Baxter

VANCOCIN® HCl

(Vancomycin Injection, USP)

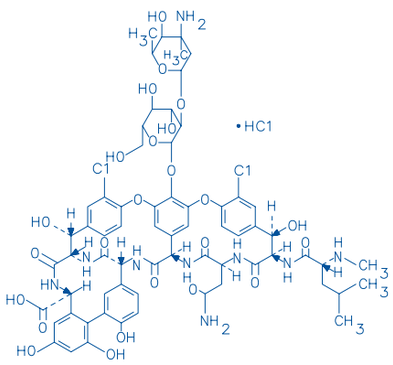
in GALAXY Plastic Container (PL 2040) For Intravenous Use Only

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 bacteria.

DESCRIPTION

Vancocin® HCl (Vancomycin Injection, USP) in the GALAXY plastic container (PL 2040) contains Vancomycin, USP as vancomycin hydrochloride. It is a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis* (formerly *Nocardia orientalis*). The molecular formula is $C_{66}H_{75}Cl_2N_9O_{24}$·HCl and the molecular weight is 1,485.74. 500 mg of the base is equivalent to 0.34 mmol.

Vancomycin hydrochloride has the following structural formula:



Vancocin® HCl (Vancomycin Injection, USP) in the GALAXY plastic container (PL 2040) is a frozen, iso-osmotic, sterile, nonpyrogenic premixed 100 mL or 200 mL solution containing 500 mg or 1 g Vancomycin, USP respectively as Vancomycin hydrochloride. Each 100 mL of solution contains approximately 5 g of Dextrose Hydrous, USP. The pH of the solution has been adjusted with hydrochloric acid and may have been adjusted with sodium hydroxide. Thawed solutions have a pH in the range of 3.0 to 5.0. After thawing to room temperature, this solution is intended for intravenous use only.

This GALAXY container is fabricated from a specially designed multilayer plastic (PL 2040). Solutions are in contact with the polyethylene layer of this container and can leach out certain chemical components of the plastic in very small amounts within the expiration period. The suitability of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

CLINICAL PHARMACOLOGY

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 µg/mL immediately after the completion of infusion, mean plasma concentrations of approximately 23 µg/mL 2 hours after infusion, and mean plasma concentrations of approximately 8 µg/mL 11 hours after the end of the infusion. Multiple dosing of 500 mg infused over 30 minutes produces mean plasma concentrations of about 49 µg/mL at the completion of infusion, mean plasma concentrations of about 19 µg/mL 2 hours after infusion, and mean plasma concentrations of about 10 µg/mL 6 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/h, and mean renal clearance is about 0.048 L/kg/h. 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 6 hours. Serum concentrations of about 10 µg/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 (see **PRECAUTIONS**).

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 µg/mL. After IV 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.

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 AND USAGE** 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 1µg/mL or less against most (≥90%) strains of streptococci listed below and MIC's of 4 µg/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[1] (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:

For testing aerobic microorganisms[a] other than streptococci:

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

[a] A ß-lactamase test using an inoculum ≥10^7 CFU/mL (or direct colony growth) and a nitrocefin-based substrate should be performed to detect either ampicillin or penicillin resistance among enterococci due to ß-lactamase production.

For testing streptococci[b] other than *Streptococcus pneumoniae*:

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

[b] Interpretative criteria applicable only to tests performed by broth microdilution method using cation-adjusted Mueller-Hinton broth with 2 to 5% lysed horse blood[1].

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 (µg/mL)
Enterococcus faecalis	ATCC 29212	1-4
Staphylococcus aureus	ATCC 29213	0.5-2
Streptococcus pneumoniae[a]	ATCC 49619	0.12-0.5

[a] Interpretative criteria applicable only to tests performed by broth microdilution method using cation-adjusted Mueller-Hinton broth with 2 to 5% lysed horse blood[1].

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[2] requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 30-µg 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-µg vancomycin disk should be interpreted according to the following criteria:

For testing aerobic microorganisms other than enterococci and streptococci:

Zone Diameter (mm)	Interpretation
≥15	Susceptible (S)
-	Intermediate (I)
-	Resistant (R)

For testing enterococci [a,b]:

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

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

[b] 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[1] (broth or agar) or equivalent.

For testing streptococci[c] other than *Streptococcus pneumoniae*:

Zone Diameter (mm)	Interpretation
≥17	Susceptible (S)

[c] Interpretative criteria applicable only to tests performed by disk diffusion method using Mueller-Hinton agar with 5% defibrinated sheep blood and incubated in 5% CO_2[2].

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-µg vancomycin disk should provide the following zone diameters in these laboratory test quality control strains:

Microorganism		Zone Diameter (mm)
Staphylococcus aureus	ATCC 25923	17-21
Streptococcus pneumoniae[a]	ATCC 49619	20-27

[a] Interpretative criteria applicable only to tests performed by disk diffusion method using Mueller-Hinton agar with 5% defibrinated sheep blood and incubated in 5% CO_2[2].

INDICATIONS AND USAGE

Vancomycin is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (beta-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 *Streptococcus 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.

CONTRAINDICATION

Vancomycin is contraindicated in patients with known hypersensitivity to this antibiotic.
Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products.

WARNINGS

Rapid bolus administration (e.g., over several minutes) may be associated with exaggerated hypotension, including shock, and, rarely, cardiac arrest. Vancomycin should be administered over a period of not less than 60 minutes to avoid rapid-infusion-related reactions. Stopping the infusion usually results in prompt cessation of these reactions.
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**).
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including vancomycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.
Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis". After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *C. difficile* colitis.

PRECAUTIONS

General—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.
In order to minimize the risk of nephrotoxicity when treating patients with underlying renal dysfunction or patients receiving concomitant therapy with an aminoglycoside, serial monitoring of renal function should be performed and particular care should be taken in following appropriate dosing schedules (see **DOSAGE AND ADMINISTRATION**). 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 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.
Drug Interactions-Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing (see *Usage in Pediatrics* under **PRECAUTIONS**) and anaphylactoid reactions (see **ADVERSE REACTIONS**).
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, when indicated, requires careful monitoring.
Pregnancy-Teratogenic Effects -Pregnancy 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.
Pediatric Use-In pediatric 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 pediatric patients (see **ADVERSE REACTIONS**). The potential for toxic effects in pediatric patients from chemicals that may leach from the plastic containers into the single-dose, premixed intravenous preparation has not been determined.
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**).
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.

ADVERSE REACTIONS

Infusion-Related Events-During or soon after rapid infusion of vancomycin, patients may develop anaphylactoid reactions, including hypotension (see **ANIMAL PHARMACOLOGY**), 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-Renal failure, principally manifested by increased serum creatinine or BUN concentrations, especially in patients administered large doses of vancomycin, has been reported rarely. Cases of interstitial nephritis have also been reported rarely. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had preexisting kidney dysfunction. When vancomycin was discontinued, azotemia resolved in most patients.
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/mm^3) 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, Stevens-Johnson syndrome, and vasculitis in association with administration of vancomycin.
Chemical peritonitis has been reported following intraperitoneal administration of vancomycin (see **PRECAUTIONS**).

Overdosage

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. The median lethal intravenous dose is 319 mg/kg in rats and 400 mg/kg in mice.
To obtain up-to-date information about the treatment of overdose, a good resource is your certified Regional Poison Control Center. Telephone numbers of certified poison control centers are listed in the *Physicians' Desk Reference (PDR)*. In managing overdosage, consider the possibility of multiple drug overdoses, interaction among drugs, and unusual drug kinetics in your patient.

Dosage and Administration

Vancocin® HCl (Vancomycin Injection, USP) in the GALAXY plastic container (PL 2040) is intended for intravenous use only.
Vancomycin in the GALAXY Container (PL 2040 Plastic) is <u>not</u> to be administered orally. 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 6 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.
Pediatric 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 may be warranted in these patients.
Neonates-In pediatric 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 1st week of life and every 8 hours thereafter up to the age of 1 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 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:

DOSAGE TABLE FOR VANCOMYCIN
IN PATIENTS WITH IMPAIRED RENAL FUNCTION
(Adapted from Moellering et al)[3]

Creatinine Clearance	Vancomycin Dose
mL/min	mg/24 h
100	1,545
90	1,390
80	1,235
70	1,080
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 1,000 mg once every several days rather than administering the drug on a daily basis. In anuria, a dose of 1,000 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.

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

$$\text{Women: } 0.85 \times \text{above value}$$

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.
Directions for use of Vancocin® HCl in GALAXY plastic container (PL 2040)
Vancocin® HCl in GALAXY plastic container (PL 2040) is for intravenous administration only.
Storage:
Store in a freezer capable of maintaining a temperature at or below -20°C (-4°F).
Thawing of Plastic Containers:
1. Thaw frozen containers at room temperature (25°C/77°F) or under refrigeration (5°C/41°F). **DO NOT FORCE THAW BY IMMERSION IN WATER BATHS OR BY MICROWAVE IRRADIATION**.
2. Check for minute leaks by squeezing the bag firmly. If leaks are detected, discard solution because sterility may be impaired.
3. **DO NOT ADD SUPPLEMENTARY MEDICATION.**
4. Visually inspect the container for particulate matter and discoloration. Components of the solution may precipitate in the frozen state and should dissolve with little or no agitation after the solution has reached room temperature. Potency is not affected. If after visual inspection, the solution is discolored or remains cloudy, an insoluble precipitate is noted, or any seals or outlet ports are not intact, the container should be discarded.
5. The thawed solution in GALAXY plastic container (PL 2040) remains chemically stable for 72 hours at room temperature (25°C/77°F) or for 30 days when stored under refrigeration (5°C/41°F).
6. **Do not refreeze thawed antibiotics.**

Preparation for Intravenous Administration:
1. Suspend container from eyelet support.
2. Remove protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.
4. Use sterile equipment.

Caution: Do not use plastic containers in series connections. Such use could result in an embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is complete.
Rx only.

HOW SUPPLIED

Vancocin® HCl (Vancomycin Injection, USP) is supplied as a frozen, iso-osmotic, premixed solution in a 100 mL or 200 mL single dose GALAXY plastic container (PL 2040) in the following vancomycin-equivalent dose:

2G3551	500 mg/100-mL container	NDC 0338-3551-48
2G3552	1 g/200 mL container	NDC 0338-3552-48

Store at or below -20°C (-4°F).
See DIRECTIONS FOR USE OF VANCOCIN® HCl (Vancomycin Injection, USP) in GALAXY plastic container (PL 2040).

ANIMAL PHARMACOLOGY

In animal studies, hypotension and bradycardia occurred in dogs receiving an intravenous infusion of vancomycin 25 mg/kg, at a concentration of 25 mg/mL and an infusion rate of 13.3 mL/min.

REFERENCES

1. National Committee for Clinical Laboratory Standards. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically—Fourth Edition. Approved Standard NCCLS Document M7-A4, Vol. 17, No.2, NCCLS, Wayne, PA, January, 1997.
2. National Committee for Clinical Laboratory Standards. Performance Standards for Antimicrobial Disk Susceptibility Tests - Sixth Edition. Approved Standard NCCLS Document M2-A6, Vol. 17, No. 1, NCCLS, Wayne, PA, January, 1997.
3. Moellering RC, Krogstad DJ, Greenblatt DJ: Vancomycin therapy in patients with impaired renal function: A nomogram for dosage. *Ann Inter Med* 1981;94:343.

Baxter Healthcare Corporation
Deerfield, IL 60015 USA

Printed in USA

07-19-38-191
Revised, May, 2003