

PRESCRIBING INFORMATION
Including Patient Medication Information

COLY-MYCIN* M PARENTERAL

(Colistimethate for Injection USP)

Sterile Colistimethate sodium
Equivalent to 150 mg colistin base

Parenteral

ANTIBIOTIC



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PRESCRIBING INFORMATION**COLY-MYCIN* M PARENTERAL****(Colistimethate for Injection USP)****Sterile Colistimethate sodium
Equivalent to 150 mg colistin base****THERAPEUTIC CLASSIFICATION**

Antibiotic

ACTION AND CLINICAL PHARMACOLOGY

COLY-MYCIN* M (Colistimethate for Injection, U.S.P.) 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.

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.

Hydrolysis of sodium colistimethate is required for antibacterial activity. 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.

INDICATIONS AND CLINICAL USE

COLY-MYCIN* M (Colistimethate for Injection, U.S.P.) 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 COLY-MYCIN* M PARENTERAL and other antibacterial drugs, COLY-MYCIN* M PARENTERAL 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.

CONTRAINDICATIONS

COLY-MYCIN* M PARENTERAL (Colistimethate for Injection, U.S.P.) is contraindicated in patients with a history of sensitivity to the drug.

PRECAUTIONS

Maximum daily dose of COLY-MYCIN* M PARENTERAL (Colistimethate for Injection, U.S.P.) should not exceed 5 mg/kg/day with normal renal function.

Occupational Hazards: 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.

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

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

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. 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.

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.

Other drugs, including curariform muscle relaxants (ether, tubocurarine, succinylcholine, gallamine, decamethonium and sodium citrate), potentiate the neuromuscular blocking effect and should be used with extreme caution in patients being treated with sodium colistimethate.

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

Susceptibility/Resistance: Prescribing COLY-MYCIN* M PARENTERAL 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.

ADVERSE REACTIONS

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 cholistimethate. 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.

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.

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.

OVERDOSE

For management of a suspected drug overdose, please contact your regional Poison Control Centre.
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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.

DOSAGE AND ADMINISTRATION

For IV or IM use: 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.

Vial Composition

Each COLY-MYCIN* M PARENTERAL (Colistimethate for Injection, U.S.P.) vial contains: colistin base activity (as sodium colistimethate) 150 mg as a fluffy, spongy, white to slightly yellow lyophilized cake which forms a clear, aqueous solution when reconstituted with 2.0 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.

Stability and Storage Recommendations

Store COLY-MYCIN* M PARENTERAL (Colistimethate for Injection, USP) at controlled room temperature 15 to 30°C.

After reconstitution, COLY-MYCIN* M PARENTERAL 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.

AVAILABILITY OF DOSAGE FORMS

COLY-MYCIN* M PARENTERAL (Colistimethate for Injection, U.S.P.) vials are available in the dosage strength equivalent to 150 mg of colistin base activity per vial.

PHARMACEUTICAL INFORMATION**Drug Substance**

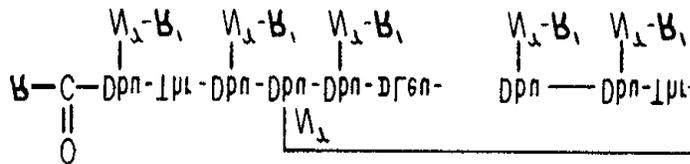
Proper Name: COLY-MYCIN* M PARENTERAL

Chemical Name: Colistimethate Sodium

Empirical Formula: $C_{58}H_{105}N_{16}NaO_{28}S_5$ (colistin A component)
 $C_{57}M_{103}N_{16}Na_5O_{28}S_5$ (colistin B component)

Molecular Weight: Colistin A component 1749.82
 Colistin B component 1735.80

Structural Formula:



CH₃

Dbu is L- α , (γ - diaminobutyric acid; R is CH₃CH₂CH(CH₂)₄ in the colistin A component

and CH₃CH(CH₂)₄ in the colistin B component. R' is CH₂SO₃Na

Patient Medication Information

COLY-MYCIN* M PARENTERAL

Colistimethate for Injection USP

Read this carefully before you start taking COLY-MYCIN* M PARENTERAL. 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 COLY-MYCIN* M PARENTERAL.

What is COLY-MYCIN* M PARENTERAL used for?

COLY-MYCIN* M PARENTERAL 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 COLY-MYCIN* M PARENTERAL treat only bacterial infections. They do not treat viral infections. Although you may feel better early in treatment, COLY-MYCIN* M PARENTERAL should be used exactly as directed. Misuse or overuse of COLY-MYCIN* M PARENTERAL could lead to the growth of bacteria that will not be killed by COLY-MYCIN* M PARENTERAL (resistance). This means that COLY-MYCIN* M PARENTERAL may not work for you in the future.

How does COLY-MYCIN* M PARENTERAL work?

COLY-MYCIN* M PARENTERAL is an antibiotic that kills bacteria in your body by damaging the cell wall of the bacteria.

What are the ingredients in COLY-MYCIN* M PARENTERAL?

Medicinal ingredients: colistin (as colistimethate sodium).

Non-medicinal ingredients: none.

COLY-MYCIN* M PARENTERAL comes in the following dosage forms:

As a sterile powder for solution in a vial containing 150 mg colistin.

Do not use COLY-MYCIN* M PARENTERAL if you:

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

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take COLY-MYCIN* M PARENTERAL. Talk about any health conditions or problems you may have, including if you:

- have kidney problems.

Other warnings you should know about:

COLY-MYCIN* M PARENTERAL may cause dizziness or light-headedness. Do not drive or use machines while you are receiving this medicine.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following medicines may interact with COLY-MYCIN* M PARENTERAL:

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

How to take COLY-MYCIN* M PARENTERAL:

- COLY-MYCIN* M PARENTERAL 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 COLY-MYCIN* M PARENTERAL 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 COLY-MYCIN* M PARENTERAL.

Overdose:

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

If you think you have received too much COLY-MYCIN* M PARENTERAL, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using COLY-MYCIN* M PARENTERAL?

These are not all the possible side effects you may feel when taking COLY-MYCIN* M PARENTERAL. If you experience any side effects not listed here, contact your healthcare professional.

Side effects may include:

- 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			✓
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If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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 (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

Storage:

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

Keep out of reach and sight of children.

If you want more information about COLY-MYCIN* M PARENTERAL:

- 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 website (<http://hc-sc.gc.ca/index-eng.php>); the manufacturer's website (www.eci2012.net), or by calling 1-800-931-3133.

This leaflet was prepared by ERFA Canada 2012 Inc.