Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

TAFOTAX-1000

2. Qualitative and quantitative composition

Each vial contains vancomycin hydrochloride USP equivalent to 500 mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Powder for injection
A white, almost white, or tan to brown, free-flowing powder.

4. Clinical particulars

4.1 Therapeutic indications

Intravenous vancomycin is indicated in the following severe infections caused by Gram-positive bacteria susceptible to vancomycin, which cannot be treated with, have failed to respond to, or are resistant to other antibiotics such as penicillins and cephalosporins:

Endocarditis.
Infections of the bones (osteomyelitis).
Pneumonia.
Soft-tissue infections.

Endocarditis caused by enterococci, Streptococcus viridans or S. bovis should be treated with a combination of vancomycin and an aminoglycoside.

Vancomycin may be used for perioperative prophylaxis against bacterial endocarditis in patients at high risk of developing bacterial endocarditis when they undergo major surgical procedures (e.g. cardiac and vascular procedures) and are unable to receive a suitable beta-lactam antibacterial agent.

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

The submitted document further states that vancomycin may be used orally for the treatment of staphylococcal enterocolitis and pseudomembranous colitis due to Clostridioides difficile, that parenteral administration is not effective for these indications, and that intravenous administration may be used concomitantly if required.

4.2 Posology and method of administration

Posology

For intravenous infusion.

For preparation of the solution for infusion, see section 6.6.

Concentrations of no more than 5 mg/mL are recommended. In selected patients in need of fluid restriction, a concentration of up to 10 mg/mL may be used; use of such higher concentrations may increase the risk of infusion-related events. Infusions should be given over at least 60

minutes. In adults, if doses exceeding 500 mg are used, a rate of infusion of no more than 10 mg/min is recommended. Infusion-related events may occur, however, at any rate or concentration.
The dose and duration of treatment should be adjusted individually according to the underlying type and severity of the infection and to patient factors such as age and renal function. Vancomycin levels can be measured to aid dose adjustment.

Measurement of serum concentrations

Following multiple intravenous doses, peak serum concentrations measured two hours after completion of the infusion range from 18 to 26 mg/L. Trough levels measured immediately prior to the next dose should be 5 to 10 mg/L. Ototoxicity has been associated with serum drug levels of 80 to 100 mg/L, but this is rarely seen when serum levels are kept at or below 30 mg/L.

Patients with normal renal function – adults and children above 12 years of age

The recommended daily intravenous dose is 2,000 mg (2 g), given as 500 mg every 6 hours or 1,000 mg (1 g) every 12 hours. Improvement is usually seen within 48 to 72 hours. The total duration of administration is determined by the type and severity of the infection and by the clinical response of the patient.
For bacterial endocarditis, the generally accepted regimen is 1,000 mg (1 g) vancomycin intravenously every 12 hours for 4 weeks, either alone or in combination with other antibiotics. Longer treatment, up to 6 weeks, may be required depending on the pathogen involved.
If vancomycin is co-administered with an aminoglycoside (e.g. gentamicin), patients should be monitored carefully for signs of neurotoxicity and ototoxicity. The dosage should be adjusted when renal disturbance occurs (see section 4.5).
Perioperative prophylaxis against bacterial endocarditis: adults receive 1,000 mg (1 g) vancomycin intravenously prior to surgery (prior to induction of anaesthesia) and, depending on the time and type of surgery, a further dose of 1,000 mg (1 g) intravenously 12 hours postoperatively may be given.

Children one month to 12 years of age

40 mg/kg/day. The dose must be divided, usually into four doses (e.g. 10 mg/kg every 6 hours). Each dose should be administered over at least 60 minutes.

Newborn infants (full term)

0–7 days of age: a starting dose of 15 mg/kg, followed by 10 mg/kg every 12 hours.
7–30 days of age: a starting dose of 15 mg/kg, followed by 10 mg/kg every 8 hours.
Each dose should be administered over at least 60 minutes. Close monitoring of serum vancomycin concentrations may be warranted in these patients.

Elderly

Dosage reduction may be necessary to a greater extent than expected because of decreasing renal function. Auditory function should be monitored (see section 4.4).

Pregnancy

It has been reported that significantly increased doses may be required to achieve therapeutic serum concentrations in pregnant patients.

Patients with impaired renal function

In patients with impaired renal function, the dosage regimen must be modified in response to the degree of renal impairment, the severity of the infection, the susceptibility of the causative organism and the serum concentrations of the medicinal product. A suggested starting dose is 15 mg/kg, with subsequent doses based mainly on renal function and serum concentrations.

Accumulation may occur with prolonged therapy and regular monitoring of serum levels should be carried out. The following guide is provided. These data are not valid for functionally anephric patients on dialysis.

Creatinine clearance (mL/min/kg)	Vancomycin dose (mg/kg/24 hours)
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 a subsequent dosage of 1.9 mg/kg/24 hours. Since individual maintenance doses of 250 mg to 1 g are convenient in patients with marked renal impairment, a dose may be given every several days rather than daily. In anuria, a dose of 1 g every 7 to 10 days has been recommended.

In patients on haemodialysis, the medicinal product is not significantly removed by haemodialysis. A dose of 1 g every seven days produces effective blood levels. Serum levels should be monitored to avoid 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 may be added to the dialysate at a concentration of 25 micrograms per mL.

Patients with impaired liver function

The availability of data in patients with impaired liver function is limited. Available data do not indicate the need for dose adjustment in mild or moderate hepatic impairment.

Oral administration:

The contents of vials for parenteral administration may be used.

Adults and the elderly: The usual daily dose given is 500 mg in divided doses for 7 to 10 days, although up to 2 g/day have been used in severe cases. The total daily dosage should not exceed 2g. Each dose may be reconstituted in 30 mL water and either given to the patient to drink, or administered by nasogastric tube.

Children:

The usual daily dose is 40 mg/kg in three or four divided doses for 7 to 10 days. The total daily dosage should not exceed 2g.
Common flavouring syrups may be added to the solution at the time of administration to improve the taste.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Infusion-related reactions

Rapid bolus administration (e.g. 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 syndrome" or "red neck syndrome"). Vancomycin should be infused in a dilute 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 these reactions (see sections 4.2 and 4.8).

Hypersensitivity

In cases of severe acute hypersensitivity reactions (e.g. anaphylaxis), treatment with vancomycin must be discontinued immediately and the usual appropriate emergency measures started. Vancomycin should be used with caution in patients with allergic reactions to teicoplanin, since cross-hypersensitivity reactions between vancomycin and teicoplanin have been reported.

Renal impairment

Vancomycin should be used with care in patients with renal insufficiency, as the possibility of developing toxic effects is much higher in the presence of prolonged high blood concentrations. The dose should be reduced according to the degree of renal impairment. The risk of toxicity is appreciably increased by high blood concentrations or prolonged therapy. Blood levels should be monitored and renal function tests performed regularly.

Ototoxicity

Ototoxicity, which may be transitory or permanent (see section 4.8), has been reported in patients with prior deafness, in those who have received excessive intravenous doses, and in those receiving concomitant treatment with another ototoxic active substance such as an aminoglycoside. 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.
Vancomycin should be avoided in patients with previous hearing loss. If it is used in such patients, the dose should be regulated by periodic determination of the drug level in the blood. The elderly are more susceptible to auditory damage.

Paediatric population
In premature neonates and young infants, it may be appropriate to confirm desired vancomycin serum concentrations. Concomitant administration of vancomycin and anaesthetic agents has been associated with erythema and histamine-like flushing in children (see section 4.5).
Elderly
The natural decrease of glomerular filtration with increasing age may lead to elevated vancomycin serum concentrations if the dosage is not adjusted (see section 4.2).
Local tolerance
Vancomycin is very irritating to tissue and causes injection site necrosis if injected intramuscularly. Pain and thrombophlebitis may occur in many patients receiving vancomycin and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised by administering the medicinal product slowly as a dilute solution (see section 6.6) and by changing the sites of infusion regularly.
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 the vancomycin by infusion over 60 minutes before anaesthetic induction.
Monitoring
Doses should be titrated on the basis of serum levels. Blood levels should be monitored and renal function tests performed regularly. It is a general recommendation to monitor the concentrations 2 to 3 times weekly. Regular monitoring of blood levels is indicated in longer-term use, particularly in patients with renal dysfunction or impaired hearing, and with concurrent administration of nephrotoxic or ototoxic substances.
Patients with borderline renal function and individuals over the age of 60 should be given serial tests of auditory function and of vancomycin blood levels. All patients receiving the medicinal product should have periodic haematological studies, urinalysis and renal function tests.
Superinfection and Clostridioides difficile
Clinically significant serum concentrations have been reported in some patients being treated for active C. difficile-induced pseudomembranous colitis after multiple oral doses of vancomycin; monitoring of serum concentrations may therefore be appropriate in these patients. Prolonged use of vancomycin may result in the overgrowth of non-susceptible organisms and 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. It is therefore important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of vancomycin. Antiperistaltic agents are contraindicated.

4.5 Interaction with other medicinal products and other forms of interaction

Anaesthetics

Concomitant administration of vancomycin and anaesthetic agents has been associated with erythema, histamine-like flushing and anaphylactoid reactions. Infusion-related events may be minimised by the administration of vancomycin as a 60-minute infusion prior to anaesthetic induction.

Other potentially nephrotoxic or ototoxic medicinal products

Concurrent or sequential systemic or topical use of other potentially neurotoxic or nephrotoxic medicinal products, such as gentamicin, amphotericin B, streptomycin, neomycin, kanamycin, amikacin, tobramycin, bacitracin, polymyxin B, colistin, viomycin or cisplatin, may potentiate the nephrotoxicity and/or ototoxicity of vancomycin and consequently requires careful monitoring. See section 4.2 with regard to dosage adjustment in the case of use with an aminoglycoside.

Muscle relaxants

There is an increased potential for neuromuscular blockade with concomitant administration of vancomycin and neuromuscular blocking agents.

4.6 Pregnancy and Lactation

Pregnancy

No sufficient safety experience is available regarding vancomycin during human pregnancy. Reproduction toxicology studies in animals do not suggest any effects on the development of the embryo or foetus or on the gestation period (see section 5.3). However, vancomycin penetrates the placenta and a potential risk of embryonal and neonatal ototoxicity and nephrotoxicity cannot be excluded. Vancomycin should therefore be given in pregnancy only if clearly needed and after a careful risk/benefit evaluation.

Breast-feeding

Vancomycin is excreted in human milk. Caution should be exercised when it is given to breast-feeding mothers, because of potential adverse reactions in the infant (disturbances of the intestinal flora with diarrhoea, colonisation with yeast-like fungi and possibly sensitisation). Considering the importance of this medicinal product for the nursing mother, the decision whether to stop breast-feeding should be considered.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

The most common adverse reactions are phlebitis and pseudo-allergic reactions in connection with too rapid intravenous infusion of vancomycin.

Infusion-related events

During or shortly after rapid infusion, anaphylactoid reactions may occur, including hypotension, dyspnoea, urticaria or pruritus. Redness of the skin on the upper body (red man syndrome) and pain and cramps in the chest or back muscles can occur. The reactions abate when administration is stopped, generally between 20 minutes and 2 hours. Vancomycin should be infused slowly, over more than 60 minutes (see section 4.4).
Ototoxicity has primarily been reported in patients given high doses, in those receiving concomitant treatment with another ototoxic medicinal product, and in those with a pre-existing reduction in kidney function or hearing.

Tabulated list of adverse reactions

The following terminology has been used to classify the occurrence of adverse reactions: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Rare	Thrombocytopenia, neutropenia, agranulocytosis, eosinophilia
Immune system disorders	Rare	Anaphylactic reactions, hypersensitivity reactions
Ear and labyrinth disorders	Uncommon	Transient or permanent loss of hearing
	Rare	Tinnitus, dizziness
Cardiac disorders	Very rare	Cardiac arrest
Vascular disorders	Common	Decrease in blood pressure, thrombophlebitis
	Very rare	Vasculitis
Respiratory, thoracic and mediastinal disorders	Common	Dyspnoea, stridor
Gastrointestinal disorders	Rare	Nausea, diarrhoea
	Very rare	Pseudomembranous enterocolitis
Skin and subcutaneous tissue disorders	Common	Exanthema and mucosal inflammation, pruritus, urticaria
	Very rare	Exfoliative dermatitis, Stevens-Johnson syndrome, linear IgA bullous dermatosis, Lyell's syndrome
Renal and urinary disorders	Common	Renal insufficiency, manifested primarily by increased serum creatinine
	Rare	Interstitial nephritis, acute renal failure
General disorders and administration site conditions	Common	Phlebitis, redness of the upper body and the face, pain and spasm of the chest and back muscles
	Rare	Drug fever, shivering

Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome) has been reported.

Reporting of suspected adverse reactions

Healthcare professionals are asked to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS): https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms

Toxicity due to overdose has been reported. A dose of 500 mg administered intravenously to a child of 2 years of age resulted in lethal intoxication. Administration of a total of 56 g over 10 days to an adult resulted in renal insufficiency. In certain high-risk conditions, for example severe renal impairment, high serum levels and oto- and nephrotoxic effects can occur.

Management

A specific antidote is not known. Symptomatic treatment while maintaining renal function is required.

Vancomycin is poorly removed from the blood by haemodialysis or peritoneal dialysis.

Haemofiltration or haemoperfusion with polysulfone resins have been used to reduce serum concentrations of vancomycin.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other antibacterials, glycopeptide antibacterials. ATC code: J01XA01.

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 medicinal product is bactericidal for dividing microorganisms.

Pharmacokinetic/pharmacodynamic relationship

Vancomycin activity is considered to be time-dependent; that is, antimicrobial activity depends on the duration for which the drug level exceeds the minimum inhibitory concentration of the target organism.

Mechanism of resistance

Acquired resistance to glycopeptides is based on the acquisition of various van gene complexes and alteration of the D-alanyl-D-alanine target to D-alanyl-D-lactate or D-alanyl-D-serine, which bind vancomycin poorly because a critical site for hydrogen bonding is missing. This form of resistance is especially seen in Enterococcus faecium. Reduced susceptibility or resistance to vancomycin in Staphylococcus is not well understood; several genetic elements and multiple mutations are required. Cross-resistance with teicoplanin has been reported.

Susceptibility

Vancomycin is active against Gram-positive bacteria; Gram-negative bacteria are resistant. The MIC breakpoints separating susceptible from resistant organisms are as follows.

Organism	Susceptible	Resistant
Staphylococcus species	≤ 2 mg/L	> 2 mg/L
Enterococcus species	≤ 4 mg/L	> 4 mg/L
Streptococcus species	≤ 2 mg/L	> 2 mg/L
Streptococcus pneumoniae	≤ 2 mg/L	> 2 mg/L
Gram-positive anaerobes	≤ 2 mg/L	> 2 mg/L

Organism	Susceptible	Resistant
Non-species related*	≤ 2 mg/L	> 4 mg/L

*Non-species related breakpoints have been determined mainly on the basis of pharmacokinetic/pharmacodynamic data and are independent of MIC distributions of specific species. They are for use only for species that have not been given a species-specific breakpoint, and not for species for which susceptibility testing is not recommended.

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 infection is questionable.

Commonly susceptible species

Gram-positive: Enterococcus faecalis; Staphylococcus aureus; coagulase-negative staphylococci; Streptococcus species; Streptococcus pneumoniae; Clostridium species.

Species for which acquired resistance may be a problem

Enterococcus faecium.

Inherently resistant organisms

Gram-negative bacteria; Chlamydia species; Mycobacteria; Mycoplasma species; Rickettsia species.

5.2 Pharmacokinetic properties

Distribution

Vancomycin appears in various body fluids, including pleural, pericardial, synovial and ascitic fluids. A single intravenous dose of 1 g in adults produces plasma concentrations of 15 to 30 micrograms/mL one hour after a 1- to 2-hour infusion. The volume of distribution is 0.4 to 1 L/kg. The binding of vancomycin to protein has been reported in the literature to range from 10% to 50%. Factors that affect the overall activity of vancomycin include its tissue distribution, inoculum size and protein-binding effects.

Biotransformation and elimination

Vancomycin is metabolised only to a low extent. After parenteral administration it is excreted almost completely as microbiologically active substance (approximately 75–90% within 24 hours) through glomerular filtration via the kidneys. Biliary excretion is insignificant (less than 5% of a dose).

The serum elimination half-life is about 4 to 6 hours in adults with normal renal function and 2.2 to 3 hours in children. In patients with impaired renal function the serum elimination half-life can be significantly increased, up to 7.5 days. The total systemic and renal clearance of vancomycin may be reduced in the elderly due to the natural decrease in glomerular filtration.

Oral administration

Vancomycin is not significantly absorbed from the normal gastrointestinal tract and is therefore not effective by the oral route for infections other than staphylococcal enterocolitis and pseudomembranous colitis due to C. difficile. Orally administered vancomycin does not usually enter the systemic circulation even when

inflammatory lesions are present. Measurable serum concentrations may occur infrequently in patients with active C. difficile-induced pseudomembranous colitis and, in the presence of renal impairment, the possibility of accumulation exists.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology and repeated-dose toxicity. Limited data on mutagenic effects show negative results; long-term studies in animals regarding carcinogenic potential are not available.

In teratogenicity studies in which rats and rabbits received doses approximately corresponding to the human dose based on body surface area, no direct or indirect teratogenic effects were observed.

Animal studies of use during the perinatal and postnatal period and regarding effects on fertility are not available.

6. Pharmaceutical Particulars

6.1 List of Excipients

Not applicable

6.2 Incompatibilities

Not applicable

6.3 Shelf-Life

24 months.

6.4 Special Precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and Content of container

A 10 mL clear moulded glass vial containing lyophilised powder, packed into a carton with a leaflet.

The pack contains 1 vial together with a diluent of 10 mL sterilised water for injections BP.

6.6 Special precautions for disposal and other handling

No special requirements for disposal

7. Marketing Authorization Holder

TAWWAB PHARMA PRIVATE LIMITED

8. Marketing Authorization Number

H2025/CTD10954/23726

9. Date of first authorization/renewal of the authorization

2025 May 26

10. Date of revision of the text

2025 May 26