

Package leaflet: Information for the user
Vancomycin 500mg and 1g Powder for Solution for Infusion
vancomycin hydrochloride

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or nurse.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What vancomycin is and what it is used for
2. What you need to know before you are given vancomycin
3. How to use vancomycin
4. Possible side effects
5. How to store vancomycin
6. Contents of pack and further information

1. What vancomycin is and what it is used for

Vancomycin is an antibiotic that belongs to a group of antibiotics called "glycopeptides". Vancomycin works by eliminating certain bacteria that cause infections.

Vancomycin powder is made into a solution for infusion or oral solution.

Vancomycin is used in in all age groups by infusion for the treatment of the following serious infections:

- Infections of the skin and tissues below the skin.
- Infections of bone and joints.
- An infection of the lungs called "pneumonia".
- Infection of the inside lining of the heart (endocarditis) and to prevent endocarditis in patients at risk when undergoing major surgical procedures.
- Infection in central nervous system,
- Infection in the blood linked to the infections listed above.

Vancomycin can be given orally in adults and children for the treatment of infection of the mucosa of the small and the large intestines with damage to the mucosae (pseudomembranous colitis), caused by the *Clostridium difficile* bacterium.

2. What you need to know before you are given vancomycin

Do not use Vancomycin

- If you are allergic to vancomycin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or hospital pharmacist or nurse before using Vancomycin if:

- You suffered a previous allergic reaction to teicoplanin because this could mean you are also allergic to vancomycin.
- You have a hearing disorder, especially if you are elderly (you may need hearing tests during treatment).
- You have kidney disorder (you will need to have your blood and kidneys tested during treatment).
- You are receiving vancomycin by infusion for the treatment of the diarrhoea associated to *Clostridium difficile* infection instead of orally.

Talk to your doctor or hospital pharmacist or nurse during treatment with Vancomycin if:

- You are receiving vancomycin for a long time (you may need to have your blood, hepatic and kidneys tested during treatment).
- You develop any skin reaction during the treatment.
- You develop severe or prolonged diarrhoea during or after using vancomycin, consult your doctor immediately. This may be a sign of bowel inflammation (pseudomembranous colitis) which can occur following treatment with antibiotics.

Children

Vancomycin will be used with particular care in premature infants and young infants, because their kidneys are not fully developed and they may accumulate vancomycin in the blood. This age group may need blood tests for controlling vancomycin levels in blood.

Concomitant administration of vancomycin and anaesthetic agents has been associated with skin redness (erythema) and allergic reactions in children.

Similarly, concomitant use with other medicines such as aminoglycoside antibiotics, nonsteroidal anti-inflammatory agents (NSAIDs, e.g., ibuprofen) or amphotericin B (medicine for fungal infection) can increase the risk of kidney damage and therefore more frequent blood and renal test may be necessary.

Other medicines and vancomycin

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. This is especially important of the following, as they may interact with your vancomycin:

- anaesthetics – these may cause redness, flushing, fainting, collapse or even heart attacks. You should, therefore, tell your doctor that you are taking vancomycin if you are going to have an operation.
- any drug that affects your nerves or kidneys such as amphotericin B (treats fungal infections), aminoglycosides, bacitracin, polymixin B, colistin, viomycin (antibiotics) or cisplatin (a chemotherapy drug).
- potent diuretics (strong medicines which are given to encourage the production of urine) such as furosemide.

It may still be all right for you to be given vancomycin and your doctor will be able to decide what is suitable for you.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

Vancomycin should not affect your ability to drive or use machines.

3. How to use vancomycin

You will be given Vancomycin by medical staff while you are in hospital. Your doctor will decide how much of this medicine you should receive each day and how long the treatment will last.

Dosage

The dose given to you will depend on:

- your age,
- your weight,
- the infection you have,
- how well your kidneys are working,
- your hearing ability,
- any other medicines you may be taking.

Intravenous administration

Adults and adolescents (from 12 years and older)

The dosage will be calculated according to your body weight. The usual infusion dose is 15 to 20 mg for each kg of body weight. It is usually given every 8 to 12 hours. In some cases, your doctor may decide to give an initial dose of up to 30 mg for each kg of body weight. The maximum daily dose should not exceed 2 g.

Use in children

Children aged from one month to less than 12 years of age

The dosage will be calculated according to your body weight. The usual infusion dose is 10 to 15 mg for each kg of body weight. It is usually given every 6 hours.

Preterm and term newborn infants (from 0 to 27 days)

The dosage will be calculated according to post-menstrual age (time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (post-natal age).

The elderly, pregnant women and patients with a kidney disorder, including those on dialysis, may need a different dose.

Oral administration

Adults and adolescents (from 12 to 18 years)

The recommended dose is 125 mg every 6 hours. In some cases, your doctor may decide to give a higher daily dose of up to 500 mg every 6 hours. The maximum daily dose should not exceed 2 g.

If you suffered other episodes (infection of the mucosa) before you may need different dose and different duration of the therapy.

Use in children

Neonates, infants and children less than 12 years old

The recommended dose is 10 mg for each kg of body weight. It is usually given every 6 hours. The maximum daily dose should not exceed 2 g.

INFORMATION FOR THE HEALTHCARE PROFESSIONAL

Vancomycin 500mg Powder for Solution for Infusion

Vancomycin 1g Powder for Solution for Infusion

Please refer to the Summary of Product Characteristics (SmPC) for further details on this product.

Qualitative and Quantitative Composition

Vancomycin 500mg Powder for Solution for Infusion - Each vial contains 500 mg vancomycin hydrochloride equivalent to 500,000 IU vancomycin.

Vancomycin 1g Powder for Solution for Infusion - Each vial contains 1000 mg vancomycin hydrochloride equivalent to 1,000,000 IU vancomycin.

Pharmaceutical Form

Powder for solution for intravenous infusion

Powder for solution for oral use

'A white to cream coloured porous cake'

Therapeutic indications

Intravenous administration

Vancomycin is indicated in all age groups for the treatment of the following infections:

- complicated skin and soft tissue infections (cSSTI)
- bone and joint infections
- community acquired pneumonia (CAP)
- hospital acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP)
- infective endocarditis

Vancomycin is also indicated in all age groups for the perioperative antibacterial prophylaxis in patients that are at high risk of developing bacterial endocarditis when undergoing major surgical procedures.

Oral administration

Vancomycin is indicated in all age groups for the treatment of *Clostridium difficile* infection (CDI).

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

Posology and method of administration

Posology

Where appropriate, vancomycin should be administered in combination with other antibacterial agents.

Intravenous administration

The initial dose should be based on total body weight. Subsequent dose adjustments should be based on serum concentrations to achieve targeted therapeutic concentrations. Renal function must be taken into consideration for subsequent doses and interval of administration.

Patients aged 12 years and older

The recommended dose is 15 to 20 mg/kg of body weight every 8 to 12 h (not to exceed 2 g per dose).

In seriously ill patients, a loading dose of 25–30 mg/kg of body weight can be used to facilitate rapid attainment of target trough serum vancomycin concentration.

Infants and children aged from one month to less than 12 years of age:

The recommended dose is 10 to 15 mg/kg body weight every 6 hours.

Term neonates (from birth to 27 days of post-natal age) and preterm neonates (from birth to the expected date of delivery plus 27 days)

For establishing the dosing regimen for neonates, the advice of a physician experienced in the management of neonates should be sought. One possible way of dosing vancomycin in neonates is illustrated in the following table:

PMA (weeks)	Dose (mg/kg)	Interval of administration (h)
<29	15	24
29-35	15	12
>35	15	8

PMA: post-menstrual age ((time elapsed between the first day of the last menstrual period and birth (gestational age) plus the time elapsed after birth (post-natal age)).

Peri-operative prophylaxis of bacterial endocarditis in all age groups

The recommended dose is an initial dose of 15 mg/kg prior to induction of anaesthesia. Depending on the duration of surgery, a second vancomycin dose may be required.

Duration of treatment

Suggested treatment duration is shown in table below. In any case, the duration of treatment should be tailored to the type and severity of infection and the individual clinical response.

Indication	Treatment duration
Complicated skin and soft tissue infections - Non necrotizing - Necrotizing	7 to 14 days 4 to 6 weeks*
Bone and joint infections	4 to 6 weeks**
Community-acquired pneumonia	7 to 14 days
Hospital-acquired pneumonia, including ventilator-associated pneumonia	7 to 14 days
Infective endocarditis	4 to 6 weeks***

*Continue until further debridement is not necessary, patient has clinically improved, and patient is afebrile for 48 to 72 hours

**Longer courses of oral suppression treatment with suitable antibiotics should be considered for prosthetic joint infections

***Duration and need for combination therapy is based on valve-type and organism

Special populations

Elderly

Lower maintenance doses may be required due to the age-related reduction in renal function.

Renal impairment

In adult and paediatric patients with renal impairment, consideration should be given to an initial starting dose followed by serum vancomycin trough levels rather than to a scheduled dosing regimen, particularly in patients with severe renal impairment or those who undergo renal replacement therapy (RRT) due to the many varying factors that may affect vancomycin levels in them.

In patients with mild or moderate renal failure, the starting dose must not be reduced. In patients with severe renal failure, it is preferable to prolong the interval of administration rather than administer lower daily doses.

Appropriate consideration should be given to the concomitant administration of medicinal products that may reduce vancomycin clearance and/or potentiate its undesirable effects.

Vancomycin is poorly dialyzable by intermittent hemodialysis. However, use of high-flux membranes and continuous renal replacement therapy (CRRT) increases vancomycin clearance and generally requires replacement dosing (usually after the haemodialysis session in case of intermittent haemodialysis).

Adults

Dose adjustments in adult patients could be based on glomerular filtration rate estimated (eGFR) by the following formula:

Men: $[\text{Weight (kg)} \times 140 - \text{age (years)}] / 72 \times \text{serum creatinine (mg/dl)}$

Women: 0.85 x value calculated by the above formula.

The usual starting dose for adult patients is 15 to 20 mg/kg that could be administered every 24 hours in patients with creatinine clearance between 20 to 49 ml/min. In patients with severe renal impairment (creatinine clearance below 20 ml/min) or those on renal replacement therapy, the appropriate timing and amount of subsequent doses largely depend on the modality of RRT and should be based on serum vancomycin trough levels and on residual renal function. Depending on the clinical situation, consideration could be given to withhold the next dose while awaiting the results of vancomycin levels.

In the critically ill patient with renal insufficiency, the initial loading dose (25 to 30 mg/kg) should not be reduced.

Paediatric population

Dose adjustments in paediatric patients aged 1 year and older could be based on glomerular filtration rate estimated (eGFR) by the revised Schwartz formula:

$eGFR (\text{mL/min}/1.73 \text{ m}^2) = (\text{height cm} \times 0.413) / \text{serum creatinine (mg/dl)}$

$eGFR (\text{mL/min}/1.73 \text{ m}^2) = (\text{height cm} \times 36.2 / \text{serum creatinine } (\mu\text{mol/L}))$

For neonates and infants below 1 year of age, expert advice should be sought as the revised Schwartz formula is not applicable to them.

Oriental dosing recommendations for the paediatric population are shown in table below that follow the same principles as in adult patients.

GFR (mL/min/1.73 m²)	IV dose	Frequency
50-30	15 mg/kg	12 hourly
29-10	15 mg/kg	24 hourly
< 10	10-15 mg/kg	Re-dose based on levels*
Intermittent haemodialysis		
Peritoneal dialysis	15 mg/kg	Re-dose based on levels*
Continuous renal replacement therapy		

*The appropriate timing and amount of subsequent doses largely depends on the modality of RRT and should be based on serum vancomycin levels obtained prior

Method of administration

Intravenous infusion means that the medicinal product flows from an infusion bottle or bag through a tube to one of your blood vessels and into your body. Your doctor, or nurse, will always give vancomycin into your blood and not in the muscle. Vancomycin will be given into your vein for at least 60 minutes.

If given for treatment of gastric disorders (so called Pseudomembranous colitis), the medicinal product must be administered as a solution for oral use (you will take the medicine by mouth).

Duration of treatment

The length of treatment depends on the infection you have and may last a number of weeks.

The duration of the therapy may be different depending on the individual response to treatment for every patient.

During the treatment, you might have blood tests, be asked to provide urine samples and possibly have hearing tests to look for signs of possible side effects.

If you think you have received too much vancomycin

As vancomycin will be given to you whilst you are in hospital is unlikely that you will be given too little or too much, however, tell your doctor or nurse if you have any concerns.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Vancomycin can cause allergic reactions, although serious allergic reactions (anaphylactic shock) are rare. Tell your doctor immediately if you get any sudden wheeziness, difficulty in breathing, redness on the upper part of the body, rash or itching.

The absorption of vancomycin from the gastrointestinal tract is negligible. However, if you have an inflammatory disorder of the digestive tract, especially if you also have a kidney disorder, side effects that occur when vancomycin is administered by infusion may appear.

Common side effects (may affect up to 1 in 10 people):

- Fall in blood pressure
- Breathlessness, noisy breathing (a high pitched sound resulting from obstructed air flow in the upper airway)
- Rash and inflammation of the lining of the mouth, itching, itching rash, hives
- Kidney problems which may be detected primarily by blood tests
- Redness of upper body and face, inflammation of a vein

Uncommon side effects (may affect up to 1 in 100 people):

- Temporary or permanent loss of hearing

Rare side effects (may affect up to 1 in 1,000 people):

- Decrease in white blood cells, red blood cells and platelets (blood cells responsible for blood clotting)
- Increase in some of the white cells in the blood
- Loss of balance, ringing in your ears, dizziness
- Blood vessel inflammation
- Nausea (feeling sick)
- Inflammation of the kidneys and kidney failure
- Pain in the chest and back muscles
- Fever, chills

Very rare side effects (may affect up to 1 in 10,000 people):

- Sudden onset of severe allergic skin reaction with skin flaking blistering or peeling skin. This may be associated with a high fever and joint pains
- Cardiac arrest
- Inflammation of the bowel which causes abdominal pain and diarrhea, which may contain blood

Not known (frequency cannot be estimated from the available data):

- Being sick (throwing up), diarrhoea
- Confusion, drowsiness, lack of energy, swelling, fluid retention, decreased urine
- Rash with swelling or pain behind the ears, in the neck, groin, under the chin and armpits (swollen lymph nodes), abnormal blood and liver function tests
- Rash with blisters and fever.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes

any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store vancomycin

Keep this medicine out of the sight and reach of children.

Your doctor, nurse or pharmacist will usually be responsible for storing and preparing vancomycin before use and for checking that the vials have not passed their expiry date. The vials will be stored below 25°C. Made-up solutions may be stored for up to 24 hours in a refrigerator (2°C - 8°C).

Do not use this medicine after the expiry date which is stated on the carton and label. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste.

Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of pack and further information

What vancomycin contains

Each vial contains the active substance vancomycin (as vancomycin hydrochloride), as a powder for solution for intravenous infusion or powder for solution for oral use. There are no other ingredients included in the product.

What vancomycin looks like and contents of the pack

Vancomycin infusion comes in a glass vial with a rubber stopper capped with a flip-off cap. The powder is a white to cream coloured solid.

Each 500mg vial contains 500,000IU vancomycin. Each 1g vial contains 1,000,000IU vancomycin.

It is available in packs of one, two, five or ten vials. Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Wockhardt UK Limited, Ash Road North, Wrexham, LL13 9UF, UK.

Manufacturer: CP Pharmaceuticals Ltd, Ash Road North, Wrexham, LL13 9UF, UK.

Other formats:

To listen to or request a copy of this leaflet in Braille, large print or audio please call, free of charge:

0800 198 5000 (UK Only)

Please be ready to give the following information:

Product Name	Reference Number
Vancomycin 500mg Powder for Solution for Infusion	29831/0319
Vancomycin 1g Powder for Solution for Infusion	29831/0322

This is a service provided by the Royal National Institute of Blind People

This leaflet was last revised in 04/2018.

Other sources of information

Advice/medical education

Antibiotics are used to cure bacterial infections. They are ineffective against viral infections.

If your doctor has prescribed antibiotics, you need them precisely for your current illness.

Despite antibiotics, some bacteria may survive or grow. This phenomenon is called resistance: some antibiotic treatments become ineffective.

Misuse of antibiotics increases resistance. You may even help bacteria become resistant and therefore delay your cure or decrease antibiotic efficacy if you do not respect appropriate:

- dosage
- schedules
- duration of treatment

Consequently, to preserve the efficacy of this drug:

1. Use antibiotics only when prescribed.
2. Strictly follow the prescription.
3. Do not re-use an antibiotic without medical prescription, even if you want to treat a similar illness.

103385/7

WOCKHARDT

to dosing and on residual renal function. Depending on the clinical situation, consideration could be given to withhold the next dose while awaiting the results of vancomycin levels.

Hepatic impairment:

No dose adjustment is needed in patients with hepatic insufficiency.

Pregnancy

Significantly increased doses may be required to achieve therapeutic serum concentrations in pregnant women.

Obese patients

In obese patients, the initial dose should be individually adapted according to total body weight as in non-obese patients.

Oral Administration

Patients aged 12 years and older

Treatment of *Clostridium difficile* infection (CDI):

The recommended vancomycin dose is 125 mg every 6 hours for 10 days for the first episode of non-severe CDI. This dose can be increased to 500 mg every 6 hours for 10 days in case of severe or complicated disease. The maximum daily dose should not exceed 2 g.

In patients with multiple recurrences, consideration may be given to treat the current episode of CDI with vancomycin, 125 mg four times daily for 10 days followed by either tapering the dose, i.e., gradually decreasing it until 125 mg per day or a pulse regimen, i.e., 125–500 mg/day every 2–3 days for at least 3 weeks.

Neonates, infants and children less than 12 years old

The recommended vancomycin dose is 10 mg/kg orally every 6 hours for 10 days. The maximum daily dose should not exceed 2 g.

Treatment duration with vancomycin may need to be tailored to the clinical course of individual patients. Whenever possible the antibacterial suspected to have caused CDI should be discontinued. Adequate replacement of fluid and electrolytes should be ensured.

Monitoring of vancomycin serum concentrations

The frequency of therapeutic drug monitoring (TDM) needs to be individualized based on the clinical situation and response to treatment, ranging from daily sampling that may be required in some hemodynamically unstable patients to at least once weekly in stable patients showing a treatment response. In patients with normal renal function, the serum concentration of vancomycin should be monitored on the second day of treatment immediately prior to the next dose.

In patients on intermittent haemodialysis, vancomycin levels should be usually obtained before the start of the haemodialysis session.

After oral administration, monitoring vancomycin serum concentrations in patients with inflammatory intestinal disorders should be performed.

Therapeutic trough (minimum) vancomycin blood levels should normally be 10–20 mg/l, depending on the site of infection and susceptibility of the pathogen. Trough values of 15–20 mg/l are usually recommended by clinical laboratories to better cover susceptible-classified pathogens with MIC \geq 1 mg/L.

Model-based methods may be useful in the prediction of individual dose requirements to reach an adequate AUC. The model-based approach can be used both in calculating the personalized starting dose and for dose adjustments based on TDM results.

Method of administration

Intravenous administration

Intravenous vancomycin is usually administered as an intermittent infusion and the dosing recommendations presented in this section for the intravenous route correspond to this type of administration.

Vancomycin shall only be administered as slow intravenous infusion of at least one hour duration or at a maximum rate of 10 mg/min (whichever is longer) which is sufficiently diluted (at least 100 ml per 500 mg or at least 200 ml per 1000 mg).

Patients whose fluid intake must be limited can also receive a solution of 500 mg/50 ml or 1000 mg/100 ml, although the risk of infusion-related undesirable effects can be increased with these higher concentrations.

Continuous vancomycin infusion may be considered, e.g., in patients with unstable vancomycin clearance.

Oral administration

The contents of vials for parenteral administration may be used.

Common flavouring syrups may be added to the solution at the time of administration to improve the taste.

Capsules are also available.

Pharmaceutical Particulars

List of excipients

None

Incompatibilities

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

This medicinal product must not be mixed with other medicinal products except those mentioned under the subheading "special precautions for disposal and other handling".

Shelf life

Unopened - 36 months

Reconstituted solution intended for parenteral administration

Physical and chemical stability have been demonstrated for a period of 24 hours when stored at 2° to 8°C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution and dilution has taken place in controlled and validated aseptic conditions.

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

Reconstituted solution intended for oral administration

Solution intended for oral administration may be stored in a refrigerator (2° to 8°C) for up to 24 hours.

Special precautions for storage

Unopened: Do not store above 25°C

After reconstitution: Store at 2-8°C.

Nature and contents of container

Vancomycin 500mg Powder for Infusion:-

Packs* of one, two, five or ten Type II colourless glass 10ml vials stoppered with Type I rubber stopper, capped with a flip-off cap.

Vancomycin 1g Powder for Infusion:-

Packs* of one, two, five or ten Type II colourless glass 20ml vials stoppered with Type I rubber stopper, capped with a flip-off cap. *Not all pack sizes may be marketed

Special precautions for disposal and other handling

Preparation of solution: At the time of use, add 10ml of water for Injections to the 500mg vial. And add 20ml of water for injections to the 1g vial. Vials reconstituted in this manner will give a solution of 50mg/ml. The reconstituted solution is clear and colourless.

Further dilution is required. Read instructions which follow:

1. Intermittent infusion is the preferred method of administration. Reconstituted solutions containing 500mg vancomycin must be diluted with at least 100ml diluent. Reconstituted solutions containing 1g vancomycin must be diluted with at least 200ml diluent. 0.9% sodium chloride intravenous infusion or 5% dextrose intravenous infusion are suitable diluents. The desired dose should be given by intravenous infusion over a period of at least 60 minutes. If administered over a shorter period of time or in higher concentrations, there is the possibility of inducing marked hypotension in addition to thrombophlebitis. Rapid administration may also produce flushing and a transient rash over the neck and shoulders.
2. Continuous infusion (should be used only when intermittent infusion is not feasible).
1-2g can be added to a sufficiently large volume of sodium chloride intravenous infusion or 5% dextrose intravenous infusion to permit the desired daily dose to be administered slowly by intravenous drip over a 24 hour period.
3. Oral administration

The contents of vials for parenteral administration may be used.

Common flavouring syrups may be added to the solution at the time of administration to improve the taste.

Vials are for single use only and any unused product or waste material should be disposed of immediately in accordance with local requirements.

Marketing Authorisation Holder

Wockhardt UK Limited, Ash Road North, Wrexham LL13 9UF, United Kingdom

Marketing Authorisation Number

Vancomycin 500mg Powder for Infusion – PL 29831/0319

Vancomycin 1g Powder for Infusion – PL 29831/0322

DATE OF REVISION OF THE TEXT

04/2018

103385/7

WOCKHARDT