PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

Pr VANCOMYCIN HYDROCHLORIDE FOR INJECTION USP

500 mg/vial, 1 g/vial, 5 g/vial and 10 g/vial Vancomycin

Sterile lyophilized powder for solution

Antibiotic

SteriMax Inc.
2770 Portland Drive
Oakville, Ontario
L6H 6R4

DATE OF REVISION:
November 05, 2018

Control No.: 220151

PRODUCT MONOGRAPH

[Pr] VANCOMYCIN HYDROCHLORIDE FOR INJECTION USP

500 mg/vial, 1 g/vial, 5 g/vial and 10 g/vial Vancomycin

Sterile lyophilized powder for solution

THERAPEUTIC CLASSIFICATION

Antibiotic

ACTIONS AND CLINICAL PHARMACOLOGY

The bactericidal action of vancomycin against most gram-positive bacteria results from the inhibition of the biosynthesis of peptidoglycan polymers during the second stage of cell wall synthesis in dividing organisms. This effect occurs at a site different from that of penicillins and cephalosporins. The cytoplasmic membrane composition may also be affected and membrane permeability altered. There is also evidence that vancomycin selectively inhibits RNA synthesis.

Vancomycin is a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis* (formerly *Nocardia orientalis*). It is primarily active against gram-positive organisms including staphylococci and streptococci. It is active against methicillin-resistant strains of *Staphylococcus aureus* and *Staphylococcus epidermidis.*

Vancomycin is poorly absorbed from the gastrointestinal tract. It is given intravenously for therapy of systemic infections.

Following intravenous administration, vancomycin is widely distributed and inhibitory concentrations of vancomycin can be documented in the pericardial, pleural, ascitic, and synovial fluids. Low concentrations of the drug may appear in CSF if meninges are inflamed. The volume of distribution for vancomycin ranges from 0.43 to 1.25 L/kg. At a concentration of 10 to 100 µg/mL *in vitro*, vancomycin is reportedly 52 to 60% bound to serum proteins.

Pharmacokinetics

In subjects with normal kidney function, multiple intravenous dosing of 1 g of vancomycin (15 mg/kg), infused over 60 minutes, produces mean plasma concentrations of approximately 63 mg/L immediately at the completion of infusion, mean plasma concentrations of approximately 23 mg/L 2 hours after infusion, and mean plasma concentrations of approximately 8 mg/L 11 hours after the end of the infusion. Multiple dosing of 500 mg, infused over 30 minutes, produces mean plasma concentrations of about 49 mg/L at the completion of infusion, mean

plasma concentrations of about 19 mg/L 2 hours after infusion, and mean plasma concentrations of about 10 mg/L 6 hours after infusion. Plasma concentrations are slightly higher than those following a single dose, as accumulation tends to occur after 2 to 3 days of intravenous administration at 6- or 12-hour intervals. The serum elimination half-life of vancomycin in adults with normal renal function has been reported to average 4 to 6 hours.

Vancomycin is excreted by the kidneys primarily by glomerular filtration; approximately 80 to 90% of the dose is excreted in the urine within 24 hours. Impairment of renal function results in delayed excretion and in high blood levels associated with an increase in drug toxicity. The total systemic and renal clearance may be reduced in the elderly.

INDICATIONS AND CLINICAL USE

Vancomycin Hydrochloride for Injection USP, administered intravenously, is indicated for the treatment of severe or life-threatening staphylococcal infections in patients who cannot receive or have failed to respond to the penicillins or cephalosporins or who have infections with staphylococci resistant to other antibiotics, including methicillin.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin Hydrochloride for Injection USP and other antibacterial drugs, Vancomycin Hydrochloride 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.

Vancomycin has been used effectively alone in the treatment of staphylococcal endocarditis. Vancomycin has been reported to be effective alone or in combination with an aminoglycoside for treatment of endocarditis, caused by *S. viridans* or *S. bovis*. For endocarditis caused by enterococci (*S. faecalis*), vancomycin has been reported to be effective only in combination with an aminoglycoside.

Vancomycin has been reported to be effective for the treatment of diphtheroid endocarditis. It has been used successfully in combination with either rifampin, an aminoglycoside, or both, in early-onset prosthetic valve endocarditis caused by *S. epidermidis* or diphtheroids.

The effectiveness of vancomycin has been documented in other infections due to staphylococci including osteomyelitis, pneumonia, septicemia and soft- tissue infections. When staphylococcal infections are localized and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

Specimens for bacteriologic cultures should be obtained in order to isolate and identify causative organisms and to determine their susceptibilities to vancomycin.

Although no controlled clinical efficacy studies have been conducted, intravenous vancomycin has been suggested by the American Heart Association and the American Dental Association for prophylaxis against bacterial endocarditis, in patients who are at risk, in the following situations:

a) In Dental, Oral or Upper Respiratory Tract Procedures
   As an alternate prophylactic regime in ampicillin/amoxicillin/penicillin-allergic patients considered high risk.

b) In Genitourinary and Gastrointestinal Procedures
   In combination with gentamicin in ampicillin/amoxicillin/penicillin-allergic patients.

When selecting antibiotics for the prevention of bacterial endocarditis, the physician or dentist should read the full joint statement of the American Heart Association and the American Dental Association (JAMA 1990;264:2919-2922).

The parenteral form of vancomycin may be administered orally for the treatment of staphylococcal enterocolitis and antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. **Parenteral administration of vancomycin is not effective for these indications. Vancomycin has not been shown to be effective by the oral route for the treatment of other types of infections. Vancomycin is not effective *in vitro* against gram-negative bacilli, mycobacteria, or fungi.**

CONTRAINDICATIONS

Vancomycin Hydrochloride for Injection USP is contraindicated in patients with known hypersensitivity to vancomycin hydrochloride.

WARNINGS

Rapid bolus administration (e.g. over several minutes) of vancomycin may result in an exaggerated hypotension including shock and, rarely, cardiac arrest.

Vancomycin Hydrochloride for Injection USP should be administered in a dilute solution over a period of not less than 60 minutes to avoid rapid infusion-related reactions. Stopping the infusion usually results in a prompt cessation of these reactions (see **PRECAUTIONS** and **DOSAGE AND ADMINISTRATION).**

The dosage of Vancomycin Hydrochloride for Injection USP must be adjusted for patients with kidney dysfunction (see **PRECAUTIONS** and **DOSAGE AND ADMINISTRATION).**

Toxic serum levels can occur when vancomycin is given intravenously. Vancomycin is excreted by the kidney and blood levels increase markedly with decreased renal clearance. The risk of

ototoxicity and nephrotoxicity appears appreciably increased during parenteral therapy by high blood concentrations or prolonged treatment in patients who have kidney dysfunction or underlying hearing loss or who are receiving concurrent therapy with another ototoxic agent such as an aminoglycoside. Vancomycin is poorly absorbed orally and toxic serum levels have not been reported from oral dosage.

Ototoxicity has occurred in patients receiving vancomycin. Reports of ototoxicity have been associated with serum vancomycin levels ranging from 40 to 80 μg/mL. Deafness may be preceded by tinnitus. Ototoxicity may be transient or permanent. The elderly are more susceptible to auditory damage. Experience with other antibiotics suggests that deafness may be progressive despite cessation of treatment.

Careful monitoring is required with concurrent and sequential use of other neurotoxic and/or nephrotoxic agents, particularly aminoglycoside antibiotics, loop diuretics, neuromuscular blocking agents, cephaloridine, polymyxin B, colistin, viomycin, paromomycin, bacitracin, amphotericin B and cisplatin.

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 these situations, careful monitoring of serum levels is recommended.

Susceptibility/Resistance

Development of Drug Resistant Bacteria

Vancomycin Hydrochloride 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.

PRECAUTIONS

Vancomycin Hydrochloride for Injection USP should be administered in a dilute solution over a period of not less than 60 minutes to avoid rapid infusion-related reactions. To minimize the risk of a hypotensive reaction, the patient's blood pressure should be monitored during the infusion. Stopping the infusion usually results in a prompt cessation of these reactions (see **DOSAGE AND ADMINISTRATION** and **ADVERSE REACTIONS**).

Vancomycin should be used with care in patients with renal insufficiency because of its ototoxicity and nephrotoxicity. The dose and/or dose intervals should be adjusted carefully. Vancomycin blood levels should be monitored and serial tests of renal and auditory functions administered if it is necessary to use vancomycin parenterally in patients with renal impairment and in individuals over the age of 60 (see **DOSAGE AND ADMINISTRATION**).

In patients with previous hearing loss, use of vancomycin should be avoided (if possible). If therapy is deemed essential, the dose of vancomycin should be monitored by periodic testing of auditory function and determination of drug levels in the blood.

Audiometric and renal function testing should be monitored in patients using other concurrent or sequential systemic or topical nephrotoxic or ototoxic drugs.

All patients receiving vancomycin should have periodic hematologic studies, urinalyses, liver and renal function tests.

Overgrowth of non-susceptible organisms may result with the use of vancomycin. If new infections due to bacteria or fungi appear during therapy with this product, appropriate measures should be taken, including withdrawal of vancomycin. In rare instances, there have been reports of antibiotic-associated pseudomembranous colitis due to *Clostridium difficile* developing in patients receiving anti-infective agents including intravenous vancomycin.

Reversible neutropenia has been reported in patients receiving vancomycin (see **ADVERSE REACTIONS**). Periodic monitoring of the leukocyte count should be performed in patients who will undergo prolonged therapy with vancomycin or those who are receiving concomitant drugs which may cause neutropenia.

VANCOMYCIN SHOULD NEVER BE GIVEN INTRAMUSCULARLY. Vancomycin is irritating to tissue and must be given by a secure intravenous route of administration. Pain, tenderness and necrosis occur with intramuscular injection of vancomycin or with inadvertent extravasation.

Pain and thrombophlebitis may occur in patients receiving vancomycin intravenously and can be severe. The frequency and severity of these infusion-related events can be minimized by administering the drug slowly as a dilute solution (2.5 to 5 mg/mL) and by rotating the sites of infusion.

There have been reports that the frequency of infusion-related events (including hypotension, flushing, erythema, urticaria and pruritis) increases with the concomitant administration of anesthetic agents. Infusion- related events may be minimized by the administration of vancomycin as a 60-minute infusion prior to anesthetic induction.

The safety and efficacy of administering Vancomycin Hydrochloride for Injection USP by the intrathecal (intralumbar and intraventricular) routes have not been evaluated.

Vancomycin is not indicated for intraperitoneal administration as safety and efficacy have not been determined.

Some patients with inflammatory disorders of the intestinal mucosa may have significant systemic absorption of oral vancomycin and may thus be at risk of developing adverse reactions

associated with parenteral administration of vancomycin. This risk is greater in the presence of renal impairment. Total systemic and renal clearance of vancomycin are reduced in the elderly.

Use in the Elderly

Since geriatric patients usually excrete vancomycin more slowly, they are at greater risk of vancomycin-induced ototoxicity and nephrotoxicity. Dosage adjustments are required to avoid excessive vancomycin serum concentrations (see **DOSAGE AND ADMINISTRATION**).

Use in Children

In prematures, neonates and young infants, close monitoring of serum vancomycin concentrations may be warranted, as the renal immaturity of these patients may lead to increased serum concentrations of the drug. Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing in children. These adverse reactions may be minimized by administering vancomycin over at least one hour prior to induction of anesthesia (see **DOSAGE AND ADMINISTRATION** and **ADVERSE REACTIONS).**

Use in Pregnancy

Safe use of Vancomycin Hydrochloride for Injection USP during pregnancy has not as yet been established. Vancomycin should be used during pregnancy only when clearly needed. In a controlled clinical study, vancomycin was administered to 10 pregnant women for serious staphylococcus infections complicating intravenous drug abuse. Vancomycin levels of 13.2 and 16.7 μg/mL were measured in cord blood of two patients. No sensorineural hearing loss or nephrotoxicity attributable to vancomycin was noted. Because the number of patients treated in this study was small and vancomycin administered only in the second and third trimester, it is not known whether vancomycin causes fetal harm.

Use in Nursing Mothers

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

Burn Patients

Burn patients reportedly have higher total body clearance rates for vancomycin and may thus require more frequent and higher doses. When vancomycin is used in these patients, dosage individualisation and close monitoring are recommended.

ADVERSE REACTIONS

Infusion-Related Events

Rapid administration of Vancomycin Hydrochloride for Injection USP may be associated with anaphylactoid reactions including hypotension, wheezing, dyspnea, and pruritus. Additionally, flushing of the skin over the neck and shoulder area ("red neck") with transitory fine rash including urticaria and a throbbing type of pain in the muscles of the back and neck has been reported during rapid administration. These reactions usually resolve within 20 to 30 minutes but may persist for several hours. Infusion-related events may be minimized or avoided by slower administration (see **DOSAGE AND ADMINISTRATION**).

Nephrotoxicity

Renal failure has been reported in patients treated with vancomycin, principally manifested by increased serum creatinine or BUN, particularly in patients given large doses. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had pre-existing kidney dysfunction. When vancomycin was discontinued, azotemia resolved in most patients. Rare cases of interstitial nephritis have been reported in patients treated with vancomycin.

Ototoxicity

There have been reports of hearing loss in patients receiving vancomycin. Most of these patients also had kidney dysfunction, pre-existing hearing loss, or concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have been reported rarely.

Hematopoietic

Reversible neutropenia, usually starting one week or more after onset of therapy with vancomycin or after a total dose of more than 25 g, has been reported. Neutropenia appeared to be, in several patients, promptly reversible when vancomycin was discontinued. Thrombocytopenia has rarely been reported. Reversible agranulocytosis (granulocyte count less than 5 000/mm^3) has been reported rarely.

Phlebitis

Inflammation at the injection site and thrombophlebitis have been reported.

Miscellaneous

Anaphylaxis, nausea, chills, drug fever, urticaria, eosinophilia, and rashes including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and rare cases of vasculitis, have been associated with the administration of vancomycin.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Supportive treatment is advised with maintenance of glomerular filtration. Plasma concentrations of vancomycin are reported to be minimally affected by conventional hemodialysis. Increased vancomycin clearance has been reported with highly permeable membranes used in high-flux hemodialysis. At 4-6 hours following the onset of high-flux hemodialysis, steady state concentrations of vancomycin may be reduced by 10-15% of the pre-dialysis concentrations. Peritoneal dialysis, although it may decrease concentrations, does not remove significant amounts.

Hemofiltration and hemoperfusion with polysulfone resin has been reported to result in increased clearance of vancomycin.

DOSAGE AND ADMINISTRATION

DOSAGE

Solutions of Vancomycin Hydrochloride for Injection USP reconstituted with Sterile Water for Injection contain no bacteriostat and are intended for single-use. When smaller doses are required, the unused portion should be discarded. Further dilution is required before use (see **PHARMACEUTICAL INFORMATION – Reconstitution**).

EACH DOSE SHOULD BE ADMINISTERED AT A RATE OF NO MORE THAN 10 mg/min OR OVER A PERIOD OF AT LEAST 60 MINUTES.

Within 48 to 72 hours, most patients with infections susceptible to vancomycin show a therapeutic response. The type and severity of the infection and the clinical response of the patient determine the duration of therapy.

Intravenous Dosage

Adults with Normal Renal Function

The usual daily intravenous dose is 2 g divided either as 500 mg every 6 hours or 1 g every 12 hours. Each dose should be administered over a period of at least 60 minutes. Other patient factors, such as age or obesity, may call for modification of the usual daily dose.

Adults with Impaired Renal Function

Dosage adjustment must be made in patients with impaired renal function to avoid toxic serum levels. Since accumulation in such patients has been reported to occur over several weeks of treatment, serum levels should be checked regularly. Because of decreasing renal function in the elderly, dosage reduction may be necessary.

Measurement of vancomycin serum concentrations can be helpful in optimizing therapy, especially in seriously ill patients with changing renal function.

For most patients with renal impairment or the elderly, the dosage can be calculated by using the following table if creatinine clearance is known. The dosage of Vancomycin Hydrochloride for Injection USP per day in mg is about 15 times the glomerular filtration rate in mL/min (see Table 1).

Table 1
Dosage for Vancomycin in Patients with Impaired Renal Function[+]
(adapted from [*]Moellering, RC, *et al.,* 1981)

Creatinine Clearance (mL/min)	Vancomycin Dose (mg/24 hrs)
100	1545
90	1390
80	1235
70	1080
60	925
50	770
40	620
30	465
20	310
10	155

[+] The initial dose should be no less than 15 mg/kg even in patients with mild to moderate renal insufficiency.
[*] Moellering RC, *et al*.: Vancomycin therapy in patients with impaired renal function: A monogram for dosage. Ann Int Med 1981;94:343.

The table is not valid for functionally anephric patients on dialysis. For such patients, an initial dose of 15 mg/kg body weight should be given in order to achieve prompt therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 hr. Since individual maintenance doses of 250 to 1000 mg are convenient, one dose may be given every several days rather than on a daily basis in patients with marked renal impairment.

When only the serum creatinine concentration is known, the following formula (based on sex, weight, and age of the patient) may be used to estimate creatinine clearance. Calculated creatinine clearances (mL/min) are only estimates.

Men:	$\frac{\text{Weight (kg)} \times (140 - \text{age in years})}{72 \times \text{serum creatinine concentration (mg/dL)}}$
Women:	0.85 x above value

The serum creatinine must represent a steady state of renal function; otherwise, the estimated value for clearance is not valid. Such a calculated clearance is an overestimate of actual clearance in patients with conditions:

1) characterized by decreasing renal function, such as shock, severe heart failure, or oliguria;

2) in which a normal relationship between muscle mass and total body weight is not present, such as in obese patients or those with liver disease, edema, or ascites; and

3) accompanied by debilitation, malnutrition, or inactivity.

Pediatric Use

The following dosage schedule has been used. Infusion should be over a period of at least 60 minutes and can be incorporated into the child's 24-hour fluid requirements.

Neonates

In neonates, an initial dose of 15 mg/kg is suggested, followed by 10 mg/kg every 12 hours for neonates in the first week of life, and every 8 hours thereafter up to the age of one month. Close monitoring of serum concentrations of vancomycin may be warranted in these patients.

Infants and Children

The usual intravenous dosage of vancomycin is 10 mg/kg/dose given every 6 hours. The majority of patients with infections caused by organisms susceptible to the antibiotic show a therapeutic response by 48 to 72 hours. The total duration of therapy is determined by the type and severity of infection and clinical response of the patient.

Oral Dosage

Adults

The usual daily dose for antibiotic-associated pseudomembranous colitis caused by *C. difficile* and/or staphylococcal enterocolitis is 125 to 500 mg orally every 6 to 8 hours for 7 to 10 days.

Children

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

ADMINISTRATION

Intermittent infusion is the recommended method of administration.

Intermittent Intravenous Infusion

The reconstituted solution must be further diluted with 0.9% Sodium Chloride or 5% Dextrose in Sterile Distilled Water for Injection (D5-W). This should be infused over a period of at least 60 minutes (see **PHARMACEUTICAL INFORMATION – Reconstitution).**

Continuous Intravenous Infusion

Continuous intravenous infusion should be used only when intermittent infusion is not practical.
Note: Infusion-related events are related to both concentration and rate of administration of vancomycin. Concentration of no more than 5 mg/mL and rates of no more than 10 mg/min are recommended in adults (see age-specific recommendations). In selected patients in need of fluid restriction, a concentration up to 10 mg/mL may be used; use of such higher concentrations may increase risk of infusion-related events. Infusion-related events may occur, however, at any rate or concentration.

Oral Administration

The contents of the intravenous vial (500 mg) may be diluted in 30 mL of water and given to the patient to drink, or the diluted material may be administered via nasogastric tube.

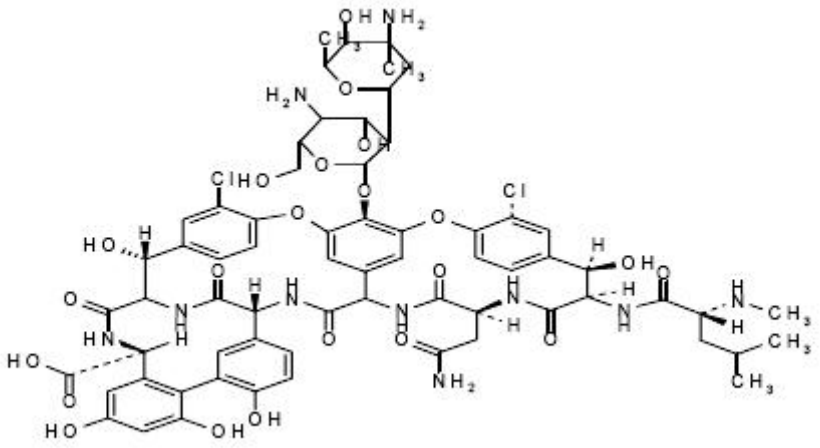
PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name: Vancomycin hydrochloride

Chemical Name: (S_a)–(3S,6R,7R,22R,23S,26S,36R,38aR)-44-[[2-O-(3-amino-2,3,6-trideoxy-3-C-methyl-α-L-lyxo-hexopyranosyl)-β-D-glucopyranosyl]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-[(2*R*)-4-methyl-2-(methylamino)valeramido]-2,5,24,38,39-pentaoxo-22*H*-8,11:18,21-dietheno-23,36-(iminomethano)-13,16:31,35-dimetheno-1*H*,16*H*-[1,6,9]oxadiazacyclohexadecino[4,5-*m*]-[10,2,16]benzoxadiazacyclotetracosine-26-carboxylic acid,monohydrochloride.

Structural Formula:



.HCl

Molecular Formula: $C_{66}H_{75}Cl_2N_9O_{24}.HCl$

Molecular Weight: 1485.73

Description: Vancomycin hydrochloride is a tricyclic glycopeptide antibiotic. It is an off-white, free-flowing powder, very soluble in water at pH 4, moderately soluble in aqueous methanol, but insoluble in higher alcohols, acetone or ether. The melting point is 105°C.

Composition

Sterile vials contain vancomycin hydrochloride equivalent to either 500 mg, 1 g, 5 g or 10 g of vancomycin base as a lyophilized drug. When reconstituted in Sterile Water for Injection USP, it forms a clear solution with a pH of 4.0 (2.5 to 4.5). May contain hydrochloric acid and/or sodium hydroxide for pH adjustment.

Reconstitution

Flip-Top Vial

Solution for Reconstitution: Sterile Water for Injection USP
Reconstitute as follows (see Table 2):

Table 2
Reconstitution

Flip-Top Vial Sizes	Volume to be Added to Vial	Approx. Available Volume	Vancomycin Concentration
500 mg	10 mL	10.3 mL	50 mg/mL
1 g	20 mL	20.6 mL	50 mg/mL
5 g	100 mL	103.0 mL	50 mg/mL
10 g	95 mL	97.85 mL	100 mg/mL

Note: FURTHER DILUTION IS REQUIRED

For Intermittent Intravenous Infusion

500 mg vial: Reconstituted solutions must be diluted with at least 100 mL of 0.9% Sodium Chloride Injection or 5% Dextrose in Sterile Water for Injection.

1 g vial: Reconstituted solutions must be diluted with at least 200 mL of 0.9% Sodium Chloride Injection or 5% Dextrose in Sterile Water for Injection.

5 g vial: **Further dilution of the reconstituted solution is required.** The 5 g vial is a Pharmacy Bulk Package intended for pharmacy use only.

10 g vial: **Further dilution of the reconstituted solution is required.** The 10 g vial is a Pharmacy Bulk Package intended for pharmacy use only.

For Continuous Intravenous Infusion

The vials reconstituted according to **Table 2 (Reconstitution)** should be further diluted to the desired volume with one of the following intravenous solutions:

5% Dextrose Injection
3.3% Dextrose Injection and 0.3% Sodium Chloride Injection
Lactated Ringer's Injection
0.9% Sodium Chloride Injection

A concentration of no greater than 5 mg/mL is recommended.

Directions for Dispensing from Pharmacy Bulk Package:

Pharmacy bulk packages (5 g and 10 g) are for use in a pharmacy admixture service only in suitable work area such as a laminar flow hood. The pharmacy bulk package should be hung by the integral labeling hanger and suspended in the laminar flow hood. The container closure should be penetrated only one time utilizing a suitable sterile dispensing set which allows measured distribution of the contents. Use of a syringe and needle is not recommended as it may cause leakage. Insert the dispensing set into the pharmacy bulk package using aseptic technique.

Once the sterile dispensing set has been inserted into the container, withdrawal of the contents should be accomplished without delay. However, if this is not possible, a maximum time of **8 hours** from the initial entry may be allowed to complete fluid aliquoting/transferring operations. This time limit should begin with the introduction of solution or diluent into the pharmacy bulk package. Discard the container no later than **8 hours** after initial closure puncture.

Stability and Storage Recommendations

Dry Powder

Vancomycin hydrochloride powder should be stored between 15ºC and 25ºC.

Solutions

Reconstituted solutions and further diluted infusion mixtures should be used within 24 hours if kept at room temperature or within 72 hours if stored under refrigeration (5°C). If prepared in a facility with a recognized parenteral intravenous admixture program, such mixtures may be kept up to 96 hours if stored under refrigeration (5°C).

NOTE: As with all parenteral drug products, intravenous admixtures should be inspected visually for clarity, particulate matter, precipitation, discolouration and leakage prior to administration whenever solution and container permit. Solutions showing haziness, particulate matter, precipitate, discolouration or leakage should not be used. Discard unused portion.

Incompatibility

Vancomycin solution has a low pH and may cause physical instability of other compounds.

Some of the specific substances found to be incompatible are aminophylline, chloramphenicol sodium succinate, chlorthiazide sodium, dexamethasone sodium phosphate, diphenylhydantoin sodium, methicillin sodium, vitamin B_{12} complex with C, sulfisoxazole diethanolamine, heparin sodium, potassium penicillin G, hydrocortisone sodium succinate, amobarbital sodium, nitrofurantoin sodium, pentobarbital sodium, phenobarbital sodium, secobarbital sodium, sodium bicarbonate, sulfadiazine sodium, and warfarin sodium.

NOTE: Common flavouring syrups have been added to the solution to improve the taste for oral administration. There is no information to indicate that the potency or efficacy of the drug is affected by the addition of these agents.

AVAILABILITY OF DOSAGE FORMS

Vancomycin Hydrochloride for Injection USP is supplied as a sterile, lyophilized powder of vancomycin hydrochloride equivalent to:

- 500 mg vancomycin base in 10 or 20 mL single-dose glass vials, closed with rubber stoppers and flip-off caps. Packages of 10 (20 mL vials) or 25 (10 mL vials).

- 1 g vancomycin base in 20 mL single-dose glass vials, closed with rubber stoppers and flip-top caps. Packages of 10.

- 5 g vancomycin base in 100 mL single-use glass vials, closed with rubber stoppers and flip-top caps. Vials are individually packaged.*

- 10 g vancomycin base in 100 mL single-use glass vials, closed with rubber stoppers and flip-top caps. Vials are individually packaged.*

* The 5 g and 10 g vials have labels with integrated hangers which can be peeled back and used to suspend the bottle as a unit in a laminar air flow hood.

MICROBIOLOGY

Cross-resistance has not been demonstrated between vancomycin hydrochloride and other classes of antibiotics. Laboratory-induced resistance has been reported to occur in a slow stepwise fashion. The development of resistance to vancomycin by staphylococci has not been reported in clinical use. Changes in pH or presence of serum do not significantly alter vancomycin's activity.

Vancomycin is active *in vitro* against staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains); Streptococci including *Streptococcus pyogenes, Streptococcus pneumoniae* (including penicillin-resistant strains); *Streptococcus agalactiae,* the viridans group*, Streptococcus bovis*, and enterococci (e.g. *Streptococcus faecalis*); Clostridium species including *Clostridium difficile*, (e.g. toxigenic strains implicated in pseudomembranous enterocolitis); and diphtheroids. Other organisms that are susceptible to vancomycin *in vitro* include *Listeria monocytogenes*, Lactobacillus species, Actinomyces species, Clostridium species and Bacillus species.

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

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

Susceptibility data showing the antibacterial activity of vancomycin are compiled in Table 3.

Table 3
In Vitro Antibacterial Activity of Vancomycin

Organism	No. Isolates	MIC_{50} (mg/L)	MIC_{90} (mg/L)
S. aureus	90	1.6	3.1
S. aureus	22	0.7	0.9
S. aureus (methicillin-resistant)	22	1.6	3.1
S. aureus (methicillin- resistant)	26	0.4	0.4
S. epidermis	50	1.6	6.3
S. *epidermis* (methicillin-resistant)	27	1.6	3.1
S. *epidermis* (methicillin-resistant)	25	2.0	4.0
Coagulase-negative staphylococci	200	2.0	4.0
Streptococcus pyogenes	110	0.5	0.5
Streptococcus pneumoniae	74	0.5	0.5
S. pneumoniae (penicillin-resistant)	10	1.0	2.0
S. bovis	100	0.25	0.5
*Streptococcus mutans (*viridans group)	82	0.8	1.6
Streptococcus agalactiae (Group B)	148	1.6	1.6
Streptococcus faecalis	347	1.6	1.6
Diphtheroids (including CDC-JK strains)	98	0.8	0.8
Listeria sp	26	0.8	1.6
Clostridium difficile	78	1.0	2.0
Clostridium sp	14	0.8	3.1
Lactobacillus sp	3	1.25	--
Actinomyces sp	58	5.0	--
Bacillus cereus	10	2.2 (mean)	--

Synergy

The combination of vancomycin and an aminoglycoside acts synergistically *in vitro* against many strains of *S. aureus,* nonenterococcal group D Streptococci, enterococci, and Streptococcus species (viridans group).

Susceptibility Testing/Diffusion and Dilution Techniques

The following recommendations are based on current NCCLS antimicrobial susceptibility testing standards M2-A5, M7-A3 and M2-A5 for the disk diffusion and dilution techniques. The performance standards for the susceptibility testing are based on the tables found in the NCCLS document M100-S5.

The standard single disc susceptibility test (using 30 µg vancomycin hydrochloride disc) and the dilution susceptibility test for gram positive organisms other than *S. pneumoniae* and enterococci should be interpreted according to the criteria in Table 4.

Table 4
Criteria for the interpretation of standard single disc and dilution susceptibility tests

	Zone Diameter (mm)	**Appropriate MIC Correlate (mg/L)**
Susceptible	≥ 12	≤ 4
Intermediate	10 – 11	4 to < 16
Resistant	≤ 9	≥ 16
Note: These criteria and the definition are in agreement with NCCLS. Order Code M100-55.		

Table 5 and Table 6 provide the criteria for the interpretation of standard disc and dilution susceptibility tests for *S. pneumoniae* and for enterococci, respectively.

Table 5
Criteria for the interpretation of standard disc and dilution susceptibility tests for *S. pneumoniae*

	Zone Diameter (mm)	**Appropriate MIC Correlate (mg/L)**
Susceptible	≥ 17	≤ 1
Note: Strains yielding results suggestive of a "Nonsusceptible" category should be submitted to a reference laboratory for further testing.		

Table 6 Criteria for the interpretation of standard disc and dilution susceptibility tests for enterococci		
	Zone Diameter (mm)	**Appropriate MIC Correlate (mg/L)**
Susceptible	≥ 17	≤ 4
Intermediate	15 – 16	-
Resistant	≤ 14	≥ 32

A report of "Susceptible" indicates that the test organism is likely to respond to therapy.

A report of "Intermediate" indicates that the organisms in this category are likely to respond if the infection is confined to tissues or fluids in which high antibiotic concentrations are attained.

A report of "Resistant" indicates that achievable drug concentrations are unlikely to be inhibitory, and other therapy should be selected.

Standardized Diffusion Techniques

Standardized procedures require the use of laboratory control organisms. The 30 µg vancomycin hydrochloride disk should give zone diameters as presented in Table 7.

Table 7 Zone Diameter for the 30 µg vancomycin disk	
Organisms	**Zone Diameter (mm)**
S. aureus ATCC 25923	15 - 19

Standardized Dilution Techniques

As with standardized diffusion techniques, dilution procedures require the use of laboratory control organisms. Standard vancomycin powder should provide the MIC values presented in Table 8.

Table 8 Standard vancomycin powder MIC values	
Organisms	**MIC (mg/L)**
S. aureus ATCC 29213	0.5 to 2.0
E. faecalis ATCC 29212	1.0 to 4.0

PHARMACOLOGY

HUMAN

Pharmacodynamics

Vancomycin is bactericidal and appears to bind to the bacterial cell wall causing blockage of glycopeptide polymerization. This effect occurs at a site different from that affected by the penicillins and produces immediate inhibition of cell wall synthesis and secondary damage to the cytoplasmic membrane.

Pharmacokinetics

In subjects with normal kidney function, multiple intravenous dosing of 1 g of vancomycin (15 mg/kg) infused over 60 minutes produces mean plasma concentrations of approximately 63 mg/L immediately at the completion of infusion, mean plasma concentrations of approximately 23 mg/L 2 hours after infusion, and mean plasma concentrations of approximately 8 mg/L 11 hours after the end of the infusion. Multiple dosing of 500 mg infused over 30 minutes produces mean plasma concentrations of about 49 mg/L at the completion of infusion, mean plasma concentrations of about 19 mg/L 2 hours after infusion, and mean plasma concentrations of about 10 mg/L 6 hours after infusion. Plasma concentrations are slightly higher than those following single dose as accumulation tends to occur after 2 to 3 days of intravenous administration at 6 or 12-hour intervals.

In normal subjects, the elimination half-life of vancomycin from plasma ranges from 4 to 6 hours. About 80 to 90% of an administered dose of vancomycin is excreted in urine by glomerular filtration in the first 24 hours. Excretion of vancomycin is slowed by renal dysfunction. The average half-life of elimination is 7.5 days in anephric patients.

There is no apparent metabolism of the drug. Vancomycin is not effectively removed by either hemodialysis or peritoneal dialysis. Plasma concentrations of vancomycin are reported to be minimally affected by conventional hemodialysis. Increased vancomycin clearance has been reported with highly permeable membranes used in high-flux hemodialysis. At 4-6 hours following the onset of high-flux hemodialysis, steady state concentrations of vancomycin may be reduced by 10-15% of the pre-dialysis concentrations. Peritoneal dialysis, although it may decrease concentrations, does not remove significant amounts. Reduction in total systemic and renal clearance may be observed in the elderly.

Following oral administration of vancomycin to normal subjects, serum levels are undetectable but trace amounts are recovered in the urine. Vancomycin is excreted by the fecal route after oral administration.

At vancomycin serum concentrations of 10 to 100 mg/L, vancomycin is approximately 55% serum protein bound. After intravenous administration of vancomycin HCl, inhibitory concentrations are present in pleural, pericardial, ascitic and synovial fluids. Vancomycin does

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

TOXICOLOGY

Acute Toxicity

The acute toxicity of vancomycin was evaluated in the rat, mouse, and dog. Table 9 gives the LD_{50} values obtained in these animals after the administration of vancomycin by various routes.

Table 9
LD_{50} of Vancomycin in Various Animals

Route of Administration	Rat	Mouse	Dog
Intravenous	319 ± 14	489 ± 41	292 ± 29
Intraperitoneal	2 218 ± 240	1 734 ± 227	--
Subcutaneous	--	> 5000	--
Oral	--	> 5000	--

In rats and mice following intravenous vancomycin, death resulted quickly from clonic convulsions, being a direct CNS effect. Following subcutaneous administration, no deaths were observed in rats, but extensive necrosis and sloughing of the subcutaneous tissue was observed. No death was observed in mice after oral administration, even at doses of 5 mg/kg. Death in dogs resulted generally from kidney failure, several days after drug administration. Vancomycin, when administered intravenously in a 5% solution to dogs at a rate of 0.6 mL/min., caused a slight dose-related drop in blood pressure. When the same dogs were given the same doses at a rate of 15 mL/min., blood pressure dropped dramatically, as much as 40%. This effect appears to be a histaminergic response.

Subacute Toxicity

Dogs were given daily intravenous doses of vancomycin at 12.5 mg and 50 mg/kg for 21 to 311 days. In 4 of 22 dogs receiving 50 mg/kg/day, slight renal damage was seen.

Monkeys tolerated intravenous doses of 25 and 50 mg/kg/day for 16 to 178 days, with irritation at the injection site as the only toxic effect.

No systemic toxicity was observed in cats receiving intravenous doses of 25 and 50 mg/kg/day for three months.

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

REFERENCES

1. AHFS Drug Information. American Society of Hospital Pharmacists Inc., Bethesda, MD, U.S.A. 1994:357-359.

2. Barna JCJ, Williams DH. The structure and mode of action of glycopeptide antibiotics of the vancomycin group. Am Rev 19 Microbial 1984;38:339-57.

3. Bartlett JG. Treatment of antibiotic-associated pseudomembranous colitis. Rev Infect Dis 1984;6(Suppl L):S235-41.

4. Benner EJ, Morthland V. Methicillin-resistant *Staphylococcus aureus.* N Engl J Med 1967;227:678.

5. Bunke CM, Aronoff GR, Brier ME, Sloan RS, Luft FC. Vancomycin kinetics during continuous ambulatory peritoneal dialysis. Clin Pharmacol Ther 1983;34:631.

6. Cantu TG, Yamanake-Yuen NA, Lietman PS. Serum vancomycin concentrations: reappraisal of their clinical value. Clin Infect Dis 1994;18(4):533-543.

7. Cooper GL, Given DB. Vancomycin, a comprehensive review of 30 years of clinical experience. Park Row Publishers, Inc. March 1986.

8. Dudley MN, Quintiliani R, Nightingale CH, Gontarz N. Absorption of vancomycin. Ann Intern Med 1984;104:144.

9. Geraci JE, Heilman ER, Nichols DR, Wellman WE. Antibiotic therapy of bacterial Endocarditis VII. Vancomycin for acute micrococcal endocarditis. Proc Staff Meet Mayo Clin 1958;33:172.

10. Geraci JE, Heilman ER. Vancomycin in the treatment of staphylococcal endocarditis. Proc Staff Meet Mayo Clin 1960;35:316.

11. Gilbert DN, Wood CA, Kimbrough RC. Failure of treatment with teicoplanin at 6 mg/kg/day in patients with *Staphylococcus aureus* intravascular infections. The infectious disease consortium of Oregon. Antimicrob Agents Chemother 1991;35(ISS1):79-87.

12. Griffith RS. Vancomycin: Continued clinical studies. In: Antibiotics Annual. New York. 1956-1957; Medical Encyclopedia, pp. 118-122.

13. Guay DR, Vance-Bryan K. Gilliland S, Rodvold K, Rotschafer J. Comparison of vancomycin pharmacokinetics in hospitalized elderly and young patients using a Bayesian forecaster. J Clin Pharmacol 1993;33(10):918-922.

14. Kavanagh KT, McCabe BF. Ototoxicity of oral neomycin and vancomycin. Laryngoscope 1983;93:649-53.

15. Kirby WMM, Divelbiss CL. Vancomycin, clinical and laboratory studies. In: Antibiotics Annual. New York. 1956-1957; Medical Encyclopedia, pp. 107-117.

16. Kirby WMM. Vancomycin therapy of severe staphylococcal infections. J Antimicrob Chemother 1984;14(Suppl D):73-8.

17. Kirby WMM. Vancomycin therapy in severe staphylococcal infections. Rev Infect Dis 1981;3(Suppl):S236-9.

18. Krogstad DJ, Moellering RC, Greenblatt DJ. Single-dose kinetics of intravenous vancomycin. J Clin Pharmacol 1980;20:197.

19. Moellering RC Jr, Krogstad DJ, Greenblatt DJ. Vancomycin therapy in patients with impaired renal function; a nomogram for dosage. Ann Intern Med 1981;94:343.

20. Moellering RC. Pharmacokinetics of vancomycin. J Antimicrob Chemother 1984;14(Suppl D):43-52.

21. Mogg GAG, Keighley MRB, Burdon DW, Alexander-Williams J, Youngs D, Johnson M, Bentley S, George RH. Antibiotic-associated colitis - a review of 66 cases. Br J Surg 1979;66:738-742.

22. National Committee for Clinical Laboratory Standards, M100-S5. Performance standards for antimicrobial disk susceptibility tests. NCCLS M100-S5, Vol. 14, No. 16. Villanova, PA;1994.

23. National Committee for Clinical Laboratory M7-T. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically. NCCLS, Villanova, PA;1983.

24. Pancorbo S, Conty C. Peritoneal transport of vancomycin in four patients undergoing continuous ambulatory peritoneal dialysis. Nephron 1982;31:37.

25. Pauly DJ, Musa DM, Lestico MR, Lindstrom MJ, Hetsko CM. Risk of nephrotoxicity with combination vancomycin-aminoglycoside antibiotic therapy. Pharmacotherapy 1990;10(6):378-382.

26. Redfield DC, et al. Cerebrospinal fluid penetration of vancomycin. In: Nelson JD, Grassi C. (eds); Current chemotherapy and infectious disease. Proceedings of the 11th International Congress on Chemotherapy and the 19th Interscience Conference on Antimicrobial Agents and Chemotherapy. American Society for Microbiology 1980;1:638-640.

27. Rice TL. Simplified dosing and monitoring of vancomycin for the burn care clinician. Burns 1992;18(5):355-361.

28. Romanelli VA, Howie MB, Myerowitz PD, Zvara DA, Rezaei A, Jackman DL, Sinclair DS, McSweeny TD. Intraoperative and postoperative effects of vancomycin administration in cardiac surgery patients: a prospective, double-blind, randomized trial. Crit Care Med 1993;21(ISS8):1124-1131.

29. Santre C, Leroy O, Simon M, Georges H, Guery B, Buescart C, Beaucaire G. Pharmacokinetics of vancomycin during continuous hemodialfiltration. Intensive Care Med 1993;19(6):347-350.

30. Sato K, Lin TY, Weintrub L, Olsen K, McCraken GH. Bacteriological efficacy of nafcillin and vancomycin alone or in combination with rifampicin or amikacin in experimental meningitis due to methicillin-susceptible or – resistant *Staphylococcus aureus*. Jap J Antibiot 1985;38:145-152.

31. Sheldrick GM, Jones PG, Kennard O, Williams DH, Smith GA. Structure of vancomycin and its complex with acetyl-D-alanyl-D-alanine. Nature 1978;271:223-5.

32. Silva J, Batts DH, Fekety R, Plouffe JF, Rifkin GD, Baird L. Treatment of *Clostridium difficile* colitis and diarrhea with vancomycin. Am J Med 1981;71:815-821.

33. Sorrell TC, Collignon PJ. A prospective study of adverse reactions associated with vancomycin therapy. J Antimicrob Chemother 1985;16:235-41.

34. USPDI Drug Information for the Health Care Professional. United States Pharmacopeial Convention, Inc. Rockville, MD, USA 1995;1:2755-2758.

35. Watanakunakorn C, Glotzbecker C. Enhancements of the effects of antistaphylococcal antibiotics by aminoglycosides. Antimicrob Agents Chemother 1974;6:802.

36. Watanakunakorn C, Glotzbecker C. Synergism with aminoglycosides of penicillin, ampicillin and vancomycin against nonenterococcal group D Streptococci and viridans streptococci. J Med Microb 1977;10:133.

37. Wold JS, Turnipseed SA. Toxicology of vancomycin in laboratory animals. Rev Infect Dis 1981;3(Suppl):224.

38. Daljani A, Bisno A, Chung KJ et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. JAMA 1990;264:2919-2922.

39. Vancomycin Hydrochloride for Injection, USP Product Monograph. Pfizer Canada Inc. Date of Revision: June 7, 2018. Control Number: 213061.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

Pr VANCOMYCIN HYDROCHLORIDE FOR INJECTION USP

500 mg/vial, 1 g/vial, 5 g/vial and 10 g/vial Vancomycin

Sterile lyophilized powder for solution

Read this carefully before you start taking Vancomycin Hydrochloride 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 Vancomycin Hydrochloride for Injection USP.

What is Vancomycin Hydrochloride for Injection USP used for?

Vancomycin is used to treat bacterial infections in many different parts of the body such as:

- Heart
- Bone
- Lung
- Blood
- Skin and muscle

Vancomycin is typically used for serious infections for which other medicines may not work.

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

How does Vancomycin Hydrochloride for Injection USP work?

Vancomycin hydrochloride is in a family of medications called glycopeptide antibiotics. It works by preventing the growth of certain types of bacteria.

What are the ingredients in Vancomycin Hydrochloride for Injection USP?

Medicinal ingredients: Vancomycin hydrochloride
Non-medicinal ingredients: Sodium hydroxide and hydrochloric acid

Vancomycin Hydrochloride for Injection USP comes in the following dosage forms:

Vancomycin Hydrochloride for Injection USP comes as a sterile powder. It is supplied in a vials. Each vial may contain:

- 500 mg of vancomycin (as vancomycin hydrochloride)
- 1 g of vancomycin (as vancomycin hydrochloride)
- 5 g of vancomycin (as vancomycin hydrochloride)
- 10 g of vancomycin (as vancomycin hydrochloride)

Do not use Vancomycin Hydrochloride for Injection USP if:

- You are allergic to vancomycin hydrochloride.

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

- Have kidney problems
- Have hearing problems
- Are pregnant or planning to become pregnant
- Are breastfeeding

Other warnings you should know about Vancomycin Hydrochloride for Injection USP:

While you are using Vancomycin Hydrochloride for Injection USP

- **Elderly:** Vancomycin Hydrochloride for Injection USP may cause damage to your hearing and kidneys (see the "Serious side effects and what to do about them" table below). These side effects may be more likely to occur in elderly patients. During your treatment your healthcare professional may require that you do blood, kidney and hearing tests.
- If you are going to have surgery, including dental surgery, tell your healthcare professional that you are receiving vancomycin. Vancomycin may affect other medicines used during surgery.
- If you develop severe diarrhea (very loose or watery stool), tell your healthcare professional right away. Diarrhea may mean that you have a serious condition affecting your bowel (colitis). You may need urgent medical care. Do not try to treat loose stools without first checking with your healthcare professional (see the "Serious side effects and what to do about them" table below).
- Stop taking vancomycin at the first sign of a skin rash and call your healthcare professional. Skin rash may be a sign of a more serious reaction to vancomycin (see the "Serious side effects and what to do about them" table below).
- **Driving and using machines:** This medicine may cause dizziness in some people. If this occurs, do not drive, use machines or do anything else that could be dangerous.

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 Vancomycin Hydrochloride for Injection USP:

- Other medications in the antibiotics family such as:
  - aminoglycoside antibiotics such as amikacin, gentamicin, kanamycin, paramomycin, tobramycin etc.
  - cephaloridine (not marketed in Canada)
  - polymixin B
  - colistin
  - viomycin (not marketed in Canada)
- Cisplatin, a medicine used to treat cancer
- Medications given during surgery to relax the muscles (neuromuscular blocking agents)

Always keep a list of your medicines and show it to your healthcare professional when you get new medicine. It is important that your healthcare professional reviews all medications and supplements you are taking before prescribing Vancomycin Hydrochloride for Injection USP.

How to take Vancomycin Hydrochloride for Injection USP:

- Vancomycin Hydrochloride for Injection USP is usually injected slowly into the vein over a period of at least 60 minutes. You may receive it at the hospital, or clinic.
- Under certain circumstances, Vancomycin Hydrochloride for Injection USP may also be given orally to treat colitis (inflammation of the intestine caused by certain bacteria) that may occur after antibiotic treatment.

Usual dose:

- Your healthcare professional will work out the right amount (dose) of medicine for you. The dose will depend on:
  - the medical problem for which you are using vancomycin
  - your weight, age
  - how well your kidneys are working and other factors.
- Your healthcare professional will explain to you the dosing instructions for Vancomycin Hydrochloride for Injection USP (amount of medicine to take each day, the time allowed between doses, and how long you need to take this medicine).
- Ask your healthcare professional if you have any questions about the dosing instructions.

Overdose:

Your healthcare professional is trained to recognize the symptoms of an overdosage, and deal with its symptoms.

If you think you have taken too much Vancomycin Hydrochloride for Injection USP, contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed dose:

If you have missed a dose of medication, call your healthcare professional to find out what to do.

What are possible side effects from using Vancomycin Hydrochloride for Injection USP?

These are not all the possible side effects you may feel while taking Vancomycin Hydrochloride for Injection USP. If you experience any side effects not listed here, contact your healthcare professional.

See also the "To help avoid side effects and ensure proper use…" section.

Check with your healthcare professional if any of these side effects persist or become troublesome:

- Headache.
- Shortness of breath.
- Sick to stomach.
- Rash.
- Tiredness.
- Vomiting.
- Fever.
- 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**	
Unknown frequency			
Reactions that may occur during your infusion or soon after your infusion is completed: • chills, • itching or skin irritation, • flushing of the skin over the neck and shoulder ("red neck")		✓	

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**	
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 genital • 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			✓
Rare			
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			✓
Kidney problems: • unable to pass urine • change in the amount of urine you pass • pain in urinating, blood in the urine • tiredness, nausea, vomiting • swollen hands and feet			✓
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			✓

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**	
Blood problems (neutropenia, agranulocytosis) (usually found when your doctor orders tests) • more likely to develop infections, sore throat, fever, chills, and other signs of infection			✓

Bowel infection (Clostridium difficile colitis):
May happen 2 or more months after your treatment
• diarrhea that does not go away (bloody or watery) with or without:
  ○ fever
  ○ stomach cramps
			✓

Vasculitis (inflammation of your blood vessels): • fever • headache • fatigue • weight loss • general aches and pains • night sweats • rash • nerve problems, such as numbness or weakness		✓	

If you have troublesome symptoms or side effects that are not listed here or become 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 (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 Vancomycin Hydrochloride for Injection USP powder between 15ºC and 25ºC.
- Reconstituted solutions and further diluted infusion mixtures should be used within 24 hours if kept at room temperature or within 72 hours if stored under refrigeration (5°C).
- Most of the time, Vancomycin Hydrochloride for Injection USP will be given in the hospital.

Keep out of reach and sight of children.

If you want more information about Vancomycin Hydrochloride 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 website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.sterimaxinc.com, or by calling 1-800-881-3550.

This leaflet was prepared by:

SteriMax Inc.
Oakville, Ontario
L6H 6R4

Last revised: November 05, 2018