Colistin-150
FOR IV / IM

Composition :
Each vial contains :- Sterile Colistimethate Sodium equivalent to Colistin 150 mg

Product description :
White or yellowish white sterile powder to be dissolved in sterile solution for injection.

Pharmacodynamic :
Colistimethate Sodium is hydrolyzed in aqueous solution and body fluids to colistin which has bactericidal action to susceptible organisms. It acts primarily by binding to membrane phospholipids and disrupting the bacterial cytoplasmic membrane. It is particularly effective against *Pseudomonas aeruginosa.* Colistimethate Sodium has a bactericidal action on most gram-negative bacilli and of the other gram-negative organisms, *Acinetobacter* spp., *Escherichia coli*, *Enterobacter* spp., *Klebsella* spp., *Haemophilus influenzae*, *Bordetella pertussis*, *Salmonella* spp. and *Shigella* spp. are sensitive.

Pharmacokinetics :
Peak plasma concentrations usually occur 2 to 3 hours after an intramuscular injection of colistimethate sodium. Plasma protein binding of colistimethate sodium is low. The serum half-life of colistimethate sodium is 2 to 3 hours but is prolonged in renal impairment (values of 10 to 20 hours have been reported in patients with a creatinine clearance of less than 20 mL/minute). Colistimethate is mainly excreted by glomerular filtration as changed and unchanged drug and up to 80% of a parenteral dose may be recovered in the urine within 24 hours. Excretion is more rapid in children than in adults. Colistin crosses the placenta. It is distributed into breast milk.

Indication :
COLISTIN -150 has been used in the treatment of severe gram-negative infections, especially those due to *Pseudomonas aeruginosa* and in multidrug-resistant *Pseudomonas* or *Acinetobacter* CNS infections.

Recommended dose :
Each mg of colistin base has a potency of 30,000 I.U. and each mg of colistimethate sodium has a potency of 12,500 I.U.

Parenteral dosage
The usual IM or IV dosage of colistimethate sodium for adults and children with normal renal function is 2.5-5 mg/kg of colistin daily given in 2-4 divided doses, depending on the severity of the infection.

The maximum IM or IV dosage of colistimethate sodium for patients with normal renal function is 5 mg/kg of colistin daily.

Oral inhalation dosage
Colistimethate sodium has been given by oral inhalation by nebulization in a dosage of 33.33 – 66.66 mg (1-2 million I.U.) of colistin 2 or 3 times daily.

Administration in renal impairment
The dose and frequency of IM or IV colistimethate sodium should be decreased in proportion to the degree of renal impairment.
- Serum creatinine 1.3 to 1.5 mg/100 mL : 2.5-3.8 mg/kg daily given IM or IV in 2 divided doses.
- Serum creatinine 1.6 to 2.5 mg/100 mL : 2.5 mg/kg daily given IM or IV in a single dose or in 2 divided doses.
- Serum creatinine 2.6 to 4.0 mg/100 mL : 1.5 mg/kg daily given IM or IV every 36 hours.

Mode of administration :
COLISTIN -150 is administered by IM injection, IV injection, or continuous IV infusion. The drug also has been administered by oral inhalation via nebulization.

Parenteral administration : COLISTIN-150 is reconstituted by adding 2 mL of sterile water for injection to a vial, swirled gently. The resultant solution contains 75 mg of colistin per mL.

- IV injection : For direct intermittent IV administration, one-half of the total daily dose should be injected directly into a vein over a 3- to 5- minute period every 12 hours.

- IV infusion : For continuous IV infusion, one-half of the total daily dose should be injected directly into a vein over a 3- to 5-minute period; the remaining one-half of the total daily dose should be added to a compatible IV solution (0.9% NaCl, 5% dextrose, 5% dextrose and 0.225% or 0.45% or 0.9% NaCl, Lactate Ringer 's, 10% invert sugar) and administered 1-2 hours later (over the next 22-23 hours) by slow IV infusion. The infusion rate should be 5-6 mg/hour in patients with normal renal function. For patients with impaired renal function, the infusion rate should be reduced depending on the degree of renal impairment.

The specific IV solution and volume of the solution used should be based on the patients ' fluid and electrolyte requirements.

- IM administration : For IM injection, the appropriate dose of reconstituted solution should be given IM.

Stability of reconstituted solution : Following reconstitution with sterile water for injection, COLISTIN -150 solutions contain 75 mg of colistin per mL and should be stored at 2-8 °C or 25 °C and used within 7 days. However, reconstituted solutions should be used freshly prepared.

Oral Inhalation : For oral inhalation via nebulization, an isotonic solution of COLISTIN-150 has been prepared by diluting the appropriate dose in 2-4 mL of preservative-free 0.9% sodium chloride injection, sterile water, or a mixture of 0.9% sodium chloride injection and sterile water. The solution should be used promptly after prepared.

Contraindication :
1. Hypersensitivity to colistimethate sodium
2. Patients who have myasthenia gravis.

Precaution :
- Neurotoxic reactions such as dizziness, confusion, and visual disturbances can occur during parenteral therapy and patients so affected should not drive or operate machinery.
- Plasma-concentration monitoring during systemic treatment is recommended in neonates, patient with renal impairment, and those with cystic fibrosis. Peak plasma-colistin concentrations of 10 to 15 mg/litre are recommended.
- Premixing of colistimethate in an aqueous solution and storing it for longer than 24 hours results in increased concentrations of colistin in solution and increases the potential for lung toxicity. Therefore, should be given promptly after preparation.
- Colistin has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions with other medicaments :
- Use with cephalosporins group, vancomycin, capreomycin, minocycline, amphotericin B, bacitracin, cisplatin, methoxyflurane and polymyxin B may result in additive side effect of neurotoxic, ototoxic and nephrotoxic.
- If use before, during or after surgical procedures in which a neuromuscular blocking agent is administered, the possibility of prolonged duration of neuromuscular blockade (or recurarization, particularly postoperatively) should be considered.

Pregnancy and Lactation :
Pregnancy : Avoid. Possible risk of fetal toxicity especially in second and third trimesters.
Lactation : Avoid. It is distributed into breast milk.

Undesirable effects :
- Dizziness, confusion and visual disturbances
- Pain and local irritation are reported to be less troublesome after intramuscular injection.
- Neurotoxicity reported especially with excessive doses (including apnoea, perioral and peripheral paraesthesia, vertigo; rarely vasomotor instability, slurred speech, confusion, psychosis, visual disturbances); nephrotoxicity; hypersensitivity reactions including rash; injection-site reactions.

Overdose and Treatment :
Overdosage may cause apnoea, muscle weakness, vertigo, slurred speech, vasomotor instability, visual disturbances, confusion, psychosis and renal insufficiency.
Treatment of overdose
No antidote is available. Management of overdose is by means of supportive treatment and measures designed to increase clearance of colistimethate sodium such as inducing an osmotic diuresis with mannitol, peritoneal dialysis or prolonged haemodialysis.

Storage condition :
Store below 30 °C

Dosage forms and packaging available :
Clear colorless glass vial with flip-off cap contains sterile colistimethate sodium equivalent to colistin 150 mg packed or unpacked in paper box of 1, 2, 3, 4, 5, 10, 12, 20, 24, 25, 50 and 100 vials.

Manufactured by : ABLE MEDICAL CO., LTD.
Mahasarakham 44160, Thailand
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