and prostration. Severe and occasionally fatal anaphylaxis has occurred.

Hemolytic anemia, leucopenia, thrombocytopenia, nephropathy, and neuropathy are rarely observed adverse reactions and are usually associated with high intravenous dosage.

Cardiac arrhythmias and cardiac arrest may also occur. (High dosage of penicillin G sodium may result in congestive heart failure due to high sodium intake.)

Overdose

Excessive blood levels of benzylpenicillin sodium can be corrected by haemodialysis.

5. Pharmacological properties

Pharmacodynamic properties

Pharmacotherapeutic group: Beta-lactamase sensitive penicillins.

ATC code: J01 CE01.

General Properties:

Benzylpenicillin sodium is a beta-lactam antibiotic. It is bacteriocidal by inhibiting bacterial cell wall biosynthesis.

Breakpoints:

The tentative breakpoints (British Society for Antimicrobial Chemotherapy, BSAC) for benzylpenicillin sodium are as follows:

Organism	S ≤ (mg/L)	I (mg/L)	R ≥ (mg/L)
Streptococcus pneumonia Neisseria gonorrhoea	0.06	0.12-1.0	2.0
Neisseria meningitides	0.06		0.12
Haemolytic streptococci Staphylococci Moraxella catarrhalis Haemophilus influenzae	0.12		0.25
Rapidly growing anaerobes	1.0		2.0

S = Susceptible, I = Intermediate susceptibility, R = Resistant

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. The following table gives only approximate guidance on probabilities whether microorganisms will be susceptible to benzylpenicillin sodium or not.

Susceptible and intermediately susceptible microorganisms		
Type of Microorganism	Microorganism	Range of acquired resistance
Aerobic Gram-positive microorganisms	• Bacillus anthracis	0%**
	• Corynebacterium diphtheriae	0%*
	• Haemolytic streptococci (including Streptococcus pyogenes)	0%*-3%**

	• Listeria monocytogenes	0%**
	• Streptococcus pneumoniae	4%*-40%**
	• Streptococcus viridans	3-32%*
Aerobic Gram-negative microorganisms	• Neisseria gonorrhoeae	9-10%*
	• Neisseria meningitidis	18%*
	• Pasteurella multocida	0%***
Anaerobic microorganisms	• Actinomyces israelii	8%**
	• Fusobacterium nucleatum and Fusobacterium necrophorum	Usually sensitive
	• Gram-positive sporing bacilli (including Clostridium tetani and Clostridium perfringens (welchii))	14%**
	• Gram-positive cocci (including peptostreptococcus)	7%*

* UK data; ** European data, ***Global data

Insusceptible microorganisms		
Type of Microorganism	Microorganism	Range of acquired resistance
Aerobic Gram-positive microorganisms	• Coagulase negative Staphylococcus	71-81%*
	• Enterococcus Spp	Resistant
	• Staphylococcus aureus	79-87%*
Aerobic Gram-negative microorganisms	• Acinetobacter	Resistant

	• Bordetella pertussis	Generally resistant
	• Brucella spp.	Resistant
	• Enterobacteriaceae (including Escherichia coli, Salmonella, Shigella, Enterobacter, Klebsiella, Proteus, Citrobacter).	Generally resistant
	• Haemophilus influenzae	Resistant
	• Pseudomonas	Resistant
Anaerobic microorganisms	• Bacteroides fragilis	100%***

* UK data; ** European data, *** Global data

Pharmacokinetic properties

Benzylpenicillin sodium rapidly appears in the blood following intramuscular injection of water-soluble salts and maximum concentrations are usually reached in 15-30 minutes. Peak plasma concentrations of about 12 mcg/ml have been reported after doses of 600 mg with therapeutic plasma concentrations for most susceptible organisms detectable for about 5 hours. Approximately 60% of the dose injected is reversibly bound to plasma protein.
In adults with normal renal function the plasma half-life is about 30 minutes. Most of the dose (60-90%) undergoes renal elimination, 10% by glomerular filtration and 90% by tubular secretion. Tubular secretion is inhibited by probenecid, which is sometimes given to increase plasma penicillin concentrations. Biliary elimination of benzylpenicillin sodium accounts for only a minor fraction of the dose.

Preclinical safety data

No further information of relevance.

6. Pharmaceutical particulars

List of excipients

Not applicable

Incompatibilities

Not applicable

Shelf life

3 years

Special precautions for storage

Store below 30℃.

Nature and contents of container

Packed with 7 ml mould vial, Rubber stopper and Aluminium cap.

Special precautions for disposal and other handling

After contact with skin, wash immediately with water. In case of contact with eyes, rinse immediately with plenty of water and seek medical advice if discomfort persists.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Manufacturer

CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co., Ltd.

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