120x320mm

Venjar

(Vancomycin)

Highnoon

COMPOSITION:
Venjar 500mg Injection: Each Vial contains:
Vancomycin HCl eq. to Vancomycin 500mg
Venjar 1g injection: Each Vial contains:
Vancomycin HCl eq. to Vancomycin 1g

DESCRIPTION:
Vancomycin hydrochloride is a tricyclic glycopeptide antibacterial derived from amycolatopsis orientalis (formerly Nocardia orientalis).

MECHANISM OF ACTION
The bactericidal action of vancomycin results primarily from inhibition of cell-wall biosynthesis. In addition, vancomycin alters bacterial-cell-membrane permeability and RNA synthesis.

MICROBIOLOGY:
Resistance
There is no cross-resistance between vancomycin and other antibacterial(s). Vancomycin is not active in vitro against gram-negative bacilli, mycobacteria, or fungi.
Interaction with Other Antimicrobials
The combination of vancomycin and an aminoglycoside acts synergistically in vitro against many isolates of Staphylococcus aureus, Streptococcus gallolyticus (previously known as Streptococcus bovis), Enterococcus spp, and the viridans group streptococci.
Antimicrobial Activity
Vancomycin has been shown to be active against most isolates of the following bacteria, both in vitro and in clinical infections.

Aerobic bacteria
Gram-positive bacteria
- Corynebacterium spp.
- Enterococcus spp. (including Enterococcus faecalis)
- Staphylococcus aureus (including methicillin-resistant and methicillin-susceptible isolates)
- Coagulase negative staphylococci (including S. epidermidis and methicillinresistant isolates)
- Streptococcus gallolyticus (previously known as Streptococcus bovis)
- Viridans group streptococci

The following in vitro data are available, but their clinical significance is unknown. At least 90 percent of the following bacteria exhibit an in vitro minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for vancomycin against isolates of similar genus or organism group. However, the efficacy of vancomycin in treating clinical infections caused by these bacteria has not been established in adequate and well-controlled clinical trials.

Aerobic bacteria
Gram-positive bacteria
- Listeria monocytogenes
- Streptococcus pyogenes
- Streptococcus pneumoniae
- Streptococcus agalactiae

Anaerobic bacteria
Gram-positive bacteria
- Actinomyces spp
- Lactobacillus spp

PHARMACOKINETICS:
Vancomycin is only poorly absorbed from the gastrointestinal tract, although absorption may be somewhat greater when the gastrointestinal tract is inflamed. Infusion of a 1-g dose intravenously over 60 minutes has reportedly been associated with plasma concentrations of up to about 60 micrograms/mL immediately after completion of the infusion, and about 25 micrograms/mL 2 hours later, falling to under 10 micrograms/mL after 11 hours. However, there may be considerable individual variation in the pharmacokinetics of vancomycin: a range of half-lives between 3 and 13 hours has been reported, with an average of about 6 hours, in patients with normal renal function. Half-life may be prolonged in patients with renal impairment, to 7 days or more in anephric patients. About 55% is bound to plasma proteins, although large variations have been reported.

Vancomycin diffusion into extracellular fluid, including plural, pericardial, ascitic, and synovial fluid. Small amounts are found in the bile. Vancomycin concentration in lung tissue is relatively low, accounting for 20 to 30% of serum concentration. There is little diffusion into the CSF and even when the meninges are inflamed effective concentration may not be achieved. Vancomycin crosses the peritoneal cavity; about 60% of an intraperitoneal dose is reported to be absorbed in 6 hours. It is reported to cross the placenta. It is also distributed into breast milk. Little or no metabolism of vancomycin is thought to take place. It is excreted unchanged by the kidney, mostly by glomerular filtration, some 80 to 90% of the dose is excreted in urine within 24 hours. There appears to be a small amount of non-renal clearance, although the mechanism for this has not been determined.

The pharmacokinetics of vancomycin may be altered conditions which affect renal clearance: clearance of vancomycin has been reported to be enhanced in burn patients, where in those in renal impairment, or reduced renal function (such as neonates or the elderly), clearance is reduced and plasma-concentration and half-lives increased. Dosage adjustment is often necessary in patients with reduced or impaired renal function; ideally, this should be based on plasma-concentration monitoring. Although clearance is also altered in hepatic impairment, it has been suggested that dosage adjustment is not necessary in the absence of other factors. Plasma concentration of vancomycin is reported to be little affected by conventional hemodialysis, although the use of high-flux membranes may significantly reduce vancomycin concentrations. Peritoneal dialysis, although it may decrease concentration, is also thought not to do by significant amounts, but hemoperfusion or hemofiltration effectively removes vancomycin from the blood.

INDICATIONS AND USAGE:
- It is indicated in adults and pediatric patients for whom appropriate dosing with this formulation can be achieved and use in specific populations for the treatment of septicemia due to:
  - Susceptible isolates of methicillin-resistant Staphylococcus aureus (MRSA) and coagulase negative staphylococci.
  - Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins
- It is indicated in adults and pediatric patients for whom appropriate dosing with this formulation can be achieved and use in specific Populations for the treatment of infective endocarditis due to:
  - Susceptible isolates of MRSA.
  - Viridans group streptococci or Streptococcus gallolyticus (previously known as Streptococcus bovis) and Enterococcus species and corynebacterium species. For enterococcal endocarditis (e.g., E. faecalis), use vancomycin injection in combination with an aminoglycoside.
  - Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins. Vancomycin injection is indicated in adults and pediatric patients for the treatment of early-onset prosthetic valve endocarditis caused by Staphylococcus epidermidis in combination with rifampin and an aminoglycoside.
- It is indicated in adults and pediatric patients for whom appropriate dosing with this formulation can be achieved and use in specific populations for the treatment of skin and skin structure infections due to:
  - Susceptible isolates of MRSA and coagulase negative staphylococci.
  - Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.
- It is indicated in adults and pediatric patients (and older) for whom appropriate dosing with this formulation can be achieved and use in specific populations for the treatment of bone infections due to:
  - Susceptible isolates of MRSA and coagulase negative staphylococci.
  - Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.
- It is indicated in adults and pediatric patients for whom appropriate dosing with this formulation can be achieved and use in specific populations for the treatment of lower respiratory tract infections due to:
  - Susceptible isolates of MSRA.
  - Methicillin-susceptible staphylococci in penicillin-allergic patients, or those patients who cannot receive or who have failed to respond to other drugs, including penicillins or cephalosporins.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Vancomycin injection and other antibacterial drugs, Vancomycin injection 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.

DOSAGE AND ADMINISTRATION:
Important administration Instruction
- Venjar (Vancomycin) injection is intended for intravenous use only.
- Venjar (Vancomycin) injection is not to be administered orally.
- To reduce the risk of infusion related adverse reactions, administer Venjar (Vancomycin) injection by intravenous infusion over 60 minutes or greater. An infusion rate of 10 mg/min or less is associated with fewer infusion-related adverse reactions. Infusion related adverse reactions may occur, however, at any rate or concentration.
- Drug additives should not be made to this solution.
- Venjar (Vancomycin) injection concentrations of no more than 5 mg/mL are recommended in adults.
- Administer Venjar (Vancomycin) by a secure intravenous route of administration to reduce the risk of local irritation and phlebitis reactions.
- Administer Venjar (Vancomycin) injection prior to intravenous anesthetic agents to reduce the risk of infusion related adverse reactions.

Recommended Dosage in Adult Patients with normal renal function
The usual daily intravenous dosage of Venjar (Vancomycin) injection is 2 grams (g) divided either as 500 mg every 6 hours or 1 g every 12 hours. Administer each dose by intravenous infusion over a period of 60 minutes or greater. Other patient factors, such as age or obesity, may call for modification of the usual intravenous daily dose. The initial daily dose should be no less than 15 mg/kg.

Recommended Dosage in Pediatric Patients with normal renal function
Pediatric Patients (Aged 1 Month and Older): The usual intravenous dosage of Venjar (Vancomycin) is 10 mg/kg per dose given every 6 hours. Each dose should be administered over a period of at least 60 minutes. Close monitoring of serum concentrations of vancomycin may be warranted in these patients.
Pediatric Patients (Younger than 1 Month Old): 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 1st week of life and every 8 hours thereafter up to the age of 1 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.

Recommended Dosage in Patients with Renal Impairment
Dosage adjustment must be made in patients with renal impairment. The initial dose should be no less than 15 mg/kg in patients with any degree of renal impairment. Measure trough vancomycin serum concentrations to guide therapy, especially in seriously ill patients with changing renal function. For functionally anephric patients, an initial dose of 15 mg/kg of body weight should be given to achieve prompt therapeutic serum concentrations. Measure vancomycin serum concentrations at 24 hours following the first dose to guide further intravenous therapy.

Preparation of Venjar (Vancomycin) for Administration
Preparation and Administration Instructions
Vancomycin Injection, is for intravenous administration only. Intermittent infusion is the recommended method of administration. Do not add supplemental medication. Visually inspect the container, if after visual inspection the solution remains cloudy or if an insoluble precipitate is noted or if any seals are not intact, discard the container. The diluted solution remains chemically stable for 12 hours at room temperature (25°C - 30°C) or for 14 days when stored under refrigeration (2°C - 8°C).
Reconstitution with 10 mL water for injection (500 mg vancomycin injection); Almost white to off white colored powder filled in transparent glass vial. Reconstitute with 10 mL water for injection to obtain colorless clear solution. Dilute the reconstituted solution with one of the following compatible solutions (100 mL) prior to intravenous infusion;
- 0.9% Sodium Chloride (NaCl) injection
- 5% Dextrose injection
- Ringer lactate injection

Reconstitution with 20 mL (10x2) water for injection (1000 mg / 2000 mg, vancomycin injection); Almost white to off white colored powder filled in transparent glass vial. Reconstitute with 20 mL water for injection to obtain colorless clear solution. Dilute the reconstituted solution with one of the following compatible solutions (100 mL) prior to intravenous infusion;
- 0.9% Sodium Chloride (NaCl) injection
- 5% Dextrose injection
- Ringer lactate injection

CONTRAINDICATIONS:
- It is contraindicated in patients with known hypersensitivity to vancomycin.

WARNINGS AND PRECAUTIONS:
- Hypotension including shock and cardiac arrest, wheezing, dyspnea, urticaria or pruritus, muscular and chest pain may occur with rapid Vancomycin injection administration. (e.g., over several minutes). The reactions may be more severe in pediatric patients. Rapid intravenous administration of Vancomycin injection may also be associated with “vancomycin infusion reaction”, which manifests as pruritus and erythema that involves the face, neck and upper body or pain and muscle spasm of the chest and back. There have been reports that the frequency of infusion-related reactions (including hypotension, flushing, erythema, urticaria, and pruritus) increases with the concomitant administration of anesthetic agents. Infusion-related adverse reactions are related to both the concentration and the rate of administration of Vancomycin for injection. Infusion-related adverse reactions may occur, however, at any rate or concentration. Administer Vancomycin injection over a period of 60 minutes or greater to reduce the risk of rapid-infusion-related adverse reactions. 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 adverse reactions. Administer Vancomycin injection as a 60-minute infusion prior to administration of anesthetic agents when feasible to minimize infusion-related adverse reactions. Stop the infusion if a reaction occurs because this usually results in prompt cessation of these reactions.
- Vancomycin injection can result in acute kidney injury (AKI), including acute renal failure, mainly due to interstitial nephritis or less commonly acute tubular necrosis. AKI is manifested by increasing blood urea nitrogen (BUN) and serum creatinine (Cr). The risk of AKI increases with higher vancomycin serum levels, prolonged exposure, concomitant administration of other nephrotoxic drugs, concomitant administration of piperacillin-tazobactam, volume depletion, pre-existing renal impairment and in critically ill patients and patients with co-morbid conditions that predispose to renal impairment. Monitor serum vancomycin concentrations and renal function in all patients receiving Vancomycin injection. More frequent monitoring is recommended in patients with comorbidities that predispose to impairment in renal function or are concomitantly receiving other nephrotoxic drugs, in critically ill patients, in patients with changing renal function, and in patients requiring higher therapeutic vancomycin levels. If acute kidney injury occurs, discontinue Vancomycin injection, or reduce the dose.
- Ototoxicity has occurred in patients receiving Vancomycin injection. It may be reversible or permanent. Ototoxicity manifests as tinnitus, hearing loss, dizziness or vertigo. The risk is higher in older patients, patients who are receiving higher doses, who have an underlying hearing loss, who are receiving concomitant therapy with another ototoxic agent, such as an aminoglycoside or who have underlying renal impairment. Monitor for signs and symptoms of ototoxicity during therapy. Monitor serum vancomycin concentrations and renal function in all patients receiving parenteral vancomycin. Discontinue Vancomycin injection if ototoxicity occurs. Dosage of Vancomycin injection must be adjusted for patients with renal impairment. Serial tests of auditory function may be helpful in order to minimize the risk of ototoxicity.
- Severe dermatologic reactions such as toxic epidermal necrolysis (TEN), Stevens Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), and linear IgA bullous dermatosis (LABD) have been reported in association with the use of vancomycin. Cutaneous signs or symptoms reported include skin rashes (including exfoliative dermatitis), mucosal lesions, and blisters. Discontinue Vancomycin injection at the first appearance of signs and symptoms of TEN, SJS, DRESS, AGEP, or LABD.
- Clostridioides difficile-associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Vancomycin injection, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile. C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibacterial use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents. If CDAD is suspected or confirmed, ongoing antibacterial use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibacterial treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated. Prolonged use of vancomycin may result in the overgrowth of non-susceptible microorganisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken. In rare instances, there have been reports of pseudomembranous colitis due to C. difficile developing in patients who received intravenous vancomycin.
- Hemorrhagic occlusive retinal vasculitis, including permanent loss of vision, occurred in patients receiving intracameral or intravitreal administration of vancomycin during or after cataract surgery. The safety and efficacy of vancomycin administered by the intracameral or the intravitreal route have not been established by adequate and well controlled trials. Vancomycin is not indicated for prophylaxis of endophthalmitis.
- Reversible neutropenia has been reported in patients receiving vancomycin. Patients who will undergo prolonged therapy with vancomycin or those who are receiving concomitant drugs that may cause neutropenia should have periodic monitoring of the leukocyte count. Reversible neutropenia, usually starting 1 week or more after onset of therapy with vancomycin 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 is discontinued. Thrombocytopenia has been reported. Although a causal relationship has not been established, reversible agranulocytosis (granulocyte <50/mm3) has been reported.
- Inflammation at the injection site has been reported. Vancomycin is irritating to tissue and must be given by a secure intravenous route of administration. Thrombophlebitis may occur, the frequency and severity of which can be minimized by slow infusion of the drug and by rotation of venous access sites. Administration of Vancomycin injection by intramuscular (IM), intraperitoneal, intrathecal intraventricular, or intravitreal routes has not been approved and is not recommended. The safety and efficacy of vancomycin administered by these routes of administration have not been established by adequate and well controlled trials. Pain, tenderness, and necrosis occur with intramuscular (IM) injection of vancomycin or with inadvertent extravasation. 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 as a 60-minute infusion prior to anesthetic induction.
  Administration of sterile vancomycin by the intraperitoneal route during continuous ambulatory peritoneal dialysis (CAPD) has been reported to result in a syndrome of chemical peritonitis. Manifestations of this syndrome range from a cloudy dialysate alone to a cloudy dialysate accompanied by variable degrees of abdominal pain and fever. This syndrome appears to be resolved after discontinuation of intraperitoneal vancomycin. About 60% of an intraperitoneal dose of vancomycin administered during peritoneal dialysis is absorbed systemically in 6 hours. Serum concentrations of about 10 mcg/mL are achieved by intraperitoneal injection of 30 mg/kg of vancomycin. However, the safety and efficacy of the intraperitoneal use of vancomycin has not been established in adequate and well-controlled trials.
- Prescribing Vancomycin injection in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
- Avoid use of Vancomycin injection, in patients with congestive heart failure, elderly patients and patients requiring restricted sodium intake.

ADVERSE REACTIONS:
The reported adverse events are; infusion reactions, nephrotoxicity, ototoxicity, severe dermatologic reactions, clostridioides difficile-associated diarrhea, hemorrhagic occlusive retinal vasculitis, neutropenia, phlebitis, other administration site reactions, anaphylaxis and “vancomycin infusion reaction”, acute kidney injury, interstitial nephritis, hearing loss, vertigo, tinnitus, rashes including exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), clostridioides difficile colitis, nausea, agranulocytosis, neutropenia, pancytopenia, leukopenia, thrombocytopenia, eosinophilia cardiac arrest, chest pain, general discomfort, drug fever, chills, phlebitis, injection site irritation, injection site pain, necrosis following intramuscular injection, chemical peritonitis following intraperitoneal administration, elevated blood urea nitrogen, elevated serum creatinine, muscle pain, dizziness, wheezing, dyspnea, hypotension, shock, vasculitis, severe dermatologic reactions such as toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalized exanthematous pustulosis (AGEP), and linear IgA bullous dermatosis (LABD).

DRUG INTERACTIONS:
- Concomitant administration of vancomycin and anesthetic agents has been associated with erythema and histamine-like flushing.
- An increased incidence of acute kidney injury in patients administered concomitant piperacillin/tazobactam and vancomycin as compared to vancomycin alone. Monitor kidney function in patients receiving concomitant piperacillin/tazobactam and Vancomycin injection.
- Concurrent and/or sequential systemic or topical use of other potentially neurotoxic and/or nephrotoxic drugs with Vancomycin injection requires more frequent monitoring of renal function.

USE IN SPECIFIC POPULATIONS:
Pregnancy
Risk Summary:
Available data over several decades of vancomycin use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

Lactation:
Vancomycin is present in human milk following intravenous administration, however, there are insufficient data to inform the levels. There are no data on the effects of vancomycin on the breastfed infant or milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for vancomycin and any potential adverse effects on the breastfed infant from vancomycin or from the underlying maternal condition.

Pediatric Use:
Vancomycin injection is indicated in pediatric patients for the treatment of septicemia, infective endocarditis, skin and skin structure infections, bone infections and lower respiratory tract infections for whom appropriate dosing with this formulation can be achieved. More severe infusion related reactions related to vancomycin administration may occur in pediatric patients. In pediatric patients, monitor vancomycin serum concentration and renal function when administering Vancomycin injection. Concomitant administration of vancomycin and intravenous anesthetic agents has been associated with erythema and histamine-like flushing in all patients including pediatric patients.

Geriatric Use:
Vancomycin injection is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Renal Impairment:
Dosage adjustment of Vancomycin injection must be made in patients with impaired renal function. Measure trough vancomycin serum concentrations to guide intravenous therapy, especially in patients with impaired renal function or fluctuating renal function.

OVERDOSAGE:
Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Hemofiltration and hemoperfusion with polysulfone resin have been reported to result in increased vancomycin clearance.

PRESENTATION
Venjar 500mg Injection: I vial of 500mg vancomycin and I ampoule of 10mL sterile water for injection.
Venjar 1g Injection: I vial of 1g vancomycin and I ampoule of 20mL sterile water for injection.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from ligh.

وینجار

(وینکومائیسین)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

Manufactured by: BIO-LABS (PVT) LTD
Plot No. 145, Industrial Triangle,
Kahuta Road, Islamabad, Pakistan. Mfg. Lic. No. 000296
Manufactured for: BIO-NEXT PHARMACEUTICALS
Plot No. 50, St. No. S-10, RCCI Industrial Estate Rawat,
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