"A NEW CONJUGATE OF VANCOMYCIN AND TRANSPORTAN 10 FOR USE IN ANTIBACTERIAL TREATMENT"

Description of the product

The proposed innovative bioconjugate is a combination of a commonly known antibiotic - vancomycin, with a transport protein - transportan 10 (Van-TP10). Van-TP10 can be used for the treatment of bacterial meningitis, which is a serious diagnostic and therapeutic problem in contemporary medicine. In addition to being a life-threatening condition, meningitis can lead to permanent sequelae associated with mental and physical disability. While it may be caused by viruses, bacteria, fungi and parasites, bacterial infections are the most serious, given their prevalence and clinical severity. According to epidemiological data, meningitis continues to be a major cause of morbidity and mortality in children despite the advances in medicine. A key aspect in the management of meningitis is the appropriate selection of an antibiotic that is carried to the brain with the blood. The newly developed conjugate is characterised by an improved penetrability to the cerebrospinal fluid compared to the other known antibiotics.

Key words

Vancomycin, transportan 10, bacterial meningitis

Legal status of the product

Polish Patent Office:

– 31 January 2019 patent application P.428782. The Medical University of Gdańsk is a co-assignee of the patent.

Subject of the offer

Subject of the offer is a new glycopeptide antibiotic which is a conjugate of vancomycin and transportan 10. This compound exerts antibacterial effects against meticillin-resistant *Staphylococcus aureus* (MRSA), *Enterococcus* spp. and *Neisseria* spp.

Analysis of the market competition

The wholesale distribution of pharmaceuticals in Poland increased from 2008 to 2015 by 26.6%, with the worldwide forecasts estimating a further, very dynamic growth of expenditure in this sector. Poland currently ranks 8th among the EU countries in terms of wholesale distribution of medicines, with antibacterial products being among the bestselling groups. The newly developed Van-TP10, is an alternative to the traditional vancomycin, which is successfully used in severe infections caused by gram-positive bacteria resistant to other antibiotics and in patients with hypersensitivity to penicillins and cephalosporins. The poor blood-brain barrier penetration of the traditional vancomycin has been a limitation of using this antibiotic in the treatment of bacterial meningitis. With its much improved property of penetrating the blood-brain barrier, the modified vancomycin, Van-TP10, can be used as a

modern medicine for the treatment of dangerous bacterial infections of the central nervous system, especially those caused by MRSA.

Advantages of the proposed product

The new Van-TP10 conjugate is characterised by an improved antibacterial efficacy and penetrability of the brain tissue. These improved properties have been possible to achieve by conjugating vancomycin with transportan 10. Transportan 10 is a member of the family of cell-penetrating peptides, it transports various molecules, including drugs, across cell membranes into the intracellular space and it has also an antibacterial properties. The development of the Van-TP10 conjugate has improved the pharmacokinetic and pharmacodynamic properties of vancomycin while maintaining low cellular toxicity. The Van-TP10 conjugate exerts better antibacterial effect against the clinical strains of MRSA and achieves 200-fold higher brain concentrations compared to vancomycin alone. The proposed compound has may potentially be used for the treatment of life-threatening MRSA infections, especially those of the central nervous system.

Product development stage

A total of 4 conjugates of vancomycin and transportan 10 have been synthesised, differing in the site of vancomycin substitution (*C*-terminus, *N*-terminus, and Lys7). The purity of the resulting compounds has been determined at more than 98%. The chemical structure has been identified and confirmed using MALDI-TOF or ESI mass spectrometry. All the synthesised conjugates have been tested for antibacterial action by determining MIC values for three *S. aureus* strains and two clinical strains of vancomycin-resistant enterococci. The ability of one of the conjugates to penetrate into the brain following intravenous administration has been estimated in BALB mice using fluorescent microscopy. The amounts of the conjugate in the brains of the mice were determined by LC/MS. The brain concentration of the conjugate was more than 200-fold higher than that of vancomycin alone. The toxicity of the conjugates has been tested using an *ex vivo* red blood cell haemolysis assay. The conjugates proved non-toxic within the antibacterial concentration range.