Gigabac

Colistimethate Sodium USP

Composition
Gigabac™ 1 M Injection: Each vial contains Colistimethate Sodium USP equivalent to 1 Million IU or 34 mg Colistin.

Gigabac™ 4.5 M Injection: Each vial contains Colistimethate Sodium USP equivalent to 4.5 Million IU or 150 mg Colistin.

Pharmacology
Colistimethate sodium is a surface active agent which penetrates into and disrupts the bacterial cell membrane. It has been shown to have bactericidal activity against Aerobic gram-negative microorganisms e.g. *Enterobacter aerogenes, E. coli, Klebsiella pneumoniae* and *Pseudomonas*

Indication
Gigabac™ is indicated for the treatment of acute or chronic infections caused by sensitive strains of certain gram-negative bacilli. It is particularly indicated in the infection caused by sensitive strains of *Pseudomonas aeruginosa*. **Gigabac**™ is not indicated for infections due to Proteus or Neisseria. Gigabac TM is very effective in the treatment of infections due to the following gram-negative organisms: *Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa.*

Dosage & Administration
The dose of **Gigabac**™ should be 2.5 to 5mg/kg per day of colistin base in 2 to 4 divided doses for patients with normal renal function, depending on the severity of the infection.

Adults and adolescents:
Maintenance dose 9 million IU/day in 2-3 divided doses
In patients who are critically ill, a loading dose of 9 MIU should be administered.
Renal impairment:
Dose adjustments in renal impairment are necessary.
Dose reductions are recommended for patients with creatinine clearance < 50 ml/min:
Twice daily dosing is recommended.
Creatinine clearance:

Creatinine clearance (ml/min)	Daily dose
< 50- 30	5.5- 7.5 MIU
<30- 10	4.5- 5.5 MIU
<10	3.5 MIU

MIU = million IU

Haemodialysis (HD) patients:
No-HD days: 2.25 MIU/day (2.2-2.3 MIU/day). HD days: 3 MIU/day (Should be given after the HD session) Twice daily dosing is recommended.
Paediatric population:
The dose should be based on lean body weight. Children ≤40kg: 75,000-150,000 IU/kg/day divided into 3 doses. Children >40kg: >150,000 IU/kg/day has been reported in children with cystic fibrosis.
Hepatic impairment patients:
There are no data in patients with hepatic impairment. Caution is advised when administering Colistimethate sodium in these patients.

Reconstitute the contents of the vial with not more than 10ml water for injection or 0.9% sodium chloride.

Reconstitution
For IM injection:
Reconstitute the contents of the vial with 2 ml water for injection only.
For bolus injection:
Reconstitute the contents of the vial with 5 ml water for injection.
For infusion:
The contents of the reconstituted vial may be diluted, usually with 50 ml-100ml 0.9% sodium chloride.

Intravenous Administration
1. Direct Intermittent Administration - Slowly inject one-half of the total daily dose over a period of 3 to 5 minutes every 12 hours.
2. Continuous Infusion - Slowly inject one-half of the total daily dose over 3 to 5 minutes. Add the remaining half of the total daily dose of Colistimethate for injection to one of the following:

0.9% NaCl
5% dextrose in 0.9% NaCl
5% dextrose in water
5% dextrose in 0.45% NaCl
5% dextrose in 0.225% NaCl
Lactated Ringer's solution

There are not sufficient data to recommend usage of Colistimethate for injection with other drugs or other than the above listed infusion solutions.

Administer the second half of the total daily dose by slow intravenous infusion, starting 1 to 2 hours after the initial dose, over the next 22 to 23 hours. In the presence of impaired renal function, reduce the infusion rate depending on the degree of renal impairment.

The choice of intravenous solution and the volume to be employed are dictated by the requirements of fluid and electrolyte management.

Any infusion solution containing Colistimethate sodium should be freshly prepared and used for no longer than 24 hours.

3. Alternative method – As per specialized references for intermittent infusion: Prescribed dose can be diluted in 50 - 100 ml 0.9% NaCl and administer over 30-60 minutes in IV route.

Adverse Effects
The following adverse reactions have been reported: gastrointestinal upset, tingling of extremities and tongue, slurred speech, dizziness, vertigo and paresthesia, generalized itching, urticaria and rash, fever, increased blood urea nitrogen (BUN), elevated creatinine and decreased creatinine clearance, respiratory distress and apnea, nephrotoxicity and decreased urine output.
Precautions
Colistimethate Sodium should be used with caution in patient with impaired renal function. When actual renal impairment is present, Colistimethate Sodium may be used, but the greatest caution should be exercised and the dosage should be reduced in proportion to the extent of the impairment. Colistimethate Sodium should be used with caution in neonates, infants and children.

Use in Pregnancy & Lactation
There are no adequate and well-controlled studies about the use of Colistimethate Sodium in pregnant women. Since Colistimethate Sodium is transferred across the placental barrier in humans, it should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
It is not known whether Colistimethate sodium is excreted in human breast milk. Therefore, caution should be exercised when administered to nursing women.

Drug Interaction
Colistimethate Sodium should not be given with certain antibiotics like-aminoglycosides and polymyxin due to report of interfere with the nerve transmission at the neuromuscular junction. It should not be given with muscle relaxants e.g., tubocurarine and other drugs including ether, succinylcholine, gallamine, decamethonium and sodium citrate. The concomitant use of Sodium Cephalothin and Colistimethate Sodium should be avoided.

Over Dose
Overdosage with Colistimethate Sodium can cause neuromuscular blockade characterized by paresthesia, lethargy, confusion, dizziness, ataxia, nystagmus, disorders of speech and apnea. Respiratory muscle paralysis may lead to apnea, respiratory arrest and death. Overdosage with the drug can also cause acute renal failure, manifested as decreased urine output and increases in serum concentrations of B.U.N and creatinine. As in any case of overdose, Colistimethate Sodium therapy should be discontinued and general supportive measures should be utilized.

Pharmaceutical Precaution
Before reconstitution: Store at 30^0 C, protect from light and moisture.
After reconstitution: Store at 2^0C to 8^0 C (Do not freeze) and use within 24 hours.

How Supplied
Gigabac™ 1 M Injection: Each box contains 1 vial filled with Colistimethate Sodium powder accompanied by one ampoule of 5 ml Water for Injection BP and one 5ml sterile disposable syringe.
Gigabac™ 4.5 M Injection: Each box contains 1 vial filled with Colistimethate Sodium powder accompanied by one ampoule of 5 ml Water for Injection BP and one 5ml sterile disposable syringe.

Manufactured by
SQUARE
PHARMACEUTICALS LTD.
BANGLADESH