VANOCIN CP (Sterile Vancomycin Hydrochloride) has the chemical formula \( \text{C}_{66}\text{H}_{75}\text{Cl}_{2}\text{N}_{9}\text{O}_{24}.\text{HCl} \).

The formula weight is 1449; 500 mg of the base is equivalent to 0.35 mmol. The CAS number is 1404-93-9.

The following structure of vancomycin hydrochloride has been confirmed by X-ray diffraction:

![Structure of Vancomycin Hydrochloride](image)

DESCRIPTION

Vancocin CP (Sterile Vancomycin Hydrochloride), Intravenous, is a chromatographically purified tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis* (formerly *Nocardia orientalis*) which is bactericidal against many gram-positive bacteria. It should be administered intravenously in dilute solution (see DOSAGE AND ADMINISTRATION).
Vancocin CP is available as sterile vials containing vancomycin equivalent to either 500 mg (500,000 IU) or 1 g (1,000,000 IU) of vancomycin activity. It is an off-white lyophilised plug. When reconstituted in water, it is a clear solution with a pH range of 2.8 to 4.5. Disodium edetate has been added during processing. Sodium hydroxide and/or hydrochloric acid may be used during manufacture for pH adjustment.

**CLINICAL PHARMACOLOGY**

Vancocin CP 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 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, and 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. 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 0.06 L/kg/hr, and mean renal clearance is about 0.05 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 0.69 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 mg/L are achieved by intraperitoneal injection of 30 mg/kg of vancomycin.

Although vancomycin is not effectively removed by either haemodialysis or peritoneal dialysis; there have been reports of increased vancomycin clearance with haemoperfusion and haemofiltration.

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

Protein binding is approximately 55% as measured by ultrafiltration at vancomycin serum concentrations of 10 to 100 mg/L. Clinically effective concentrations of this antibiotic in the blood are usually achieved and maintained by its intravenous administration, moreover, inhibitory concentrations can be demonstrated in pleural, pericardial, ascitic and synovial fluids, in urine, in peritoneal dialysis fluid, and in atrial appendage tissue. This antibiotic does not readily diffuse across the meninges into the cerebrospinal fluid.
Measurable serum concentrations of vancomycin may occur in patients treated for active pseudomembranous colitis due to *Clostridium difficile*.

**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 active 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., *Enterococcus faecalis* [formerly *Streptococcus faecalis*]); *C. difficile* (e.g., toxigenic strains implicated in pseudomembranous enterocolitis); and diphtheroids. The following in vitro data are available, but their clinical significance is unknown. Other organisms that are susceptible to vancomycin in vitro include *Listeria monocytogenes*, *Lactobacillus* species, *Actinomyces* species, *Clostridium* species, and *Bacillus* species.

**ACTIVITY OF VANCOMYCIN IN VITRO**

<table>
<thead>
<tr>
<th>Organism</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Number of Isolates)</td>
<td>(mg/L)</td>
<td>(mg/L)</td>
</tr>
<tr>
<td>S. aureus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>methicillin-susceptible</td>
<td>(90)</td>
<td>1.6</td>
</tr>
<tr>
<td>methicillin-susceptible</td>
<td>(22)</td>
<td>0.7</td>
</tr>
<tr>
<td>methicillin-resistant</td>
<td>(22)</td>
<td>1.6</td>
</tr>
<tr>
<td>methicillin-resistant</td>
<td>(26)</td>
<td>0.4</td>
</tr>
<tr>
<td>S. epidermidis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>methicillin-susceptible</td>
<td>(50)</td>
<td>1.6</td>
</tr>
<tr>
<td>methicillin-resistant</td>
<td>(27)</td>
<td>1.6</td>
</tr>
<tr>
<td>methicillin-resistant</td>
<td>(20)</td>
<td>2</td>
</tr>
<tr>
<td>Coagulase-negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>staphylococcus</td>
<td>(200)</td>
<td>2</td>
</tr>
<tr>
<td>Strep. pyogenes</td>
<td>(110)</td>
<td>0.5</td>
</tr>
<tr>
<td>Strep. pneumoniae</td>
<td>(74)</td>
<td>0.5</td>
</tr>
<tr>
<td>Strep. pneumoniae (penicillin-resistant)</td>
<td>(10)</td>
<td>1</td>
</tr>
<tr>
<td>Strep. bovis</td>
<td>(100)</td>
<td>0.25</td>
</tr>
<tr>
<td>Strep. mutans (viridans group)</td>
<td>(82)</td>
<td>0.8</td>
</tr>
<tr>
<td>E. faecalis (enterococcus)</td>
<td>(347)</td>
<td>1.6</td>
</tr>
<tr>
<td>Diphtheroids (JK strain)</td>
<td>(98)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

VANCOCIN CP powder for injection vial - Product Information  Page 3 of 14
<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Resistance (μg)</th>
<th>Zone Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Listeria sp.</em></td>
<td>(26)</td>
<td>0.8</td>
</tr>
<tr>
<td><em>C. difficile</em></td>
<td>(78)</td>
<td>1</td>
</tr>
<tr>
<td><em>Clostridium sp.</em></td>
<td>(14)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

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 *S. aureus*, nonenterococcal group D streptococci, enterococci, and *Streptococcus* sp. (viridans group). The combination of vancomycin and a cephalosporin acts synergistically against some strains of *S. epidermidis* (methicillin-resistant). The combination of vancomycin and rifampin acts with partial synergism against some strains of *S. aureus* and with synergism against *S. epidermidis*. Synergy testing is helpful because the combination of vancomycin and a cephalosporin may act antagonistically against some strains of *S. epidermidis*, and the combination of vancomycin and rifampin may act antagonistically against some strains of *S. aureus*.

**Disc Susceptibility Tests**—Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. The Bauer-Kirby-Sherris-Turck Method has been recommended for use with discs for testing susceptibility to vancomycin. Results of standard single-dose susceptibility tests with a 30 μg vancomycin hydrochloride disc should be interpreted according to the following criteria. Susceptible organisms produce zones greater than or equal to 12mm, indicating that the test organism is likely to respond to therapy. Organisms that produce zones of 10 or 11 mm are considered to be of intermediate susceptibility. Organisms in this category are likely to respond if the infection is confined to tissues or fluids in which high antibiotic concentrations are attained. Resistant organisms produce zones of 9 mm or less, indicating that other therapy should be selected. With a standardised dilution method, a bacterial isolate may be considered susceptible if the MIC value for vancomycin is 4 mg/L or less. Organisms are considered resistant to vancomycin if the MIC is greater than or equal to 16 mg/L. Organisms having an MIC value of less than 16 mg/L but greater than 4 mg/L are considered to be of intermediate susceptibility.

Standardised procedures require the use of laboratory control organisms. The 30 μg vancomycin disc should give zone diameters between 15 and 19 mm for *S. aureus* ATCC 25923. As with the standard diffusion methods, dilution procedures require the use of laboratory control organisms. Standard vancomycin powder should give MIC values in the range of 0.5 mg/L to 2.0 mg/L for *S. aureus* ATCC 29213. For *E. faecalis* ATCC 29212, the MIC range should be 1.0 to 4.0 mg/L.
INDICATIONS

Vancocin CP is indicated in potentially life-threatening infections which cannot be treated with another effective, less toxic antimicrobial drug, including the penicillins and cephalosporins.

Vancocin CP is useful in therapy of severe staphylococcal (including methicillin-resistant staphylococcal) infections in patients who cannot receive or who failed to respond to the penicillins and cephalosporins or who have infections with staphylococci that are resistant to other antibiotics. Once sensitivity data are available, therapy should be adjusted accordingly.

Vancocin CP is 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*), Vancocin CP is effective only in combination with an aminoglycoside. Vancocin CP is effective for the treatment of diphtheroid endocarditis. Vancocin CP is used in combination with rifampin, an aminoglycoside, or both in early-onset prosthetic valve endocarditis caused by *S. epidermidis* or diphtheroids.

The effectiveness of Vancocin CP has been documented in other infections due to staphylococci including osteomyelitis, pneumonia, septicaemia, and soft tissue infections. When staphylococcal infections are localised 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 Vancocin CP.

Vancocin CP should be administered orally for the treatment of Staphylococcal enterocolitis and antibiotic associated pseudomembranous colitis produced by *C. difficile*. Parenteral administration of Vancocin CP alone is inappropriate for this indication. Vancomycin is not effective by the oral route for other types of infections. For oral administration the parenteral formulation may be used. Some systemic absorption may occur following oral administration in patients with pseudomembranous colitis.

CONTRAINDICATION

Vancocin CP is contraindicated in patients with known hypersensitivity to this antibiotic.
PRECAUTIONS

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

Vancocin CP 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 DOSAGE AND ADMINISTRATION and ADVERSE REACTIONS).

Complications of occasional severe hypotension, histamine like responses and rash can be avoided by slow administration of the recommended dilute solutions over at least one hour for both adults and children.

Vancomycin should be administered with caution in patients allergic to teicoplanin, since allergic cross reactions between vancomycin and teicoplanin have been reported.

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 (see DOSAGE AND ADMINISTRATION, Compatability with Other Drugs and Intravenous Fluids).

Although intravitreal injection is not an approved route of administration for vancomycin, precipitation has also been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles (see DOSAGE AND ADMINISTRATION, Compatability with Other Drugs and Intravenous Fluids).

Because of its ototoxicity and nephrotoxicity, Vancocin CP should be used with care in patients with renal insufficiency. The risk of toxicity is appreciably increased by high blood concentrations or prolonged therapy. If it is necessary to use Vancocin CP in such patients, blood levels should be monitored and appropriate dosage modifications made.

Vancocin CP should be avoided in patients with previous hearing loss. If it is used in such patients, the dose of Vancocin CP should be regulated, if possible by periodic determination of the drug level in the blood. Deafness may be preceded by tinnitus. The elderly are more susceptible to auditory damage. Experience with other antibiotics suggests that deafness may be progressive despite cessation of treatment.

Patients with borderline renal function and individuals over the age of sixty should be given serial tests of auditory function and of vancomycin blood levels.
Vancomycin serum levels may be determined by use of the modified Rammelkamp serial twofold dilution technique with streptococcus C203 as the indicator organism.

All patients receiving the drug should have periodic haematologic studies, urinalyses and liver and renal function tests.

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 Vancocin CP may result in the overgrowth of nonsusceptible organisms. 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.

Vancocin CP is irritating to tissue and causes necrosis when injected intramuscularly; it must be administered intravenously. Pain and thrombophlebitis occur in many patients receiving Vancocin CP and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised if the drug is administered in a volume of at least 200 mL of glucose or saline solution and if the sites of injection are rotated.

Reversible neutropenia has been reported in patients receiving Vancocin CP (see ADVERSE REACTIONS). Patients undergoing prolonged therapy with Vancocin CP or who are receiving concomitant drugs which may cause neutropenia should have periodic monitoring of the leukocyte count.

Neither the safety nor the efficacy of vancomycin administration by the intrathecal or intraventricular routes have been studied. Vancomycin should not be administered by these routes.

Reports have revealed that administration of sterile vancomycin HCl 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 varying degrees of abdominal pain and fever. This syndrome appears to be short-lived after discontinuation of intraperitoneal vancomycin.

**DRUG INTERACTIONS**

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, requires careful monitoring.

In animal studies designed to evaluate nephrotoxicity in the rat, renal impairment occurred with high serum concentrations of vancomycin alone and with lower concentrations when vancomycin was administered with an aminoglycoside.
Combining vancomycin with a loop diuretic in the rat model did not potentiate the renal impairment that occurred with vancomycin alone. When treating patients with underlying renal dysfunction or those 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 in order to minimise the risk of nephrotoxicity.

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

**USE IN PREGNANCY** - Category B2

Animal reproduction studies have not been conducted with VANCOCIN CP. It is also not known whether VANCOCIN CP can affect reproduction capacity. In a controlled clinical study, vancomycin was administered to pregnant women for serious staphylococcal infections complicating intravenous drug abuse to evaluate potential ototoxic and nephrotoxic effects on the infant. 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. As only 10 patients were treated with vancomycin in this study, and administration was only in the second and third trimesters, it is not known whether vancomycin causes foetal harm. VANCOCIN CP should be given to a pregnant woman only if clearly needed.

**USE IN LACTATION**

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

**USE IN PAEDIATRICS**

(see PRECAUTIONS)—In premature neonates, infants and children, it is appropriate to confirm vancomycin serum concentrations. Concomitant administration of vancomycin and anaesthetic agents has been associated with erythema and histamine-like flushing in children (see ADVERSE REACTIONS).
USE IN GERIATRICS

(see PRECAUTIONS)--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).

ADVERSE REACTIONS

Infusion-Related Events--During or soon after infusion of Vancocin CP, patients may develop anaphylactoid reactions including hypotension, palpitations, substernal pressure, tachycardia, wheezing, dyspnoea, urticaria, or pruritus. Severe anaphylactoid reactions require immediate treatment with adrenaline, corticosteroids and oxygen. Rapid infusion may 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. In animal studies, hypotension and bradycardia occurred in animals given large doses of vancomycin at high concentrations and rates. Such events are infrequent if Vancocin CP is given by a slow infusion over 60 minutes and at a sufficient dilution. In a study using multiple infusion rates, infusion-related events were not reported by the 4 volunteers administered vancomycin hydrochloride at a rate of 10 mg/min or less.

Gastrointestinal--Oral doses of vancomycin are extremely unpalatable and have been associated with nausea, diarrhoea and occasional vomiting.

Nephrotoxicity--Rarely, renal failure, principally manifested by increased serum creatinine or urea concentrations, especially in patients given large doses of vancomycin hydrochloride, has been reported. Rare cases of interstitial nephritis have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had preexisting kidney dysfunction. When Vancocin CP was discontinued, uraemia resolved in most patients.

Transient elevations of urea and granular casts in the urine occasionally occur.

Ototoxicity--There have been reports of hearing loss associated with Vancocin CP. Most of these patients had kidney dysfunction, preexisting hearing loss, or concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have also been reported rarely.

Haematological--Some patients have been reported to have developed reversible neutropenia, usually starting one week or more after onset of therapy with Vancocin CP or after a total dose of more than 25 g. Neutropenia appears to be promptly reversible when Vancocin CP is discontinued. Thrombocytopenia has rarely been reported. Eosinophilia has also been reported. Although a causal relationship has not been established, reversible agranulocytosis (granulocyte count less than 500/mm³) has been reported rarely.
Liver Function—Elevation of liver transaminases.

Phlebitis--Inflammation at the injection site has been reported.

Immunological--Hypersensitivity reactions with chills, nausea, urticaria, rashes, including exfoliative dermatitis, Linear IgA bullous dermatosis; Stevens-Johnson Syndrome, toxic epidermal necrolysis and rare cases of vasculitis, fever and rigors. Anaphylactoid reactions have been reported infrequently.

General--The use of Vancocin CP may result in overgrowth of nonsusceptible organisms. If new infections due to bacteria or fungi appear during therapy with this product, appropriate measures should be taken.

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

**DOSAGE AND ADMINISTRATION**

Infusion-related events are related to both concentration and 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. Infusion-related events may occur, however, at any rate or concentration.

Patients with Normal Renal Function:

**Adults:**
The usual intravenous dose is 500 mg (in 0.9 percent Sodium Chloride injection or 5 percent glucose in Sterile Water for Injection) every six hours or 1 g every twelve 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 daily dose.

The majority of patients with infections caused by organisms susceptible to the antibiotic show a therapeutic response by forty-eight to seventy-two hours. The total duration of therapy is determined by the type and severity of the infection and the clinical response of the patient. In staphylococcal endocarditis, therapy for three weeks or longer is recommended.

**Children:**
The paediatric dosage of Vancocin CP is calculated on the basis of 10 mg/kg of body weight every six hours after an initial loading dose of 15 mg/kg. Each dose should be administered over a period of at least 60 minutes.
Infants and Neonates:
In neonates and young infants, the total daily intravenous dosage may be lower. An initial dose of 15 mg/kg is suggested, followed by 10 mg/kg every 12 hours in the first week of life and every 8 hours thereafter until one month of age. Each dose should be administered over 60 minutes. Close monitoring of serum vancomycin concentrations is mandatory 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 in the elderly, dosage reduction may be necessary to a greater extent than expected because of decreasing renal function. Measurement of vancomycin serum concentrations is required to optimise therapy, especially in seriously ill patients with changing renal function. Vancomycin serum concentrations may be determined by use of a microbiologic assay, a radioimmunoassay, a fluorescence polarisation immunoassay, a fluorescence immunoassay, or high-pressure liquid chromatography.

For most patients with renal impairment or the elderly, the dosage calculations may be made by using the following table. The Vancocin CP dose per day in mg is about 15 times the glomerular filtration rate in mL/min. (see table below).

### DOSAGE TABLE FOR VANCOMYCIN IN ADULT PATIENTS WITH IMPAIRED RENAL FUNCTION

<table>
<thead>
<tr>
<th>Creatinine Clearance mL/min</th>
<th>Vancomycin Dose mg/24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>1545</td>
</tr>
<tr>
<td>90</td>
<td>1390</td>
</tr>
<tr>
<td>80</td>
<td>1235</td>
</tr>
<tr>
<td>70</td>
<td>1080</td>
</tr>
<tr>
<td>60</td>
<td>925</td>
</tr>
<tr>
<td>50</td>
<td>770</td>
</tr>
<tr>
<td>40</td>
<td>620</td>
</tr>
<tr>
<td>30</td>
<td>465</td>
</tr>
<tr>
<td>20</td>
<td>310</td>
</tr>
<tr>
<td>10</td>
<td>155</td>
</tr>
</tbody>
</table>

**Loading dose** The initial dose should be no less than 15 mg/kg even in patients with mild to moderate renal insufficiency.

**Anephric patients** 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 in order to promptly achieve therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 h. Since individual maintenance doses of 250 to 1000 mg are convenient, in patients with marked renal impairment, a dose may be
given every several days rather than on a daily basis. In anuria a dose of 1000 mg every 7 to 10 days has been recommended.

**PREPARATION OF SOLUTION:** At the time of use, add 10 mL of Sterile Water for Injection to the vial of dry, sterile Vancocin CP, 500 mg or 20 mL of Sterile Water for Injection to the vial of Vancocin CP, 1 g.

**FURTHER DILUTION IS REQUIRED, READ INSTRUCTIONS WHICH FOLLOW:**

1. Intermittent infusion is the preferred method of administration. The solution containing 500 mg (500,000 IU) vancomycin activity can be added to 100-200 mL of 0.9 percent Sodium Chloride Injection or 5 percent Glucose in Sterile Water for Injection. The solution containing 1 g (1,000,000 IU) vancomycin activity can be added to 200-400 mL of 0.9 percent Sodium Chloride injection or 5 percent Glucose in Sterile Water for Injection. The desired dose, diluted in this manner to a concentration of 2.38-4.55 g per L may be administered by intravenous infusion over a period of at least 60 minutes every 6 or 12 hours.

2. Continuous infusion (should be used only when intermittent infusion is not feasible). One to 2 g (1,000,000 to 2,000,000 IU) vancomycin activity can be added to a sufficiently large volume of 0.9 percent Sodium Chloride Injection or 5 percent Glucose in Sterile Water for Injection to permit the desired daily dose to be administered slowly by intravenous infusion over a twenty-four hour period.

**Compatibility with Other Drugs and Intravenous Fluids--**The following diluents are physically and chemically compatible (with 4 g/L Vancocin CP):

- 5% Glucose Solution
- 5% Glucose and 0.9% Sodium Chloride Solution
- Hartmann's Solution
- Hartmann's and 5% Glucose Solution
- 0.9% Sodium Chloride Solution

To avoid microbiological hazards, the solutions should be used as soon as possible after preparation.

Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution or container permits.

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 also been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles.

For Oral Administration:--The usual adult total daily dosage for antibiotic-associated pseudomembranous colitis produced by *C. difficile* and Staphylococcal enterocolitis is 500 mg to 2 g given in 3 or 4 divided doses for 7 to 10 days. The total daily dosage in children is 40 mg/kg of body weight in 3 or 4 divided doses. The total daily dosage should not exceed 2 g. The appropriate dose may be diluted in 30 mL of distilled or deionised water and given to the patient to drink, or the diluted material may be administered via nasogastric tube. Common flavouring syrups may be added to the solution to improve the taste for oral administration.

**STABILITY OF PREPARED SOLUTION**

After reconstitution with Water for Injection, 5% Glucose injection or 0.9% Sodium Chloride Injection, the solution may be stored in a refrigerator for 24 hours without significant loss of potency. To reduce microbiological hazards, the solution should be used as soon as practicable after reconstitution.

**OVERDOSAGE**

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Haemoperfusion with Amberlite resin XAD-4 has been reported to be of limited benefit. Haemofiltration and haemoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance.

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

Contact the Poisons Information Centre on 13 11 26 for advice on management.

**PRESENTATION AND STORAGE CONDITIONS**

Vancocin CP (vancomycin hydrochloride) 500 mg (500,000 IU) vancomycin activity, 10 mL size, rubber-stoppered vials. Available in packs of 1 vial and packs of 10 vials.

Vancocin CP (vancomycin hydrochloride) 1 g (1,000,000 IU) vancomycin activity, 20 mL size, rubber-stoppered vials. Available in packs of 1 vial and packs of 10 vials.
Prior to reconstitution: store below 25°C.

POISON SCHEDULE

Prescription Only Medicine (S4)

SPONSOR

Aspen Pharmacare Australia Pty Ltd
34-36 Chandos St
St Leonards NSW 2065
Australia

DATE OF TGA APPROVAL

Approved by the Therapeutic Goods Administration: February 23 1995
Date of most recent amendment: 18 August 2010