

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Vancomycin 500 mg & 1000 mg Powder for concentrate for solution for infusion

Vancomycin hydrochloride

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 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 or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

The name of your medicine is one of the following:

- Vancomycin 500 mg Powder for concentrate for solution for infusion
- Vancomycin 1000 mg Powder for concentrate for solution for infusion

In the rest of this leaflet your medicine is called Vancomycin.

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
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1. What Vancomycin is and what it is used for

Vancomycin contains the active ingredient vancomycin. 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 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.

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 *Clostridioides difficile* bacterium.

2. What you need to know before you use 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

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

Signs of an allergic reaction to this medicine, including breathing problems and chest pain, have been reported with Vancomycin. Stop immediately Vancomycin and contact immediately your doctor or medical emergencies if you notice any of these signs.

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

-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.

- 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 *Clostridioides 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.

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 using, have recently used or might use any other medicines, including medicines obtained without a prescription. This is especially important for 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), cisplatin (a chemotherapy drug) or piperacillin/tazobactam.
- 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, 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, pharmacist or nurse for advice before taking this medicine.

Driving and using machines

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

Vancomycin contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

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 child's 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.

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 use more Vancomycin than you should

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.

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).
- Chest pain, which can be a sign of a potentially serious allergic reaction called Kounis syndrome.

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
- Increase of liver enzymes

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.
- Excessive breakdown of red blood cells causing tiredness and pale skin (haemolytic anaemia).

Reporting of side effects

If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.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 or nurse knows how to store Vancomycin.

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 carton and the label on the glass container (vial) after (EXP). The expiry date refers to the last day of that month.

Store below 25 °C. Keep the vial in the outer carton in order to protect from light.

Once reconstituted, Vancomycin solution for infusion should be used immediately. Chemical and physical in-use stability has been demonstrated for 24 hours at 2 – 8 °C.

Your doctor will ensure that the solution is not discoloured or contains particles.

Solutions intended for oral dosing may be stored in a refrigerator (2 – 8 °C) for 96 hours.

The vials are for single use and your doctor will dispose of any Vancomycin solution that is left over after you have been given your dose.

Do not throw away any medicines via wastewater or household waste. Ask your doctor 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 substance is vancomycin hydrochloride 500 mg or 1000 mg.

The other ingredient is hydrochloric acid.

Each glass container will contain either 500 mg vancomycin hydrochloride equivalent to 500,000 IU vancomycin or 1000 mg vancomycin hydrochloride equivalent to 1,000,000 IU vancomycin.

What Vancomycin looks like and contents of pack

Vancomycin is a powder for concentrate for solution for infusion. This means liquid must be added to make a solution and more liquid must then be added to dilute the solution before it can be given to you intravenously (by infusion).

Normally your doctor or nurse will prepare your medicine before it is given to you.
Each pack contains 1, 5, 10 or 20 vials (glass containers). Not all pack sizes may be available.

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.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: Noridem Enterprises Limited, Evagorou & Makariou, Mitsi Building 3, Office 115, 1065 Nicosia, Cyprus.

Manufacturer: Demo S.A. PHARMACEUTICAL INDUSTRY, 21st km National Road Athens, Lamia, 14568 Krioneri, Attiki, Greece, **T:** +30 210 8161802, **F:** +30 2108161587.

This medicine is authorised in the Member States of the European Economic Area under the following names:

Ireland:	Vancomycin 500 mg & 1000 mg Powder for concentrate for solution for infusion
Germany:	Vancomycin Noridem 500 mg & 1000 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Austria:	Vancomycin Noridem 500 mg & 1000 mg Pulver für ein Konzentrat zur Herstellung einer Infusionslösung
Greece:	Vancomycin/Noridem 500 mg & 1000 mg Κόνις για πυκνό σκεύασμα για παρασκευή διαλύματος προς έγχυση
Spain:	Vancomicina Noridem 500mg & 1000 mg polvo para concentrado para solución para perfusión EFG
Cyprus:	Vancomycin Noridem 500mg & 1000mg κόνις για πυκνό σκεύασμα για παρασκευή διαλύματος προς έγχυση
Czech Republic:	Vancomycin Noridem
Slovakia:	Vancomycin Noridem 500mg & 1000mg prášok na koncentrát na infúzny roztok
Finland:	Vancomycin Noridem 500mg & 1000mg kuiva-aine välikonsentraatiksi infuusionestettä varten, liuos
Sweden:	Vancomycin Noridem
Denmark:	Vancomycin Noridem
Norway:	Vancomycin Noridem
France:	VANCOMYCINE NORIDEM 500mg & 1000mg, poudre pour solution à diluer pour perfusion ou pour solution buvable
Hungary:	Vancomycin Noridem 500 mg & 1000mg por oldatos infúzióhoz való koncentrátumhoz

Italy:	Vancomicina Noridem
Netherlands:	Vancomycine Noridem 500 mg & 1000mg poeder voor concentraat voor oplossing voor infusie
Poland:	Vancomycin Noridem
Portugal:	Vancomicina Noridem
Romania:	Vancomicină Noridem 500 mg & 1000mg pulbere pentru concentrat pentru soluție perfuzabilă

This leaflet was last revised in

The following information is intended for medical or healthcare professionals only:

Instructions for reconstitution

For single use only. Discard any unused content.

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

Preparation of the reconstituted solution

Vancomycin 500 mg:

At the time of use, add 10 mL of Water for Injections Ph. Eur. to the vial.

Vancomycin 1000 mg:

At the time of use, add 20 mL of Water for Injections Ph. Eur. to the vial.

Vials reconstituted in this manner will give a solution of 50 mg / mL. When reconstituted in water, it forms a clear solution.

FURTHER DILUTION IS REQUIRED. Read instructions which follow:

Preparation of final diluted solution for infusion:

Intermittent infusion is the preferred method of administration. Reconstituted solutions containing 500 mg vancomycin hydrochloride must be diluted with at least 100 mL 0.9 % Sodium Chloride (9 mg / mL) or 5 % Dextrose.

Reconstituted solutions containing 1000 mg vancomycin hydrochloride must be diluted with at least 200 mL 0.9 % Sodium Chloride (9 mg / mL) or 5 % Dextrose. 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.

Continuous infusion (should be used only when intermittent infusion is not feasible).

Vancomycin 500 mg:

Two to four vials (1 – 2 g) can be added to a sufficiently large volume of 0.9 % Sodium Chloride (9 mg / mL) or 5 % Dextrose to permit the desired daily dose to be administered slowly by intravenous drip over a 24 hour period.

Vancomycin 1000 mg:

One to two vials (1 – 2 g) can be added to a sufficiently large volume of 0.9 % Sodium Chloride (9 mg / mL) or 5 % Dextrose to permit the desired daily dose to be administered slowly by intravenous drip over a 24 hour period.

Concentrations of no more than 5 mg/mL are recommended. In selected patients in need of fluid restriction, a concentration up to 10 mg/mL may be used.

Each dose should be administered at no more than 10 mg / min.

Before administration, the reconstituted and diluted solutions should be inspected visually for particulate matter and discoloration.

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.

Incompatibilities

Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds. Mixing with alkaline solutions should be avoided. Each parenteral solution should be checked visually for precipitation and discolouration prior to use.

Mixtures of solutions of vancomycin and beta-lactam antibiotics have been shown to be physically incompatible. The likelihood of precipitation increases with higher concentrations of vancomycin. It is recommended to adequately flush the intravenous lines between the administrations of these antibiotics. It is also recommended to dilute solutions of vancomycin to 5 mg / mL or less.

Although intravitreal injection is not an approved route of administration for vancomycin, precipitation has been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles. The precipitates dissolved gradually, with complete clearing of the vitreous cavity over two months and with improvement of visual acuity.

Shelf life after reconstitution of the concentrate and diluted solutions:

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage items and conditions prior to use are the responsibility of the user.

Chemical and physical in-use stability has been demonstrated for 24 hours at 2-8 °C.

Solutions of the parenteral powder intended for oral administration may be stored in a refrigerator (2°-8°C) for 96 hours.

Prior to administration, parenteral medicinal products should be inspected visually for particulate matter and discolouration whenever solution or container permits. Only clear and colourless to slightly yellowish brown solution free from particles should be used.

Disposal

Any unused product or waste material should be disposed of in accordance with local requirements.