This preparation for the treatment of colitis is for oral use only. Vancocin must be given orally for treatment of staphylococcal enterocolitis and antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*. If parenteral vancomycin therapy is desired, use VANCOCIN CP (Sterile Vancomycin Hydrochloride), Intravenous, and consult package insert accompanying that preparation. Parenteral administration of VANCOCIN CP is not effective for treatment of staphylococcal enterocolitis and antibiotic-associated pseudomembranous colitis produced by *Clostridium difficile*; therefore, Vancocin HCl must be given orally for these indications. Orally administered VANCOCIN is not effective for other types of infections.

**NAME OF THE MEDICINE**

Vancomycin hydrochloride  
Chemical formula: C_{66}H_{75}Cl_{2}N_{9}O_{24}.HCl  
The molecular weight is 1486; 500 mg of the base is equivalent to 0.34 mmol.  
The CAS number is 1404-93-9.

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

Vancomycin hydrochloride is a mixture of related glycopeptides, consisting principally of vancomycin B, a substance produced by certain strains of *Amycolatopsis orientalis* or obtained by any other means. It is a white or almost white, hygroscopic powder; freely soluble in water; slightly soluble in alcohol. A 5% solution in water has a pH of 2.5 to 4.5.

Vancocin Capsules contain vancomycin hydrochloride as the active ingredient. It is available in strengths of 125 mg and 250 mg. The excipients are macrogol 6000, gelatin, indigo carmine, iron oxide red, iron oxide yellow (125 mg), iron oxide black (250 mg) and titanium dioxide.

CLINICAL PHARMACOLOGY

Vancomycin is poorly absorbed after oral administration. In a comparative bioavailability study of the capsule dosage form and the oral solution dosage form, there were no significant differences in serum or faecal concentrations. During multiple dosing of 250 mg every 8 hours for seven doses, faecal concentrations of vancomycin in volunteers exceeded 100 mg/kg in the majority of samples. No blood levels were detected and urinary recovery did not exceed 0.76%.

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 *C. difficile* (e.g. toxigenic strains implicated in pseudomembranous enterocolitis). It is also active against staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains).

Many strains of streptococci and *C. difficile*, are susceptible *in vitro* to concentrations of less than 5 mg/L. A small proportion of *S. aureus* strains require 10 to 20 mg/L for inhibition.

Vancomycin is not active *in vitro* against gram-negative bacilli, mycobacteria or fungi.

Disc Susceptibility Tests. – Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One such procedure has been recommended for use with discs for testing susceptibility to vancomycin. Interpretations correlate zone diameters of the disc test with minimum inhibitory concentrations (MIC) values for Vancocin. With the procedure, a report from the laboratory of “resistant” indicates that the infecting organism is not likely to respond to therapy. A report of “intermediate susceptibility” suggests that the organism would be susceptible if the infection is confined to the urine, in which high antibiotic levels can be obtained, or if high dosage is used in other types of infection.
If the Bauer-Kirby method of disc susceptibility testing is used, a 30 µg disc of Vancocin should produce a zone of more than 11 mm when tested against a vancomycin-susceptible bacterial strain.

INDICATIONS

Vancocin capsules may be administered orally for the treatment of staphylococcal enterocolitis and antibiotic-associated pseudomembranous colitis produced by *C. difficile*. Parenteral administration of Vancocin is not effective for the above indications; therefore Vancocin must be given orally. Vancocin is not effective by the oral route for other types of infection.

CONTRAINDICATION

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

PRECAUTIONS

Clinically significant serum concentrations have been reported in some patients who have taken multiple oral doses of vancomycin for active *C. difficile*-induced pseudomembranous colitis; therefore, monitoring of serum concentrations may be appropriate in these patients.

Significant systemic absorption of orally administered vancomycin has been reported in some patients with inflammatory disorders of the intestinal mucosa. Therefore, patients treated with Vancocin capsules may be at risk for the development of adverse reactions associated with the parenteral administration of vancomycin. See package insert accompanying the intravenous preparation. 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. The need for estimation of serum levels and dosage adjustment should be considered in such cases.

Ototoxicity has occurred in patients receiving Vancocin. It may be transient or permanent. It has been reported mostly in patients who have been given excessive intravenous doses, who have an underlying hearing loss, or who are receiving concomitant therapy with another ototoxic agent such as an aminoglycoside or have impaired renal clearance of vancomycin (e.g. in the elderly). Serial tests of auditory function may be helpful in order to minimise the risk of ototoxicity and are recommended, particularly in patients at risk and those with other special sensory impairment (e.g. blindness). Vancocin capsules should be avoided in patients with previous hearing loss unless no other appropriate therapy is available.

When treating patients with underlying renal dysfunction or those patients receiving concomitant therapy with a potentially nephrotoxic drug, including aminoglycosides, serial monitoring of renal function should be performed.

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Prolonged use of vancomycin 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.

**Use in Pregnancy:** Category B2

Animal reproduction studies have not been conducted with Vancocin. It is also not known whether Vancocin can affect reproduction capacity. In a controlled clinical study vancomycin was administered intravenously 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 capsules should be given to a pregnant woman only if clearly needed.

**Use in Lactation**

Vancomycin hydrochloride is excreted in human milk after intravenous administration. 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.

**ADVERSE REACTIONS**

Vancocin capsules may cause indigestion, stomach ache, nausea, chills, diarrhea and occasionally vomiting. Because oral vancomycin may be absorbed in some patients, the possibility of other adverse effects normally associated with parenteral administration (see below) should be borne in mind.

**Nephrotoxicity** – Cases of increased serum creatinine or BUN concentrations and rare cases of interstitial nephritis in patients given intravenously administered Vancocin have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had pre-existing kidney dysfunction. When Vancocin was discontinued, azotemia resolved in most patients.

**Ototoxicity** – Cases of hearing loss associated with intravenously administered Vancocin have been reported. Most of these patients had kidney dysfunction, pre-existing hearing loss, or concomitant treatment with an ototoxic drug. Vertigo, dizziness and tinnitus have been reported rarely.

**Haematological** – Patients have been reported to have developed reversible neutropenia, usually starting one week or more after onset of intravenous therapy with Vanocin or after a total dose of more than 25 g. Neutropenia appears to be promptly reversible when Vancocin 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/mm$^3$) has been reported rarely.

**Liver Function** - elevation of liver transaminases

**Sensitivity Reactions** – Infrequently, patients have been reported to have anaphylaxis, urticaria, pruritis, drug fever, hypotension, wheezing, dyspnoea, flushing of the upper body (“red neck”), pain and muscle spasm of the chest and back, and rashes including exfoliative dermatitis, Stevens-Johnson Syndrome, toxic epidermal necrolysis and rare cases of vasculitis in association with Vancocin.

**DOSAGE AND ADMINISTRATION**

**Adults** – The usual daily dosage for staphylococcal enterocolitis and for antibiotic induced pseudomembranous colitis produced by *C. difficile* is 250 mg 6 hourly for 5-10 days. However doses of 500 mg to 2 g orally administered in 3 or 4 divided doses for 7-10 days have been used for the treatment of antibiotic associated pseudomembranous colitis produced by *C. difficile*. Vancomycin is not effective by the oral route for other types of infections.

**Children** – The usual daily dose is 20 mg/kg orally in 4 divided doses but doses of up to 40 mg/kg/day may be used. The total daily dose should not exceed 2 g.

**OVERDOSAGE**

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Haemofiltration and haemoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance.

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

**PRESENTATION AND STORAGE CONDITIONS**

VANCOCIN 125 mg Capsules are peach and dark blue in colour (20’s)
VANCOCIN 250 mg Capsules are mushroom grey and dark blue in colour (20’s)

Store at controlled room temperature, below 25°C.

**POISON SCHEDULE**

Prescription Only Medicine (S4)

**SPONSOR**

Aspen Pharmacare Australia Pty Ltd
34-36 Chandos St
St Leonards NSW 2065
TGA Approval: 13 August 1992
Date of most recent amendment: 17 March 2009