**NAME OF THE MEDICINE**

Active ingredient: Vancomycin hydrochloride

**DESCRIPTION**

Vancomycin is an amphoteric glycopeptide antimicrobial substance produced by the growth of certain strains of *Amycolatopsis orientalis* (formerly *Nocardia orientalis*). It is bactericidal against many gram-positive organisms. Vancomycin is not chemically related to any of the presently used antimicrobial agents.

Vancomycin Hydrochloride is freely soluble in water and insoluble in alcohol.

Vancomycin Hydrochloride for Intravenous Infusion is a lyophilized powder for reconstitution. When reconstituted in water, it is a clear solution with a pH of 2.8 to 4.5. It should be administered intravenously in dilute solution. (See **Dosage and administration**).
PHARMACOLOGY

Pharmacokinetics

Vancomycin is poorly absorbed by mouth. It is given intravenously for the treatment of systemic infections. In subjects with normal renal function participating in a multi-dose study, 1 g (1,000,000 IU) given over 60 minutes produced mean plasma levels of approximately 63 microgram/mL immediately after the completion of infusion, and mean plasma levels of approximately 23 microgram/mL and approximately 8 microgram/mL at 2 hours and 11 hours respectively, after completion of the infusion. Serum levels will be higher in patients with renal impairment, and toxicity may result.

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 the urine by glomerular filtration. Mean plasma clearance is about 0.06 L/kg/hour, and mean renal clearance is about 0.05 L/kg/hour. 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.

Vancomycin is not effectively removed by either haemodialysis or peritoneal dialysis; there have been no reports of vancomycin clearance with haemoperfusion.

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 microgram/mL. 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. Vancomycin does not readily diffuse across the meninges into the cerebrospinal fluid.

Measurable serum concentrations of vancomycin may occur in patients treated with oral vancomycin for active pseudomembranous colitis due to Clostridium difficile.

Microbiology

Vancomycin is active against many gram-positive organisms (See below). Gram-negative bacteria, mycobacteria and fungi are resistant. Many strains of gram-positive bacteria are sensitive in vitro to vancomycin concentrations of 0.5 to 5 microgram/mL, but a few Staph. aureus strains require 10 to 20 microgram/mL for inhibition.

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); Clostridium difficile (e.g. toxigenic strains implicated in pseudomembranous enterocolitis); diphtheroids (e.g. JK corynebacterium). The in vitro susceptibility data are listed in Table 1, 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.

**Table 1** – Vancomycin *in vitro* activity

<table>
<thead>
<tr>
<th>Organism</th>
<th>Number of isolates</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt; (mg/L)</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt; (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>methicillin susceptible</td>
<td>90</td>
<td>1.6</td>
<td>3.1</td>
</tr>
<tr>
<td>methicillin susceptible</td>
<td>22</td>
<td>0.7</td>
<td>0.9</td>
</tr>
<tr>
<td>methicillin resistant</td>
<td>22</td>
<td>1.6</td>
<td>3.1</td>
</tr>
<tr>
<td>methicillin resistant</td>
<td>26</td>
<td>0.4</td>
<td>0.4</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>methicillin susceptible</td>
<td>50</td>
<td>1.6</td>
<td>6.3</td>
</tr>
<tr>
<td>methicillin resistant</td>
<td>27</td>
<td>1.6</td>
<td>3.1</td>
</tr>
<tr>
<td>methicillin resistant</td>
<td>20</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Coagulase negative staphylococcus</td>
<td>200</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>110</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td><em>Streptococcus pneumoniae</em></td>
<td>74</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>(penicillin resistant)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Streptococcus bovis</em></td>
<td>100</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td><em>Streptococcus mutans</em></td>
<td>82</td>
<td>0.8</td>
<td>1.6</td>
</tr>
<tr>
<td>(viridans group)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>347</td>
<td>1.6</td>
<td>1.6</td>
</tr>
<tr>
<td>Diphtheroids (JK strain)</td>
<td>98</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Listeria sp.</td>
<td>26</td>
<td>0.8</td>
<td>1.6</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>78</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><em>Clostridium sp.</em></td>
<td>14</td>
<td>0.8</td>
<td>3.1</td>
</tr>
</tbody>
</table>

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

The combination of vancomycin and a cephalosporin acts synergistically against some strains of *S. epidermidis* (methicillin-resistant). The combination of vancomycin and rifampicin 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 rifampicin may act antagonistically against some strains of *S. aureus*.

Vancomycin appears to act by inhibiting the production of bacterial cell wall mucopeptide. This effect occurs at a site different from that affected by penicillins and produces immediate inhibition of cell wall synthesis and secondary damage to the cytoplasmic membrane. There is also evidence that vancomycin alters the permeability of the cell membrane and selectively inhibits RNA synthesis.

**Susceptibility tests**

Dilution or diffusion techniques, either quantitative (MIC) or breakpoint, should be used following a regularly updated, recognised and standardised method (e.g. NCCLS). Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.
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 medicine 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.

Note: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

**INDICATIONS**

Vancomycin Hydrochloride for Intravenous Infusion is indicated for potentially life threatening infections which cannot be treated with another effective, less toxic antimicrobial drug, including the penicillins and cephalosporins.

Vancomycin is useful in therapy of severe staphylococcal (including methicillin-resistant staphylococcal) infections in patients who cannot receive or who have 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.

Vancomycin is effective alone or in combination with an aminoglycoside for endocarditis caused by *Strep. viridans* or *Strep. bovis*. For endocarditis caused by Enterococci (eg *Enterococcus faecalis*), vancomycin is effective only in combination with an aminoglycoside. Vancomycin is effective for the treatment of diphtheroid endocarditis. Vancomycin is used in combination with rifampicin, an aminoglycoside, or both in early onset prosthetic valve endocarditis caused by *Staph. epidermidis* or diphtheroids.

The effectiveness of vancomycin has been documented in other infections due to staphylococci including osteomyelitis, pneumonia, sepsicaemia and, skin and skin structure infections. When staphylococcal infections are localised and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

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

Vancomycin should be administered orally for the treatment of staphylococcal enterocolitis and antibiotic associated pseudomembranous colitis (produced by *C. difficile*). Parenteral administration of vancomycin 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.
CONTRAINDICATIONS

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

PRECAUTIONS

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

Vancomycin Hydrochloride for Intravenous Infusion should be administered in a dilute solution at a rate not exceeding 500 milligram/hour to avoid rapid infusion related reactions, e.g. hypotension, flushing, erythema, urticaria and pruritus. Stopping the infusion usually results in a prompt cessation of these reactions (See Dosage and Administration and Adverse Effects).

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.

When given intravenously, toxic serum levels can occur. Vancomycin is excreted fairly rapidly by the kidney and blood levels increase markedly with decreased renal clearance. During parenteral therapy, the risk of toxicity and nephrotoxicity appears appreciably increased by high blood concentrations or prolonged treatment.

Because of its ototoxicity and nephrotoxicity, vancomycin should be used with care in patients with renal insufficiency. If it is necessary to use vancomycin parenterally in patients with renal impairment, the dose and/or dose intervals should be adjusted carefully (See Dosage and Administration) and blood levels monitored. Serial monitoring of renal function should be performed.

When patients receive concomitant therapy with an aminoglycoside, serial monitoring of renal function should be performed.

Ototoxicity has occurred when serum levels exceeded 80 microgram/mL. It may be transient or permanent. 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.

Vancomycin should be avoided (if possible) in patients with previous hearing loss. If it is used in such patients, the dose of vancomycin should be regulated by periodic determination of medicine levels in the blood. Patients with renal insufficiency and individuals over the age of 60 should be given serial tests of auditory function and of vancomycin blood levels. All patients receiving the medicine should have periodic hematologic studies, urinalyses, and liver and renal function tests.

Some patients with inflammatory disorders of the intestinal mucosa may have significant systemic absorption of oral vancomycin and, therefore, may be at risk for the development of adverse reactions associated with the parenteral administration of vancomycin. The risk is greater if renal impairment is present. It should be noted that the total systemic and renal clearances of vancomycin are reduced in the elderly.
Concurrent and sequential use of other neurotoxic and/or nephrotoxic antibiotics, particularly ethacrynic acid, neuromuscular blocking agents, aminoglycoside antibiotics, polymixin B colistin, viomycin and cisplatin requires careful monitoring.

Reversible neutropenia has been reported in patients receiving Vancomycin Hydrochloride (See Adverse Effects). Patients who will undergo prolonged therapy with vancomycin or those who are receiving concomitant medicines which may cause neutropenia should have periodic monitoring of the leukocyte count.

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 Compatibility with other medicines and intravenous fluids).

Since vancomycin is irritating to tissue and causes medicine fever, pain and possibly necrosis, it should never be injected intramuscularly; it must be administered intravenously. Pain and thrombophlebitis occur in many patients receiving vancomycin and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised if the medicine is administered in a volume of at least 200 mL of glucose or saline solution and if the injection sites are rotated.

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

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.

If parenteral and oral vancomycin are administered concomitantly, an additive effect can occur. This should be taken into consideration when calculating the total dose. In this situation, serum levels of the antibiotic should be monitored.

In surgical patients, the administration of vancomycin should be carefully timed in relation to the induction of anaesthesia (See Interactions with other medicines).

The use of vancomycin may result in overgrowth of non-susceptible organisms. If new infections due to bacteria or fungi appear during therapy with this product, appropriate measures should be taken including withdrawal of vancomycin. In rare instances there have been reports of pseudomembranous colitis due to *C. difficile* developing in patients who received intravenous vancomycin.

Patients taking oral vancomycin should be warned of its offensive taste.

**Carcinogenicity and mutagenicity**

No long term carcinogenicity studies have been performed using vancomycin in animals. There are no studies available demonstrating the mutagenic potential of vancomycin.
Effects on Fertility

No definitive fertility studies have been performed.

Use in Pregnancy (Category B2)

Animal reproduction studies have not been conducted with vancomycin hydrochloride. It is not known whether vancomycin hydrochloride can affect reproduction capacity. In a controlled clinical study, vancomycin was administered to pregnant women for serious staphylococcal infections complicating intravenous medicine 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. Vancomycin Hydrochloride for Intravenous Infusion should be given to a pregnant woman only if clearly needed.

Australian categorisation definition of Category B2:

Medicines which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of foetal damage.

Use in Lactation

Vancomycin is excreted in breast milk but it is not known whether it is harmful to the newborn. Therefore, it is not recommended for nursing mothers unless the expected benefits outweigh any potential risk.

Paediatric use

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 Effects).

Use in the elderly

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).

Interactions with other medicines

Concurrent administration with other neurotoxic or nephrotoxic medicines, e.g. streptomycin, neomycin, gentamicin, kanamycin, amikacin, amphotericin B, bacitracin, tobramycin, polymyxin B, colistin and cisplatin, requires careful monitoring.

In order to minimise the risk of nephrotoxicity 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 (See Dosage and Administration).

Diuretics such as ethacrynic acid and frusemide may aggravate ototoxicity.

Cholestyramine has been shown to bind vancomycin in vitro. Therefore, if oral vancomycin is used with cholestyramine, the two medicines should be administered several hours apart.

Reversible neutropenia has been reported in patients receiving Vancomycin Hydrochloride (See Adverse Effects). Patients who are receiving concomitant medicines which may cause neutropenia should have periodic monitoring of the leukocyte count.

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 vancomycin at a rate not exceeding 500 milligram/hour prior to anaesthetic induction.

Vancomycin may enhance neuromuscular blockade produced by medicines such as suxamethonium or vecuronium.

**ADVERSE EFFECTS**

**Infusion related events**

During or soon after infusion of vancomycin, 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. Such events are infrequent if vancomycin is given by a slow infusion at a rate not exceeding 500 milligram/hour and at an appropriate dilution.

**Auditory and vestibular disorders**

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

**Cardiovascular**

Hypotension, palpitations, substernal pressure, tachycardia (See Infusion related events).

**Dermatological**

Pruritus at injection site, generalised flushing, erythematous macular rash with intense pruritus over face, neck and upper body have occurred after too rapid injection of the medicine. Tissue irritation and necrosis occurs after intramuscular injection or extravasation from the intravenous site.
Gastrointestinal

Oral doses are extremely unpalatable. In leukaemic patients, oral dosing regimens are associated with frequent nausea, diarrhoea and occasional vomiting.

Haematological

Some patients have been reported to have developed reversible neutropenia, usually starting one week or more after onset of therapy with vancomycin or after a total dose of more than 25 grams. Neutropenia appears to be promptly reversible when vancomycin is discontinued. Thrombocytopenia has rarely been reported. Eosinophilia has also been reported. Although a casual relationship has not been established, reversible agranulocytosis (granulocyte count less than 500/mm$^3$) has been reported rarely.

Immunological

Hypersensitivity reactions with chills, nausea, urticaria, macular rash, fever and rigors. The types of rashes that can occur include exfoliative dermatitis, Linear IgA bullous dermatosis, Stevens-Johnson syndrome, toxic epidermal necrolysis and rare cases of vasculitis. Anaphylactoid reactions have been reported infrequently (See Infusion related events).

Renal and Urinary tract disorders

Rarely, renal failure, principally manifested by increased serum creatinine or urea concentrations, especially in patients given large doses of vancomycin, has been reported. Rare cases of interstitial nephritis have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had pre-existing kidney dysfunction. When vancomycin was discontinued, uraemia resolved in most patients. Transient elevations of urea and granular casts in the urine occasionally occur.

Hepatobiliary disorders

Elevation of liver transaminases.

General disorders

The use of vancomycin may result in overgrowth of non-susceptible organisms resulting in new bacterial or fungal infections. If the 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).

Phlebitis (Inflammation at the injection site has been reported).

DOSAGE AND ADMINISTRATION

This product is for single use in one patient only. Discard any residue.

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/minute are recommended in adults (see also age specific recommendations). In selected patients in need of fluid restriction, a
concentration of up to 10mg/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.

**Normal renal function - Adults**

The usual intravenous dose is 500 milligrams every 6 hours or 1 g every 12 hours. A 500 milligram dose of vancomycin should be infused over a period of at least 60 minutes, whereas a 1 g dose should be administered over a period of at least two hours. Vancomycin must not be given by intramuscular injections (See Precautions).

Each dose should be administered at no more than 10 mg/minute 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.

**Adults with impaired renal function and the elderly**

Dosage adjustment must be made in patients with impaired renal function to avoid toxic serum levels. 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 microbiological 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 vancomycin dose per day in milligrams is about 15 times the glomerular filtration rate in mL/minute (See table below).

**Vancomycin**

Dosage in patients with impaired renal function

<table>
<thead>
<tr>
<th>Creatinine clearance mL/minute</th>
<th>Vancomycin dose milligram/24 hours</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 milligram/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 milligram/kg bodyweight should be given in order to promptly achieve therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 milligram/kg/24 hours. Since individual maintenance doses of 250 (250,000 IU) to 1,000 (1,000,000 IU) milligrams 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 1,000 milligrams every seven to ten days has been recommended.

The majority of patients with infections caused by organisms susceptible to the antibiotic show a therapeutic response by 48 to 72 hours. The total duration of therapy is determined by the type and severity of 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 vancomycin is calculated on the basis of 10 milligram/kg bodyweight every six hours after an initial loading dose of 15 milligram/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 milligram/kg is suggested, followed by 10 milligram/kg every twelve hours in the first week of life and every eight hours thereafter until one month of age. Close monitoring of serum vancomycin concentrations is mandatory in these patients. Each dose should be administered over a period of at least 60 minutes.

Oral administration

The usual adult total daily dosage for antibiotic associated pseudomembranous colitis produced by *C. difficile* and staphylococcal enterocolitis is 500 milligrams to 2 g given in three or four divided doses for 7 to 10 days. The total daily dosage in children is 40 milligram/kg bodyweight in three or four divided doses. The total daily dosage should not exceed 2 g.

After initial reconstitution of the vial 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.

Preparation of solution for injection

At the time of use, the 500 milligram (500,000 IU) vial should be reconstituted with 10 mL of Water for Injections. The resulting solution contains vancomycin 50 milligram/mL. The 1 g (1,000,000 IU) vial should be reconstituted with 20 mL of Water for Injections. The resulting solution contains vancomycin 50 milligram/mL. The reconstituted solution containing 500 milligrams of vancomycin must be further diluted with at least 100 mL of Sodium Chloride Intravenous Infusion 0.9% or Glucose Intravenous Infusion 5%. The reconstituted solution containing 1 g of vancomycin must be further diluted with at least 200 mL of Sodium Chloride Intravenous Infusion 0.9% or Glucose Intravenous Infusion 5%. The resulting solution should be infused over a period of at least 60 minutes when 500 milligrams of vancomycin is to be
administered, or at least 2 hours when 1 g of vancomycin is to be given. In selected patients in need of fluid restriction, a concentration of up to 10 mg/mL may be used; use of such higher concentration may increase the risk of infusion related events. Infusion related events may occur, however, at any rate of concentration.

Stability of reconstituted solution

To reduce microbiological hazard, use as soon as practicable after dilution. If storage is necessary, hold at 2 to 8°C for not more than 24 hours.

Compatibility with other medicines and intravenous fluids

Vancomycin hydrochloride solutions have a low pH and may cause chemical or physical instability when mixed with other compounds. All parenteral medicine products should be inspected visually for both particulate matter and discoloration prior to administration, whenever solution or container permits.

OVERDOSAGE

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is not effectively removed by either haemodialysis or peritoneal dialysis. Haemoperfusion with Amberlite resin XAD-4 has been reported to be of limited benefit. Haemofiltration and heamoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance.

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

Contact the Poisons Information Centre on 131126 (Australia) for advice on the management of overdosage.

PRESENTATION AND STORAGE CONDITIONS

Store vials prior to reconstitution below 25°C. Protect from light. See also Dosage and Administration Stability of reconstituted solution.

Vials containing 500 mg (500,000 IU) of vancomycin, activity, freeze dried powder:

Vancomycin Alphapharm 500 mg (as hydrochloride) powder for Injection Vial

Vials containing 1 g (1,000,000 IU) of vancomycin activity, freeze dried powder:

Vancomycin Alphapharm 1 g (as hydrochloride) powder for Injection Vial

POISON SCHEDULE OF THE MEDICINE

S4 – Prescription Only Medicine
NAME AND ADDRESS OF THE SPONSOR

Alphapharm Pty Limited

Cnr Wentworth Park Road & Bay Street

Glebe NSW 2037

ABN 93 002 359 739

www.alphapharm.com.au

DATE OF APPROVAL

Approved by the Therapeutic Goods Administration on 6 July 2010.