Colistimethate sodium is no longer listed as an antimicrobial for use in renal impairment. C. difficile. This antibiotic is indicated for infections due to susceptible gram-negative pathogenic bacilli. Colistimethate sodium is a surface active agent which penetrates into the bacterial cell membrane, it has been shown to have bactericidal activity against most strains of the following microorganisms, both in vitro and in clinical infections described in the INDICATIONS AND USAGE section:

**INDICATIONS AND USAGE**

Coly-Mycin M Parenteral may be used to initiate therapy in serious infections that are caused by drug-susceptible Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa. Respiratory arrest has been reported following intramuscular administration of colistimethate sodium. Impaired renal function increases the possibility of apnea and respiratory arrest.

Overdosage can result in renal insufficiency, muscle weakness, and apnea (see OVERDOSAGE section). Nephrotoxicity can occur and is probably a dose-dependent effect of colistimethate sodium. Impaired renal function increases the possibility of apnea and respiratory arrest.

Colistimethate sodium is a polypeptide antibiotic with an approximate molecular weight (150 mg colistin base activity). Each vial contains colistimethate sodium or pentasodium colistimethane sulfate (150 mg colistin base activity).

**DESCRIPTION**

Colistimethate sodium is a polypeptide antibiotic with an approximate molecular weight of 1720. The empirical formula is C_{40}H_{60}N_{30}O_{18}S_2 and the structural formula is represented below:

Higher serum levels were obtained at 10 minutes following IV administration. Serum levels were maintained with a half-life of 2.3 hours following oral intramuscular or intravenous administration in adults and in the pediatric population, including neonates and infants.

Average urine levels ranged from about 270 mcg/mL at 2 hours to about 15 mcg/mL, at 8 hours after intravenous administration and from 0.02 to about 25 mcg/mL during a 48-hour period after oral administration.

**Microbiology:** Colistimethate sodium is a surface active agent which penetrates into the bacterial cell membrane, it has been shown to have bactericidal activity against most strains of the following microorganisms, both in vitro and in clinical infections described in the INDICATIONS AND USAGE section:


**Susceptibility Tests:** Colistimethate sodium is no longer listed as an antimicrobial for routine testing and reporting by clinical microbiology laboratories.

**INDICATIONS AND USAGE**

Coly-Mycin M Parenteral is indicated for the treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacteria. It is particularly indicated when the infection is caused by sensitive strains of Pseudomonas aeruginosa. This antibiotic is not indicated for infections with Proteus or Klebsiella. Colistimethate sodium has proven clinically effective in treatment of infections due to the following gram-negative organisms:

- Enterobacter aerogenes, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa.

Coly-Mycin M Parenteral may be used to initiate therapy in serious infections that are caused by drug-susceptible Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa.

**CONTRAINDICATIONS**

The use of Coly-Mycin M Parenteral is contraindicated for patients with a history of sensitivity to the drug or any of its components.

**WARNINGS**

Maximum daily doses calculated from colistin base activity should not exceed 5 mg/kg/day with normal renal function. Transient neurological disturbances may occur. These include circulatory paraneuritis or numbness, tingling or formication of the extremities, generalized pruritus, vertigo, dizziness, nausea, vomiting, diarrhea, muscle weakness, and apnea.

Overdosage can result in renal insufficiency, muscle weakness, and apnea (see OVERDOSAGE section). Nephrotoxicity can occur and is probably a dose-dependent effect of colistimethate sodium. Impaired renal function increases the possibility of apnea and respiratory arrest.

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Nursing Mothers

It is not known whether colistimethate sodium is excreted in human breast milk. However, colistimethate sodium may be excreted in human breast milk. Therefore, caution should be exercised when colistimethate sodium is administered to nursing women.

Geriatric Use

Clinical studies of colistimethate sodium did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be based on age, general condition, and concomitant disease.

Pediatric Use

In clinical studies, colistimethate sodium was administered to the pediatric population (infants, children, and adolescents). Although adverse reactions appear to be similar in the adult and pediatric populations, subjective symptoms of toxicity may not be reported by pediatric patients. Closer clinical monitoring of pediatric patients is recommended.

Information for Patients

Patients should be counseled that antibacterial drugs such as colistimethate sodium may cause overgrowth of non-sensitive bacteria. If this occurs, patients should report to their physician.

ADVERSE REACTIONS

The following adverse reactions have been reported:

Gastrointestinal:

- nausea
- vomiting
- abdominocutaneous upset

Nervous System:

- loss of appetite
- fatigue
- weakness
- drowsiness
- dizziness
- headache
- neck stiffness
- meningismus
- myalgia
- chills
- fever

Cutaneous: Integumentary:

- local injection site reactions (erythema, pain, swelling, induration) and paresthesia

Respiratory System:

- dyspnea
- respiratory arrest
- bronchospasm

Renal System:

- decreased creatinine clearance

OVERDOSAGE

Colistimethate sodium can cause neuromuscular blockade characterized by paresthesia, lethargy, confusion, dizziness, ataxia, nystagmus, dysarthria, laryngospasm, apnea, and respiratory arrest. Overdosage with the drug can also cause acute renal failure, manifested as decreased urine output and increases in serum concentrations of BUN and creatinine.

As in any case of overdose, colistimethate sodium therapy should be discontinued and general supportive measures should be utilized. If death occurs, blood should be withdrawn and, if possible, a sample for colistin base activity should be sent to the pharmaceutical manufacturer. There is no information available on the use of hemodialysis or peritoneal dialysis in overdosage cases.

DOSEAGE AND ADMINISTRATION

Important: Colistimethate sodium is supplied as a white to slightly yellow lyophilized powder equivalent to 150 mg of colistin base activity per vial.

Reconstitution for Intravenous or Intramuscular Administration: The 150 mg vial should be reconstituted with 2 mL Sterile Water for Injection, USP. The reconstituted solution provides colistimethate sodium at a concentration equivalent to 75 mg/mL colistin base activity. During reconstitution swirl gently to avoid frothing.

Parenteral drug products should be inspected visually for particulate matter and foreign matter. The reconstituted solution is a clear, colorless, phosphate-buffered, isotonic solution. It is not necessary to filter the product prior to administration. The reconstituted solution is stable for 7 days when stored at controlled room temperature.

DOSAGE

DOSAGE Schedule

2.5 – 5 mg/kg, divided into 2 or 4 doses per day

DOSAGE and ADMINISTRATION

Pediatres and Pediatric Patients—Intravenous or Intramuscular Administration: The daily dose of Coly-Mycin M Parenteral should be 2.5 to 5 mg/kg by slow intravenous injection over a period of 3 to 5 minutes every 12 hours.

Adults and Pediatric Patients—Intravenous Administration: Slowly inject one-half of the total daily dose over a period of 3 to 5 minutes every 12 hours.

Intramuscular Administration: For Intramuscular Injection, administer by deep intramuscular injection into a large muscle mass (such as the gluteal muscles or lateral part of the thigh).

In obese individuals, dosage should be based on ideal body weight.

In obese individuals, dosage should be based on ideal body weight.

The daily dose and frequency should be reduced for the patients with renal impairment. Suggested modifications of dosage schedule for patients with renal impairment are presented in Table 1.

Table 1: Suggested Modification of Dosage Schedules of Coly-Mycin M Parenteral for Adults with Impaired Renal Function

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Normal</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 – 49</td>
<td>2.5 mg/kg, divided into 2 or 4 doses per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50 – 79</td>
<td>2.5 mg/kg, divided into 2 doses per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 – 49</td>
<td>2.5 mg/kg, divided into 2 doses per day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 – 29</td>
<td>1.5 mg/kg every 36 hours</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: The suggested total daily dose is calculated from colistin base activity.

INTRAVENOUS ADMINISTRATION

1. Direct Intravenous 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 Coly-Mycin M Parenteral to one of the following:

- 0.9% NaCl
- 5% dextrose in 0.9% NaCl
- 5% dextrose in water
- 0.45% NaCl
- 0.225% NaCl
- lactated Ringer’s solution
- 10% invert sugar solution

There are not sufficient data to recommend usage of Coly-Mycin M Parenteral with other drugs or other than the above listed infusion solutions.

Administration:

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 33 hours. In the presence of impaired renal function, the infusion rate should be adjusted according to 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 final intravenous infusion solution containing colistimethate sodium should be freshly prepared and used for no longer than 24 hours.

INTRAVASCULAR ADMINISTRATION

1. For Intramuscular Injection, administer by deep intramuscular injection into a large muscle mass (such as the gluteal muscles or lateral part of the thigh).

Store reconstituted solution for intravenous infusion in a refrigerated 2° to 8°C (36° to 46°F) or between 20° to 25°C (68° to 77°F) and use within 7 days.

HOW SUPPLIED

Coly-Mycin M Parenteral is supplied in vials containing colistimethate sodium (equivalent to 150 mg colistin base activity per vial) as a white to slightly yellow lyophilized powder. It is not necessary to filter the product prior to administration. When solution and container are in use, the product is considered to be sterile.

Nursing Mothers

It is not known whether colistimethate sodium is excreted in human breast milk. However, colistin sulphate is excreted in human breast milk. Therefore, caution should be exercised when colistimethate sodium is administered to nursing women.

Geriatric Use

Clinical studies of colistimethate sodium did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be based on age, general condition, and concomitant disease.

Pediatric Use

In clinical studies, colistimethate sodium was administered to the pediatric population (infants, children, and adolescents). Although adverse reactions appear to be similar in the adult and pediatric populations, subjective symptoms of toxicity may not be reported by pediatric patients. Closer clinical monitoring of pediatric patients is recommended.

Information for Patients

Patients should be counseled that antibacterial drugs such as colistimethate sodium may cause overgrowth of non-sensitive bacteria. If this occurs, patients should report to their physician.

ADVERSE REACTIONS

The following adverse reactions have been reported:

Gastrointestinal:

- nausea
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Nervous System:

- loss of appetite
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- decreased creatinine clearance

OVERDOSAGE

Colistimethate sodium can cause neuromuscular blockade characterized by paresthesia, lethargy, confusion, dizziness, ataxia, nystagmus, dysarthria, laryngospasm, apnea, and respiratory arrest. Overdosage with the drug can also cause acute renal failure, manifested as decreased urine output and increases in serum concentrations of BUN and creatinine.

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DOSEAGE AND ADMINISTRATION

Important: Colistimethate sodium is supplied as a white to slightly yellow lyophilized powder equivalent to 150 mg of colistin base activity per vial.

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During reconstitution swirl gently to avoid frothing.

Parenteral drug products should be inspected visually for particulate matter and foreign matter. The reconstituted solution is a clear, colorless, phosphate-buffered, isotonic solution. It is not necessary to filter the product prior to administration. When solution and container are in use, the product is considered to be sterile.

DOSAGE

DOSAGE Schedule

2.5 – 5 mg/kg, divided into 2 or 4 doses per day

DOSAGE and ADMINISTRATION

Pediatres and Pediatric Patients—Intravenous or Intramuscular Administration: The daily dose of Coly-Mycin M Parenteral should be 2.5 to 5 mg/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.