Package leaflet: Information for the user

Vancomycin 500 mg and 1000 mg Powder for Concentrate for Solution for Infusion

Vancomycin

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

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on 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

How does the medicine work?

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.

What is the medicine used for?

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 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.

2. What you need to know before you use Vancomycin

Do not use Vancomycin

- If you are allergic to vancomycin.

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 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.

Rapid injection of vancomycin may cause low blood pressure, shock and rarely cardiac arrest. Stopping the infusion usually results in a prompt cessation of the reactions.

Injection site pain, inflammation of the vein wall and blood clotting can occur and is occasionally severe, slow administration also reduces these side effects.

Other medicines and Vancomycin
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

The following medicines may interact with Vancomycin:
- anaesthetic agents
- medicine for muscle relaxation
- medicines for infections caused by bacteria (e.g. polymyxin B, colistin, bacitracin, aminoglycosides)
- medicine for fungal infection (amphotericin B)
- medicine for tuberculosis (viomycin)
- medicine for cancer (cisplatin).

Drugs that can affect the kidneys and hearing
If you receive vancomycin together with other drugs that may be harmful to the kidneys and the hearing (e.g. aminoglycoside antibiotics), the harmful effect may be increased. In such cases, careful and regular monitoring of renal function and hearing is necessary.

Anaesthetic agents
Use of anaesthetic agents increases the risk of side effects of vancomycin such as hypotension, rash, hives and itching.

Muscle relaxants
If you receive muscle relaxants (e.g. succinylcholine), together with vancomycin the effect of these may be enhanced or extended.

Pregnancy, breast-feeding and fertility
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.
Vancomycin should be given during pregnancy and breast-feeding only if clearly needed. The doctor may decide that you should stop breast-feeding.

Driving and using machines
Vancomycin has no or very little effect on your 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.

Do not tamper with the bag/bottle. Follow the doctor's instructions.

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.

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 receive too much Vancomycin
Your doctor monitors the amount of Vancomycin you receive. If blood tests and other tests show that you have too much in your body, the amount of Vancomycin will be reduced or treatment may be interrupted or stopped. The level remaining in your blood will be lowered.

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

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.

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 or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6767836. 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

Your doctor will be responsible for storing the medicine.

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

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

Powder as packaged for sale:
Store below 25 °C.
Keep the vial in the outer carton in order to protect from light.

The stability of the reconstituted concentrate and further diluted product is stated below in the additional information for medical or healthcare professionals.

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

6. Contents of the pack and other information

What Vancomycin contains:

The active ingredient is vancomycin.

- Vancomycin 500 mg Powder for Concentrate for Solution for Infusion: Each vial contains 500 mg vancomycin (as vancomycin hydrochloride) equivalent to 500,000 IU.

- Vancomycin 1000 mg Powder for Concentrate for Solution for Infusion: Each vial contains 1000 mg vancomycin (as vancomycin hydrochloride) equivalent to 1,000,000 IU.

What Vancomycin looks like and contents of the pack:
Vancomycin 500 mg Powder for Concentrate for Solution for Infusion:
- A white to cream coloured porous cake powder in a clear glass vial with a grey flip-off cap.

Pack size: 1 vial.

Vancomycin 1000 mg Powder for Concentrate for Solution for Infusion:
- A white to cream coloured porous cake powder in a clear glass vial with a green flip-off cap.

Pack size: 1 vial.

The medicine is a powder that has to be dissolved before you receive it.

Marketing Authorisation Holder:
Actavis Group PTC ehf.
Reykjavíkurvegi 76-78
220 Hafnarfjörður
Iceland

Manufacturer
Xellia Pharmaceuticals ApS
Dalslandsgade 11
2300 Copenhagen S
Denmark

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Other sources of information

<u>Advice/medical education</u>
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.

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The following information is intended for healthcare professionals only.

Vancomycin Powder for Concentrate for Solution for Infusion is for single use only and any unused solution should be discarded.

The powder must be reconstituted and the resulting concentrate must then be immediately diluted further prior to use.

Preparation of the reconstituted concentrate
Dissolve the content of each 500 mg vial in 10 ml of sterile water for injections.
Dissolve the content of each 1000 mg vial in 20 ml of sterile water for injections.
One ml of reconstituted solutions contains 50 mg vancomycin. pH of the reconstituted solutions is 2.5 to 4.5.
The solution should be clear colourless to pale yellow and free from fibre and visible particulate matters.

Preparation of final diluted solution for infusion
Reconstituted concentrate containing 50 mg/ml of vancomycin should be further diluted depending on the method of administration.
Suitable diluents are: 5% Glucose Injection, 0.9% Sodium Chloride Injection, 0.9% Sodium Chloride and 5% Glucose Injection or Ringer acetate Injection.

Intermittent infusion
Reconstituted concentrate containing 500 mg of vancomycin (50 mg/ml) must be diluted further with at least 100 ml diluent.
Reconstituted concentrate containing 1000 mg of vancomycin (50 mg/ml) must be diluted further with at least 200 ml diluent.
The concentration of vancomycin in solution for infusion should not exceed 5 mg/ml.

The desired dose should be administrated slowly by intravenous infusion at a rate of no more than 10 mg/minute, for at least 60 minutes or even longer.

Before administration, the reconstituted and diluted solutions should be inspected visually for particulate matter and discolouration. Only clear and colourless solution free from particles should be used.

Shelf-life of reconstituted concentrate:
The reconstituted concentrate should be further diluted immediately after reconstitution.

Shelf-life of diluted product:
From a micobiological point of view, the product should be used immediately.