SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

VANSAFE-CP 500mg (Vancomycin Hydrochloride for Injection USP)

2. Qualitative and quantitative composition

Each vial contains:

Vancomycin Hydrochloride USP

Equivalent to Vancomycin……...500 mg

3. Pharmaceutical form

Dosage form: Dry Powder for Injection

Description: White to almost white or tan to brown free flowing powder

4. Clinical particulars

4.1 Therapeutic indications

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 penicillinallergic patients, or in those who have failed to respond to other medicines, including the penicillins or cephalosporins, and for infections caused by vancomycin -susceptible organisms that are resistant to other antimicrobial medicines. Vancomycin is indicated as an initial therapy when methicillin-resistant staphylococci are suspected. However, when the susceptibility data is available, therapy should be adjusted accordingly.

Vancomycin is effective in the treatment of Staphylococcal endocarditis. Effectiveness has also been documented in other infections due to staphylococci, including septicaemia, bone infections, lower respiratory tract infections, and skin and skin-structure infections. When staphylococcal infections are localized and purulent, is recommended that the antibiotics be used as adjuncts to appropriate surgical measures.

Vancomycin is reported to be effective alone or in combination with an aminoglycoside for endocarditis caused by S. viridans or S. bovis. For endocarditis caused by enterococci (e.g., Enterococcus faecalis), vancomycin has been reported to be effective only in combination with an aminoglycoside.

Vancomycin has been reported to be effective for the treatment of diphtheroid endocarditis. Vancomycin has been used successfully in combination with either rifampin an aminoglycoside, or both in early-onset prosthetic valve endocarditis caused by S.epidermidis or diphtheroids. It is

recommended that specimens for bacteriologic cultures be obtained to isolate and identify causative organisms, and determine 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.

4.2 Posology and method of administration

VANSAFE-CP is for intravenous use only. Each intravenous dose should be administered over a period of at least 60 minutes. Concentrations of no more than 5 mg/ml and rates of no more than 10 mg/min are recommended.

Adults: The usual total daily intravenous dose is 2g, divided either as 500mg every 6 hours or 1g every 12 hours. Aged and obese patients may require modification of the usual daily dose.

Children: The total daily intravenous dosage of vancomycin is calculated on the body weight basis. (e.g. a 40mg/kg of body weight dose should be given in 4 divided doses at 10mg/kg, every 6 hourly and incorporated into the child's 24-hour fluid requirement).

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 15mg/kg is suggested, followed by 10mg/kg every 12 hours for neonates in the 1st week of life and every 8 hours thereafter up to the age of 1 month. Close monitoring of serum concentrations of vancomycin may be warranted in these patients.

Patients with Impaired Renal Function and Elderly Patients:

After an initial loading dose of 750 mg to 1 g, but not less than 15mg per kg of body weight, adults with impaired renal function may require a reduction in dose as indicated in the table below.

Clcr (ml/min)	Dose Interval
>90	Every 12 hours
40-90	Every 24 hours
30-40	Every 48 hours
20-30	Every 72 hours

10-20	Every 96 hours
<10	Every 5-7 days

However, the preferred method is to adjust dosage based on serum vancomycin concentrations as follows.

Men : $\frac{\text{Weight (kg) X (140 - age in years)}}{\text{72 X serum creatinine concentration (mg/dl)}}$

Women : 0.85 X above value

Monitoring Parameters:

In patients with renal dysfunction or receiving concomitant therapy with neurotoxic and/or nephrotoxic drugs such as amphotericin B, aminoglycosides, bacitracin, polymycin B, colistin, viomycin or cisplatin requires careful serial monitoring of renal function and vancomycin dosage adjustment. Serial tests of auditory function should be carried out to minimize the risk of ototoxicity. Patients on long term Vancomycin therapy or receiving concomitant drugs that may cause neutropenia should have periodic monitoring of the leukocyte count.

Stability and Compatibility

Reconstitute the vial by adding Sterile Water for Injection I.P. The solution so obtained must be further diluted before use. Use immediately after preparation if it is clears. Vancomycin is incompatible with HEPARIN and PHENOBARBITAL

Patient Information:

Patients should be advised to report pain at infusion site, dizziness, fullness or ringing in ears with I.V. use. The dose schedule should be followed exactly as directed by the physician. Missing doses or not completing the full course of therapy may decrease the effectiveness of the immediate treatment and increase the likelihood that bacteria will develop resistance and will not be treatable by vancomycin or other antibacterial drugs in the future.

4.3 Contraindications

Vancomycin is contraindicated in patients showing hypersensitivity to Vancomycin or any component of the formulation. It should be avoided in patients who have an underlying hearing loss.

4.4 Special warnings and precautions for use

Vancomycin should be used with caution in patients with renal impairment or those receiving other nephrotoxic or ototoxic drugs due to the increased risk of toxicity. Dosage modification is required in patients with impaired renal function (especially elderly).

Vancomycin should be administered slowly over a period of not less than 60 minutes to avoid rapid-infusion-related reactions. Pseudomembranous colitis has been found associated with Vancomycin as with virtually all antibiotics: therefore, its diagnosis should be considered in patients who develop diarrhea during Vancomycin therapy. In moderate to severe cases, management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug effective against Clostridium difficile is necessary. Repeated evaluation of each patient is essential due to increased risk of overgrowth of non-susceptible organisms.

Since Vancomycin is irritating to tissue, it must be given by a secure intravenous route of administration. Vancomycin should be prescribed only when a bacterial infection is proved or strongly suspected, failing which may increase the risk of the development of drug-resistant bacteria.

4.5 Interaction with other medicinal products and other forms of Interaction

Anesthetic agents: Concomitant administration of Vancomycin and anesthetic agents may result in erythema and histamine-like flushing and anaphylactic 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.

4.6 Pregnancy and lactation

Pregnancy Risk Factor C: Vancomycin is known to cross the placenta and there are reports of hearing loss and kidney damage in infants of mothers on Vancomycin treatment during pregnancy. Therefore, Vancomycin should be used with caution in pregnant women.

Vancomycin is secreted in human milk. The safety of Vancomycin in nursing infant is not established. It is recommended that mothers should avoid breastfeeding when on Vancomycin Therapy.

4.7 Effects on ability to drive and use machines

Although visual disorders belong to the rare adverse reactions, caution is recommended by patients driving cars and/or using machines.

4.8 Undesirable effects

Side effect	**> 10%**	
Gastrointestinal	Oral: Bitter taste, nausea, vomiting: Parenteral: Hypotension accompanied by flushing and erythematous rash on face and upper body (red neck or red man syndrome)	
Side effect	**1% to 10%**	**< 1%**
Central nervous system	Chills	-
Haematologic	Eosinophilia	Thrombocytopenia
Miscellaneous	Fever	-
Cardiovascular	-	
Otic	-	
Renal	-	Renal failure, intestinal nephritis

4.9 Overdose

Symptoms of overdose include ototoxicity, nephrotoxicity; there is no specific therapy for an overdosage with vancomycin. Care is symptomatic and supportive in nature. Peritoneal filtration and hemofiltration (not dialysis) have been shown to reduce the serum concentration of vancomycin; high flux dialysis may remove up to 25%.

5. Pharmacological Characteristics

5.1 Mechanism of Action

Anatomic Therapeutic Chemical Classification and Distribution Category

ATC Classification: J01XA01, Anti-bacterial Agent

Distribution category: Prescription only drug

Vancomycin is a bactericidal agent, effective against bacterial infections. Vancomycin is a tricyclic glycopeptides antibiotic. It inhibits bacterial cell wall synthesis by blocking glycopeptides polymerization through binding tightly to D-alanyl-D-alanine portion of the cell wall precursor.

Microbiology

The bactericidal action of vancomycin 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 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 Staphylococcus aureus, Streptococcus bovis, enterococci, and the viridans group streptococci. Vancomycin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.

Gram-positive bacteria

Diphtheroids Enterococci (e.g., *Enterococcus faecalis*), Staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains) in adequate and well-controlled clinical trials.

Aerobic gram-positive microorganisms

Listeria monocytogenes, Streptococcus pyogenes, Streptococcus pneumoniae (including penicillin-resistant strains) *Streptococcus agalactiae*

Anaerobic gram-positive microorganisms

Actinomyces species

Lactobacillus species

5.2 Pharmacokinetics:

Route of Aministration: Intravenous infusion.

Distribution: Widely distributed to most tissues and body fluids; adequate therapeutic concentrations in serum and in pleural, pericardial, peritoneal, ascitc and synovial fluids; high concentrations in urine; inadequate concentrations in bile; does not readily cross normal bloodbrain barrier into cerebrospinal fluid (CSF); however, penetrates into CSF when meninges are inflamed and may achieve therapeutic concentrations. Crosses the placenta.

Volume of distribution: Approx. 0.39 to 0.92 liter per kg.

Mean Plasma concentration: 63 mcg/ml after an infusion of 60 minutes.

Time to peak serum concentration: Within 45-65 minutes.

Mean Elimination half-life: 4 to 6 hours

Serum protein binding: 55%

Elimination: About 75% of an administered dose of Vancomycin is excreted in urine by glomerular filtration.

6. Pharmaceutical Particulars

6.1 List of excipients

None

6.2 Incompatibilities

Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds.

This medicinal product must not be mixed with other medicinal products except those mentioned.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30º C. protected from light. Do not freeze

6.5 Nature and contents of container

10 ml flint molded Glass vial closed with 20mm rubber stoppers and sealed with 20mm Flip-Off aluminium seal is placed in a carton along with pack insert.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. Marketing Autorization Holder

M/S VHB MEDI SCIENCES LTD.

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8. Marketing authorisation holder

TAN 21 HM 0382

9. Marketing authorisation number

2021-10-09

10. Date of revision of the text