



Sodium cephalothin may enhance the nephrotoxicity of colistimethate for injection. The concomitant use of sodium cephalothin and colistimethate for injection should be avoided.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term animal carcinogenicity studies and genetic toxicology studies have not been performed with colistimethate sodium. There were no adverse effects on fertility or reproduction in rats at doses of 9.3 mg/kg/day (0.3 times the maximum daily human dose when based on mg/m<sup>2</sup>).

**Pregnancy - Teratogenic Effects**

Pregnancy Category C: Colistimethate sodium given intramuscularly during organogenesis to rabbits at 4.15 and 9.3 mg/kg resulted in talipes varus in 2.6% and 2.9% of fetuses, respectively. These doses are 0.25 and 0.55 times the maximum daily human dose based on mg/m<sup>2</sup>. In addition, increased resorption occurred at 9.3 mg/kg. Colistimethate sodium was not teratogenic in rats at 4.15 or 9.3 mg/kg. These doses are 0.13 and 0.3 times the maximum daily human dose based on mg/m<sup>2</sup>. There are no adequate and well-controlled studies 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.

**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.

**Pediatric Use**

In clinical studies, colistimethate sodium was administered to the pediatric population (neonates, 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. Close clinical monitoring of pediatric patients is recommended.

**Information for Patients**

Patients should be counseled that antibacterial drugs including colistimethate for injection should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When colistimethate for injection 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 will not be treatable by colistimethate for injection or other antibacterial drugs in the future.

**ADVERSE REACTIONS**

The following adverse reactions have been reported:

**Gastrointestinal:** gastrointestinal upset

**Nervous System:** tingling of extremities and tongue, slurred speech, dizziness, vertigo and paresthesia

**Integumentary:** generalized itching, urticaria and rash

**Body as a Whole:** fever

**Laboratory Deviations:** increased blood urea nitrogen (BUN), elevated creatinine and decreased creatinine clearance

**Respiratory System:** respiratory distress and apnea

**Renal System:** nephrotoxicity and decreased urine output

**OVERDOSAGE**

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 BUN and creatinine.

As in any case of overdose, colistimethate sodium therapy should be discontinued and general supportive measures should be utilized.

It is unknown whether colistimethate sodium can be removed by hemodialysis or peritoneal dialysis in overdose cases.

**DOSE AND ADMINISTRATION**

**Important:** Colistimethate for injection is supplied in vials containing colistimethate sodium equivalent to 150 mg colistin base activity per vial.

**Reconstitution:** The 150 mg vial should be reconstituted with 2.0 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 discoloration prior to administration, whenever solution and container permit. If these conditions are observed, the product should not be used.

**Dosage**

**Adults and pediatric patients – Intravenous or Intramuscular Administration:** Colistimethate for injection should be given in 2 to 4 divided doses at dose levels of 2.5 to 5 mg/kg per day for patients with normal renal function, depending on the severity of the infection.

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

The daily dose should be reduced in the presence of renal impairment. Modifications of dosage in the presence of renal impairment are presented in Table 1.

**TABLE 1. Suggested Modification of Dosage Schedules of Colistimethate for Injection for Adults with Impaired Renal Function**

Renal Function	Degree of Impairment			
	Normal	Mild	Moderate	Considerable
Plasma creatinine, mg/100 mL	0.7–1.2	1.3–1.5	1.6–2.5	2.6–4.0
Urea clearance, % of normal	80–100	40–70	25–40	10–25
<b>Dosage</b>				
Unit dose of Colistimethate for injection, mg	100–150	75–115	66–150	100–150
Frequency, times/day	4 to 2	2	2 or 1	every 36 hr
Total daily dose, mg	300	150–230	133–150	100
Approximate daily dose, mg/kg/day	5	2.5–3.8	2.5	1.5

**Note:** The suggested unit dose is 2.5 to 5 mg/kg; however, the time INTERVAL between injections should be increased in the presence of impaired renal function.

**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
- 10% invert sugar 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.**

**HOW SUPPLIED**

Colistimethate for injection is supplied in vials containing colistimethate sodium (equivalent to 150 mg colistin base per vial). Colistimethate sodium appears as a white to slightly yellow lyophilized cake and is available as one vial per carton.

NDC 0574-0858-01

**Store between 20° - 25°C (68° - 77°F)[See USP Controlled Room Temperature].**

**Store reconstituted solution in refrigerator 2° to 8°C (36° to 46°F) or between 15° to 30°C (59° to 86°F), and use within 7 days.**

Manufactured for:  
Paddock Laboratories, Inc.  
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Manufactured by:  
Draxis Pharma Inc.  
Kirkland, Quebec H9H 4J4  
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Revised: April 2004



<b>NOM DU PRODUIT/PRODUCT NAME: COLISTIMETHATE</b> <b>NUMÉRO DU PRODUIT / PRODUCT NUMBER: 214160</b> <b>NUMÉRO DU PHARMACODE / PHAMACODE NUMBER: N/A</b>	<b>APPROBATION/APPROVAL</b>  <b>DRAXIS PHARMA</b>
<b>SPÉCIFICATIONS</b> COULEURS / COLORS (RECTO/FRONT): BLACK (VERSO/BACK): BLACK TYPE DE PAPIER / PAPER TYPE: ALLIANCE POID DU PAPIER / PAPER WEIGHT: 60 M DIMENSIONS (MM): À PLAT / FLAT: 101,6 x 355,6 PLIÉ / FOLDED: 51 x 30 POINT DE COLLE / GLUE SPOTS: N/A CONFORMITÉ DU PLIAGE / CONFORMITY OF FOLDING: <input type="checkbox"/>	APP.: _____ DATE: _____  APP.: _____ DATE: _____  APP.: _____ DATE: _____  APP.: _____ DATE: _____