SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the product:

1.1 Product name:

PolyMxB

Polymyxin B for Injection USP (Lyophilized)

1.2 Strength

5, 00, 000 units

1.3 Pharmaceutical dosage form:

Powder for Injection

2. Qualitative and quantitative composition:

Qualitative and quantitative composition of PolyMxB

Ingredients	**Indication**	**Specification**	**Each vial contains**
Polymyxin B Sulphate	Active	USP	5,00,000 Units
Water for Injection	Aqueous vehicle	USP	q.s. to 1 ml

3. Pharmaceutical form:

Lyophilized Injection.

4. Clinical particulars:

4.1 Therapeutic Indications :

1. 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 Ps. aeruginosa. It may also be used as subconjunctival injection in the treatment of infections of the eye caused by susceptible strains of Ps. aeruginosa.

2. It may be indicated in serious infections caused by susceptible strains of the following organisms,

***** H. influenzae, specifically meningeal infections.

***** Escherichia coli, specifically urinary tract infections.

***** Aerobacter aerogenes, specifically bacteremia.

***** Klebsiella pneumoniae, specifically bacteremia.

4.2 Posology and Method of Administration

Intravenous :

Dissolve 5,00,000 Units Polymyxin B Sulfate in 300 to 500ml of 5% dextrose in water 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 up to 40,000 units / kg / day without adverse effects.

Intramuscular:

Not recommended routinely because of severe pain at injection sites, particularly in infants and children. Dissolve 5,00,000 Units Polymyxin B Sulfate in 2ml sterile distilled water (Sterile Water for Injection U.S.P.) or sterile physiologic saline (Sodium Chloride Injection U.S.P.) or 1% procaine hydrochloride solution.

Adults and 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: Infants with normal kidney function may receive up to 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 prematures and newborn infants for sepsis caused by Ps. aeruginosa.

Intrathecal :

A treatment of choice for Ps. aeruginosa meningitis.

Dissolve 5,00,000 Units Polymyxin B Sulfate in 5ml of sterile physiologic saline (Sodium Chloride Injection U.S.P.) for 50,000 units per ml dosage un

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 cerebrospinal fluid are negative and sugar content has returned to normal.

Ophthalmic Use : (For Subconjunctival Injection only).

For the treatment of Ps aeruginosa infections of the eye, a subconjunctival injection of up to 100,000 units / day may be used for the treatment of Ps aeruginosa infections of the cornea and conjunctiva.

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

4.3 Contra-indications:

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

4.4 Special warning and precautions for use :

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.

Patients with nephrotoxicity due to POLY-MxB 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, peripheral paresthesia, 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 POLY-MxB can result in respiratory paralysis from neuromuscular blockade, especially when the drug is given soon after anesthesia and / or muscle relaxants

Precautions:

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 nonsusceptible organisms, including fungi. If superinfection occurs, appropriate therapy should be instituted.

4.5 Interaction with other medicinal products and other forms of interactions

The concurrent use of polymyxins with curariform muscle relaxants and other neurotoxic drugs such as ether, tubocurarine, succinylcholine, gallamine, decamethonium, and sodium citrate must be avoided, since these agents may trigger the development of neuromuscular blockade [55]. Co-administration of sodium cephalothin and polymyxins may enhance the development of neurotoxicity, so this combination of antimicrobial medication should also be avoided [4]. In addition, antimicrobial agents with known neurotoxic effect, such as aminoglycosides, should generally be avoided or given with great caution in patients who receive polymyxins. In such instances, close monitoring of the patients receiving these antibiotics is mandatory. Experimental studies showed that application of polymyxins in combination with glutamic acid to a peripheral nerve could cause transgaglionic degenerative atrophy [65].

4.6 Pregnancy and lactation

The safety of this drug in human pregnancy has not been established.

4.7 Effects on ability to drive and use machine

No effects on ability to drive and use machines have been observed

4.8 Undesirable effects

Nephrotoxic reactions :

* Albuminuria,
* Cylindruria,
* Azotemia,
* Rising serum drug 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.
* Signs of meningeal irritation with intrathecal administration, e.g. fever, headache, stiff neck and increased cell count and protein in cerebrospinal fluid.

Other reactions occasionally reported:

* Drug fever,
* Urticarial rash,
* Pain (severe) at intramuscular injection sites,
* Thrombophlebitis at intravenous injection sites.

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4.9 Overdose:

Overdoses with polymyxins, mainly with colistimethate sodium, have been reported several times in the old literature. Although, one case of a three year old child who received intramuscularly450 mg (approximately 5.5 million IU) of colistimethate sodium reported no adverse effects, the majority of cases with Polymyxin overdose resulted in acute renal failure and various manifestations of neurotoxicity, including neuromuscular blockade and apnea [3,31,33,34]. It should be emphasized that cases of Polymyxin overdose with fatal consequences are scarce [29]. There is no antidote for

Polymyxin overdose. Management requires early cessation of the medication and appropriate supportive treatment. In the presence of established acute renal failure, haemodialysis and peritoneal dialysis can only manage renal complications, since they have little influence on the elimination of polymyxins, as discussed above. If apnea occurs, mechanical ventilation support is needed.

5. Pharmaceutical particulars :

Pharmacological properties:

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 grampositive bacteria, fungi, and the gram-negative cocci, *N gonorrhoeae* and *N meningitidis*, are resistant.

Susceptibility plate testing: If the Kirby-Bauer method of disc susceptibility testing is used, a 300-unit Polymyxin B disc 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. 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

6.1 List of Excipients:

1. Water for Injection USP

6.2 Incompatibilities:

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life:

36 months.

6.4 Special precautions for storage:

Store at 25°C, Protect from light.

6.5 Nature and contents of container:

The lyophilized powder is filled in USP type – I, 5 ml glass vial, further packed in a carton along with a pack insert.

7. Marketing authorization holder

Bharat Serums & Vaccines Ltd.
1st floor, Building No1. Business Development Centre,
DIL Complex, Near Tatwagyan Vidyapeeth,
Ghodbunder Road,
Thane – (West)
Mumbai -400 610. India.

8. Marketing authorization number

Not Applicable.

9. Date of first authorization / renewal of authorization

Not Applicable

10. Date of revision of the text

Not Applicable.