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Vancosol Injection
(Vancomycin HCl)

وینکوسول انجیکشن
(وینکومائی سین ایچ سی ایل)

COMPOSITION
Vancosol Injection 500mg
Each vial contains:
Vancomycin (as hydrochloride) powder for reconstitution.....500mg
(USP Specification)

Vancosol Injection 1g
Each vial contains:
Vancomycin (as hydrochloride) powder for reconstitution.....1000mg
(USP Specification)

DESCRIPTION
Vancosol contains vancomycin hydrochloride as an active moiety. Vancomycin is an antibiotic produced by soil bacillus Streptococcus orientalis. Vancomycin (HCl) is a complex glycopeptide. Vancomycin (HCl) is highly effective against cocci, especially staphylococci and other gram positive bacteria. Vancomycin (HCl) is administered intravenously or by intravenous infusion. It is used for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (beta-lactam-resistant) staphylococci.

MODE OF ACTION
The bactericidal action of vancomycin results primarily from inhibition of cell-wall biosynthesis. Specifically, vancomycin prevents incorporation of N-acetylmuramic acid (NAM) - and N-acetylglucosamine (NAG)-peptide subunits from being incorporated into the peptidoglycan matrix; which forms the major structural component of Gram-positive cell walls. The large hydrophilic molecule is able to form hydrogen bond interactions with the terminal D-alanyl-D-alanine moieties of the NAM/NAG-peptides. Normally this is a five-point interaction. This binding of vancomycin to the D-Ala-D-Ala prevents the incorporation of the NAM/NAG-peptide subunits into the peptidoglycan matrix. In addition, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis. There is no cross-resistance between vancomycin and other antibiotics. Vancomycin is not active in vitro against gram-negative bacilli, mycobacteria, or fungi.

INDICATIONS
Vancomycin HCl is indicated for the treatment of serious or severe infections caused by susceptible strains of methicillin-resistant (Beta-lactam-resistant) Staphylococcal, It is indicated for penicillin-allergic patients who cannot receive or who have failed to respond to other drugs including the penicillins or cephalosporins, and for infections caused by Vancomycin HCl-susceptible organisms that are resistant to other antimicrobial drugs. Vancomycin HCl is indicated for initial therapy when Methicillin resistant staphylococci are suspected, but after susceptibility data are available, therapy should be adjusted accordingly.
Vancomycin HCl is effective in the treatment of Staphylococcal endocarditis. Its effectiveness has been documented in other infections due to staphylococcal, including septicemia, bone infections, lower respiratory tract infections, and skin and skin structure infections. When Staphylococcal infections are localised and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

Vancomycin HCl has been reported to be effective alone or in combination with an aminoglycoside for endocarditis caused by streptococcus viridans or Bovis. For endocarditis caused by enterococci (e.g. Faecalis). Vancomycin HCl has been reported to be effective only in combination with an aminoglycoside.
Vancomycin HCl has been reported to be effective for the treatment of diphtheroids endocarditis. Vancomycin HCl has been used successfully in combination with rifampin, and aminoglycoside, or both in early onset of prosthetic value endocarditis caused by S.epidermidis or diphtheroids. Specimens for bacteriologic cultures should be obtained in order to isolate and identify causative organisms and to determine their susceptibilities to Vancomycin HCl.
The parenteral form of Vancomycin may be administered orally for treatment of antibiotic-associated-pseudomembranous colitis produced by C. difficile and Staphylococcal ileocolitis, parenteral administration of Vancomycin HCl alone is of unproven benefit for this indication. Vancomycin HCl is not effective by the oral route for other types of infection.
Although on controlled clinical efficacy studies have been conducted, intravenous Vancomycin HCl has been utilized for prophylaxis against bacterial endocarditis in patients with congenital heart disease, rheumatic or other acquired valvular disease who are allergic to penicillin and undergoing dental procedures or surgical procedures of upper respiratory tract.

DOSAGE AND ADMINISTRATION
Patients with Normal Renal Function
Adults: The usually daily intravenous dose is 2 g divided either as 500 mg every 6 hours or 1g every 12 hours. Each dose should be administered over a period of at least 60 minutes. Other patient factors such as age or obesity, may call for modification of the usual daily dose.

Children: The total daily intravenous dosage of Vancomycin Hydrochloride calculated on the basis of 40 mg/kg of body weight, can be divided and incorporated into the Child's 24 hours fluid requirement. Each dose should be administered over a period of at least 60 minutes.

Infants and Neonates: In neonates and young infants, the total daily intravenous dosage may be lower. In both neonates and infants, 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 8 hours there after upto the age of 1 month.
Close monitoring of serum concentrations of Vancomycin HCl may be warranted in these patients. The safety and efficacy of Vancomycin HCl administration by the intrathecal (intralumbar or intraventricular) route have not been assessed.

Patients with impaired renal function and elderly:
Dosage adjusted must be made in patients with impaired renal function in the elderly dosage reduction may be necessary to a greater extent than expected because of decreasing renal function. Measurement of Vancomycin serum concentration can be helpful in optimizing therapy, especially in seriously ill patients with changing renal function. Vancomycin serum concentration can be determined by use of microbiological assay, radio immunoassay, fluorescence polarization immunoassay, and 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 Hydrochloride per day in mg is about 15 times the glomerular filtration rate in mL/min.

DOSAGE TABLE FOR VANCOMYCIN HYDROCHLORIDE
In patients with impaired renal function
(Adapted from Moellering et al)
Vancomycin Hydrochloride dose: mg/24 hr

Creatinine Clearance ml/min	Vancomycin Hydrochloride dose: mg/24 hr
100	1,545
90	1,390
80	1,235
70	1,080
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 in order to achieve prompt therapeutic serum concentrations. The dose required to maintain stable concentrations is 1.9 mg/kg/24 h since individual maintenance dose of250 to 1.000 mg are convenient. 1 dose may be given every several days rather than on a daily basis in patients with marked renal impairment in anuria, a dose of1.000 mg every 7 to 10 days has been recommended.
The safety and efficacy of Vancomycin Hydrochloride by the intrathecal (intralumbar or intraventricular) route have not been assessed.
Intermittent infusion is the recommended method of administration.
Intraperitoneal administration is not recommended.

Method Of Reconstitutuion
At the time of use reconstitute by adding either 10mL of sterile water for injection to the 500 mg vial or 20 mL of sterile water for injection to the 1gm vial of dry. Sterile Vancomycin HCl powder. FURTHER DILUTION IS REQUIRED.
After reconstitution the vial may be stored with in a refrigerator for 14 days without significant loss of potency. Reconstituted solutions containing 500 mg of Vancomycin must be diluted with at least 100 ml of diluent. Reconstituted solutions containing 1g of Vancomycin HCl must be diluted with at least 200 ml of diluent.
The desired dose, diluted in the manner, should be administered by intermittent intravenous infusion over a period of at least 60 minutes.

Compatibility with other Drugs and Intravenous Fluids
Solutions that are diluted with 5% Dextrose injection or 0.9% Sodium Chloride injection may be stored in a refrigerator for 14 days without significant loss of potency. Solutions that are diluted with the following infusion fluids may be stored in a refrigerator for 96 hours.
5% Dextrose Injection and 0.9% Sodium Chloride Injection. Lactated Ringer's Injection Lactated Ringers and 5% Dextrose Injection Normosol-M and 5% Dextroselsolyte E.
Vancomycin HCl solution has a low pH and may Cause physical instability of other compounds.
Parenteral drug products should be inspected visually for paniculate matter and discolorations prior to administration. Whenever solution or container permits.

PHARMACOKINETICS
Vancomycin Hydrochloride is poorly absorbed after oral administration: It is given intravenously for therapy of systemic injections.
In subjects with normal kidney function, multiple intravenous dosing of 1g of Vancomycin (15 mg/kg) infused over 60 minutes produces mean plasma concentrations of approximately 63 mg/L immediately at the completion of infusion, mean plasma concentrations of approximately 23mg/L 2 hours after infusion, and mean plasma concentrations of approximately 8 mg/L 11 hours after the end of the infusion. Multiple dosing of500 mg infused over 30 minutes produces mean plasma concentrations of about 49 mg/L at the completion of infusion, mean plasma concentrations of about 19 mg/L 2 hours after infusion, and mean plasma concentrations of about 10 mg/L 6 hours after infusion. The plasma concentrations during multiple dosing are similar to those after a single dose.
The mean elimination half-life of Vancomycin from plasma is 4 to 6 hours in subjects with normal renal functions. In the first 24 hours, about 75% of an administered dose of Vancomycin is excreted in urine by glomerular filtration. Mean plasma clearance is about 0.058 L/kg/hr and mean renal clearance is about 0.048 L/kg/hr. renal dysfunction slows excretion of Vancomycin. There is no apparentmetabolism of a drug. About 60 percent of an intraperitoneal dose of vancomycin Hydrochloride administered during peritoneal dialysis is absorbed systematically in 6 hours, Serum concentrations of about 10 mg/L are achieved by intraperitoneal injection of 30 mg/kg of Vancomycin. Vancomycin is not effectively removed by either hemodialysis or peritoneal dialysis, there have been no reports of Vancomycin clearance with hemoperfusion.
Total systematic and renal clearance ofVancomycin may be reduced in the elderly.

MICROBIOLOGY
The bactericidal action ofVancomycin results primarily from inhibition of cell-wall biosynthesis. In addition. Vancomycin alters bacterial-cell membrane permeability and RNA synthesis. There is no cross-resistance between Vancomycin and other antibiotics. Vancomycin is active against Staphylococci, including Staphylococcus aureus and Staphylococcus epidemidis (including heterogeneous methicillin-resistant strains); Streptococci including streptococcus pyogenes. Streptococcus pneumoniae
(including penicillin resistant strains), streptococcus agalactiae, the viridans group, streptococcus bovis, and enterococci (e.g. Streptococcus faecalis); clostridium difficile (e.g. toxigenic strains implicated in pseudomembranous enterocolitis): diphtheroids. (E.g. JK Corynebacterium) and Propionibacterium. Other organisms that are susceptible to Vancomycin in vitro include Listeria monocytogenes. Lactobacillus species. Actinomyces species, Clostridium species and Bacillus species.
Vancomycin is not active in vitro against Gram-negative bacilli, mycobacteria, or fungi.

Synergy
The combination of Vancomycin and an aminoglycoside acts synergistically in vitro against many strains of S.aureus, nonenterococcal group D streptococci, enterococci and

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Streptococcus species (viridans group).

WARNINGS

Rapid bolus administration (e.g. Over several minutes) may be associated with exaggerated hypotension and rarely cardiac a rest.

Vancomycin HCl should be administered in a diluted solution over a period of not less than 60 minutes to avoid rapid-infusion-related reactions. Stopping the infusion usually results in prompt cessation of there reactions.

Ototoxicity has occurred in patients receiving Vancomycin HCl. It may be transient, or permanent. It has been reported mostly in patients who have given excessive doses, who have an underlying hearing loss, or who are receiving concomitant therapy with another ototoxic agent, such as an aminoglycoside. Vancomycin HCl should be used with caution in patients with renal insufficiency because the risk of toxicity is appreciably increased by high, prolonged blood concentrations. Dosage of Vancomycin HCl must be adjusted for patients with renal dysfunction.

PRECAUTIONS

General - Clinically significant serum concentrations have been reported in some patient being treated for active C-difficile induced pseudomembranous colitis after multiple oral doses of Vancomycin Hydrochloride.

In order to minimise the risk of nephrotoxicity when treating patients with underlying renal dysfunction or patients receiving concomitant therapy with an aminoglycoside. Serial monitoring or renal function should be performed and particular care should be taken in following appropriate dosing schedules

Serial tests of auditory function may be helpful in orderto minimise the risk of ototoxicity.

Reversible neutropenia has been reported in patients receiving Vancomycin HCl. Patients who will undergo prolonged therapy with Vancomycin HCl or those who are receiving concomitant drugs that may cause neutropenia should have periodic monitoring of the leukocyte count.

Vancomycin HCl is irritating to tissue and must be given by a secure intravenous route of administration. Pain, tenderness and necrosis occur with intramuscular injection of Vancomycin HCl or with inadvertent extravasation. Thrombophlebitis may occur, the frequency and severity of which can be minimized by administering the drug slowly as a dilute solution (2.5 to 5 g/L) and by rotating the sites of infusion. There have been reports that the frequency of infusion related events (including hypotension, flushing, erythema, urticaria and pruritus) increases with the concomitant administration of anesthetic agents. Infusion-related events may be minimized by the administration of Vancomycin HCl as a 60 minute infusion prior to anesthetic induction.

The safety and efficacy of Vancomycin HCl administration by the intrathecal (intralumbar intraventricular) routes have not been assessed.

Vancomycin HCl is not indicated for intraperitoneal administration, safety and efficacy has not been determined. Concurrent and /or sequential systemic or topical use of other potentially neurotoxic and / or nephrotoxic drugs, such as amphotericin Aminoglycosides, bacitracin, polymyxin Colistin, viomycin or cisplatin, requires careful monitoring.

Usage in pregnancy:

Pregnancy Category C-Animal reproduction studies have not been conducted with Vancomycm HCl. It is not known whether Vancomycin HCl can causes fetal harm when administered to a pregnant woman or can affect reproduction capacity. Vancomycin HCl should be given to a pregnant woman only if clearly needed

Nursing Mothers: It is not known whether this drug is excreted in human milk, because many drugs are excreted in human milk caution should be exercised when Vancomycin HCl is administered to a nursing woman. It is unlikely that a nursing infant can absorb a significant amount of Vancomycin from the normal gastrointestinal tract.

Usage in Pediatrics: - In premature neonates and young infants. It may be appropriate to confirm desired Vancomycin serum concentrations. Concomitant administration of Vancomycin HCl and anesthetic agents has been associated with erythema and histamine-likeflushing in children.

Geriatrics: The natural decrement of glomerular filtration with increasing age may lead to elevated Vancomycin HCl serum concentrations if dosage is not adjusted. Vancomycin HCl dosage schedules should be adjusted in elderly patients (see DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS

Infusion Related Events - During or soon after rapid infusion of Vancomycin HCl Patients may develop anaphylactoid reactions, including hypotension, wheezing, dyspnea, urticaria, or pruritus. Rapid infusion may also cause flushing of the upper body ("red neck") or pain and muscle spasm of the chest and back. These reactions usually resolve within 20 minutes but may persist for several hours.

Such events are infrequent if Vancomycin HCl is given by a slow infusion over 60 minutes. In studies of normal volunteers. Infusion related events did not occur when Vancomycin HCl was administered at a rate of l0mg/min or less.

Nephrotoxicity - A few dozen cases of increased serum creatinine or BUN concentrations, in patients given Vancomycin HCl have been reported. Most of these have occurred in patients who were given aminoglycosides concomitantly or who had preexisting kidney dysfunction. When Vancomycin HCl was discontinued, azotemia resolved in most patients.

Ototoxicity - A few dozen cases of hearing loss associated with Vancomycin HCl have been reported. Most of these patients had kidney dysfunction preexisting hearing loss, or concomitant treatment with an ototoxic drug. Vertigo, dizziness, and tinnitus have been reported rarely.

Hematopoietic - Reversible neutropenia, usually starting 1 week or more after onset of therapy with Vancomycin HCl or after a total dosage of more than 25 g. has been reported for several dozen patients. Neutropenia appears to be promptly reversible when Vancomycin HCl is discontinued. Thrombocytopenia has rarely been reported.

Injection site reactions: Inflammation at the injection site and thrombophlebitis have been reported.

Miscellaneous - Infrequently, patients have been reported to have had anaphylaxis, drug fever, chills, and rashes in association with Vancomycin HCl.

DRUG INTERACTIONS

Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing and anaphylactoid reactions. Concurrent and/or sequential systemic or topical use of other potentially neurotoxic and/or nephrotoxic drugs, such as amphotericin B, aminoglycosides, bacitracin, polymyxin B, colistin, viomycin, or cisplatin, when indicated, requires careful monitoring.

CONTRAINDICATIONS

Vancomycin is contraindicated in patients with known hypersensitivity to this antibiotic. Solutions containing dextrose may be contraindicated in patients with known allergy to corn or corn products.

OVER DOSAGE

Supported care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Hemoperfusion with Amberlite XAD-4 Resin has been, reported to be limited benefit-

STORAGE & INSTRUCTIONS

Store between 15-25°C.
Protect from heat, sunlight and moisture. Do not freeze.
Keep away from the reach of children.
Initial reconstituted solution is stable for two weeks in a refrigerator.
Discard the remaining portion after administration.
To be sold on prescription of registered medical practitioner only.

HOW SUPPLIED

VANCOSOL Injection 500mg
I vial + 10ml sterile water for injection.
VANCOSOL Injection 1g
I vial + 20ml sterile water for injection.

خوراک وطریقہ استعمال:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۱۵-۲۵ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

تیار کردہ محلول ریفریجریٹر میں رکھنے پر دو ہفتے تک قابل استعمال رہتا ہے۔

استعمال کے بعد بچ جانے والا محلول ضائع کر دیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔

Manufactured by:
PHARMASOL
PRIVATE LIMITED
Plot # 549,Sundar Industrial Estate, Lahore, Pakistan.