For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

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Polymyxin B for Injection IP (Lyophilized)

Polyhope™
पॉलिहोप
5,00,000 Units / Vial

Lyophilized Cake Form
For Intrathecal / IM / IV Use

Composition: Each Vial Contains:
Polymyxin B Sulphate IP
Eq. to Polymyxin B ..... 5,00,000 IU
Excipients ..... q.s.

PHARMACEUTICAL FORM
Injection for Infusion

CLINICAL PARTICULARS

Indications:

Acute infections caused by susceptible strai9ns of Pseudomonas aeruginosa. Polymyxin B sulfate is a drug of choice in the treatment of infections of the urinary tract, meninges and blood stream caused by susceptible strains of Pseudomonas aeruginosa.

It may be indicated in serious infections caused by susceptible strains of the following organisms, when less potentially toxic drugs are ineffective or contraindicated. Haemophilus influenza, specifically meningeal infections. Escherichia coli, specifically urinary tract infections. Enterobacter aerogenes, specifically bacteremia. Klebsiella pneumonia, specifically bacteremia.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of polymyxin B and other bacterial drugs, Polymyxin B should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria.

NOTE: IN MENINGEAL INFECTIONS, POLYMYXIN B SULPHATE SHOULD BE ADMINISTERED ONLY BY THE INTRATHECAL ROUTE.

Dosage and Administration:

PARENTERAL:

Intravenous: Dissolve 5,00,000 polymyxin B units in 300 to 500 ml of 5% Dextrose Injection for continuous intravenous drip.

Adults and Children: 15,000 to 25,000 units/kg body weight/day in individuals with normal kidney function. This amount should be reduced from 15,000 units/kg downward for individuals with kidney impairment. Infusions may be given every 12 hours, however the total daily dose must not exceed 25,000 units/kg/day

Infants: Infants with normal kidney function may receive upto 40,000 units/kg/day without adverse effects.

Intramuscular: Not recommended routinely because of severe pain at injection sites, particulary in infants and children. Dissolve 5,00,000 polymyxin B units in 0.9% sodium chloride injection.

Adults and Children: 25,000 to 30,000 units/kg/day. This should in the presence of renal impairment. The dosage may be divided and given at either 4 or 6 hours intervals.

Infants: Infants with normal kidney function may receive upto 40,000 units/kg/day without adverse effects.

Note: Doses as high as 45,000 units/kg/day have been used in limited clinical studies in treating premature and newborn infants for sepsis caused by Pseudomonas aeruginosa.

Intrathecal: A treatment of choice for Pseudomonas aeruginosa meningitis. Dissolve 5,00,000 polymixin B units in 5 ml 0.9% sodium chloride injection for 1,00,000 units per ml. dilute further using 5 ml of same solvent to obtain 50,000 units per ml. dosage units.

Adults and Children: Over 2 years of age dosage is 50,000 units once daily intrathecally for 3 to 4 days, then 50,000 units once every other day for at least 2 weeks after cultures of the cerebrospinal fluid are negative and sugar content has returned to normal

Children under 2 years of age: 20,000 units once daily. Intrathecally for 3 to 4 days or 25,000 units once every other day. Continue with a dose of 25,000 units once every other day for atleast 2 weeks after cultures of the cerebrospinal fluid are negative and sugar content has returned to normal.

IN THE INTEREST OF SAFETY, SOLUTIONS OF PARENTERAL USE SHOULD BE STORED UNDER REFRIGERATION AND ANY UNUSED PORTIONS SHOULD BE DISCARDED AFTER 72 HOURS.

Contraindications:

This drug is contraindicated in persons with a prior history of hypersensitivity reactions to polymyxins.

Warnings:

When this drug is given intramuscularly and/or intrathecally. It should be given only to hospitalized patients, so as to provide constant supervision by a physician. Renal function should be carefully determined and patients with renal damage and nitrogen retention should have reduced dosage. Patients with nephrotoxicity due to polymyxin B sulfate usually show albuminuria, cellular casts and azotemia. Diminishing urine output and a rising BUN are indications for discontinuing therapy with this drug. Neurotoxic reactions may be manifested by irritability, weakness, drowsiness, ataxia, perioral paraesthesia, numbness of the extremities and blurring of vision. These are usually associated with high serum levels found in patients with impaired renal function and/or nephrotoxicity. The neurotoxicity of polymyxin B sulfate can result in respiratory paralysis from neuromuscular blockade especially whenthe drug is given soon after anesthesia and/or muscle relaxants. Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Polymyxin B for injection and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management protein supplementation, antibiotic treatment of C. difficile and surgical evaluation should be instituted as clinically indicated.

Precautions

Prescribing polymyxin B in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increase the risk of the development of drug resistant bacteria. Baseline renal function should be done prior to therapy with frequent monitoring of renal function and blood levels of the drug during parenteral therapy. Avoid concurrent use of a curariform muscle relaxant and other neurotoxic drugs (ether, tubocurarine, succinylcholine, gallamine, decamethonium and sodium citrate) which may precipitate respiratory depression. If signs of respiratory paralysis appear, respiration should be assisted as required and the drug discontinued. As with other antibiotics use of this drug may result in overgrowth of non susceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be instituted.

Drug Interactions

The concurrent or sequential use of other neurotoxic and/or nephrotoxic drugs, particularly bacitracin, streptomycin, neomycin, kanamycin, gentamycin, tobramycin, amikacin, cephaloridine, paromomycin and colistin should be avoided.

Pregnancy and Lactation

The safety of this drug inhuman pregnancy has not been established.

Effects on Ability to Drive and Use Machine.

No studies on the effect on the ability to drive and use machines have been performed.

Adverse Reactions

Nephrotoxic reactions: Albuminuria, cylinduria, azotemia and rising blood levels without any increase in dosage.

Neurotoxic reactions: Facial flushing, dizziness progressing to ataxia, drowsiness, peripheral paraesthesia (circumoral and stocking glove) apnoea due to concurrent use of curariform muscle relaxants other neurotoxic drugs or in advertent over dosage and signs of meningeal irritation with intrathecal administration, e.g. fever, headache, stiff neck and increased cell count and protein cerebrospinal fluid.

Other reactions occasionally reported: Drug fever, urticarial rash, pain (severe) at intramuscular injection sites and thrombophlebitis at intravenous injection sites.

Overdose

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

Polymyxin B sulfate is the sulfate salt of Polymyxin B1 and B2. Each milligram of pure polymyxin B base is equivalent to 10,000 units of polymyxin B and each microgram of pure polymyxin B base is equivalent to 10 units of polymyxin B.

Polymyxin B has bactericidal action against almost all Gram – negative bacilli except the Proteus group. Polymyxins increase the permeability of the bacterial cell membrane leading to death of the cell. All Gram-positive bacteria, fungi and Gram-negative cocci are resistant to polymyxin B. Appropriate methods should be used when performing in vitro susceptibility testing of polymyxin B. The following in vitro susceptibility test criteria should only be used for interpreting the results of polymyxin B susceptibility testing when the indicated quality control parameters are met during testing. In vitro susceptibility test interpretive criteria for polymyxin B sulfate against pseudomonas aeruginosa.

In vitro susceptibility test interpretive criteria for Polymyxin B against Non-fermenters			
	Minimal Inhibitory Concentration (MIC) (µg/ml)		
Pathogen			
Pseudomonas aeruginosa	≤ 2	4	≥ 8
Acinetobacter spp.& other Non-Enterobacteriaceae	≤ 2	-	≥ 4

Pharmacokinetics

Polymyxin B sulfate is not absorbed from the normal alimentary tract. Since the drug loses 50 percent of its activity in the presence of serum, active blood levels are low. Repeated injections may give a cumulative effect. Levels tend to be higher in infants and children. The drug is excreted slowly by the kidneys. Tissue diffusion is poor and the drug does not pass the blood brain barrier into the cerebrospinal fluid. In therapeutic dosage, polymyxin B sulfate causes some nephrotoxicity with tubule damage to a slight degree.

Storage: Store at a temperature not exceeding 25°C. Protect from light.

Reconstituted solution is stable upto 72 hours with 0.9% Sodium Chloride Injection and 5% Dextrose solution at 2°C-8°C and remain stable upto 2 hrs after dilution with 5% Dextrose solution at room temperature.

Keep all the medicines out of reach of children.

Presentation

One vial of Polyhope packed in a carton

Reference:

1. Clinical Laboratory and Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing : 24th Informational Supplement. CLSI document M 100-S24. CLSI, 940 West Valley Rd., Suite 2500, Wayne, PA 19087, USA.

URIHK

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