SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1-Name of the Medicinal Product : Benzylpenicillin Sodium for Injection 1mega

1.1 Product Name: Benzylpenicillin Sodium for Injection

1.2 Strength: 1mega

1.3 Pharmaceutical Dosage Form: powder for injection

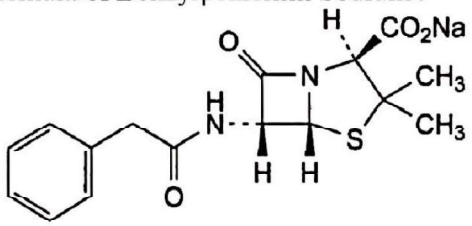
2-Quality and Quantitative Composition :

2.1 Qualitative Declaration
The active substance of the Benzylpenicillin Sodium for Injection is Benzylpenicillin Sodium.

Benzylpenicillin Sodium: White or almost white, crystalline powder.

The molecular formula of Benzylpenicillin Sodium: $C_{16}H_{17}N_2NaO_4S$

The structural formula of Benzylpenicillin Sodium :



The molecular weight of Benzylpenicillin Sodium : 356.4

The CAS number of Benzylpenicillin Sodium : 69-57-8

2.2 Quantitative Declaration

Benzylpenicillin Sodium for Injection 1mega

Dosage form: powder for injection

Concentration: 1mega

Product description: 1 mega of white or almost white, crystalline powder is filled in the glass vial.

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Ingredients	Quantity per vial	Function of ingredients
Benzylpenicillin Sodium	1 mega	Active substance

3-Pharmaceutical Form :

Dosage form：powder for injection
1 mega of white or almost white, crystalline powder is filled in the glass vial.

4-Clinical Particulars

4.1 Therapeutic indications
Penicillin is suitable for a variety of infections caused by sensitive bacteria, such as abscesses, bacteremia, pneumonia and endocarditis. Penicillin is the drug of choice for the following infections:
1. Hemolytic streptococcal infections, such as pharyngitis, tonsillitis, scarlet fever, erysipelas, cellulitis and puerperal fever.
2. Pneumococcal infections such as pneumonia, otitis media, meningitis and bacteremia.
3. Staphylococcal infection without penicillinase production.
4. Anthrax.
5. Clostridium infection such as tetanus and gas gangrene.
6. Syphilis (including congenital syphilis).
7. Leptospirosis.
8. Recurrent fever.
9. Diphtheria.
10. Penicillin combined with aminoglycosides for the treatment of streptococcus viridis endocarditis.
Penicillin can also be used to treat:
1. Epidemic cerebrospinal meningitis.
2. Actinomycosis.
3. Gonorrhea.
4. Vincent's angina.
5. Lyme disease.
6. Rat bite fever.
7. Listeria infection.
8. Many anaerobic bacterial infections other than Bacteroides fragilis.
Penicillin can be used to prevent infective endocarditis in patients with rheumatic heart disease or congenital heart disease before oral, dental, gastrointestinal, or urogenital tract surgery and procedures.

4.2 Posology and method of administration
- Recommended doses:
Penicillin is administered by intramuscular injection or intravenous drip

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1. Adults: intramuscular injection, 800,000 ~ 2 million units (1 ~ 2.5) per day, divided into 3 ~ 4 doses; Intravenous infusion, 2 million to 20 million units (2.5 to 25 sticks) per day, divided into 2 to 4 times.
2. Children: intramuscular injection, according to the weight of 25,000 units /kg, administered once every 12 hours; Intravenous infusion: daily according to body weight 50,000 ~ 200,000 units /kg, divided into 2 ~ 4 times.
3. Newborns (full-term) : each time according to the weight of 50,000 units /kg, intramuscular injection or intravenous infusion; Once every 12 hours during the first week of life, once every 8 hours for those more than a week, and once every 6 hours for severe infections.
4. Premature infants: 30000 units /kg per time, once every 12 hours in the first week of birth, once every 8 hours in 2 to 4 weeks; Every six hours after that.
5. Patients with renal dysfunction: those with mild or moderate renal impairment do not need to reduce the conventional dose, and those with severe renal impairment should extend the administration interval or adjust the dose. When the endogenous creatinine clearance rate was 10-50 ml/ hour, the administration interval was extended from 8 hours to 8-12 hours or the administration interval was unchanged and the dose was reduced by 25%. When the endogenous creatinine clearance is less than 10ml/, the administration interval is extended to 12-18 hours or each dose is reduced to 25% to 50% of the normal dose, while the administration interval is unchanged.
6. For intramuscular injection, every 500,000 units of penicillin sodium should be dissolved in 1ml of sterilization water for injection, and more than 500,000 units should be added with 2ml of sterilization water for injection, and sodium chloride injection should not be used as the solvent; The rate of administration should not exceed 500,000 units per minute during intravenous infusion to avoid central nervous system toxicity.

4.3 Contraindications
Patients with a history of penicillin allergy or a positive penicillin skin test are prohibited.

4.4 Special warning and precautions for use
1. Before applying this product, ask about the history of drug allergy in detail and conduct penicillin skin test. The skin test solution contains 500 units of penicillin per 1ml, and intradermal injection is 0.05 ~ 0.1ml. Must be used after user desensitization, should be ready for allergic reaction first aid.
2. People who are allergic to one kind of penicillin may be allergic to other penicillins and penicillamine. Patients with allergic diseases such as asthma, eczema, hay fever and urticaria should use this product with caution.
3. Penicillin solution is unstable at room temperature, the aging price of 20 units /ml penicillin solution placed at 30℃ for 24 hours decreases by 56%, and the content of penicillenic acid increases by 200 times, so the application of this product must be prepared fresh.
4. The electrolyte should be tested regularly when using the product in large doses;
5. Interference with diagnosis:
(1) During the application of penicillin, false positives may occur in the determination

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of urine sugar by the copper sulfate method, but the glucase method is not affected.
(2) Intravenous injection of this product can cause an increase in blood sodium determination value.
(3) This product can increase serum alanine aminotransferase or aspartate aminotransferase.

4.5 Interaction with other medicinal products and other forms of Interactions
1. Chloramphenicol, erythromycin, tetracycline, sulfonamides can interfere with the activity of this product, so this product should not be used with these drugs.
2. Prosulfanilamide, aspirin, indomethacin, butazone and sulfanilamide reduce the renal tubule secretion of penicillin and prolong the serum half-life of this product. Penicillin can enhance the anticoagulant effect of warfarin.
3. This product is incompatibility with heavy metals, especially copper, zinc and mercury.
4. When lincomycin, tetracycline, Vancomycin, ethylsuccinic Erythromycin, Amphotericin B, Norepinephrine, m-hydroxylamine, phenytoin sodium, hydroxyzine hydrochloride, prochlorazine, promethazine, vitamin B, vitamin C, etc. are added into penicillin intravenous infusion, turbidity will appear.
5. Instillation of this product with aminoglycoside antibiotics in the same bottle can reduce the antibacterial activity of both, so it cannot be administered in the same container.
4.6 Pregnancy and lactation
No fetal damage was found in animal reproductive test. "However, rigorous controlled trials in pregnant women have not been performed to exclude adverse effects on the fetus, so pregnant women should use this drug only when it is truly necessary." A small amount of this product is secreted from breast milk, and lactating women should suspend lactation when using it.

4.7 Child medication
The experiment was not performed and no reliable reference was available.

4.8 Elderly medication
The experiment was not performed and no reliable reference was available.

4.9 Undesirable effects
1. Allergic reactions: penicillin allergic reactions are common, including urticaria and other types of rash, leukopenia, interstitial nephritis, asthma attack, etc., and serosickness reactions. Anaphylactic shock is rare. Once it occurs, it must be rescued on the spot, and the treatment measures such as maintaining airway patency, oxygen inhalation, and using epinephrine and glucocorticoid should be given.
2. Toxic reaction: rare, but when the drug is given intravenously in large doses or intrathecally, it can cause convulsions, muscle clonus, coma and severe psychiatric symptoms due to high drug concentration in cerebrospinal fluid (penicillin encephalopathy). This reaction is more common in infants, the elderly, and patients with renal insufficiency.
3. Hessian reaction and treatment contradiction: when using penicillin to treat diseases

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such as syphilis and leptospirosis, the symptoms can be aggravated due to the death of the pathogen, which is called Hessian reaction. Treatment conflicts are also seen in patients with syphilis, which may be caused by the rapid disappearance of syphilis lesions after treatment and the relatively slow tissue repair or the contraction of fibrous tissue at the lesion site, which may hinder organ function.
4. Superinfection: Superinfection with penicillin-resistant Staphylococcus aureus, Gram-negative bacilli or Candida can occur.
5. The use of large doses of penicillin sodium can cause heart failure due to the intake of large amounts of sodium salt.

4.10 Overdose
The main manifestations of drug overdose are adverse reactions in the central nervous system. Drug overdose should be stopped in time and symptomatic and supportive treatment should be given. Penicillin is cleared by hemodialysis.

4.11 Pharmacology and toxicology
Penicillin has good antibacterial activity against Streptococcus species such as Streptococcus haemolyticus, Streptococcus pneumoniae and Staphylococci that do not produce penicillinase. It has moderate antibacterial activity against Enterococci. Neisseria gonorrhoeae, Neisseria meningitidis, Corynebacterium diphtheria, Bacillus anthracis, Actinomyces bovis, Streptobacillus moniliformis, Listeria, Leptospira and treponema pallidum are sensitive to this product. It also has certain antibacterial activity against Haemophilus influenzae and Borteria pertussis. Other Gram-negative aerobic or facultative anaerobic bacteria are less sensitive to this product. This product has good antibacterial effect on Clostridium, pepsin streptococcus anaerobes and Bacteroides melaninogens, etc., and poor antibacterial effect on Bacteroides fragilis. Penicillin plays a bactericidal role by inhibiting bacterial cell wall synthesis.

4.12 Pharmacokinetics
The peak blood concentration (Cmax) was reached 0.5 h after intramuscular injection, and the peak concentration was 20000 units /L(12mg/L) after intramuscular injection of 1 million units (600mg). The neonates were given intramuscular penicillin of 25,000 units /kg(15mg/kg) according to their body weight. After 0.5 ~ 1 hour, the average blood concentration of penicillin was about 22mg/L, and decreased to 9.6-19.2mg /L after 12 hours. The average blood concentration of the drug in adults is about 19.2mg/L when the drug is injected intravenously with 2 million units every 2 hours or 3 million units every 3 hours. Five million units (3g) of penicillin were injected intravenously within 5 minutes. The mean plasma concentrations were 400mg/L and 273mg/L at 5 minutes and 10 minutes, respectively, and decreased to 45mg/L at 1 hour and only 3.0mg/L at 4 hours.
This product is widely distributed in tissues and body fluids. Concentrations in thoracic, abdominal and joint fluid were approximately 50% of serum concentrations. It is not easy to penetrate into eye, bone tissue, non-blood supply area and abscess cavity, and easy to penetrate into inflammatory tissue. Penicillin crosses the placenta and therapeutic concentrations are generally available in both the fetus and amniotic fluid, except at low concentrations in amniotic fluid during the first 3 months of

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pregnancy. It is difficult to penetrate the blood-cerebrospinal fluid barrier, and the concentration in cerebrospinal fluid without inflammation is only 1%-3% of the blood concentration. The concentration in cerebrospinal fluid with inflammation was up to 5%-30% of the plasma concentration. Milk may contain a small amount of penicillin, the concentration of which is 5% to 20% of the blood concentration.
The plasma protein binding rate was 45%-65%. "The half-life of blood elimination (t1/2β) is about 30 minutes, and can be prolonged to 2.5 to 10 hours in persons with impaired renal function, as well as in the elderly and neonates." The t1/2β of neonates with body weight less than 2 kg was 4.9 hours at 7 days of age and 2.6 hours at 8-14 days of age. The t1/2β was 2.6 hours and 2.1 hours at 7 days and 8 ~ 14 days, respectively, in those whose body weight was more than 2 kg.
About 19% of this product is metabolized in the liver. In the presence of normal renal function, approximately 75% of the dose is excreted from the kidneys within 6 hours. Penicillin is mainly excreted by renal tubular secretion, and only about 10% of penicillin is excreted by glomerular filtration in healthy adults. "However, in neonates, penicillin is excreted mainly by glomerular filtration." A small amount of penicillin was also excreted through the biliary tract, and the concentration in the bile reached a peak of 10 ~ 20mg/L 2 ~ 4 hours after intramuscular injection of 600mg penicillin. Stool contains no or only small amounts of penicillin because it is destroyed by penicillinase produced by intestinal bacteria. It is cleared by hemodialysis but not by peritoneal dialysis.

5-Pharmaceutical Particulars :

5.1 Shelf life
24 months

5.2 Special precautions for storage
Sealed and stored in a cool, dark and dry place (no more than 20℃ away from light).

6-Marketing Authorization Holder :

SHANDONG XIER KANGTAI PHARMACEUTICAL CO., LTD.

7-Name Of Manufacturer :

SHANDONG XIER KANGTAI PHARMACEUTICAL CO., LTD.

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