VANCO® 500 mg

Vancomycin

1. WHAT IS VANCO® 500 mg?

Pharmaceutical form

Vial of lyophilized product for parenteral use

Composition

Each vial contains:

Vancomycin hydrochloride quantity corresponding to Vancomycin base : ..... 500 mg

Pharmacological properties

The Vancomycin is an antibiotic. It's a glycopeptide of which the bactericide antibiotic activity is carried out by wall bacterial biosynthesis inhibition.

Antibacterial activity

The antibacterial spectrum of Vancomycin is the following:

Sensitive species:

-gram- Aerobic germs: bacillus, enterococci, listeria, Rhodococcus equi, staphylococcus aureus, nonaureus staphylococcus, streptococcus, Streptococcus pneumoniae.

-Anaerobic germs: clostridium, eubacterium, peptostreptococcus, propionibacterium acnes.

Resistant species:

-gram+ aerobic germs: actinomyces, erysipelothrix, hetero-fermenting lactobacillus, leuconostoc, nocardia

asteroides, and pediococcus.

- Gram- aerobic germs: cocci and bacillus.
- Others: Chlamydia, mycobacterium, mycoplasma, rickettsia, treponema.

Pharmacokinetics

Absorption :

Vancomycin is administered by intravenous route in the treatment of systemic infections.

Distribution :

- In patients with normal renal function, the repeated administration of one gram of Vancomycin (15 mg/kg) in a 60 min. infusion permits to obtain mean plasmatic concentrations of 23 µg/ml two hours after the infusion, and mean plasmatic concentrations of about 8 µg /ml eleven hours after the end of the infusion. Repeated doses of 500 mg in a infused in less than 60 min. give mean plasmatic concentrations of about 49 g /ml at the end of the infusion, of 19 g /ml two hours later, and about

10 µg /ml six hours later. The plasmatic concentrations after multiple doses are therefore similar to those obtained after single dose administration.

- The serous half-life in patients with normal renal function is 4 to 8 hours.

In the first 24 hours, about 75 % of the administrated dose of Vancomycin is excreted in urines by glomerular filtration. The mean plasmatic clearance is about 0.058 l/kg/hour, and the mean renal clearance is about 0.048 l/kg/hour.

The existence of a renal impairment involves a delaying of the renal excretion Vancomycin. In case of total renal impairment (subject with anuria), the elimination half-life is 7.5 days. The distribution coefficient varies between 0.3 and 0.43 l/kg. The total and renal clearances can be reduced in the elderly.

The plasmatic protein binding level is 55 % at the therapeutic concentrations.

Vancomycin has a good diffusion in the pleural, peritoneal and pericardial fluids; but it is inexistent in the cerebrospinal fluid when the meninges are healthy and random when they are inflamed.

Biotransformation :

Vancomycin is not metabolized in the body.

Excretion :

About 90 % of the injected dose of Vancomycin is excreted by renal route in its active form (75% in 24h).

Synergistic combinations :

Vancomycin has, in vitro, a synergistic activity with aminosides in many strains of staphylococcus aureus, streptococcus and enterococcus.

2. IN WHICH CASE CAN VANCO® 500 mg BE USED?

- Infections caused by Vancomycin sensitive germs (excluding meningitis), especially staphylococci severe infections including methicillin-resistant staphylococcus (respiratory infections, osteitis, endocarditis, septicemia,) and infections caused by streptococcus (including enterococcus), or in patients allergic to β- lactamines, Vancomycin is active as a single agent or combined to aminosides in the endocarditis caused by S.Viridans or S.Bovis. In the endocarditis caused by enterococcus (for example: Streptococcus faecalis), Vancomycin must be associated with an aminoside.
- Vancomycin is indicated in the prophylaxis of post-operative infections due to Gram positive bacteria in:
- Vascular and cardiac surgery
- Neurosurgery

-Orthopedic surgery with implantation of prosthesis equipment; in case of:

• Precocious surgical re-intervention.

• Foreseeable or demonstrated colonization by the meticillin-resistant staphylococcus (previous antibiotherapy

or stay in a hospital with known meticillin-resistant infections risk).

• In case of allergy to the β-lactamines.

3. WHAT IS NECESSARY TO BE KNOWN BEFORE TAKING VANCO® 500 mg?

Contraindications

- Known hypersensitivity to one of the components
- Hypersensitivity to the teicoplanin or to the Vancomycin

Warnings and precautions of use

- Vancomycin must be delivered by slow IV perfusion: The rapid or bolus administration may cause hypotension or even cardiovascular collapse especially with child and infant.

The dose of Vancomycin must be administered in perfusion during 60 minutes in diluted solution to avoid red man syndrome due to very fast administration and imputed to the brutal release of histamine. The interruption of perfusion allows generally the regression of troubles.

- Vancomycin must be used exclusively by intravenous route because of necrosis risk.

The venous irritation risk is limited by administering the product in diluted solution (2,5 to 5 g/l) and by injecting in different veins.

- In renal insufficiency, old and new born patients and with those using another drug potentially nephrotoxic: drug dosage must be adapted and a strict monitoring of renal functions and when it's possible of auditory functions, also Vancomycin plasma concentration should be evaluated.
- Avoid Vancomycin use in fall hearing acuity patients. When its use is mandatory for such patient, we must then adapt the drug dosage according to plasma concentrations. Auditory trouble may precede deafness. The risks of auditory trouble are increased in the elderly patients. The experience acquired with other antibiotics suggests that the deafness may persist in spite of treatment arrest.

Use during pregnancy and breastfeeding

• Pregnancy

- The high therapeutic benefit of Vancomycin makes its use considered if necessary during pregnancy, whatever is the term.
- The animal studies data doesn't show teratogenic effect, however clinical data are still insufficient.
- Considering ototoxicity of Vancomycin, in case of use during pregnancy, evaluation of neonate auditory functions could be done.

• Breastfeeding

Vancomycin is contraindicated in the nursing women because of it cross over milk.

Drug interactions

- The administration of anesthetics during Vancomycin infusion can provoke anaphylactoid reactions. These disorders can be minimized by administering Vancomycin in infusion during at least 60 minutes, before the anesthetic induction.
- Avoid association of Vancomycin with other nephrotoxic or ototoxic medicines such as: amphotericine B, aminoglycosides, bacitracin, polymyxin B, colistin, viomycin, or cisplatin, and when these medicines are indicated, it is required to rigorously monitor the renal and hearing functions.

4. HOW TO USE VANCO® 500 mg?

Dosage and mode of administration

• Dosage

Curative treatment:

a. Patients with normal hepatic and renal functions

- Adult: 2 g a day (about 30 mg/ kg/ day). The usual dose is 500 mg every 6 hours or 1 g every 12 hours. Each dose must be administered during at least 60 minutes. Other factors such as the age and the obesity have to be taken into account in the daily dosage adaptation.
- Children and infant:

40 mg/kg/day (10mg/kg in perfusion every 6 hours). If the central nervous system is attacked we can increase the dosage up to 15mg/kg every 6 hours (60 mg/ kg/day).

- New-born or premature

* 0 to 7 days: 30mg/kg/day (15mg/kg in perfusion 30 min every 12 hours) then 10mg/kg every 12 hours.
* 7 to 30 days: 45 mg/kg/days (15mg/kg in perfusion every 8 hours) under the control of seric rate of the antibiotic.

b. Renal insufficient and old patients

Patients with anuria or at the end stage of renal insufficiency , the initial dose of Vancomycin is 1 g followed

by 1g or 500 every 7 to 10 days according to the results of Vancomycin serum concentrations.

At the renal insufficient, the unit dose remains the same as for the normal subject, but the therapeutic interval

is increased. Considering great variabilities of the pharmacokinetics with renal insufficient, this interval has

to be based on the control of serum concentrations.

In anticipation of these results, the dose will be determined using:

- Data is below :

Cr Cl (ml/min)	Vancomycin Dose (mg/day)
100	1545
90	1390
80	1235
70	1080
60	925
50	770
40	620
30	465
20	310
10	155

- Or, using the following formula :

Daily dosage (mg/day) = (creatinine clearance [ml/min] x 15) + 150.

c. Hepatic insufficiency

The same precautions are recommended in hepatic insufficiency.

Prophylaxis of post-operative infections in surgery

Antibioprophylaxis must be of short term, it's often limited to the post-operative period, sometimes 24 hours

but never more than 48 hours.

- Adult : 1 g during 1 hour of IV perfusion, 1 hour before the beginning of the surgery (before incision), then

reinjection of the same dose 12 hours later during 24 hours, without exceeding 48 hours.

- child : the usual dosage is 15 mg/kg in IV then reinjection of the same dose 12 hours later during

24 hours, without exceeding 48 hours.

• Mode of administration

Dissolve the content of a vial with 10 ml of water for injectable preparations.

Do never inject this solution as it is but dilute it as follows:

1) In case of discontinuous perfusion: add the primitive solution to 100 ml or 200 ml of solvent (5% Dextrose injection or 0, 9% Sodium Chloride Injection). We can administer the diluted solution by infusion over a period of at least 60 minutes, every 6 hours.

2) In case of continuous perfusion, dilute the primary solution to a sufficiently important volume of solvent to allow the administration of the daily dose, over a period 24 hours.

• Incompatibility with all drugs :

In the absence of appropriate physicochemical compatibility studies, association's infusion with other drugs

is not recommended.

Overdose

Patient should be closely monitored, with a maintaining of the glomerular filtration

Vancomycin is slightly eliminated by dialysis. It was reported that the hemofiltration and hemoperfusion using polysulfane resin increases Vancomycin clearance.

5. WHAT ARE THE UNDESIRABLE EFFECTS?

Like all other drugs, vanco 500mg is susceptible to induce undesirable effects:

- Nausea, vomiting, fever, urticaria, cutaneous macular eruption and exfoliative dermatitis have been noted

in patients receiving Vancomycin.

- Eosinophilia has been observed. Neutropenia which is quickly reversible when the treatment is

discontinued has been reported.

- Anaphylactoid reaction. pulsatory pain in the muscles of back and neck have been reported. These reactions

may be avoided or reduced by a slow perfusion (minimum 60 minutes). Hypotension have been noted, it can

occur more particularly in case of rapid injection. A reaction of cutaneous "flush" of the neck or shoulders with fine transitory eruption, being able to be urticarian has been observed during rapid perfusion.

-Nephrotoxicity, Ototoxicity: with patients presenting a renal insufficiency the ototoxicity and

nephrotoxicity risks are increased when the blood concentrations of Vancomycin are increased or if the treatment is extended.

- Veinitis, especially when the Vancomycin is administrated by peripheral route.

6. HOW TO STORE VANCO® 500 mg?

- Keep away from heat
- After reconstitution:

The reconstituted solution can be preserved during 24 hours at an ambient temperature (+ 25°C) and

96 hours in refrigerator (+ 2° C to + 8° C). It is recommended to use the product in this time, although the

solution is stable during 14 days in refrigerator.

7. WHAT ARE THE DELIVERY CONDITIONS OF VANCO® 500 mg?

List I

Reserved to the hospital use.

8. PRESENTATION AND M.A NUMBER

Speciality	Presentation	M.A number
VANCO® 500mg	Box of 1 lyophilised vial	923 322 1H
VANCO® 500mg	Box of 10 lyophilised vial	923 322 2H

Marketing Authorization Holder and Manufacturer:

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This is a medicine

- A medicine is a product but not like any other product.
- A medicine is a product that affects your health,if it's not used properly : it can be health threatening.
- Strictly adhere to the prescription of you Doctor and the use instructions prescribed, follow your pharmacist advice.
- Your doctor and you pharmacist know the medicine, its use and side effect.
- Don't stop the use of the treatment on your own during the prescribed time.
- Don't retake, Don't increase the doses without doctor's advice.

Keep the medicines out of reach of children

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