IDEAGRAFICA S.r.l.

IMPIANTO DI PROPRIETÁ/OWNER: FISIOPHARMA

PRODOTTO/PRODUCT	CODICE/CODE	IDG FUST.	TRACCIATO/ DIE CUT NUMBER	DIMENSIONI/SIZE	DIMENSIONE PIEG./ FOLDED SIZE
FI VANCOTEX 500MG ING-MALAYSIA PHARMATEX	3510579-02			125x310	125x30

N. COLORI/ No OF COLORS	COLOR 1	COLOR 2	COLOR 3	COLOR 4	COLOR 5	COLOR 6	COLOR 7
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DATA/DATE	IDG Nr.	OPERATOR	TESTO BRAILLE/BRAILLE TEXT	LAETUS	CARTONE/CARTON TYPE
17/10/23	Bozza 1	GIORGIO		310	UM 60g.

"SI PREGA DI LEGGERE ATTENTAMENTE LA PRESENTE BOZZA.
NON CI ASSUMIAMO RESPONSABILITÁ SUCCESSIVAMENTE ALL'APPROVAZIONE DELLA STESSA DA PARTE DEL CLIENTE"

Vancotex Injection 500mg
Vancomycin (as hydrochloride)

Product Description
Dry powder for reconstitution in clear glass vials. The free-flowing powder is tan to brown.

Composition
Each vial contains Vancomycin hydrochloride 512.57 mg corresponding to Vancomycin 500 mg.

Pharmacodynamic
Vancomycin is bactericidal for most organisms and bacteriostatic for enterococci. Vancomycin inhibits bacterial cell wall synthesis at a site different from that of penicillin and cephalosporin by binding tightly to the D-alanyl- D-alanine portion of cell wall precursors and interfering with bacterial growth. This leads to activation of bacterial autolysins that destroy the cell wall by lysis. Vancomycin also may alter the permeability of bacterial cytoplasmic membranes and may selectively inhibit ribonucleic acid (RNA) synthesis. Vancomycin does not compete with penicillin for binding sites.

Pharmacokinetics
Vancomycin is widely distributed to most tissues and body fluids; adequate therapeutic concentrations in serum and in pleural, pericardial, peritoneal, ascitic, and synovial fluids; high concentrations in urine; inadequate concentrations in bile; does not readily cross normal blood-brain barrier into cerebrospinal fluid (CSF); however, penetrates into CSF when meninges are inflamed and may achieve therapeutic concentrations.
Vancomycin crosses the placenta. Vancomycin has moderate binding with plasma protein in healthy adults and low in adults with infections. Normal renal function for adults is approximately 6 hours (range, 4 to 11 hours),newborn infants is approximately 6 to 10 hours, older infants is approximately 4 hours and children is approximately 2 to 3 hours.
Vancomycin is approximately 75 to 90% or more excreted by passive glomerular filtration unchanged in urine within 24 hours; slowly eliminated by unknown route and mechanism in anephric patients. Small, into moderate amounts may be excreted in bile. Vancomycin not appreciably removed from the blood by hemodialysis or peritoneal dialysis.

Indications
Vancomycin is indicated in the serious or severe infections caused by susceptible strains of beta-lactam resistant staphylococci for penicillin-allergic patients, for infections caused by Vancomycin susceptible organism that are resistant to other antimicrobial drugs.

Recommended Dosage
Vancomycin is administered by slow intravenous infusion.

Adults
The usual adult dose is the equivalent of 500 mg of Vancomycin every 6 hours or 1 g every 12 hours, diluted with sodium chloride or 5% glucose solution. Therapeutic response is generally verified in 48-72 hours. The treatment duration should be adjusted with respect to the disease and other clinical infection circumstances. In staphylococcal endocarditis the recommended duration of the treatment is at least 3 weeks.

Children
Children may be given 44 mg per kg bodyweight daily in daily in divided dose (every 6 hours). The quantity of diluted solution must be for a 24 hours administration.

Neonates and nurslings
Neonates and nurslings may be given an initial dose of 15 mg per kg followed, in neonates, by 10 mg per kg every 12 hours in the first week of life, and every 8 hours up to the age of one month. Each infusion should be used over 60 minutes. In these patients serum-vancomycin concentrations should be monitored.

With impaired renal function
In patients with impaired renal function, dosage regimen of vancomycin must be modified in response to degree of renal impairment, severity of infection, susceptibility of causative organism and serum concentrations of the drug. A suggested starting dose in patients with impaired renal function is 15 mg/kg with subsequent doses based mainly on renal function and serum concentrations of the drug. Accumulation of the drug may occur with prolonged therapy and regular monitoring of serum levels should be carried out. The following guide is provided. This data is not valid for functionally anephric patients on dialysis.

Creatinine Clearance ml/min/kg	Vancomycin Dose Mg/kg/24 hrs
2.0	30.9
1.5	23.2
1.0	15.4
0.5	7.7
0.2	3.1

In anephric patients, a loading dose of 15 mg/kg body weight should be given with subsequent dosage of 1.9 mg/kg/24hrs. Since individual maintenance doses of 250 mg -1 g are convenient in patients with marked renal impairment, a dose may be given every several days rather than on a daily basis. In anuria a dose of 1g every 7-10 days has been recommended.
In patients on haemodialysis, the drug is not significantly removed by haemodialysis. A dose of 1 g of vancomycin every seven days produces effective blood levels. Serum levels should be monitored to avoid drug accumulation and resultant toxicity. The serum half-life ranges from 120 to 216 hours.
In patients undergoing peritoneal dialysis, the half-life of vancomycin has been reported at around 18 hours. To prevent undue lowering of serum levels during peritoneal dialysis, an additional amount of vancomycin could be added to the dialysate in a concentration of 25 microgram per ml.

Preparation of the Solution
Reconstitute each 500 mg vial with 10ml of Water for Injections and dilute with infusion fluid (either Glucose 5% or Sodium Chloride 0.9%) to a concentration of up to 5mg/ml. The concentration can be increased to 10mg/ml in fluid restriction but increased risk of infusion-related effects. The injection is to be injected intermittently over at least 60 minutes and at a rate not exceeding 10mg/minute for doses over 500mg. Use continuous infusion only if intermittent not feasible.

Incompatibilities
Intravenous:
Albumin, amphotericin B, cholesteryl sulfate complex, bivalirudin, ciprofloxacin, drotrecogin alfa, idarubicin.

Contraindication
Vancomycin is contraindicated in individuals with a history of a hypersensitive reaction to Vancomycin.

Warning and Precautions
Warning
Rapid bolus administration (e.g. over several minutes) may be associated with exaggerated hypotension, including shock, and, rarely cardiac arrest. Vancomycin should be infused in a dilute solution at a rate not greater than 10mg/min to avoid rapid infusion-related reactions. Stopping the infusion usually results in a prompt cessation of these reactions. Because of its toxicity and nephrotoxicity, vancomycin should be used with care in patients with renal impairment. The risk of toxicity is increased by high blood concentrations or prolonged therapy. Therefore, blood levels should be monitored and dosage adjusted if it is necessary to use vancomycin in such patients. The concurrent or sequential use of other nephrotoxic drugs requires careful monitoring and should be avoided if possible.
Some patients with inflammatory disorders of the intestinal mucosa may have significant systemic absorption of oral vancomycin and, therefore, may be at risk for the development of adverse reactions associated with the parenteral administration of vancomycin. The risk is greater in patients with renal impairment. It should be noted that the total systemic and renal clearances of vancomycin are reduced in the elderly.
Vancomycin should, if possible, be avoid-

ed in patients with previous hearing loss. Serial testing of auditory function in those aged more than 60 years is advised. If used it is very important that the dose be adjusted by monitoring the blood concentrations of the drug. Deafness may be preceded by tinnitus. The elderly are more susceptible to auditory damage. Experience with other antibiotics suggests that deafness may be progressive despite cessation of treatment.

Precaution
Vancomycin is very irritating to tissue and causes injection site necrosis if injected intramuscularly. Pain and thrombophlebitis occur in many patients receiving vancomycin and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised if the drug is administered as a dilute solution (2.5-5 mg/ml) of Dextrose 5% or Normal Saline 0.9% solution and if the sites of injection are changed regularly.
All patients receiving vancomycin should have periodic haematological studies, urine analysis, liver and renal function tests.
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.

Interaction 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, viomycin, bacitracin, polymyxin B, colistin and cisplatin requires careful monitoring. Diuretics such as ethacrynic acid and frusemide may aggravate ototoxicity. Cholestyramine has been shown to bind vancomycin in-vitro.

Pregnancy and Lactation
Intravenous vancomycin crosses the placenta. In one small controlled study, infants whose mothers were treated with vancomycin in their second or third trimester of pregnancy had no sensory neural hearing loss or nephrotoxicity that was attributed to vancomycin therapy. Vancomycin concentration monitoring is essential to reduce risk of fetal toxicity. Vancomycin should only be used if the potential benefit outweighs the potential risk. Parenteral vancomycin distributed into breast milk. Although available data regarding the use of vancomycin while breast-feeding are limited, problems in humans have been documented.

Side Effects
Adverse Reactions
Auditory and Vestibular:
Sensorineural deafness which may be accompanied by tinnitus has occurred but the incidence is low. Permanent deafness is more likely to occur in patients with compromised auditory or renal function but reversible deafness has been reported in normal patients. Vertigo and dizziness have been reported rarely.

Cardiovascular:
Hypotension, palpitations, substernal pressure, phlebitis, rare cases of vasculitis, and tachycardia. (All effects due to excessively rapid infusion or insufficient dilution of drug.)

Dermatological:
Pruritus at injection site, generalised flushing, erythematous macular rash with intense pruritus over face,
neck and upper body have occurred after too rapid injection of the drug. Tissue irritation and necrosis occurs after IM injection or extravasation from IV site. Vancomycin has been associated with the bullous eruption disorders, rashes including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis and linear IgA bullous dermatosis. If a bullous disorder is suspected, the drug should be discontinued and specialist dermatological assessment should be carried out.

Gastrointestinal:
Oral doses are extremely unpalatable. In leukaemic patients, oral dosing regimens are associated with frequent nausea, diarrhoea and occasional vomiting.

General:
The use of vancomycin may result in overgrowth of non-susceptible organisms resulting in new bacterial or fungal infections.

Genitourinary:
Transient elevations of urea and granular casts in the urine occasionally occur. Nephrotoxicity in the presence of normal renal function at therapeutic serum levels is rare. Rare cases of interstitial nephritis have been reported.

Haematological:
Reversible neutropenia, usually starting one week or more after onset of intravenous therapy or after a total dose of more than 25 g. Neutropenia appears to be promptly reversible when vancomycin is discontinued. Thrombocytopenia has been rarely reported. Reversible agranulocytosis (less than 500 granulocytes per mm^3) has been reported rarely, although causality has not been established. Eosinophilia has been reported.

Immunological:
Histamine release with chills, nausea, urticaria, macular rash, fever and rigors, even at normal doses but usually following rapid drug administration. Anaphylactoid reactions, hypersensitivity reactions and anaphylaxis have been reported.

Ocular:
Subconjunctival injections have infrequently been used in the treatment of bacterial corneal ulcers but may cause severe inflammation or sloughing.

Miscellaneous:
Pain and muscle spasm of the chest and back.

Symptoms and Treatment of Overdose
Vancomycin overdose may result in oliguria and acute renal function failure. Supportive care must be provided, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Hemofiltration and hemoperfusion with polysulfone resin have been used to reduce elevated serum concentrations of vancomycin. Patients should be monitored for electrolytes, fluid, hearing function, hematologic status (especially platelet and white blood cell counts), renal function, and vestibular function.

Presentation
This injection is available in 500 mg. 1 or 10 vials is packed into one folder paper box.

Storage Condition
Protect from light and store below 30°Celsius. Keep out of reach of children.

Shelf Life
The injections can be used within 36 months from the date of manufacture if kept as recommended.
After being reconstituted the solution may be kept in a refrigerator from 2°C and 8°C for 14 days without loosing efficacy.

Registration number
Vancotex Injection for injection 500mg–
MAL06051288AZ
BRU15041846P

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