Package leaflet: Information for the patient

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 are given 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 or pharmacist.
- 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 infusion is and what it is used for

Vancomycin infusion is a medicine that belongs to a group of antibiotics called “glycopeptides”. Vancomycin infusionworks 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.

Vancomycin can be given orally in all age groups for the treament of infection of the mucosa of the small and the large intestines with damage to the mucosae (pseudomembranous colitis), caused by the *Clostridioides difficile* bacterium.

2. What you need to know before you are given Vancomycin infusion

You must not be given Vancomycin infusion:

- If you are allergic to vancomycin
- Into a muscle, due to the risk of tissue damage at the site of administration

Warnings and precautions

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

Talk to your doctor or hospital pharmacist or nurse before you are given Vancomycin infusionif:

- You suffered a previous allergic reaction to a medicine called 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 *Clostridioides difficile* infection instead of orally.
- You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking vancomycin.

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, as this may be a sign of bowel swelling (pseudomembranous colitis) which can occur following treatment with antibiotics.

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.

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 kidney test may be necessary.

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

The following medicine may interact with Vancomycin infusion:

- Medicines for preventing pain during surgery (anaesthetic agents)
- Medicine for muscle relaxation
- Medicines for infections caused by bacteria (e.g polymixin B, piperacillin/tazobactam, colistin, bacitracin, aminoglycosides)
- Medicine for fungal infection (amphotericin B)
- Medicine for tuberculosis (viomycin)
- Medicine for cancer (cisplatin)
- Potent diuretics (strong medicines which are given to encourage the production of urine) such as furosemide.

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 you are given 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 Vancomycin infusion is given

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

Use in 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 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.

Use in 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
Use in 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.

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 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
As Vancomycin will be given to you whilst you are in hospital it 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.

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).**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.

The following side effects have been reported:

Common (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 (may affect up to 1 in 100 people):
- temporary or permanent loss of hearing

Rare (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 (may affect up to 1 in 10,000 people):
- severe allergic skin reaction with skin flaking blistering or peeling skin. This may be associated with a high fever and joint pains.
- cardiac arrest (sudden loss of heart function)
- inflammation of the bowel which causes stomach 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 national reporting system listed below. By reporting side effects you can help provide more information on the safety of this medicine.

For UK – via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

For Ireland – via:
HPRA Pharmacovigilance,
Earlsfort Terrace,
IRL Dublin 2;
Tel: +353 16764971;
Fax: +353 1 6762517.
Website: www.hpra.ie;
E-mail: medsafety@hpra.ie

5. How to store Vancomycin infusion

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 outer carton and vial as 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 any medicines via wastewater or household waste. Ask your phamacist how to throw away medicines you no longer use. These measures will help to protect the enviroment.

6. Content of the pack and other information

What Vancomycin infusioncontains:
The active substance is vancomycin.

Vancomycin infusion500 mg powder for concentrate for solution for infusion:
Each vial contains 500 mg vancomycin hydrochloride equivalent to 500,000 IU vancomycin.

Vancomycin infusion1000 mg powder for concentrate for solution for infusion:
Each vial contains 1000 mg vancomycin hydrochloride equivalent to 1,000,000 IU vancomycin.

What Vancomycin infusionlooks like and contents of the pack:
Vancomycin infusion500 mg powder for concentrate for solution for infusion:
- A white to cream coloured powder in a colourless glass vial with a chlorobutyl silicone coated stopper and a grey aluminium/polypropylene flip-off cap.

Pack size: 1 vial, 10 vials

Vancomycin infusion1000 mg powder for concentrate for solution for infusion:
- A white to cream coloured powder in a colourless glass vial with a chlorobutyl silicone coated stopper and a green aluminium/polypropylene flip-off cap.

Pack size: 1 vial, 10 vials

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

Marketing Authorisation Holder

For UK:
Fresenius Kabi Limited
Cestrian Court, Eastgate Way,
Manor Park, Runcorn,
Cheshire, WA7 1NT
UK

For IE:
Fresenius Kabi Deutschland GmbH
Else-Kröner-Straße 1,
Bad Homburg v.d.H. 61352,
Germany

Manufacturer
Xellia Pharmaceuticals ApS
Dalslandsgade 11
2300 Copenhagen S
Denmark

This medicinal product is authorised in the Member States under the following names:

Name of the Member State	Name of the medicinal product
Belgium	Vancomycine Fresenius Kabi 500 mg poeder voor concentraat voor oplossing voor infusie
Bulgaria	Ванкомицин Каби 500 mg прах за концентрат за инфузионен разтвор
Czech Republic	Vancomycin Kabi
Denmark	Vancomycin Fresenius Kabi
Estonia	Vancomycin Kabi 500 mg
Germany	Vancomycin Kabi 500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung oder einer Lösung zum Einnehmen
Greece	Vancomycin/Kabi 500 mg κόνις για πυκνό σκεύασμα για παρασκευή διαλύματος προς έγχυση
Hungary	Vancomycin Kabi 500 mg por oldatos infúzióhoz való koncentrátumhoz
Iceland	Vancomycin Fresenius Kabi
Ireland	Vancomycin 500 mg powder for concentrate for solution for infusion
Latvia	Vancomycin Kabi 500 mg pulveris infūziju šķīduma koncentrāta pagatavošanai
Lithuania	Vancomycin Kabi 500 mg milteliai infuzinio tirpalo koncentratui
Luxembourg	Vancomycin Kabi 500 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung oder einer Lösung zum Einnehmen
Netherlands	Vancomycine Fresenius Kabi 500 mg poeder voor concentraat voor oplossing voor infusie
Norway	Vancomycin Fresenius Kabi 500 mg pulver til konsentrat til infusjonsvæske, oppløsning
Poland	Vancomycin Kabi
Portugal	Vancomicina Kabi
Romania	Vancomicina Kabi 500 mg pulbere pentru concentrat pentru soluție perfuzabilă
Slovakia	Vancomycin Kabi 500 mg
Slovenia	Vankomicin Kabi 500 mg prašek za koncentrat za raztopino za infundiranje
United Kingdom	Vancomycin 500 mg powder for concentrate for solution for infusion

Name of the Member State	Name of the medicinal product
Belgium	Vancomycine Fresenius Kabi 1000 mg poeder voor concentraat voor oplossing voor infusie
Bulgaria	Ванкомицин Каби 1000 mg прах за концентрат за инфузионен разтвор
Czech Republic	Vancomycin Kabi
Denmark	Vancomycin Fresenius Kabi
Estonia	Vancomycin Kabi 1000 mg
Germany	Vancomycin Kabi 1000 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung oder einer Lösung zum Einnehmen
Greece	Vancomycin/Kabi 1000 mg κόνις για πυκνό σκεύασμα για παρασκευή διαλύματος προς έγχυση
Hungary	Vancomycin Kabi 1000 mg por oldatos infúzióhoz való koncentrátumhoz
Iceland	Vancomycin Fresenius Kabi
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Lithuania	Vancomycin Kabi 1000 mg milteliai infuzinio tirpalo koncentratui
Luxembourg	Vancomycin Kabi 1000 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung oder einer Lösung zum Einnehmen

Netherlands	Vancomycine Fresenius Kabi 1000 mg poeder voor concentraat voor oplossing voor infusie
Norway	Vancomycin Fresenius Kabi 1000 mg pulver til konsentrat til infusjonsvæske, oppløsning
Poland	Vancomycin Kabi
Portugal	Vancomicina Kabi
Romania	Vancomicina Kabi 1000 mg pulbere pentru concentrat pentru soluție perfuzabilă
Slovakia	Vancomycin Kabi 1 000 mg
Slovenia	Vankomicin Kabi 1000 mg prašek za koncentrat za raztopino za infundiranje
United Kingdom	Vancomycin 1000 mg powder for concentrate for solution for infusion

This leaflet was last revised in January 2021.

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 medicine:
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.

The following information is intended for healthcare professionals only.

Preparation

<u>Reconstituted concentrate</u>

500 mg:
Dissolve the content of the vial in 10 ml of sterile water for injection.

1000 mg:
Dissolve the content of the vial in 20 ml of sterile water for injection.

<u>Solution for infusion</u>

500 mg:
Dilute the reconstituted concentrate with at least 100 ml Sodium Chloride 9 mg/ml (0.9%) Injection, Glucose 50 mg/ml (5%) Injection, Sodium Chloride 9 mg/ml (0.9 %) and Glucose 50 mg/ml (5%) Injection or Ringer acetate Injection.

1000 mg:

Dilute the reconstituted concentrate with at least 200 ml Sodium Chloride 9 mg/ml (0.9%) Injection, Glucose 50 mg/ml (5%) Injection, Sodium Chloride 9 mg/ml (0.9 %) and Glucose 50 mg/ml (5%) Injection or Ringer acetate Injection.

The concentration in the prepared infusion fluid must not exceed 0.5% w/v (5 mg/ml).
In selected patients whose fluid intake must be limited, a concentration up to 10 mg/ml can be used; use of such higher concentrations may increase the risk of infusion-related undesirable effects.

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

The infusion should not be mixed with other medicines.

Infusion
Must be given by slow intravenous infusion of at least one hour duration or at a maximum rate of 10 mg/min (whichever is longer), equal to 2 ml/min of an infusion with a concentration of 5 mg/ml.

Solution for oral administration

An aliquot of 2.5 ml from the reconstituted concentrate contains 125 mg vancomycin hydrochloride and should be diluted with 5 ml of water i.e. 1 volume of aliquot should be diluted with 2 volumes of water.
The diluted solution can be given to the patient to drink or administered via nasogastric tube.
Common flavouring syrups may be added to the solution at the time of administration to improve the taste.

Dosage

Intravenous use:
The initial dose is adjusted individually and according to total body weight. The usual dose is:

Patients aged 12 years and older: 15 to 20 mg/kg of body weight every 8 to 12 h (not to exceed 2 g per dose).
Infants and children aged from one month to 12 years of age: 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)].

Oral use:

Patients aged 12 years and older
Treatment of *Clostridioides 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.

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.

Storage

Vancomycin infusionpowder for concentrate for solution for infusion should be stored below 25°C. Keep the vial in the outer carton in order to protect from light.

Vancomycin infusionpowder for concentrate for solution for infusion should not be used after the expiry date which is stated on the carton.

Reconstituted concentrate:
For intravenous administration the concentrate should be further diluted immediately after reconstitution.

For oral administration the chemical and physical in-use stability of the concentrate has been demonstrated for 96 hours at 2-8°C.

Diluted solution:
From a microbiological and physicochemical point of view, the product should be used immediately.