POLYMIXIN B FOR INJECTION USP

Rx only

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

WARNING
CAUTION: WHEN THIS DRUG IS GIVEN INTRAVENOUSLY, INTRAVASCULARLY AND/OR INTRATHYMICALLY, 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 SHOULDN'T HAVE REDUCED DOSAGE. PATIENTS WITH NEPHROTOXICITY DUE TO POLYMYXIN B SULFATE USUALLY SHOW ABLATION OF CELLS, CAST FORMATION, AND AZOTEMIA. DIMINISHING URINE OUTPUT AND A RISING BUN ARE INDICATIONS FOR CONTINUING THERAPY WITH THIS DRUG.

NEUROTOXIC REACTIONS MAY BE MANIFESTED BY IRRITABILITY, WEAKNESS, DROWSINESS, ATAXIA, PERORAL PARESTHESIAS, NUMBNESS OF THE EXTREMITIES, AND BLURRING OF VISION. THESE ARE USUALLY ASSOCIATED WITH HIGH SERUM LEVELS FOUND IN PATIENTS WITH IMPAIRED RENAL FUNCTION OR NEPHROTOXICITY.

THE CONCURRENT OR SEQUENTIAL USE OF OTHER NEUROTOXIC AND/OR NephROTOXIC DRUGS WITH POLYMYXIN B SULFATE, PARTICULARLY BACITRACIN, STREPTOMYcin, NEomycin, KANAMYcin, GENTAMycin, TOBramycin, Amikacin, CEPHALORidine, PAROMYcin, VOXYcin, AND COLOSfIN SHOULD BE AVOIDED.

THE NEUROTOXICITY OF POLYMYXIN B SULFATE CAN RESULT IN RESPIRATORY PARALYSIS FROM NEUROMUSCULAR BLOCKADE, ESPECIALLY WHEN THE DRUG IS GIVEN SOON AFTER ANESTHESIA AND/OR MUSCLE RELAXANTS.

USAGE AND NAVIGATION: THE SAFETY OF THIS DRUG IN HUMAN PREGNANCY HAS NOT BEEN ESTABLISHED.

DESCRIPTION:
Polymyxin B Sulfate is one of a group of basic polypeptide antibiotics derived from B polymyxin (B aerosporous). Polymyxin B Sulfate is the sulfate salt of Polymyxin B1 and B2, which are produced by the growth of Bacillus polymyxa (B polymyxin) Migula (Bacillus). It has a potency of not less than 6000 polymyxin B units per mg, calculated on the anhydrous basis. The structural formulae are:

**Polymyxin B (R=CH₃)**

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CH₃
RCH(CH₂)_nCO-Dab-Thr-Dab-Dab • xH₂O
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**Polymyxin B₂ (R=H)**

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Nh₂
Dab-D-Phe-Leu
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Each vial contains 500,000 polymyxin B units for parenteral or ophthalmic administration. Polymyxin B for Injection is in powder form suitable for preparation of sterile solutions for intramuscular, intravenous drip, intrathecal, or ophthalmic use.

In the medical literature, dosages have frequently been given in terms of equivalent weights of pure polymyxin B base. Equivalent weights of pure polymyxin B base is equal to 10,000 units of polymyxin B and each microgram of pure polymyxin B base is equal to 10 units of polymyxin B. Aqueous solutions of polymyxin B sulfate may be stored up to 12 months without significant loss of potency if kept under refrigeration. In the interest of safety, solutions for parenteral use should be stored under refrigeration and any unused portion should be discarded after 72 hours. Polymyxin B sulfate should not be stored in alkaline solutions.

CLINICAL PHARMACOLOGY:
Polymyxin B Sulfate has a bactericidal action against almost all gram-negative bacilli except the Proteus group. Polymyxins increase the permeability of bacterial cell wall membranes. All gram-negative aerobic and anaerobic rods, and also the aerobic cocci, N gonorrhoeae and N meningitidis, are resistant. Susceptibility plate testing: If the Kirby-Bauer method of disc susceptibility testing is used, a 300 units polymyxin B disk should give a zone of over 11 mm when tested against a polymyxin B susceptible bacterial strain. Polymyxin B Sulfate is not absorbed from the normal alimentary tract. When the drug is given intravenously, intrathecally, or ophthalmically, it may produce nephrotoxic reactions.

INDICATIONS AND USAGE:
Acute Infections Caused by Susceptible Strains of Pseudomonas aeruginosa. Polymyxin B Sulfate is a drug of choice in the treatment of infections of the urinary tract, meninges, and bloodstream caused by susceptible strains of Ps. aeruginosa. It may also be used topically and subconjunctivally to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Polymyxin B for Injection USP is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and not be treatable by Polymyxin B for Injection USP or other antibacterial drugs in the future.

ADVERSE REACTIONS: See "WARNING" box.

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

Neurotoxic reactions: Facial flushing, dizziness progressing to ataxia, drowsiness, peripheral paresthesias (circumoral and stocking glove), apnea due to concurrent use of curariform muscle relaxants, other neurotoxic drugs or inadvertent overdosage, 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.

DOSE AND ADMINISTRATION:

PARENTERAL:
• Intravenous.
• Intrathecal.
• Ophthalmic.

Intravenous Use: Dosage is 5000 units/kg/dose, 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. With normal kidney function may receive up to 40,000 units/kg/day without adverse effects.

Intrathecal. Not recommended routine because of severe pain at injection sites, particularly in infants and children. Dissolve 500,000 polymyxin B units in 2 mL sterile water for injection or sodium chloride injection or procaine hydrochloride injection 1 percent.

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

Infants. With normal kidney function may receive up to 40,000 units/kg/day without adverse effects.

Note: Doses as high as 46,000 units/kg/day have been used in limited clinical studies in treating prematures and newborn infants for caesarean section cases caused by Ps aeruginosa.

Intrathecal. Treatment of choice for Ps aeruginosa meningitis. Dissolve 500,000 polymyxin B units in 10 mL sodium chloride injection USP for 50,000 units per mL dosage unit.

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 at least 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 DISCARDER AFTER 72 HOURS.

TOPICAL

Ophthalmic. Dissolve 500,000 polymyxin B units in 20 to 50 mL sterile water for injection or sodium chloride injection USP for 10,000 units per mL, per cent. For the treatment of Ps aeruginosa infections of the eye, a concentration of 0.1 percent to 0.25 percent (10,000 units to 25,000 units per mL) is administered 1 to 3 drops every hour, increasing the intervals as response indicates. Subconjunctival injection of up to 100,000 units/day may be used for the treatment of Ps aeruginosa infections of the cornea and conjunctiva.

Note: Avoid total systemic and ophthalmic instillation over 25,000 units/kg/day.

HOW SUPPLIED:
POLYMYXIN B FOR INJECTION USP, 500,000 polymyxin B units per vial is available in single vial cartons NDC# 39822-0166-5.

Storage recommendations:
Before reconstitution: Store at controlled room temperature 20° to 25°C (68° to 77°F). Protect from light. Retain in carton until time of use.

After reconstitution: Product must be stored under refrigeration, between 2° to 8°C (36° to 46°F) and any unused portion should be discarded after 72 hours.

Printed in USA

POLYMYXIN B FOR INJECTION USP

Manufactured for

XGEN PHARMACEUTICALS INC

Northport, NY 11768

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