Controlled Medicine / Ubat Terkawal

VANCO-500

Vancomycin Hydrochloride USP Powder for solution for infusion 500 mg
For Intraveneous use only

COMPOSITION :
Each vial contains:
Sterile Vancomycin Hydrochloride USP
Equivalent to Vancomycin 500mg

DESCRIPTION:
Product Description: A vial contain white, almost white, or tan to brown , free flowing powder.
Appearance of reconstituted/diluted solution: Clear and free from visible particles and undissolved matters.

PHARMACOLOGY:
PHARMACODYNAMIC
Pharmacodynamics: ATC Code: J01 XA01 for intravenous use

Mechanism of action:
Vancomycin is a tricyclic glycopeptide antibiotic that inhibits the synthesis of the cell wall in sensitive bacteria by binding with high affinity to the D-alanyl-D-alanine terminus of cell wall precursor units. The drug is slowly bactericidal for dividing microorganisms. In addition, it impairs the permeability of the bacterial cell membrane and RNA synthesis.
Pharmacokinetic/Pharmacodynamics Relationship
Vancomycin displays concentration-independent activity with the area under the concentration curve (AUC) divided by the minimum inhibitory concentration (MIC) of the target organism as the primary predictive parameter for efficacy. On basis of in vitro, animal and limited human data, an AUC/MIC ratio of 400 has been established as a PK/PD target to achieve clinical effectiveness with vancomycin. To achieve this target when MICs are $\geq$ 1.0 mg/l, dosing in the upper range and high trough serum concentrations (15-20 mg/l) are required (see section Recommended Dose).

Mechanism of Resistance
Acquired resistance to glycopeptides is most common in enterococci and is based on acquisition of various van gene complexes which modifies the D-alanyl-D-alanine target to D-alanyl-D-lactate or D-alanyl-D-serine which bind vancomycin poorly. In some countries, increasing cases of resistance are observed particularly in enterococci; multi-resistant strains of Enterococcus faecium are especially alarming. Van genes have rarely been found in Staphylococcus aureus, where changes in cell wall structure result in “intermediate” susceptibility, which is most commonly heterogeneous. Also, methicillin-resistant staphylococcus strains (MRSA) with reduced susceptibility for vancomycin were reported. The reduced susceptibility or resistance to vancomycin in Staphylococcus is not well understood. Several genetic elements and multiple mutations are required.
There is no cross-resistance between vancomycin and other classes of antibiotics. Cross-resistance with other glycopeptide antibiotics, such as teicoplanin, does occur. Secondary development of resistance during therapy is rare.

Synergism
The combination of vancomycin with an aminoglycoside antibiotic has a synergistic effect against many strains of Staphylococcus aureus, non-enterococcal group Dstreptococci, enterococci and streptococci of the Viridans group. The combination of vancomycin with a cephalosporin has a synergistic effect against some oxacillinresistant Staphylococcus epidermidis strains, and the combination of vancomycin with rifampicin has a synergistic effect against Staphylococcus epidermidis and a partial synergistic effect against some Staphylococcus aureus strains. As vancomycin in combination with a cephalosporin may also have an antagonistic effect against some Staphylococcus epidermidis strains and in combination with rifampicin against some Staphylococcus aureus strains, preceding synergism testing is useful.
Specimens for bacterial cultures should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to vancomycin. Susceptibility testing breakpoints Vancomycin is active against gram-positive bacteria, such as staphylococci, streptococci, enterococci, pneumococci, and clostridia. Gram-negative bacteria are resistant.
The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable. This information only provides approximate guidance on the chance whether micro-organisms are susceptible to vancomycin. Minimum inhibitory concentration (MIC) breakpoints established by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) are as follows:

	Susceptible	Resistant
Staphylococcus aureus[1]	≤ 2mg/L	> 2mg/L
Coagulase-negative staphylococci[1]	≤ 4mg/L	> 4mg/L
Enterococcus spp.	≤ 4mg/L	> 4mg/L
Streptococcus groups A, B, C and G	≤ 2mg/L	> 2mg/L
Streptococcus pneumoniae	≤ 2mg/L	> 2mg/L
Gram positive anaerobes	≤ 2mg/L	> 2mg/L

[1 S.] aureus with vancomycin MIC values of 2 mg/L are on the border of the wild type distribution and there may be an impaired clinical response.

Commonly susceptible species
Gram positive Enterococcus faecalis Staphylococcus aureus Methicillin-resistant Staphylococcus aureus coagulase-negative Staphylococci Streptococcus spp. Streptococcuspneumoniae Enterococcus spp. Staphylococcus spp. Anaerobic species Clostridium spp. except Clostridium innocuum Eubacterium spp. Peptostreptococcus spp.
Species for which acquired resistance may be a problem Enterococcus faecium
Inherently resistant All Gram negative bacteria Gram positive aerobic species Erysipelothrixrhusiopathiae, Heterofermentative Lactobacillus, Leuconostoc spp. Pediococcus spp. Anaerobic species Clostridium innocuum
The emergence of resistance towards vancomycin differs from one hospital to another and a local microbiological laboratory should therefore be contacted for relevant local information.

PHARMACOKINETICS

Absorption
Vancomycin is administered intravenously for the treatment of systemic infections. In the case of patients with normal renal function, intravenous infusion of multiple doses of 1g vancomycin (15 mg/kg) for 60 minutes produces approximate average plasma concentrations of 50-60 mg/L, 20-25 mg/L and 5-10 mg/L, immediately, 2 hours and 11 hours after completing the infusion, respectively. The plasma levels obtained after multiple doses are similar to those achieved after a single dose.
Vancomycin is not usually absorbed into the blood after oral administration. However, absorption may occur after oral administration in patients with (pseudomembranous) colitis. This may lead to vancomycin accumulation in patients with co-existing renal impairment.

Distribution
The volume of distribution is about 60 L/1.73 m2 body surface. At serum concentrations of vancomycin of 10 mg/l to 100 mg/l, the binding of the drug to plasma proteins is approximately 30-55%, measured by ultra-filtration.
Vancomycin diffuses readily across the placenta and is distributed into cord blood. In non-inflamed meninges, vancomycin passes the blood-brain barrier only to a low extent.

Biotransformation
There is very little metabolism of the drug. After parenteral administration it is excreted almost completely as microbiologically active substance (approx. 75-90% within 24 hours) through glomerular filtration via the kidneys.

Elimination
The elimination half-life of vancomycin is 4 to 6 hours in patients with normal renal function and 2.2-3 hours in children. Plasma clearance is about 0.058 L/kg/h and kidney clearance about 0.048 L/kg/h. In the first 24 hours, approximately 80 % of an administered dose of vancomycin is excreted in the urine through glomerular filtration. Renal dysfunction delays the excretion of vancomycin. In anephric patients, the mean half-life is 7.5 days. Due to ototoxicity of vancomycin therapy-adjuvant monitoring of the plasma concentrations is indicated in such cases.
Biliary excretion is insignificant (less than 5% of a dose).
Although the vancomycin is not eliminated efficiently by haemodialysis or peritoneal dialysis, there have been reports of an increase in vancomycin clearance with haemoperfusion and haemofiltration.
After oral administration, only a fraction of the administered dose is recovered in the urine. In contrast, high concentrations of vancomycin are found in the faeces (>3100 mg/kg with doses of 2 g/day).

Linearity/non-linearity
Vancomycin concentration generally increases proportionally with increasing dose. Plasma concentrations during multiple dose administration are similar to those after the administration of a single dose.

Characteristics in specific groups
Renal impairment
Vancomycin is primarily cleared by glomerular filtration. In patients with impaired renal function the terminal elimination half- life of vancomycin is prolonged and the total body clearance is reduced. Subsequently, optimal dose should be calculated in line with dosing recommendations provided in section Recommended Dose.
Hepatic impairment
Vancomycin pharmacokinetics is not altered in patients with hepatic impairment.
Pregnant Women
Significantly increased doses may be required to achieve therapeutic serum concentrations in pregnant women (see Section Pregnancy and Lactation).
Overweight patients
Vancomycin distribution may be altered in overweight patients due to increases in volume of distribution, in renal clearance and possible changes in plasma protein binding. In these subpopulations vancomycin serum concentration was found higher than expected in male healthy adults (see section Recommended Dose).
Paediatric population
Vancomycin PK has shown wide inter-individual variability in preterm and term neonates. In neonates, after intravenous administration, vancomycin volume of distribution varies between 0.38 and 0.97 L/kg, similar to adult values, while clearance varies between 0.63 and 1.4 ml/kg/min. Half-life varies between 3.5 and 10 h and is longer than in adults, reflecting the usual lower values for clearance in the neonate.
In infants and older children, the volume of distribution ranges between 0.26-1.05 L/kg while clearance varies between 0.33-1.87 ml/kg/min.

INDICATION:
Vancomycin is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (beta-lactam-resistant) staphylococci. It is indicated for penicillin-allergic patients, for patients who cannot receive or who have failed to respond to other drugs, including the penicillins or cephalosporins, and for infections caused by vancomycin-susceptible organisms that are resistant to other antimicrobial drugs.
Vancomycin is indicated for initial therapy when methicillinresistant staphylococci are suspected, but after susceptibility data are available, therapy should be adjusted accordingly.
Vancomycin's effectiveness has been documented in other infections due to staphylococci, including septicemia, bone infections, lower respiratory tract infections, skin, and skin structure infections. When staphylococcal infections are localized and purulent, antibiotics are used as adjuncts to appropriate surgical measures.
Specimens for bacteriologic cultures should be obtained in order to isolate and identify causative organisms and to determine their susceptibilities to vancomycin. To reduce the development of drug-resistant bacteria and maintain the effectiveness of vancomycin and other antibacterial drugs, vancomycin should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

RECOMMENDED DOSE:

Vancomycin is intended for intravenous use. In selected patients in need of fluid restriction, a concentration up to 10 mg/mL may be used; use of such higher concentrations may increase the risk of infusion-related events. An infusion rate of 10 mg/min or less is associated with fewer infusion-related events (see section Side Effects). Infusion-related events are related to both concentration and rate of administration of vancomycin. Concentrations of no more than 5 mg/mL and rates of no more than 10 mg/min are recommended in adults (see also age-specific recommendations).

Patients with Normal Renal Function
Adults: The usual daily intravenous dose is 2 g divided either as 500 mg every six hours or 1 g every 12 hours. Each dose should be administered at no more than 10 mg/min, or over a period of at least 60 minutes, whichever is longer. Other patient factors, such as age or obesity, may call for modification of the usual intravenous daily dose.
Pediatric Patients: The usual intravenous dosage of vancomycin is 10 mg/kg per dose given every six hours. Each dose should be administered over a period of at least 60 minutes. Close monitoring of serum concentrations of vancomycin is recommended in these patients.
Neonates: In pediatric patients up to the age of 1 month, the total daily intravenous dosage may be lower. In neonates, an initial dose of 15 mg/kg is suggested, followed by 10 mg/kg every 12 hours for neonates in the first week of life and every eight hours thereafter up to the age of one month. Each dose should be administered over 60 minutes. In premature infants, vancomycin clearance decreases as postconceptional age decreases. Therefore, longer dosing intervals may be necessary in premature infants. Close monitoring of serum concentrations of vancomycin is recommended in these patients.

Patients with Impaired Renal Function and Elderly Patients
Dosage adjustment must be made in patients with impaired renal function. In the elderly, greater dosage reductions than expected may be necessary because of decreased renal function. Measurement of vancomycin serum concentrations can be helpful in optimizing therapy, especially in seriously ill patients with changing renal function. Vancomycin serum concentrations can be determined by use of microbiologic assay, radioimmunoassay, fluorescence polarization immunoassay, fluorescence immunoassay, or high-pressure liquid chromatography. If creatinine clearance can be measured or estimated accurately, the dosage for most patients with renal impairment can be calculated using the following table. The dosage of vancomycin per day in mg is about 15 times the glomerular filtration rate in mL/min:
Dosage Table For Vancomycin In Patients With Impaired Renal Function (Adapted from Moellering et al)

Creatinine Clearance mL/min	Vancomycin Dose mg/24h
100	1545
90	1390
80	1235
70	1080
60	925
50	770
40	620
30	465
20	310
10	155

The initial dose should be no less than 15 mg/kg, even in patients with mild to moderate renal insufficiency.
The table is not valid for functionally anephric patients. For such patients, an initial dose of 15 mg/kg of body weight should be given to achieve prompt therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 h. In patients with marked renal impairment, it may be more convenient to give maintenance doses of 250 to 1000 mg once every several days rather than administering the drug on a daily basis. In anuria, a dose of 1000 mg every 7 to 10 days has been recommended.
When only the serum creatinine concentration is known, the following formula (based on sex, weight, and age of the patient) may be used to calculate creatinine clearance. Calculated creatinine clearances (mL/min) are only estimates. The creatinine clearance should be measured promptly.
Men: Weight (kg) x (140 - age in years) / 72 x serum creatinine concentration (mg/dL)
Women: 0.85 x above value
The serum creatinine must represent a steady state of renal function. Otherwise the estimated value for creatinine clearance is not valid. Such a calculated clearance is an overestimate of actual clearance in patients with conditions: (1) characterized by decreasing renal function, such as shock, severe heart failure, or oliguria; (2) in which a normal relationship between muscle mass and total body weight is not present, such as obese patients or

those with liver disease, edema, or ascites; and (3) accompanied by debilitation, malnutrition, or inactivity.
The safety and efficacy of vancomycin administration by the intrathecal (intralumbar or intraventricular) routes have not been established.
Intermittent infusion is the recommended method of administration.

Route of Administration:

Intravenous (IV) Infusion

Preparation of solution: At the time of use, add 10ml of water for injections to the 500mg vial.
Vials reconstituted in this manner will give a solution of 50mg/ml.
The reconstituted solution is clear and colourless.
Further dilution is required. Read instructions which follow:
1. Intermittent infusion is the preferred method of administration. Reconstituted solutions containing 500mg vancomycin must be diluted with at least 100ml diluent. 0.9% sodium chloride intravenous infusion or 5% dextrose intravenous infusion is suitable diluent. 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.
2. Continuous infusion (should be used only when intermittent infusion is not feasible).
1-2g can be added to a sufficiently large volume of sodium chloride intravenous infusion or 5% dextrose intravenous infusion to permit the desired daily dose to be administered slowly by intravenous drip over a 24 hour period.

ROUTE OF ADMINISTRATION: For intravenous infusion and not for intramuscular administration.

CONTRAINDICATIONS:

Vancomycin hydrochloride is contraindicated in patients with known hypersensitivity to this antibiotic.
Vancomycin should not be administered intramuscularly due to the risk of necrosis at the site of administration.

WARNINGS AND PRECAUTIONS:

Hypersensitivity reactions:

Serious and occasionally fatal hypersensitivity reactions are. In case of hypersensitivity reactions, treatment with vancomycin must be discontinued immediately and the adequate emergency measures must be initiated.
In patients receiving vancomycin over a longer-term period or concurrently with other medications which may cause neutropenia or agranulocytosis, the leukocyte count should be monitored at regular intervals. All patients receiving vancomycin should have periodic haematologic studies, urine analysis, liver and renal function tests. Vancomycin should be used with caution in patients with allergic reactions to teicoplanin, since cross hypersensitivity, including fatal anaphylactic shock, may occur.

Spectrum of antibacterial activity:

Vancomycin has a spectrum of antibacterial activity limited to Gram-positive organisms. It is not suitable for use as a single agent for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a high suspicion that the most likely pathogen(s) would be suitable for treatment with vancomycin.
The rational use of vancomycin should take into account the bacterial spectrum of activity, the safety profile and the suitability of standard antibacterial therapy to treat the individual patient.

Ototoxicity:

Ototoxicity, which may be transitory or permanent has been reported in patients with prior deafness, who have received excessive intravenous doses, or who receive concomitant treatment with another ototoxic active substance such as an aminoglycoside.
Vancomycin should also be avoided in patients with previous hearing loss. Deafness may be preceded by tinnitus. Experience with other antibiotics suggests that deafness may be progressive despite cessation of treatment. To reduce the risk of ototoxicity, blood levels should be determined periodically and periodic testing of auditory function is recommended.
The elderly are particularly susceptible to auditory damage. Monitoring of vestibular and auditory function in the elderly should be carried out during and after treatment. Concurrent or sequential use of other ototoxic substances should be avoided.

Infusion-related reactions:

Rapid bolus administration (i.e. over several minutes) may be associated with exaggerated hypotension (including shock and, rarely, cardiac arrest), histamine like responses and maculopapular or erythematous rash ("red man's syndrome" or "red neck syndrome").
Vancomycin should be infused slowly in a dilute solution (2.5 to 5.0 mg/mL) at a rate no greater than 10 mg/min and over a period not less than 60 minutes to avoid rapid infusion related reactions. Stopping the infusion usually results in a prompt cessation of these reactions.
The frequency of infusion-related reactions (hypotension, flushing, erythema, urticaria and pruritus) increases with the concomitant administration of anaesthetic agents. This may be reduced by administering vancomycin by infusion over at least 60 minutes, before anaesthetic induction.

Severe bullous reactions:

Stevens-Johnson syndrome (SJS) has been reported with the use of vancomycin. If symptoms or signs of SJS (e.g. progressive skin rash often with blisters or mucosal lesions) are present, vancomycin treatment should be discontinued immediately and specialised dermatological assessment be sought.

Administration site related reactions:

Pain and thrombophlebitis may occur in many patients receiving intravenous vancomycin and are occasionally severe. The frequency and severity of thrombophlebitis can be minimized by administering the medicinal product slowly as a dilute solution and by changing the sites of infusion regularly.
The efficacy and safety of vancomycin has not been established for the intrathecal, intralumbar and intraventricular routes of administration.

Nephrotoxicity:

Vancomycin should be used with care in patients with renal insufficiency, including anuria, as the possibility of developing toxic effects is much higher in the presence of prolonged high blood concentrations. The risk of toxicity is increased by high blood concentrations or prolonged therapy.
Regular monitoring of the blood levels of vancomycin is indicated in high dose therapy and longer-term use, particularly in patients with renal dysfunction or impaired faculty of hearing as well as in concurrent administration of nephrotoxic or ototoxic substances, respectively.

Paediatric population:

The current intravenous dosing recommendations for the paediatric population, in particular for children below 12 years of age, may lead to sub-therapeutic vancomycin levels in a substantial number of children. However, the safety of increased vancomycin dosing has not been properly assessed and higher doses than 60 mg/kg/day cannot be generally recommended.
Vancomycin should be used with particular care in premature neonates and young infants, because of their renal immaturity and the possible increase in the serum concentration of vancomycin. The blood concentrations of vancomycin should therefore be monitored carefully in these children. Concomitant administration of vancomycin and anaesthetic agents has been associated with erythema and histamine-like flushing in children. Similarly, concomitant use with nephrotoxic agents such as aminoglycoside antibiotics, NSAIDs (e.g., ibuprofen for closure of patent ductus arteriosus) or amphotericin B is associated with an increased risk of nephrotoxicity and therefore more frequent monitoring of vancomycin serum levels and renal function is indicated.

Use in the elderly:

The natural decrement of glomerular filtration with increasing age may lead to elevated vancomycin serum concentrations if dosage is not adjusted.

Drug interactions with anaesthetic agents:

Anaesthetic induced myocardial depression may be enhanced by vancomycin. During anaesthesia, doses must be well diluted and administered slowly with close cardiac monitoring. Position changes should be delayed until the infusion is completed to allow for postural adjustment.
Pseudomembranous enterocolitis
In case of severe persistent diarrhoea the possibility of pseudomembranous enterocolitis that might be life-threatening has to be taken into account. Anti-diarrhoeic medicinal products must not be given.

Superinfection:

Prolonged use of vancomycin may result in the overgrowth of non-susceptible organisms.
Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

INTERACTIONS WITH OTHER MEDICAMENTS:

Concurrent administration of vancomycin and anaesthetic agents has been associated with erythema, histamine like flushing and anaphylactoid reactions. Concurrent administration with other neurotoxic or nephrotoxic drugs, e.g. amphotericin B, streptomycin, neomycin, gentamicin, kanamycin, amikacin, tobramycin, bacitracin, polymyxin B, colistin and cisplatin requires careful monitoring.
Diuretics such as ethacrynic acid and frusemide may aggravate ototoxicity.

PREGNANCY AND LACTATION:

Pregnancy: No sufficient safety experience is available regarding vancomycin during human pregnancy. Therefore, vancomycin should be given in pregnancy only if clearly needed and after a careful risk/benefit evaluation.
Lactation: Vancomycin Hydrochloride is excreted in breast milk but it is not known whether it is harmful to the newborn. Therefore, it is not recommended for nursing mothers unless the expected benefits outweigh any potential risk.

SIDE EFFECTS:

Summary of the safety profile

The most common adverse reactions are phlebitis, pseudo-allergic reactions and flushing of the upper body ("red-neck syndrome") in connection with too rapid intravenous infusion of vancomycin.
The absorption of vancomycin from the gastrointestinal tract is negligible. However, in severe inflammation of the intestinal mucosa, especially in combination with renal insufficiency, adverse reactions that occur when vancomycin is administered parenterally may appear.
Tabulated list of adverse reactions
Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.
The adverse reactions listed below are defined using the following MedDRA convention and system organ class database:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1000), Very rare (<1/10/1/10,000), not known (can not be estimated from the available table).

System organ class	
Frequency	Adverse reaction
Blood and the lymphatic system disorders	
Rare	Reversible neutropenia, agranulocytosis, eosinophilia, thrombocytopenia, pancytopenia
Immune system disorders	
Rare	Hypersensitivity reactions, anaphylactic reactions
Ear and labyrinth disorders	
Uncommon	Transient or permanent loss of hearing
Rare	Vertigo, tinnitus, dizziness
Cardiac disorders	
Very rare	Cardiac arrest
Vascular disorders	
Common	Decrease in blood pressure
Rare	Vasculitis
Respiratory, thoracic and mediastinal disorders	
Common	Dyspnoea, stridor
Gastrointestinal disorders	
Rare	Nausea
Very rare	Pseudomembranous enterocolitis
Not known	Vomiting, Diarrhoea
Skin and subcutaneous tissue disorders	
Common	Flushing of the upper body ("red man syndrome") exanthema and mucosal inflammation, pruritus, urticaria
Very rare	Exfoliative dermatitis, Stevens-Johnson syndrome, Lyell's syndrome, Linear IgA bullous dermatosis
Not known	Eosinophilia and systemic symptoms (DRESS syndrome), AGEP (Acute Generalized Exanthematous Pustulosis)
Renal and urinary disorders	
Common	Renal insufficiency manifested primarily by increased serum creatinine and serum urea
Rare	Interstitial nephritis, acute renal failure
Not known	Acute tubular necrosis
General disorders and administration site conditions	
Common	Phlebitis, redness of the upper body and face
Rare	Drug fever, shivering, pain and muscle spasm of the chest and back muscles

Description of selected adverse drug reactions
Reversible neutropenia usually starting one week or more after onset of intravenous therapy or after total dose of more than 25 g.
During or shortly after rapid infusion anaphylactic/anaphylactoid reactions including wheezing may occur. The reactions abate when administration is stopped, generally between 20 minutes and 2 hours. Vancomycin should be infused slowly (see sections Recommended Dose and, Warnings and Precautions). Necrosis may occur after intramuscular injection.Tinnitus, possibly preceding onset of deafness, should be regarded as an indication to discontinue treatment.
Ototoxicity has primarily been reported in patients given high doses, or in those on concomitant treatment with other ototoxic medicinal product like aminoglycoside, or in those who had a pre-existing reduction in kidney function or hearing.
If a bullous disorder is suspected, the drug should be discontinued and specialized dermatological assessment should be carried out.
Paediatric Population
The safety profile is generally consistent among children and adult patients. Nephrotoxicity has been described in children, usually in association with other nephrotoxic agents such as aminoglycosides.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

INCOMPATIBILITIES:

Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds. 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 intravenous lines between administration of these antibiotics. It is also recommended to dilute solutions of vancomycin to 5 mg/mL or less.

OVERDOSAGE: Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed from the blood by haemodialysis or peritoneal dialysis. Haemoperfusion with Amberlite resin XAD-4 has been reported to be of limited benefit.

STORAGE CONDITION: Store below 30^0C.
KEEP OUT OF REACH THE CHILDREN
Jauhkan daripada capaian kanak-kanak
MUST BE FURTHER DILUTED BEFORE USE
For single use only.

Reconstitution Detail:
List of Compatible Diluent
1) 0.9% sodium chloride intravenous infusion
2) 5% dextrose intravenous infusion

Shelf life of the reconstituted solution:

The reconstituted solution may be stored in a refrigerator (2°C - 8°C) for not more than 24 hours.

Shelf life of diluted solution:

After reconstitution, stored in a refrigerator at 2°- 8°C for 24 hours. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 - 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

DOSAGE FORM & PACKING STYLE :
Dosage Form: Powder for Injection
Packing Style: Available in a glass vial.
Date of Revision : 26.02.2024

Manufactured by:
SWISS PARENTERALS LTD.
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