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DHACOCIN

Vancomycin Hydrochloride for Injection

500 mg

PRODUCT DESCRIPTION:

Vancomycin Hydrochloride for Injection is a white to off white lyophilized plug or powder filled in glass vial. May contain hydrochloric acid and/or sodium hydroxide for pH adjustment. When reconstituted with Sterile Water for Injection, USP, it forms a clear solution. This product is oxygen sensitive. Solutions of vancomycin hydrochloride reconstituted with Sterile Water for Injection contain no bacteriostat and are intended for use only as a single-dose injection. When smaller doses are required, the unused portion should be discarded. When reconstituted with sterile water for injection, further dilution is required before use.

COMPOSITION:

Each vial contains: Vancomycin Hydrochloride (lyophilized) equivalent to Vancomycin 500 mg.

PHARMACOLOGY:

Vancomycin is a tricyclic glycopeptide antibiotic derived from Amycolatopsis orientalis (formerly Nocardia orientalis) and has the molecular formula $C_{66}H_{75}C_{12}N_9O_{24} \bullet HCl$. The molecular weight is 1485.74; 500 mg of the base is equivalent to 0.34 mmol.

Vancomycin has bactericidal action against a variety of Gram-positive bacteria. It is not active in-vitro against gram-negative bacilli, mycobacteria or fungi. It exerts its action by inhibiting cell wall biosynthesis of susceptible bacteria. There is also evidence that Vancomycin alters the permeability of the cell membrane and selectively inhibits ribonucleic acid synthesis. There is no cross-resistance between Vancomycin and other antibiotics.

Microbiology - The bactericidal action of vancomycin results primarily from inhibition of cell-wall biosynthesis. In addition, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis. There is no cross- resistance between vancomycin and other antibiotics. Vancomycin is not active in vitro against gram- negative bacilli, mycobacteria, or fungi.

Synergy - The combination of vancomycin and an aminoglycoside acts synergistically in vitro against many strains of *Staphylococcus aureus*, *Streptococcus bovis*, enterococci, and the viridans group streptococci.

Vancomycin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections as described in the **INDICATIONS** section.

Aerobic gram-positive microorganisms

Diphtheroids

Enterococci (e.g., *Enterococcus faecalis*)

Staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains)

Streptococcus bovis

Viridans group streptococci

The following *in vitro* data are available, but their clinical significance is unknown.

Vancomycin exhibits *in vitro* MIC's of 1 mcg/mL or less against most (> 90%) strains of streptococci listed below and MIC's of 4 mcg/mL or less against most (> 90%) strains of other listed microorganisms; however, the safety and effectiveness of vancomycin in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

Aerobic gram-positive microorganisms

Listeria monocytogenes

Streptococcus pyogenes

Streptococcus pneumoniae (including penicillin-resistant strains)

Streptococcus agalactiae

Anaerobic gram-positive microorganisms

Actinomyces species

Lactobacillus species

Susceptibility Tests:

Dilution Techniques:

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MIC's). These MIC's provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC's should be determined using a standardized procedure. Standardized procedures are based on a dilution method (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of vancomycin powder.

The MIC values should be interpreted according to the following criteria:

MIC (mcg/mL)	Interpretation
≤4	Susceptible (S)
8-16	Intermediate (I)
≥32	Resistant (R)

A beta-lactamase test using an inoculum >107CFU/mL (or direct colony growth) and a nitrocefin-based substrate should be performed to detect either ampicillin or penicillin resistance among enterococci due to beta-lactamase production.

For testing streptococci other than *Streptococcus pneumoniae*:

MIC (mcg/mL)	Interpretation
≤1	Susceptible (S)

Interpretative criteria applicable only to tests performed by broth microdilution method using cation-adjusted Mueller-Hinton broth with 2 to 5% lysed horse blood.

The current absence of data on resistant strains precludes defining any categories other than "Susceptible". Strains yielding MIC results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of "Intermediate" indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone which prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable; other therapy should be selected.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Standard vancomycin powder should provide the following MIC values:

Microorganism		MIC (mcg/mL)
Enterococcus faecalis	ATCC 29212	1-4
Staphylococcus aureus	ATCC 29213	0.5-2
Streptococcus pneumoniae	ATCC 49619	0.12-0.5

Interpretative criteria applicable only to tests performed by broth microdilution method using cation-adjusted Mueller-Hinton broth with 2 to 5% lysed horse blood.

Diffusion Techniques - Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 30-mcg vancomycin to test the susceptibility of microorganisms to vancomycin.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 30-mcg vancomycin disk should be interpreted according to the following criteria:

For testing aerobic microorganisms other than enterococci and streptococci:

<u>Zone Diameter (mm)</u>	<u>Interpretation</u>
≥15	Susceptible (S)
-	Intermediate (I)
-	Resistant (R)

For testing enterococci:

<u>Zone Diameter (mm)</u>	<u>Interpretation</u>
≥17	Susceptible (S)
15-16	Intermediate (I)
≤14	Resistant (R)

A direct nitrocefin-based beta-lactamase test using direct colony growth should be performed to detect either ampicillin or penicillin resistance among enterococci due to beta-lactamase production.

When testing for enterococci resistance to vancomycin, plates should be held for a full 24 hours and examined using transmitted light. The presence of a haze or any growth within the zone of inhibition indicates resistance. Those enterococci with intermediate zones of inhibition should be tested by a standardized procedure based on a dilution method (broth or agar) or equivalent.

For testing streptococci other than *Streptococcus pneumoniae*:

<u>Zone Diameter (mm)</u>	<u>Interpretation</u>
≥17	Susceptible (S)

Interpretative criteria applicable only to tests performed by disk diffusion method using Mueller-Hinton agar with 5% defibrinated sheep blood and incubated in 5% CO₂.

The current absence of data on resistant strains precludes defining any categories other than "Susceptible". Strains yielding zone diameter results suggestive of a "nonsusceptible" category should be submitted to a reference laboratory for further testing.

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for vancomycin.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms that are used to control the technical aspects of the laboratory procedures. For the diffusion technique, the 30-mcg vancomycin disk should provide the following zone diameters in these laboratory test quality control strains:

<u>Microorganism</u>	<u>Zone Diameter (mm)</u>	
<i>Staphylococcus aureus</i>	ATCC 25923	17-21
<i>Streptococcus pneumoniae</i>	ATCC 49619	20-27

Interpretative criteria applicable only to tests performed by disk diffusion method using Mueller-Hinton agar with 5% defibrinated sheep blood and incubated in 5% CO₂.

PHARMACOKINETICS:

Vancomycin is poorly absorbed after oral administration; it is given intravenously for therapy of systemic infections. Intramuscular injection is painful.

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 mcg/mL immediately after the completion of infusion, mean plasma concentrations of approximately 23 mcg/mL two hours after infusion, and mean plasma concentrations of approximately 8 mcg/mL eleven hours after the end of the infusion. Multiple dosing of 500 mg infused over 30 minutes produces mean plasma concentrations of about 49 mcg/mL at the

completion of infusion, mean plasma concentrations of about 19 mcg/mL two hours after infusion, and mean plasma concentrations of about 10 mcg/mL six hours after infusion. The plasma concentrations during multiple dosing are similar to those after a single dose.

The mean elimination half-life of vancomycin from plasma is 4 to 6 hours in subjects with normal renal function. In the first 24 hours, about 75% of an administered dose of vancomycin is excreted in urine by glomerular filtration. Mean plasma clearance is about 0.058 L/kg/hr, and mean renal clearance is about 0.048 L/kg/hr. Renal dysfunction slows excretion of vancomycin. In anephric patients, the average half-life of elimination is 7.5 days. The distribution coefficient is from 0.3 to 0.43 L/kg. There is no apparent metabolism of the drug. About 60% of an intraperitoneal dose of vancomycin administered during peritoneal dialysis is absorbed systemically in six hours. Serum concentrations of about 10 mcg/mL are achieved by intraperitoneal injection of 30 mg/kg of vancomycin.

However, the safety and efficacy of the intraperitoneal use of vancomycin has not been established in adequate and well-controlled trials.

Total systemic and renal clearance of vancomycin may be reduced in the elderly.

Vancomycin is approximately 55% serum protein bound as measured by ultrafiltration at vancomycin serum concentrations of 10 to 100 mcg/mL. After I.V. administration of vancomycin, inhibitory concentrations are present in pleural, pericardial, ascitic, and synovial fluids; in urine; in peritoneal dialysis fluid; and in atrial appendage tissue. Vancomycin does not readily diffuse across normal meninges into the spinal fluid; but, when the meninges are inflamed, penetration into the spinal fluid occurs.

INDICATIONS:

Vancomycin is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (β-lactam-resistant) staphylococci. It is indicated for penicillin-allergic patients, for patients who cannot receive or who have failed to respond to other drugs, including the penicillins or cephalosporins, and for infections caused by vancomycin-susceptible organisms that are resistant to other antimicrobial drugs. Vancomycin is indicated for initial therapy when methicillin-resistant staphylococci are suspected, but after susceptibility data are available, therapy should be adjusted accordingly.

Vancomycin is effective in the treatment of staphylococcal endocarditis. Its effectiveness has been documented in other infections due to staphylococci, including septicemia, bone infections, lower respiratory tract infections, skin, and skin structure infections. When staphylococcal infections are localized and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

Vancomycin has been reported to be effective alone or in combination with an aminoglycoside for endocarditis caused by *S. viridans* or *S. bovis*. For endocarditis caused by enterococci (e.g., *E. 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. Vancomycin 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.

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

To reduce the development of drug-resistant bacteria and maintain the effectiveness of vancomycin and other antibacterial drugs, vancomycin should be used only to treat or prevent 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.

The parenteral form of vancomycin hydrochloride may be administered orally for treatment of antibiotic-associated pseudomembranous colitis produced by *C. difficile* and for staphylococcal enterocolitis. Parenteral administration of vancomycin hydrochloride alone is of unproven benefit for these indications. Vancomycin is not effective by the oral route for other types of infections.

DOSAGE:

Infusion-related events are related to both the concentration and the rate of administration of vancomycin. Concentrations of no more than 5 mg/mL and rates of no more than 10 mg/min, are recommended in adults (see also 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 the risk of infusion-related events. An infusion rate of 10 mg/min or less is associated with fewer infusion-related events (see **ADVERSE REACTIONS**). Infusion-related events may occur, however, at any rate or concentration.

Patients with Normal Renal Function

Adults: The usual daily intravenous dose is 2 g divided either as 500 mg every six hours or 1 g every 12 hours. Each dose should be administered at no more than 10 mg/min, or over a period of at least 60 minutes, whichever is longer. Other patient factors, such as age or obesity, may call for modification of the usual intravenous daily dose.

Paediatric Patients: The usual intravenous dosage of vancomycin is 10 mg/kg per dose given every 6 hours. Each dose should be administered over a period of at least 60 minutes. Close monitoring of serum concentrations of vancomycin is recommended in these patients.



Neonates: In paediatric patients up to the age of 1 month, the total daily intravenous dosage may be lower. 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. Each dose should be administered over 60 minutes. In premature infants, vancomycin clearance decreases as postconceptional age decreases. Therefore, longer dosing intervals may be necessary in premature infants. Close monitoring of serum concentrations of vancomycin is recommended in these patients.

Patients with Impaired Renal Function and Elderly Patients

Dosage adjustment must be made in patients with impaired renal function. In premature infants and the elderly, greater dosage reductions than expected may be necessary because of decreased renal function. Measurement of vancomycin serum concentrations can be helpful in optimizing therapy, especially in seriously ill patients with changing renal function. Vancomycin serum concentrations can be determined by use of microbiologic assay, radioimmunoassay, fluorescence polarization immunoassay, fluorescence immunoassay, or high- pressure liquid chromatography. If creatinine clearance can be measured or estimated accurately, the dosage for most patients with renal impairment can be calculated using the following table. The dosage of vancomycin per day in mg is about 15 times the glomerular filtration rate in mL/min:

FRONT SIDE

ARTWORK DETAIL LABEL

PRODUCT	DHACOCIN - Vancomycin Hydrochloride for Injection 500 mg/vial					
BUYER / COUNTRY	Mylan / Singapore					
DIMENSION	300 x 290 mm	COMPONENT	Pack Insert	PACK	--	NO. OF COLOURS 1
COLOUR SHADES	 Black					
VERSION & DATE	Ver. 7; Date: 18.03.2021					
SPECIAL INSTRUCTIONS	 = For Position Only. Codes shall be assigned during commercial artwork preparation.					

DOSAGE TABLE FOR VANCOMYCIN IN PATIENTS WITH IMPAIRED RENAL FUNCTION

Creatinine Clearance mL/min	Vancomycin Dose mg/24 h
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.

The table is not valid for functionally anephric patients. For such patients, an initial dose of 15 mg/kg of body weight should be given to achieve prompt therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 h. In patients with marked renal impairment, it may be more convenient to give maintenance doses of 250 to 1000 mg once every several days rather than administering the drug on a daily basis. In anuria, a dose of 1000 mg every 7 to 10 days has been recommended.

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

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 creatinine 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 obese patients or those with liver disease, edema, or ascites; and (3) accompanied by debilitation, malnutrition, or inactivity.

The safety and efficacy of vancomycin administration by the intrathecal (intralumbar or intraventricular) routes have not been established.

Intermittent infusion is the recommended method of administration.

Reconstitution & administration:

Dissolve 500mg in 10ml of Sterile Water for Injection to give a solution of 50 mg/mL. Reconstituted solutions containing 500mg of Vancomycin must be further diluted with at least 100ml of diluent. The desired dose should be administered by intermittent IV infusion over a period of at least 60 minutes.

Compatibility with IV Fluids:

5% Dextrose Injection; 0.9% Sodium Chloride Injection.

Vancomycin solution has a low pH and may cause chemical or physical instability when it is mixed with other compounds.

Mixtures of solutions of vancomycin and beta-lactam antibiotics have been shown to be physically incompatible. The likelihood of precipitation increases with higher concentrations of vancomycin. It is recommended to adequately flush the intravenous lines between the administration of these antibiotics. It is also recommended to dilute solutions of vancomycin to 5 mg/mL or less.

Although intravitreal injection is not an approved route of administration for vancomycin, precipitation has been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles. The precipitates dissolved gradually, with complete clearing of the vitreous cavity over two months and with improvement of visual acuity.

Prior to administration, parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution or container permits.

SIDE EFFECTS:

Infusion-Related Events: During or soon after rapid infusion of vancomycin, patients may develop anaphylactoid reactions, including hypotension, wheezing, dyspnea, urticaria, or pruritus. Rapid infusion may also cause flushing of the upper body ("Red Neck") or pain and muscle spasm of the chest and back. These reactions usually resolve within 20 minutes but may persist for several hours. Such events are infrequent if vancomycin is given by a slow infusion over 60 minutes. In studies of normal volunteers, infusion-related events did not occur when vancomycin was administered at a rate of 10 mg/min or less.

Nephrotoxicity: Systemic vancomycin exposure may result in acute kidney injury (AKI). The risk of AKI increases as systemic exposure/serum levels increase. Additional risk factors for AKI in patients receiving vancomycin include receipt of concomitant drugs known to be nephrotoxic, in patients with pre-existing renal impairment, or with co-morbidities that predispose to renal impairment. Interstitial nephritis has also been reported in patients receiving vancomycin.

Gastrointestinal: Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment. (See **WARNINGS**).

Ototoxicity: A few dozen cases of hearing loss associated with vancomycin have been reported. Most of these patients had kidney dysfunction or a preexisting hearing loss, or were receiving concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have been reported rarely.

Hematopoietic: Reversible neutropenia, usually starting 1 week or more after onset of therapy with vancomycin or after a total dosage of more than 25 g, has been reported for several dozen patients. Neutropenia appears to be promptly reversible when vancomycin is discontinued. Thrombocytopenia has rarely been reported.

Although a causal relationship has not been established, reversible agranulocytosis (granulocytes < 500/mm³) has been reported rarely.

Phlebitis: Inflammation at the injection site has been reported.

Miscellaneous: Infrequently, patients have been reported to have had anaphylaxis, drug fever, nausea, chills, eosinophilia, rashes including exfoliative dermatitis, linear IgA bullous dermatosis, Stevens-Johnson syndrome, and vasculitis in association with administration of vancomycin.

Chemical peritonitis has been reported following intraperitoneal administration (see **PRECAUTIONS**).

WARNINGS:

Infusion Reactions

Rapid bolus administration (e.g., over several minutes) may be associated with exaggerated hypotension, including shock, and, rarely, cardiac arrest.

Vancomycin should be administered in a diluted 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.

Nephrotoxicity

Systemic vancomycin exposure may result in acute kidney injury (AKI). The risk of AKI increases as systemic exposure/serum levels increase. Monitor renal function in all patients, especially patients with underlying renal impairment, patients with co-morbidities that predispose to renal impairment, and patients receiving concomitant therapy with a drug known to be nephrotoxic.

Ototoxicity

Ototoxicity has occurred in patients receiving vancomycin. It may be transient or permanent. It has been reported mostly in patients who have been given excessive doses, who have an underlying hearing loss, or who are receiving concomitant therapy with another ototoxic agent, such as an aminoglycoside. Vancomycin should be used with caution in patients with renal insufficiency because the risk of toxicity is appreciably increased by high, prolonged blood concentrations.

Dosage of vancomycin must be adjusted for patients with renal dysfunction (see **PRECAUTIONS** and **DOSAGE AND ADMINISTRATION**).

Clostridium Difficile Associated Diarrhea (CDAD)

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including vancomycin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not direct against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated.

Hemorrhagic Occlusive Retinal Vasculitis (HORV)

Hemorrhagic occlusive retinal vasculitis, including permanent loss of vision, occurred in patients receiving intracameral or intravitreal administration of vancomycin during or after cataract surgery. The safety and efficacy of vancomycin administered by the intracameral or the intravitreal route have not been established by adequate and well-controlled trials. Vancomycin is not indicated for the prophylaxis of endophthalmitis.

PRECAUTIONS:

General

Clinically significant serum concentrations have been reported in some patients being treated for active *C. difficile*-induced pseudomembranous colitis after multiple oral doses of vancomycin.

Prolonged use of vancomycin may result in the overgrowth of nonsusceptible microorganisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken. In rare instances, there have been reports of pseudomembranous colitis due to *C. difficile* developing in patients who received intravenous vancomycin.

Serial tests of auditory function may be helpful in order to minimize the risk of ototoxicity. Reversible neutropenia has been reported in patients receiving vancomycin (see **ADVERSE REACTIONS**). Patients who will undergo prolonged therapy with vancomycin or those who are receiving concomitant drugs that may cause neutropenia should have periodic monitoring of the leukocyte count.

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. Thrombophlebitis may occur, the frequency and severity of which can be minimized by slow infusion of the drug and by rotation of venous access sites.

There have been reports that the frequency of infusion-related events (including hypotension, flushing, erythema, urticaria, and pruritus) 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 vancomycin administered by the intrathecal (intralumbar or intraventricular) route or by the intraperitoneal route have not been established by adequate and well-controlled trials.

Reports have revealed that administration of sterile vancomycin by the intraperitoneal route during continuous ambulatory peritoneal dialysis (CAPD) has resulted in a syndrome of chemical peritonitis. To date, this syndrome has ranged from a cloudy dialysate alone to a cloudy dialysate accompanied by variable degrees of abdominal pain and fever. This syndrome appears to be short-lived after discontinuation of intraperitoneal vancomycin.

Prescribing vancomycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Information for Patients

Patients should be counseled that antibacterial drugs including vancomycin should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When vancomycin is prescribed to treat a bacterial infection, patients should be told that although it

is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by vancomycin or other antibacterial drugs in the future.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.

Paediatric Use

In paediatric patients, 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 paediatric patients (see **PRECAUTIONS**).

Geriatric Use

The natural decrement 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 (see **DOSAGE AND ADMINISTRATION**).

USE IN PREGNANCY AND LACTATION:

Pregnancy: Teratogenic Effects - Category C - Animal reproduction studies have not been conducted with vancomycin. It is not known whether vancomycin can affect reproduction capacity. In a controlled clinical study, the potential ototoxic and nephrotoxic effects of vancomycin on infants were evaluated when the drug was administered to pregnant women for serious staphylococcal infections complicating intravenous drug abuse. Vancomycin was found in cord blood. No sensorineural hearing loss or nephrotoxicity attributable to vancomycin was noted. One infant whose mother received vancomycin in the third trimester experienced conductive hearing loss that was not attributed to the administration of vancomycin. Because the number of patients treated in this study was limited and vancomycin was administered only in the second and third trimesters, it is not known whether vancomycin causes fetal harm. Vancomycin should be given to a pregnant woman only if clearly needed.

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

CONTRAINDICATIONS:

Vancomycin is contraindicated in patients with known hypersensitivity to this antibiotic.

DRUG INTERACTIONS:

Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing (see Pediatric Use - **PRECAUTIONS**) and anaphylactoid reactions (see **ADVERSE REACTIONS**).

Monitor renal function in patients receiving vancomycin and concurrent and/or sequential systemic or topical use of other potentially neurotoxic and/or nephrotoxic drugs, such as amphotericin B, aminoglycosides, bacitracin, polymyxin B, colistin, viomycin, or cisplatin.

Carcinogenesis, Mutagenesis, Impairment of Fertility Although no long-term studies in animals have been performed to evaluate carcinogenic potential, no mutagenic potential of vancomycin hydrochloride for injection was found in standard laboratory tests. No definitive fertility studies have been performed.

OVERDOSE AND TREATMENT:

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis.

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

AVAILABILITY:

500 mg vials: Box of 1 vial Box of 10 vials.

STORAGE:

Store below 30°C. Protect from light. Keep out of reach of children.

For further information, please consult your physician or pharmacist.



Manufactured by:
Mylan Laboratories Limited
(Specialty Formulation Facility)
Bangalore - 560 105, India.

Mylan Laboratories Limited
Sterile Product Division
Bangalore - 560 076, India.

Date of revision: March, 2021

BACK SIDE

ARTWORK DETAIL LABEL

PRODUCT	DHACOCIN - Vancomycin Hydrochloride for Injection 500 mg/vial					
BUYER / COUNTRY	Mylan / Singapore					
DIMENSION	300 x 290 mm	COMPONENT	Pack Insert	PACK	--	NO. OF COLOURS 1
COLOUR SHADES	Black					
VERSION & DATE	Ver. 7; Date: 18.03.2021					
SPECIAL INSTRUCTIONS	= For Position Only. Codes shall be assigned during commercial artwork preparation.					

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