PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]pms-VANCOMYCIN

Vancomycin hydrochloride capsules

Capsules, 125 mg and 250 mg, oral

USP

Antibiotic

Pharmascience Inc.
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RECENT MAJOR LABEL CHANGES

N/A	

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

pms-VANCOMYCIN (vancomycin hydrochloride capsules) is indicated for:

- The treatment of infections caused by susceptible strains of the designated microorganisms in the following diseases and specific conditions:
    - staphylococcal enterocolitis, and
    - antibiotic associated pseudomembranous colitis produced by *Clostridium difficile*

Parenteral administration of vancomycin is not effective for the indicated conditions; therefore pms-VANCOMYCIN must be given orally.

pms-VANCOMYCIN is not effective by the oral route for the treatment of other types of infection.

1.1 Pediatrics

Pediatrics (premature neonates and young infants): Evidence from clinical studies and experience suggests that use in premature neonates and young infants are associated with differences in safety and a brief discussion can be found in the 7 WARNINGS AND PRECAUTIONS section.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of pms-VANCOMYCIN and other antibacterial drugs, pms-VANCOMYCIN 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. Because some strains are resistant to vancomycin, when applicable, appropriate specimens should be obtained before antibacterial treatment, to determine the causative organism(s) and susceptibility to vancomycin.

1.2 Geriatrics

Geriatrics (≥ 65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety and a brief discussion can be found in the 7 WARNINGS AND PRECAUTIONS section.

2 CONTRAINDICATIONS

- pms-VANCOMYCIN is contraindicated for patients who are hypersensitive to vancomycin hydrochloride or to any ingredient in the formulation or component of the container. For a complete listing, see the 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING section.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- If parenteral and oral vancomycin are administered concomitantly an additive effect can occur. This should be taken into consideration when calculating the total dose. In this situation serum levels of the antibiotic should be monitored.
- pms-VANCOMYCIN capsules are formulated in a matrix gel that prevents administration by a nasogastric tube; if this route of administration is being considered, the IV dosage form should be used.

4.2 Recommended Dose and Dosage Adjustment

Adults:

The usual daily dosage for antibiotic-associated pseudomembranous colitis produced by *C.difficile* and staphylococcal entercolitis is 125 to 500 mg administered orally every 6 to 8 hours for 7 to 10 days.

Pediatrics:

The usual daily dosage is approximately 40mg/kg in 3 or 4 divided doses for 7 to 10 days administered orally. The total daily dosage should not exceed 2 g.

4.4 Administration

Oral administration.

4.5 Missed Dose

If a dose of this medication has been missed, it should be taken as soon as possible. However, if it is almost time for the next dose, skip the missed dose and resume the regular dosing schedule. Do not double doses.

5 OVERDOSAGE

Activated charcoal may be administered to aid in the removal of unabsorbed drug. General

supportive measures are recommended.

Other than general supportive treatment, no specific antidote is known. Dialysis does not remove significant amounts of vancomycin. Hemofiltration and hemoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance.

In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in the patient.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1: Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Capsule 125 mg, 250 mg (as vancomycin HCl)	Polyethylene glycol 6000. Capsule shell contains titanium dioxide, iron oxide black, iron oxide yellow, iron oxide red, gelatin, and water. The 250 mg capsules also contain sodium lauryl sulfate. The markings on the capsules are in white ink, which contains shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, titanium dioxide, potassium hydroxide, and purified water.

pms-VANCOMYCIN capsules contain vancomycin hydrochloride, equivalent to 125 mg vancomycin and 250 mg vancomycin.

pms-VANCOMYCIN is supplied as hard gelatin capsules for oral administration:

pms-VANCOMYCIN 125 mg is a white to off white congealed liquid mixture as solid mass in size “2” grey cap and pink body.

pms-VANCOMYCIN 250 mg is a white to off white congealed liquid mixture as solid mass in size “0” brown cap and brown body.

pms-VANCOMYCIN 125 mg and 250 mg capsules are available in blister packs of 20 capsules.

7 WARNINGS AND PRECAUTIONS

General

Vancomycin is poorly absorbed orally. Toxic serum levels are therefore not expected from oral dosage. Clinically significant serum concentrations have been reported in some patients who have taken multiple oral doses of vancomycin for active *C. difficile*-induced pseudomembranous colitis; therefore, monitoring of serum concentrations may be appropriate in these patients.

When given intravenously, toxic serum levels can occur. During parenteral therapy, the risk of toxicity appears appreciably increased by high blood concentrations or prolonged treatment.

Driving and Operating Machinery

Ringing in your ears and dizziness have been reported and this may affect your ability to drive and use machines.

Ear/Nose/Throat

Ototoxicity has occurred when serum levels exceeded 80µg/mL. Deafness may be preceded by tinnitus. Deafness may be transient or permanent. The elderly are more susceptible to auditory damage. Deafness may be progressive despite cessation of treatment.

pms-VANCOMYCIN should be avoided (if possible) in patients with previous hearing loss. If it is used in such patients, the dose of pms-VANCOMYCIN should be regulated by periodic determination of drug levels in the blood. Patients with renal insufficiency and individuals over the age of 60 should be given serial tests of auditory function and of vancomycin blood levels.

Gastrointestinal

Some patients with inflammatory disorders of the intestinal mucosa may have significant systemic absorption of oral vancomycin and, therefore, may be at risk for the development of adverse reactions associated with the parenteral administration of vancomycin. The risk is greater if renal impairment is present.

Hematologic

Neutropenia can occur starting one week or more after onset of therapy with pms-VANCOMYCIN or after a total dose of more than 25 g. Neutropenia appears to be promptly reversible when treatment is discontinued.

Monitoring and Laboratory Tests

All patients receiving the drug should have periodic hematologic studies, urinalyses, and liver

and renal function tests.

Renal

Because of its ototoxicity and nephrotoxicity, pms-VANCOMYCIN should be used with care in patients with renal insufficiency. Vancomycin is excreted fairly rapidly by the kidney and blood levels increase markedly with decreased renal clearance. There is an increased risk of renal failure in patients receiving large doses of pms-VANCOMYCIN.

In patients with underlying renal dysfunction or those receiving concomitant therapy with an aminoglycoside there is a risk of developing interstitial nephritis. When these patients are being treated with pms-VANCOMYCIN, serial monitoring of renal function should be performed.

Sensitivity/Resistance

Development of Drug Resistant Bacteria

The prolonged use of pms-VANCOMYCIN may result in overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during therapy with this product, appropriate measures should be taken, including withdrawal of pms-VANCOMYCIN.

In vitro resistance to vancomycin has been reported among some entercoccal and staphylococcal isolates.

Vancomycin is not effective *in vitro* against gram-negative bacilli, mycobacteria, or fungi.

Prescribing pms-VANCOMYCIN 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

pms-VANCOMYCIN should be given to pregnant woman only if clearly needed. In a controlled study, vancomycin hydrochloride capsules were administered to 10 pregnant women for serious staphylococcal infections complicating intravenous drug abuse to evaluate potential ototoxic and nephrotoxic effects on the infant. Vancomycin levels of 13.2 and 16.6µg/mL were measured in core blood in two patients. No sensorineural hearing loss or nephrotoxicity attributable to vancomycin hydrochloride capsules was noted. One infant whose mother received vancomycin hydrochloride capsules in the third trimester experienced conductive hearing loss that was not attributed to the administration of vancomycin hydrochloride capsules. Because the number of patients treated in this study was limited and vancomycin hydrochloride capsules were administered only in the second and third trimesters, it is not

known whether vancomycin hydrochloride capsules cause fetal harm.

7.1.2 Breast-feeding

Vancomycin is excreted in human milk. Caution should be exercised if pms-VANCOMYCIN is administered to a nursing woman. Because of the potential for adverse events, a decision should be made whether to discontinue nursing or discontinue administration of the drug, taking into account the importance of the drug to the mother.

7.1.3 Pediatrics

Pediatrics (premature neonates and young infants)

It may be appropriate to confirm desired vancomycin serum concentrations. Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing in children.

7.1.4 Geriatrics

The natural decrease of glomerular filtration with increasing age may lead to elevated vancomycin serum concentrations if dosage is not adjusted. Vancomycin dosage schedules should be adjusted in elderly patients. It should be noted that the total systemic and renal clearances of vancomycin are reduced in the elderly. The elderly are more susceptible to auditory damage.

8 ADVERSE REACTIONS

8.3 Less Common Clinical Trial Adverse Reactions

Renal:

Nephrotoxicity
Rarely, renal failure, principally manifested by increased serum creatinine or blood urea nitrogen (BUN) concentrations, especially in patients given large doses of vancomycin hydrochloride capsules, has been reported. Rare cases of interstitial nephritis have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had pre-existing kidney dysfunction. When vancomycin hydrochloride capsules were discontinued, azotemia resolved in most patients.

Ear/Nose/Throat:

Ototoxicity
A few dozen cases of hearing loss associated with vancomycin hydrochloride capsules have been reported. Most of these patients had kidney dysfunction, pre-existing hearing loss, or

concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have been reported rarely.

Immune:

Hematopoietic
Reversible neutropenia, usually starting one week or more after onset of therapy with vancomycin hydrochloride capsules or after a total dose of more than 25 g, has been reported in several dozen patients. Neutropenia appears to be promptly reversible when vancomycin hydrochloride capsules are discontinued. Thrombocytopenia has rarely been reported. Although a causal relationship has not been established, reversible agranulocytosis (granulocyte count less than 500/mm^3) has been reported rarely. Eosinophilia has been associated with the administration of vancomycin hydrochloride capsules.

Drug Reaction with Eosinophilia and Systemic Symptoms Syndrome (DRESS)

Toxic Epidermal Necrolysis (TEN)

Miscellaneous:

Anaphylaxis, drug fever, nausea, chills, hypotension, wheezing, dyspnea, urticaria, pruritus flushing of the upper body ("red neck"), pain and muscle spasm of the chest and back, rashes, including exfoliative dermatitis, Stevens-Johnson syndrome, linear IgA bullous dermatosis and rare cases of vasculitis have been associated with the administration of vancomycin hydrochloride capsules.

9 DRUG INTERACTIONS

9.4 Drug-Drug Interactions

Table 2: Established or Potential Drug-Drug Interactions

Proper/Common name	Source of Evidence	Effect	Clinical comment
Anesthetic agents	C	Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing in children.	Caution is warranted.

Antibiotics such as aminoglyuoside antibiotics, polymixin B, colistin, viomycin	T		Caution is warranted and therapeutic concentration monitoring is recommended
Cysplatin	T		Caution is warranted and therapeutic concentration monitoring is recommended
Nephrotoxic agents, particularly ethacrynic acid	T		Caution is warranted and therapeutic concentration monitoring is recommended
Neuromuscular blocking agents	T		Caution is warranted and therapeutic concentration monitoring is recommended
Neurotoxic agents	T		Caution is warranted and therapeutic concentration monitoring is recommended

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

9.5 Drug-Food Interactions

Interactions studies between vancomycin hydrochloride capsules and food have not been conducted.

9.6 Drug-Herb Interactions

Interactions studies between vancomycin hydrochloride capsules and herbs have not been conducted.

9.7 Drug-Laboratory Test Interactions

Interactions studies between vancomycin hydrochloride capsules and laboratory tests have not been conducted.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

In vitro studies indicate that the bactericidal action of vancomycin hydrochloride against many gram- positive bacteria results from the inhibition of cell-wall synthesis. There is also evidence that vancomycin alters the permeability of the cell membrane and selectively inhibits RNA synthesis.

10.3 Pharmacokinetics

Absorption

Oral Administration:

Vancomycin is poorly absorbed after oral administration, only trace amounts being found in blood or urine. Following 125 mg orally 4 times daily, the mean concentration of vancomycin in stools was approximately 350µg/g. Following up to ten daily oral doses of 2 g, a mean level of 3100 µg/g with a range of 905 – 8760 µg/g was detected in feces of patients with pseudomembranous colitis.

Distribution:

Tissue Penetration and Distribution:

Central Nervous System:

Vancomycin does not readily diffuse across normal meninges into the spinal fluid; but when the meninges are inflamed, penetration into the spinal fluid occurs.

Other Tissues and Fluids:

Vancomycin concentration in human pericardial, pleural, bile, ascetic and synovial fluids reaches approximately one third of the equivalent serum level after single intravenous doses. A level of 7.6µg/mL was achieved in the brain cyst of one infant following intravenous infusion of 40 mg/kg daily for 4 days.

Special Populations and Conditions

- **Renal Insufficiency:**

  Adults
  Infusions of 1 g vancomycin in 250mL D5-W were given over 30 minutes to 29 anephric patients. After 18 days with intermittent dialysis at three-day intervals, the serum concentration was still 3.5µg/mL. The elimination half-life was about 7.5 days.

11 STORAGE, STABILITY AND DISPOSAL

Store pms-VANCOMYCIN capsules at room temperature (15° to 25°C). Protect from moisture.

Keep out of sight and reach of children.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

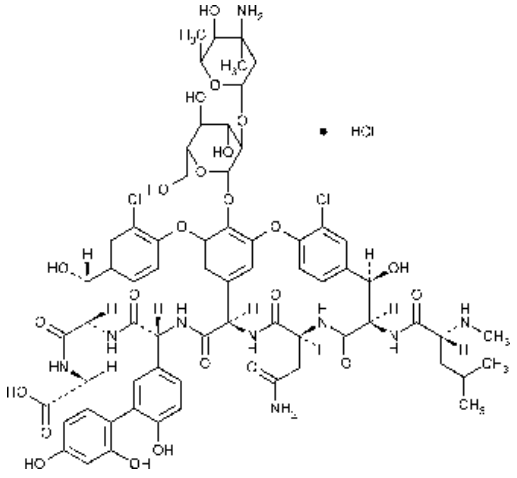
Proper name: Vancomycin hydrochloride

Chemical name: (Sa)-(3S,6R,7R,22R,23S,26S,36R,38aR)-44-[[2-0-(3-Amino-2,3,6-trideoxy-3-C-methyl-α- L-lyxo-hexopyranosyl)-β-D-glucopyrano-syl]oxy]-3-(carbamoylmethyl)-10,19- dichloro-2,3,4,5,6,7,23,24,25,26,36,37,38,38a-tetradecahydro-7,22,28,30,32- pentahydroxy-6-[(2R)-4-methyl-2-(methylamino)valeramido]-2,5,24,38,39- pentaoxo-22H-8,11:18,21-dietheno-23,36-(iminomethano)-13,16:31,35-dimetheno- 1H,16H-[1,6,9]oxadiazacyclohexadecino[4,5-m][10,2,16]-benzoxadiazacyclo-tetracosine-26,carboxylic acid, monohydrochloride

Molecular formula : $C_{66}H_{75}Cl_2N_9O_{24} \cdot HCl$

Molecular mass: 1485.68 g/mol

Structural formula:



Physicochemical properties: Vancomycin hydrochloride is a chromatographically purified tricyclic glycopeptide antibiotic derived from Amycolatopsis orientalis (formerly Nocardia orientalis). It is an off-white free flowing powder, having essentially no odour. It is soluble in water and insoluble in organic solvents.

15 MICROBIOLOGY

Cross-resistance has not been demonstrated between vancomycin hydrochloride capsules and other classes of antibiotics. Laboratory-induced resistance has been reported to occur in a slow stepwise fashion. Its activity is not significantly altered by changes in pH or by the presence of serum.

Vancomycin is active against most strains of the following organisms *in vitro* and in clinical infections as described in the section 1 INDICATIONS:

- *Staphylococcus aureus* (including heterogeneous methicillin-resistant strains)
- *Clostridium difficile*

Vancomycin is active against most strains of the following organisms *in vitro*. However, the safety and effectiveness of vancomycin hydrochloride capsules in treating clinical infections due to these organisms have not been established in adequate and well-controlled trials.

- *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains)
- *Streptococcus pneumoniae* (including multiple-resistant strains)
- *Streptococcus pyogenes* (group A beta-hemolytic)
- *Streptococcus agalactiae* (group B beta-hemolytic)
- *Streptococcus bovis*
- Alpha-hemolytic *streptococci* (*viridans* groups)
- *Enterococci (e.g. E. faecalis)*
- *Bacillus sp.*
- *Listeria monocytogenes*
- *Lactobacillus sp.*
- *Neisseria sp.*
- Diptheroids
- *Actinomyces sp.*

Note:

Many strains of *streptococci, staphylococci, C. difficile,* and other gram-positive bacteria are susceptible *in vitro* to concentrations of 0.5 to 5 µg/mL. *Staphylococci* are generally susceptible to less than 5 µg/mL of vancomycin hydrochloride, but a small proportion of *S. Aureus* strains require 10 to 20 µg/mL for inhibition.

In vitro resistance to vancomycin has been reported among some enterococcal and staphylococcal isolates.

Vancomycin is not effective *in vitro* against gram-negative bacilli, mycobacteria, or fungi.

Table 3: *In Vitro* Activity of Vancomycin

Organism	No. of Strains	MIC* (µg/mL) Range	Median
Staphylococcus aureus	55	1.0 – 2.0	1.0
	101	0.78 – 12.5	3.1
	35	0.25 – 1.0	1.0
Staphylococcus aureus	22	0.5 – 4.0	0.5
(methicillin-resistant)	38	0.3 – 12.0	1.5
	12	0.2 – 3.12	0.4
Streptococcus epidermidis	177	1.56 – 6.25	3.1
	35	0.4 – 3.1	1.6
	27	0.2 – 6.25	3.12
Streptococcus pneumonia	70	0.125 – 0.5	0.25
Streptococcus pyogenes	12	0.8 – 3.1	1.6
Streptococcus viridans	82	0.39 – 1.56	0.78
Streptococcus group D *enterococci*	382	0.8 - >100.0	3.1
Clostridium perfringens	43	0.4 – 1.6	0.8
Clostridium ramosum	49	3.1 – 12.5	6.2
Clostridium difficile	14	<1.0	<1.0
	78	1.0 – 4.0	

*Minimum Inhibitory Concentration (MIC)

Methods of Susceptibility Testing:

When the standardized method of disc susceptibility testing is used, a 30µg disc of vancomycin should produce a zone of more than 11 mm when in contact with "susceptible" organisms. A zone size of 10 – 11 mm indicates intermediate susceptibility, while a zone size of 9 mm or less indicates resistance.

With the WHO-ICS agar dilution and broth dilution methods, and MIC of <5 µg/mL indicates susceptibility to vancomycin.

Assay Methods:

Vancomycin serum and tissue levels may be determined by Bennett's agar-well diffusion method. This test can quantitatively measure vancomycin concentrations from 0.5 to

0.8 µg/mL.

Two disc-diffusion assay methods are available for vancomycin. Both use *Bacillus subtilis* as the test organism. The first method, which uses antibiotic medium No. 5, is capable of measuring vancomycin levels from approximately 5 to 40 µg/mL. The second uses minimal salt agar and is capable of detecting vancomycin concentrations from about 0.8 to 25 µg/mL. A modification of this assay permits reliable bioassay for vancomycin (in concentrations of 0.78 to 50.0 µg/mL) in the presence of rifampin or aminoglycosides. Two commercially prepared assay methods are now available and include a radioimmunoassay and an automated fluorescence polarization immunoassay.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

Acute Toxicity:

Vancomycin was administered to mice, rats and dogs by various routes.

Table 4: LD_{50} ± SE (mg/kg) Following Vancomycin Administration

Route of Administration	Rat	Mouse	Dog
Intravenous	319 ± 14	489 ± 41	292 ± 29
Intraperitoneal	2218 ± 240	1734 ± 227	
Subcutaneous		> 5000	
Oral		> 5000	

Rats died quickly from CNS-mediated effects, while dogs died, generally from kidney failure, several days after the intravenous administration.

Vancomycin, when administered intravenously in a 5 percent solution to dogs at a rate of 0.6 mL/minute, caused a slight dose-related drop in blood pressure. When the same dogs were given the same doses at a rate of 15 mL/minute, blood pressure dropped dramatically, as much as 40 percent. Whether the response is due to a direct effect on histamine receptors or to release of histamine, possibly from mast cells, is not known.

Subchronic Toxicity:

Dogs were given daily I.V. doses of vancomycin at 12.5 mg and 50 mg/kg for 21 – 311 days. Renal damage was seen in 4/22 dogs receiving 50 mg/kg/day.

Monkeys tolerated I.V. doses of 25 and 50 mg/kg/day for 16 – 187 days, with irritation at the injection site as the only toxic effect.

Cats received I.V. doses of 25 and 50 mg/kg/day for three months with no systemic toxicity. Anaphylaxis could not be induced in 9 guinea pigs that received 100 mg vancomycin subcutaneously when challenged by a 25 mg I.V. dose, 25 days later.

Intraperitoneal doses of 150 mg vancomycin or 60 mg tobramycin given subcutaneously to rats, resulted in no nephrotoxicity; however, when administered together, significant renal toxicity occurred.

Vancomycin 1000 mg/kg administered subcutaneously concurrently with ethacrynic acid 40 mg/kg intravenously did not product ototoxicity in a guinea pig model.

Neuromuscular blocking has not been demonstrated in vancomycin-treated rabbits.

17 SUPPORTING PRODUCT MONOGRAPHS

1. VANCOCIN® Vancomycin hydrochloride capsules, 125 mg and 250 mg, submission control 278879, Product Monograph, Searchlight Pharma Inc. FEB 14, 2024

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] pms-VANCOMYCIN

Vancomycin hydrochloride capsules

Read this carefully before you start taking **pms-VANCOMYCIN** 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 **pms-VANCOMYCIN.**

What is pms-VANCOMYCIN used for?

pms-VANCOMYCIN is an antibiotic. It is used to treat bacterial infections of the intestine such as pseudomembranous colitis or colitis. Colitis is the swelling or inflammation of the large intestine (colon) that can happen because of an overgrowth of a type of bacteria called *Clostridium difficile* (*C difficile*). This infection is a common cause of diarrhea after antibiotic use.

Antibacterial drugs like pms-VANCOMYCIN treat **only** bacterial infections. They do not treat viral infections such as the common cold. Although you may feel better early in treatment, pms-VANCOMYCIN should be used exactly as directed. Misuse or overuse of pms-VANCOMYCIN could lead to the growth of bacteria that will not be killed by pms-VANCOMYCIN (resistance). This means that pms-VANCOMYCIN may not work for you in the future. Do not share your medicine.

How does pms-VANCOMYCIN work?

Vancomycin is in a class of medications called glycopeptide antibiotics. It works by killing certain bacteria in the intestines.

What are the ingredients in pms-VANCOMYCIN?

Medicinal ingredients: Vancomycin hydrochloride.

Non-medicinal ingredients: Polyethylene glycol 6000.
Capsule shell contains titanium dioxide, iron oxide black, iron oxide yellow, iron oxide red, gelatin, and water. The 250 mg capsules also contain sodium lauryl sulfate.
The markings on the capsules are in white ink, which contains shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, titanium dioxide, potassium hydroxide, and purified water.

pms-VANCOMYCIN comes in the following dosage forms:

Capsules, 125mg or 250mg

Do not use pms-VANCOMYCIN if:

- you are allergic to vancomycin hydrochloride
- you are allergic to any ingredient in the formulation or component of the container (please see "What are the ingredients in pms-VANCOMYCIN?" section above).

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

- You have hearing problems
- You have had previous hearing loss
- You have kidney problems
- You have or have ever had:
    - inflammatory bowel disease (swelling of the intestine that can cause painful cramps or diarrhea)
    - Crohn's disease (a condition in which the body attacks the lining of the digestive tract, causing pain, diarrhea, weight loss, and fever)
    - ulcerative colitis (a condition which causes swelling and sores in the lining of the colon [large intestine] and rectum)
      pms-VANCOMYCIN capsules work mainly in the intestines and does not get into the blood. If you have problems in the intestines some medicine may get into the blood and you may have some side effects.
- You are pregnant or planning to become pregnant
- You are nursing or planning to nurse (Vancomycin is excreted in breast milk)

Other warnings you should know about:

While you are using pms-VANCOMYCIN

- Your healthcare professional may require that you do regular liver, kidney, blood or urine tests.
- If you are 65 or older, you could have more side effects. The risk of hearing or kidneys problems may be greater in older adults. See "Serious side effects and what to do about them" table for signs of hearing or kidneys problems.
- **Driving and using machines:** You may have ringing in your ears and dizziness. These may affect your ability to drive and use machines.

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 pms-VANCOMYCIN:

- Ethacrynic acid, a diuretic ("water pills")
- Medications that affect your kidney or your nervous systems
- Medications given during surgery to relax the muscles (neuromuscular blocking agents)
- Other antibiotics such as:
    - Aminoglycoside antibiotics such as amikacin, gentamicin, kanamycin, paromomycin, tobramycin etc.
    - Polymixin B
    - Colistin
    - Viomycin (not marketed in Canada)
- Cisplatin, a medicine used to treat cancer

How to take pms-VANCOMYCIN:

- Take pms-VANCOMYCIN capsules by mouth.

Usual dose:

- **Adults:** 125mg to 500mg 3 to 4 times a day for 7 to 10 days.

- **Children who can swallow:** The dose required will depend on the child's weight: 40mg/kg body weight daily in 3 or 4 doses for 7 to 10 days. The maximum daily dose is 2g.

Your healthcare professional will tell you exactly how much pms-VANCOMYCIN you or your child need to take and how often it must be taken each day. Ask your healthcare professional if you have any questions about pms-VANCOMYCIN dosing instructions.

Overdose:

If you think you, or a person you are caring for, have taken too much pms-VANCOMYCIN, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose of pms-VANCOMYCIN, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and continue with your next scheduled dose. Do not take two doses at the same time.

What are possible side effects from using pms-VANCOMYCIN?

These are not all the possible side effects you may have when taking pms-VANCOMYCIN. If you

experience any side effects not listed here, tell your healthcare professional.

pms-VANCOMYCIN may cause the following side effects:

- Drug fever
- Nausea
- Chills
- Itching, hives, skin rash
- Hypotension (low blood pressure): dizziness, fainting, light headedness

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**	
COMMON			
Allergic reactions: • severe rash, hives, itching • swelling of face, lips, mouth, throat or tongue • wheezing • tightness in the chest or throat • difficulty breathing or talking			✓
Redness of the skin above your waist (“red neck”)			✓
RARE			

Blood problems such as:
• Loss of blood cells that help the blood clot (platelets):
  ○ unusual bleeding or bruising,
  ○ Nosebleeds
  ○ Pinpoint red spots on the skin
• Low white blood cells (neutropenia):
  ○ more likely to develop infections, sore throat, fever, chills, and other signs of infection.
• Increased numbers of certain white blood cells (eosinophilia):
  ○ rash, weight loss, wheezing, abdominal pain.
			✓

Kidney problems: • Swelling in the arms or legs, • fatigue • loss of appetite • nausea and vomiting			✓

• thirst • unable to pass urine • change in the amount of urine you pass			
Hearing problems: • dizziness, problems with balance • vertigo (spinning sensation) • ringing in the ears (is a potential warning sign of hearing loss) • change in hearing • temporary or permanent hearing loss			✓
Pain and muscle tightness of the chest and back			✓
Serious life-threatening skin reactions (Stevens-Johnson syndrome, Toxic Epidermal Necrolysis, Drug Reaction/Rash with Eosinophilia and Systemic Symptoms (DRESS)): • unexplained widespread skin pain • flu-like symptoms (fever, sore mouth and throat, cough, fatigue, burning eyes etc.) • followed by a painful red or purplish rash that spreads and blisters on mouth, nose, eyes and genitals • shedding of your skin within days after blisters form • swelling of the face or swollen glands in the neck, armpits or groin • yellowing of your skin or eye • dark urine, light-colored bowel movements; • severe nausea or vomiting; stomach pain			✓

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 (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) 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 pms-VANCOMYCIN capsules at room temperature, 15˚ to 25˚C. Protect from moisture. Do not use beyond the expiration date.

Keep out of reach and sight of children.

If you want more information about pms-VANCOMYCIN:

- 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: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html, the manufacturer's website www.pharmascience.com; or by calling 1-888-550-6060.

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