Package Leaflet: Information for the user

Vancomycin 500 mg, Powder for concentrate for solution for infusion
Vancomycin 1000 mg, Powder for concentrate 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, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. 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 use Vancomycin
3. How to use Vancomycin
4. Possible side effects
5. How to store Vancomycin
6. Contents of the pack and other 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 an oral solution.

Vancomycin is used 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 the bones 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 the 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 use Vancomycin

Do not use Vancomycin
- If you are allergic to vancomycin or any other ingredients of this medicine (listed in Section 6).

Warnings and precautions
Talk to your doctor, 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 a 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 with 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, liver 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.
- You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking vancomycin.

Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with vancomycin treatment. Stop using vancomycin and seek medical attention immediately if you notice any of the symptoms described in section 4.

Serious side effects that may lead to loss of vision have been reported following the injection of vancomycin in the eyes.

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 tests may be necessary.
Other medicines and Vancomycin
Tell your doctor, pharmacist or nurse if you are taking, have recently taken, or might take any other medicines. Moreover, do not take any new medicine without consulting your doctor.

The following medicines may react with vancomycin if you take them at the same time, such as medicines for the treatment of:
- infections caused by bacteria (streptomycin, neomycin, gentamicin, kanamycin, amikacin, bacitracin, tobramycin, polymixin B, colistin, piperacillin/tazobactam),
- tuberculosis (viomycin),
- fungal infections (amphotericin B),
- cancer (cisplatin)

and
- medicines for muscle relaxation during anaesthesia,
- anaesthetic agents (if you are going to have general anaesthesia).

Your doctor may need to test your blood and adjust the dosage if vancomycin is given simultaneously with other medicines.

Pregnancy
If you are pregnant, think you may be pregnant or plan to become pregnant, tell your doctor before taking this medicine. Vancomycin should be given during pregnancy and breast-feeding only if clearly needed. Your doctor will decide if you should take Vancomycin.

Breast-feeding
Tell your doctor if you are breastfeeding, since Vancomycin passes into breast milk. Your doctor will decide whether vancomycin is really necessary or whether you should stop breastfeeding.

Driving and using machines
Vancomycin has no or negligible effect on the ability to drive and 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 a different dose and different duration of 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.

Method of administration
Intravenous infusion means that the medicine 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 medicine must be administrated 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 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 receive more Vancomycin than you should
As this product will be given to you while you are in the hospital, it is unlikely that you will be given too much. However, tell your doctor or nurse immediately if you have any concerns.

If you have further questions about using this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

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.

Stop using vancomycin and seek medical attention immediately if you notice any of the following symptoms:

- Reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome and toxic epidermal necrolysis).
- Widespread rash, high body temperature and enlarged lymph nodes (DRESS syndrome or drug hypersensitivity syndrome).
- A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalised exanthematous pustulosis).

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 diarrhoea, 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, hospital pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:
UK: the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
Ireland: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; E-mail: medsafety@hpra.ie.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Vancomycin

Before reconstitution: Store below 25ºC.
Keep the vial in the outer carton in order to protect from light

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

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

Do not use this medicine if you notice that the solution is cloudy or there are particles in suspension.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Vancomycin contains
The active substance is vancomycin (as hydrochloride).
Vancomycin 500 mg: Each vial contains 500 mg of vancomycin hydrochloride equivalent to 500,000 IU vancomycin.
Vancomycin 1000 mg: Each vial contains 1000 mg of vancomycin hydrochloride equivalent to 1,000,000 IU vancomycin.

The other ingredients are sodium hydroxide, hydrochloric acid for pH adjustment.

What Vancomycin looks like and contents of the pack
Vancomycin 500 mg comes in the form of a white or slightly brownish powder in clear glass vials with a rubber stopper and orange aluminium cap.
Vancomycin 1000 mg comes in the form of a white or slightly brownish powder, in clear glass vials with a rubber stopper and white aluminium cap.

Each package contains 1, 5, 10 or 20 vials.
Before use, the powder is dissolved and diluted with an intravenous liquid, obtaining a solution which will be administered to you slowly into a vein (“drip”), by a doctor or nurse.

Each 500 mg vial contains 500 mg of vancomycin hydrochloride. After reconstitution with 10 ml of water for injections is obtained a solution with a concentration of 50 mg/ml, and after further dilutions a solution with a concentration of 5 mg/ml is obtained.

Each 1000 mg vial contains 1000 mg of vancomycin hydrochloride. After reconstitution with 20 ml of water for injections is obtained a solution with a concentration of 50 mg/ml, and after further dilutions a solution with a concentration of 5 mg/ml is obtained.

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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.

Information for Healthcare Professionals

The following information is intended only for doctors and healthcare professionals.
This text is an excerpt from the Summary of Product Characteristics to help in the administration of Vancomycin.
In assessing the appropriateness of using in a particular patient, the doctor should be familiar with the Summary of Product Characteristics.

Preparation of reconstituted solution
Dissolve the contents of each 500 mg vial in 10 ml sterile water for injections.
Dissolve the contents of each 1000 mg vial in 20 ml sterile water for injections.
One ml of reconstituted solution contains 50 mg of vancomycin.

For oral administration, the reconstituted solutions containing 500 mg and 1000 mg of vancomycin can be diluted in 30 ml of water and given to the patient or administered through a naso-gastric tube.

Appearance of the reconstituted solution
After reconstitution, the solution is clear and colourless to slightly brownish yellow and has no visible particles.

Preparation of the final diluted solution for infusion
The reconstituted solution containing 50 mg/ml of vancomycin should be further diluted.

Suitable diluents are:

- Glucose 5% solution for injection
- Sodium chloride 0.9% solution for injection
- 5% Glucose Injection with 0.9% Sodium Chloride Injection

- Ringer's Lactate Injection

Intermittent infusion:
The reconstituted solution containing 500 mg of vancomycin (50 mg/ml) should first be diluted with at least 100 ml of solvent (to a concentration of 5 mg/ml).
The reconstituted solution containing 1000 mg of vancomycin (50 mg/ml) should first be diluted with at least 200 ml of solvent (to a concentration of 5 mg/ml).
The concentration of vancomycin in the infusion solution should not exceed 5 mg/ml.
The desired dose should be slowly administered intravenously at a rate not exceeding 10 mg/min for at least 60 minutes.

Continuous infusion:
Should only be used if treatment with an intermittent infusion is not possible. Dilute 1000 mg to 2000 mg of dissolved vancomycin in sufficient solvent (mentioned above) and administer as an infusion "drip", so that the patient receives the prescribed daily dose in 24 hours.

Appearance of the diluted solution
After dilution, the solution is clear, free from foreign particles.

Before administration, the reconstituted and diluted solutions should be inspected visually for particles and discoloration. Only clear, colourless solutions free of particles should be used.

Shelf life of the reconstituted solution:
For intravenous use, the reconstituted solution should be diluted immediately after preparation.
For oral use, the reconstituted solution with purified water for oral administration is stable when stored at 2-8 °C for 48 hours.

Shelf life of diluted solution:
Chemical and physical in- use stability has been demonstrated:
- for a period of 24 hours at 25 °C after reconstitution and further dilution with sodium chloride 9 mg / ml (0.9%) or glucose solution 50 mg / ml (5%);
- for a period of 96 hours when stored at 2-8 °C after reconstitution and further dilution with sodium chloride 9 mg / ml (0.9%) or glucose solution 50 mg / ml (5%), or Ringer's lactate solution or with sodium chloride 9 mg / ml (0.9%) + glucose 50 mg / ml (5%).

Patients with 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 (see section 4.4).

Vancomycin is poorly dialyzable by intermittent haemodialysis. 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).