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# REVIEW OF VANCOMYCIN ANTIBIOTIC IN CANCER THERAPY

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**Abstract:**
*Vancomycin is an antibiotic used to treat a number of bacterial infections. It is used for treatment of complicated skin infections, bloodstream infections, endocarditis, bone and joint infections, and meningitis caused by methicillin-resistantStaphylococcus aureus.]Vancomycin is also used as oral dosage form for severe Clostridium difficilecolitis. Gram-positive organisms predominate as the bacterial pathogens identified in episodes of febrile neutropenia. This has led to increased use of antibiotics with efficacy against gram-positive organisms (often vancomycin) as part of empirical antibiotic regimens for treating febrile neutropenia. Among 101 children randomized to receive amikacin, ticarcillin, and vancomycin or ticarcillin/clavulanate and amikacin along with vancomycin placebo, treatment success in those treated with vancomycin was higher (85% vs. 62%).. Results from another study and a retrospective review of a large clinical trial also support the previous conclusion.*

**Key words:** *Vancomycin, febrile neutropenia and endocarditis*

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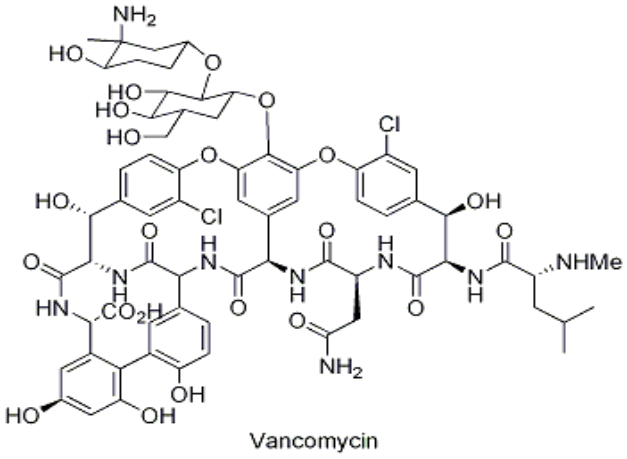
## INTRODUCTION:

Vancomycin is indicated for the treatment of serious, life-threatening infections by Gram-positivebacteria.vancomycin is used in the treatment of serious infections caused by susceptible organisms resistant to penicillins(methicillin-resistant *S. aureus (MRSA)* and multidrug-resistant *S. epidermidis* (MRSE)) or in individuals with serious allergy to penicillins Treatment of pseudomembranous colitis caused by *C. difficile*; in particular, in cases of relapse or where the infection is unresponsive to metronidazole treatment (for this indication, vancomycin is given orally, rather than by its typical intravenous route).It is also used for treatment of infections caused by Gram-positive microorganisms in patients with serious allergies to beta-lactam antibiotic. Earlier it is used as an empiric antibiotic for possible MRSA infection while waiting for culture identification of the infecting organism Halting the progression of primary sclerosing cholangitis and preventing symptoms; vancomycin does not cure the patient and success is limited. Treatment of endophthalmitis by intravitreal injection for gram-positive bacteria coverage.It use to prevent the condition, however, is not recommended due to the risk of side effects.

**Drug profile:**



Vancomycin

Trade name : Vanocin

Molecularformula : $C_{66}H_{75}Cl_2N_90_{24}$

Molecular weight: 1449.3 g.mol−1

**IUPAC name:**

(1*S*,2 *R*, 18*R*, 19*R*, 22*S*, 25*R*, 28*R*, 40*S*) - 48- {[(2*S*,3*R*,4*S*,5*S*,6*R*)- 3- {[(2*S*,4*S*,5*S*,6*S*)- 4- amino- 5- hydroxy- 4,6- dimethyloxan- 2- yl] oxy} - 4, 5- dihydroxy- 6- (hydroxymethyl)oxan- 2- yl] oxy} - 22- (carbamoylmethyl)- 5,15- dichloro- 2, 18, 32, 35, 37- pentahydroxy- 19- [(2*R*)- 4- Methyl - 2- (methylamino) pentanamido] - 20, 23, 26, 42, 44 - pentaoxo- 7,13 – dioxa - 21, 24, 27, 41, 43- pentaazaoctacyclo [26.14.2.23,6.214, 17.18, 12.129, 33.010, 25.034, 39] pentaconta- 3, 5, 8 (48), 9, 11, 14, 16, 29 (45), 30, 32, 34, 36, 38, 46, 49- pentadecaene- 40- carboxylic acid

**HISTORY:**

Vancomycin was first isolated in 1953 by Edmund Kornfeld from a soil sample collected from the interior jungles of Borneo by a missionary.The organism that produced it was eventually named *Amycolatopsis orientalis*] The original indication for vancomycin was for the treatment of penicillin-resistant *Staphylococcus.* The generic name vancomycin was derived from the term "vanquish.One advantage was that staphylococci did not develop significant resistance, despite serial passage in culture media containing vancomycin. The rapid development of penicillin resistance by staphylococci led to its approval by the Food and Drug Administration in 1958. Eli Lilly first marketed vancomycin hydrochloride under the trade name Vancocin. Vancomycin never became the first-line treatment for *S. aureus* for several reasons because it possesses poor oral bioavailability, so it must be given intravenously for most infections.

Main side effects include pain in the area of injection and allergic reactions.Occasionally, hearing loss, low blood pressure, or bone marrow suppression may occur. Safety in pregnancy is not clear, but no evidence of harm has been found,and it is likely safe for lactating women.It is a type of glycopeptide antibiotic and works by blocking the construction of a cell wall. Vancomycin was first sold in 1954.It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system. It is available as a generic medication.The wholesale cost in the developing world of an intravenous dose is about US$1.70 to 6.00. The intravenous solution may be safely taken by mouth for the treatment of *C. difficile* colitis to reduce costs.Vancomycin is made by the soil bacterium *Amycolatopsis orientalis*

**Pharmacology and chemistry:**

Vancomycin is a branched tricyclic glycosylated nonribosomal peptide produced by the Actinobacteria species *Amycolatopsis orientalis* (formerly designated *Nocardia orientalis*). Vancomycin exhibits atropisomerism — it has multiple chemically distinct rotamers owing to the rotational restriction of some of the bonds. The form present in the drug is the thermodynamically more stable conformer, so has more potent activity.

**Mechanism of action:**
Vancomycin acts by inhibiting proper cell wall synthesis in Gram-positive bacteria. Due to the different mechanism by which Gram-negative bacteria produce their cell walls and the various factors related to entering the outer membrane of Gram-negativeorganisms, vancomycin is not active against them (except some nongonococcal species of *Neisseria*).The large hydrophilic molecule is able to form hydrogen bond interactions with the terminal Dalanyl- D-alanine moieties of the NAM/NAG-peptides. Under normal circumstances, this is a fivepoint interaction. This binding of vancomycin to the D-Ala-D-Ala prevents cell wall synthesis of the long polymers of *N*-acetylmuramic acid (NAM) and *N*-acetylglucosamine (NAG) that form the backbone strands of the bacterial cell wall, and it prevents the backbone polymers that do manage to form from cross-linking with each other.

**Side effects:**
Nephrotoxicity
Ototoxicity
Common side effect;
Thrombophlebitis
localpain

**Rare side effect**;
anaphylaxis,
toxic epidermal necrolysis,
erythema multiforme,
red man syndrome,
superinfection,
thrombocytopenia,
neutropenia,
leukopenia,
tinnitus,
dizziness

**Therapeutic drug monitoring**:
Plasma level monitoring of vancomycin is necessary due to the drug's biexponential distribution, intermediate hydrophilicity, and potential for ototoxicity and nephrotoxicity, especially in populations with poor renal function and/or increased propensity to bacterial infection. Vancomycin activity is considered to be time-dependent; that is, antimicrobial activity depends on the duration that the serum drug concentration exceeds the minimum inhibitory concentration of the target organism. Thus, peak serum levels have not been shown to correlate with efficacy or toxicity; indeed, concentration monitoring is unnecessary in most cases. Circumstances in which therapeutic drug monitoring is warranted include: patients receiving concomitant aminoglycoside therapy, patients with (potentially) altered pharmacokinetic parameters, patients on haemodialysis, patients administered high-dose or prolonged treatment, and patients with impaired renal function. In such cases, trough concentrations are measured. Target ranges for serum vancomycin concentrations have changed over the years. Early authors suggested peak levels of 30 to 40 mg/l and trough levels of 5 to 10 mg/l, but current recommendations are that peak levels need not be measured and that trough levels of 10 to15 mg/l or 15 to 20 mg/l, depending on the nature of the infectionand the specific needs of thepatient, may be appropriate Vancomycin.

## CONCLUSION:

It may be noted that even after 50 years of use, adverse reactions associated with vancomycin continue with high frequency, presenting a public health problem, especially considering its current use in cases of multidrug resistant infections. Mortality associated with MRSA bacteremia was significantly higher when the empirical antibiotic was inappropriate and when vancomycin was empirically used for treatment of infection with strains with a high vancomycin MIC (>1 µg/mL).

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