Product Monograph

Including Patient Medication Information

PrColistimethate for Injection USP

Powder for solution, 150 mg colistin base (as colistimethate sodium), intravenous and intramuscular administration

Sterile

Antibiotic

Marcan Pharmaceuticals Inc.
2 Gurdwara Road, Suite #400
Ottawa, ON K2E 1A2
Canada

Date of Authorization:
2026-01-21

Control Number: 302095

Recent Major Label Changes

7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism	01/2026

Table of Contents

Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Health Professional Information

1 Indications

Colistimethate for Injection USP (colistimethate for injection) is indicated for:

- the treatment of acute or chronic infections due to sensitive strains of certain gram-negative bacilli. Particularly indicated when the infection is caused by sensitive strains of *P. aeruginosa*.

This antibiotic is not indicated for infections due to *proteus* or *neisseria*. Sodium colistimethate has proven clinically effective in treatment of infections due to the following gram-negative organisms: *A. aerogenes*, *E. coli*, *K. pneumoniae* and *P. aeruginosa*.

Pending results of appropriate bacteriologic cultures and sensitivity tests, sodium colistimethate may be used to initiate therapy in serious infections that are suspected to be due to gram-negative organisms.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Colistimethate for Injection USP and other antibacterial drugs, Colistimethate for Injection USP should be used only to treat infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

2 Contraindications

- Colistimethate for Injection USP is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 Dosage and Administration

4.1 Dosing Considerations

- Maximum daily dose of Colistimethate for Injection USP should not exceed 5 mg/kg/day with normal renal function.
- Since sodium colistimethate is eliminated mainly by renal excretion, it should be used with caution when the possibility of impaired renal function exists. The decline in renal function with advanced age should be considered.
- When actual renal impairment is present, sodium colistimethate may be used, but the greatest caution should be exercised and the dosage should be reduced in proportion to the extent of the impairment (see 7 WARNINGS AND PRECAUTIONS, Renal).

4.2 Recommended Dose and Dosage Adjustment

- Average dose is 2.5 mg/kg/day given in 2 to 4 divided doses.
- In the presence of bacteremia, septicemia or other serious infections, greater than average doses may be required.
- Maximal dose of 5 mg/kg/day should not be exceeded in patients with normal renal function.

- Overdosage can result in renal insufficiency, muscle weakness and apnea.
- Reduction of dosage may alleviate symptoms. Therapy need not be discontinued, but such patients should be observed with particular care.

4.3 Reconstitution

Table 1 - Reconstitution

Vial size	Volume of diluent to be Added to Vial	Approx. Available Volume	Concentration per mL
10 mL vial	2 mL of Sterile Water for Injection	2 mL	75 mg / mL

After reconstitution, Colistimethate for Injection USP solution should be stored refrigerated 2 to 8°C and used within 3 days (or within 24 hours, when stored at controlled room temperature 15 to 30°C).

Any infusion solution containing colistimethate sodium should be freshly prepared and used for no longer than 24 hours (see 11 STORAGE, STABILITY AND DISPOSAL).

4.4 Administration

Intravenous or intramuscular administration.

5 Overdose

Symptoms: Dizziness, ataxia, speech disturbances, generalized muscular weakness, apnea and elevated BUN.

Treatment: Usual medical regimen for treatment of oliguria or anuria. Consider dialysis, particularly if a massive overdosage is discovered shortly after administration.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 Dosage Forms, Strengths, Composition and Packaging

Table 2 - Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Intravenous, intramuscular	Powder for solution for injection 150 mg (as sodium colistimethate)	N/A

Description

Each Colistimethate for Injection USP vial contains: colistin base activity (as sodium colistimethate) 150 mg as white to pale yellow lyophilized cake which forms a clear, aqueous solution when reconstituted with 2 mL of Sterile Water for Injection USP. Each mL of reconstituted sterile solution contains: sodium colistimethate equivalent to 75 mg colistin base. Energy: nil. Sodium: <1 mmol (16.6 mg)/vial.

7 Warnings and Precautions

Driving and Operating Machinery

Transient neurological disturbances may occur. These include circumoral paresthesias or numbness, tingling or formication of the extremities, generalized pruritus, vertigo, dizziness, and slurring of speech. For these reasons, patients should be warned not to drive vehicles or use hazardous machinery while on therapy.

Endocrine and Metabolism

Cases of pseudo-Bartter syndrome have been reported in patients with the use of colistimethate sodium. In all cases hypokalemia, metabolic alkalosis, and kaliuresis were reported; some cases also involved hypomagnesemia and hypocalcemia. In case reports, electrolyte abnormalities did not completely normalize with electrolyte corrective therapy alone. In all case reports, electrolyte abnormalities eventually resolved or significantly improved following the discontinuation of colistimethate. Consider monitoring electrolytes.

Renal

Administration of amounts of sodium colistimethate in excess of renal excretory capacity will lead to high serum levels and can result in further impairment of renal function, initiating a cycle which, if not recognized, can lead to acute renal insufficiency, renal shutdown and further concentration of the antibiotic to toxic levels in the body. At this point, interference of nerve transmission at neuromuscular junctions may occur and result in muscle weakness and apnea.

Easily recognized signs indicating the development of impaired renal function are diminishing urine output, rising BUN and serum creatinine. If present, therapy with sodium colistimethate should be discontinued immediately.

If a life-threatening situation exists, therapy may be reinstated at a lower dosage after blood levels have fallen.

Respiratory

If apnea occurs it may be treated with assisted respiration, oxygen, and calcium chloride injections.

Sensitivity/Resistance

Prescribing Colistimethate for Injection USP in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

7.1 Special Populations

7.1.1 Pregnant Women

The safety of sodium colistimethate during human pregnancy has not been established.

7.1.2 Breast-feeding

It is unknown if sodium colistimethate is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

7.1.4 Geriatrics

Since sodium colistimethate is eliminated mainly by renal excretion, it should be used with caution when the possibility of impaired renal function exists. The decline in renal function with advanced age should be considered.

8 Adverse Reactions

8.5 Post-Market Adverse Reactions

Respiratory, thoracic and mediastinal disorders:

Respiratory arrest has been reported following IM administration of sodium colistimethate. Impaired renal function increases the possibility of apnea and neuromuscular blockade following administration of sodium colistimethate. This has generally been due to failure to follow recommended guidelines, usually overdosage, failure to reduce dose commensurate with degree of renal impairment, and/or concomitant use of other antibiotics or drugs with neuromuscular blocking potential.

Renal and urinary disorders:

A decrease in urine output or increase in BUN or serum creatinine can be interpreted as signs of nephrotoxicity, which is probably a dose dependent effect of sodium colistimethate. These manifestations of nephrotoxicity are reversible following discontinuation of the antibiotic.

Increases of BUN have been reported for patients receiving sodium colistimethate at dose levels of 1.6 to 5 mg/kg/day. The BUN values returned to normal following cessation of sodium colistimethate administration.

Metabolic and Nutrition Disorders:

Cases of pseudo-Bartter syndrome have been reported (see 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism).

Others:

Paresthesia, tingling of the extremities or tingling of the tongue and generalized itching or urticaria have been reported by patients who received sodium colistimethate by IM or IV injection.

In addition, the following adverse reactions have been reported for sodium colistimethate: drug fever and gastrointestinal upset, vertigo, and slurring of speech. The subjective symptoms reported by the adult may not be manifest in infants or young children, thus requiring close attention to renal function.

9 Drug Interactions

9.2 Drug Interactions Overview

Certain other antibiotics (kanamycin, streptomycin, dihydrostreptomycin, polymyxin, neomycin) have also been reported to interfere with the nerve transmission at the neuromuscular junction and thus should not be given concomitantly with sodium colistimethate except with the greatest caution. The antibiotics with a gram positive antimicrobial spectrum, e.g. penicillin, tetracycline, sodium cephalothin, have not been reported to interfere with nerve transmission and, accordingly, would not be expected to potentiate this activity of sodium colistimethate.

9.4 Drug-Drug Interactions

Table 3 - Established or Potential Drug-Drug Interactions

Proper/Common name	Source of Evidence	Effect	Clinical comment
Antibiotics such as kanamycin, streptomycin, dihydrostreptomycin, polymyxin, neomycin	C	These drugs interfere with the nerve transmission at the neuromuscular junction	They should not be given concomitantly with sodium colistimethate except with the greatest caution.
Curariform muscle relaxants such as ether, tubocurarine, succinylcholine, gallamine, decamethonium and sodium citrate	T	These drugs potentiate the neuromuscular blocking effect.	They should be used with extreme caution in patients being treated with sodium colistimethate.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 Clinical Pharmacology

10.1 Mechanism of Action

Sodium colistimethate is the pentasodium salt of the penta (methanesulfonic acid) derivative of colistin. Colistin is a basic polypeptide antibiotic substance produced by the growth of *Bacillus polymyxa var. colistinus*. Colistin derivatives appear to alter the permeability of the bacterial cytoplasmic membrane, causing leakage of intracellular nucleosides. The drugs are bactericidal in action.

10.2 Pharmacodynamics

Hydrolysis of sodium colistimethate is required for antibacterial activity.

10.3 Pharmacokinetics

Absorption

IM administration of sodium colistimethate with activity equivalent to that of 150 mg of colistin produces peak serum levels of approximately 5 to 7.5 µg/mL within 2 hours. Peak serum levels after IV administration occur within 10 minutes and are higher but decline more rapidly than those achieved after IM administration. The serum half-life is approximately 1.5 hours following IV and 2.75 to 3 hours following IM administration. Blood levels appear to decline more rapidly in children than in adults.

Metabolism:

Hydrolysis of sodium colistimethate is required for antibacterial activity.

Elimination

Sodium colistimethate and its metabolites are excreted primarily by the kidneys; urine levels of the active antibiotic are considerably higher than serum levels. In 24 hours, approximately 66% after IM administration and 75% after IV administration is excreted.

Special Populations and Conditions

- **Pediatrics:** Blood levels appear to decline more rapidly in children than in adults.
- **Renal Insufficiency**: Administration of amounts of sodium colistimethate in excess of renal excretory capacity will lead to high serum levels and can result in further impairment of renal function (see 7 WARNINGS AND PRECAUTIONS, Renal).

11 Storage, Stability and Disposal

Store Colistimethate for Injection USP at controlled room temperature between 15°C and 30°C.

After reconstitution, Colistimethate for Injection USP solution should be stored refrigerated 2°C to 8°C and used within 3 days (or within 24 hours, when stored at controlled room temperature 15°C to 30°C).

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

12 Special Handling Instructions

N/A

Part 2: Scientific Information

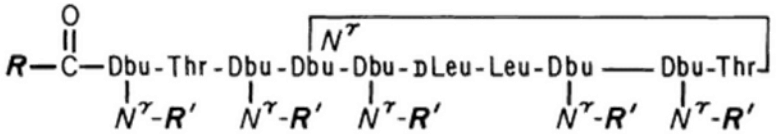
13 Pharmaceutical Information

Drug Substance

Proper name: Colistimethate Sodium USP
Chemical name: Colistimethate Sodium

Molecular formula and molecular mass: $C_{58}H_{105}N_{16}NaO_{28}S_5$ (colistin A component) 1749.82 g/ mol
$C_{57}M_{103}N_{16}Na_5O_{28}S_5$ (colistin B component) 1735.80 g/ mol

Structural formula:



(Dbu is L-α,γ-diaminobutyric acid; R is $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}H(CH_2)_4$ in the colistin A component and $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H(CH_2)_4$ in the colistin B component; R' is CH_2SO_3Na.)

14 Clinical Trials

The clinical trial data on which the original indication was authorized is not available.

15 Microbiology

No microbiological information is required for this drug product.

16 Non-Clinical Toxicology

The non-clinical data on which the original indication was authorized is not available.

17 Supporting Product Monographs

1. COLY-MYCIN M (powder for solution, 150 mg), control 282537, product monograph, Searchlight Pharma Inc. (2024-10-07)

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] Colistimethate for Injection USP

Read this carefully before you start taking **Colistimethate for Injection USP** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Colistimethate for Injection USP**.

What is Colistimethate for Injection USP used for?

Colistimethate for Injection USP is used to treat infections:

- that are sudden and severe
- or are chronic
- caused by certain bacteria
- that are proven or strongly suspected to be caused by certain bacteria

Antibacterial drugs like Colistimethate for Injection USP treat only bacterial infections. They do not treat viral infections. Although you may feel better early in treatment, Colistimethate for Injection USP should be used exactly as directed. Misuse or overuse of Colistimethate for Injection USP could lead to the growth of bacteria that will not be killed by Colistimethate for Injection USP (resistance). This means that Colistimethate for Injection USP may not work for you in the future.

How does Colistimethate for Injection USP work?

Colistimethate for Injection USP is an antibiotic that kills certain types of bacteria in your body. It works by damaging the cell wall of the bacteria.

What are the ingredients in Colistimethate for Injection USP?

Medicinal ingredients: colistin (as colistimethate sodium).

Non-medicinal ingredients: none.

Colistimethate for Injection USP comes in the following dosage forms:

As a sterile powder for solution, 150 mg

Do not use Colistimethate for Injection USP if:

- you are allergic or you have a sensitivity to this medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Colistimethate for Injection USP. Talk about any health conditions or problems you may have, including if you:

- have kidney problems.
- Are breastfeeding.
- Are pregnant

Other warnings you should know about:

- Colistimethate for Injection USP may cause dizziness or light-headedness. Do not drive or use machines while you are receiving this medicine.
- Your healthcare professional may monitor your electrolyte levels while you are taking Colistimethate for Injection USP.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.
The following may interact with Colistimethate for Injection USP:

- Other antibiotics such as dihydrostreptomycin, kanamycin, neomycin, polymyxin, streptomycin.
- Muscle relaxants such as decamethonium, ether, gallamine, sodium citrate, succinylcholine, and tubocurarine. These should be used with extreme caution.

How to take Colistimethate for Injection USP:

- Colistimethate for Injection USP will be given to you by a healthcare professional.
- It will either be infused directly into your vein or;
- It will be injected into your muscle.
- Follow all instructions given to you by your healthcare professional.

Usual dose:

- Your healthcare professional will decide how much Colistimethate for Injection USP you will receive.
- You will receive it 2, 3 or 4 times a day.
- Your healthcare professional will decide how often and for how long you will receive Colistimethate for Injection USP.

Overdose:

Overdosage can result in kidney problems, muscle weakness and difficulty breathing.

If you think you, or a person you are caring for, have received too much Colistimethate for Injection USP, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

What are possible side effects from using Colistimethate for Injection USP?

These are not all the possible side effects you may have when taking Colistimethate for Injection USP. If you experience any side effects not listed here, tell your healthcare professional.

- dizziness or vertigo (light-headedness)
- tingling of the tongue
- itching of the skin
- hives
- fever
- nausea and vomiting
- upset stomach
- diarrhea

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Breathing difficulty, breathing stops			✓
Kidney problems: abdominal or back pain, dark urine, decreased urination, nausea, swelling of the arms or legs, vomiting, weakness			✓
Slow or slurred speech			✓
Tingling, prickling, numbness or burning of hands or feet or around the mouth			✓
UNKNOWN			
Pseudo-Bartter syndrome (serious metabolic condition of electrolyte imbalances): cramping, constipation, fatigue, frequent urination, muscle weakness, muscle spasms, thirst, vomiting, irregular heartbeats			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store Colistimethate for Injection USP at room temperature (15°C to 30°C).
- After reconstitution, refrigerate Colistimethate for Injection USP solution (2°C to 8°C) and use within 3 days.
- Reconstituted Colistimethate for Injection USP solution can also be stored at room temperature (15°C to 30°C) and must be used within 24 hours.
- Infusion solution containing Colistimethate for Injection USP should be freshly prepared and used within 24 hours.

Keep out of reach and sight of children.

If you want more information about Colistimethate for Injection USP:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada Drug Product Database website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (www.marcanpharma.com), or by calling 1-855-627-2261

This leaflet was prepared by Marcan Pharmaceuticals Inc.

Date of Authorization: 2026-01-21