SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Vancomycin 125mg hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 125 mg hard capsule contains 125 mg Vancomycin as hydrochloride (equivalent to NLT 131,250 IU)

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard

125 mg capsule: Grey/pink 17.8 ± 0.40 mm hard capsule, containing white to off white congealed liquid mixture as solid mass.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Vancomycin capsules are indicated in:

- Antibiotic-associated pseudomembranous enterocolitis due to Clostridium difficile.
- Staphylococcal enterocolitis

Vancomycin is not significantly absorbed from the gastro-intestinal tract and is therefore, not effective by the oral route for other types of infection.

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

4.2 Posology and method of administration

Posology

Adults, adolescents and older people: The usual daily dose of vancomycin is 500 mg in divided doses for 7 to 10 days, although up to 2 g/day, in three or four divided doses, have been used in severe cases. The total daily dosage should not exceed 2 g.

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 2 g.

Vancomycin Capsules may not be suitable for children below the age of 6 years. Other formulations (e.g. solution) of Vancomycin are available and should be used instead.

Method of administration

The capsules should be swallowed whole with water.

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

- Clinically significant serum concentrations have been reported in some patients who have taken multiple oral doses of vancomycin for active C. difficile-induced pseudomembranous colitis. Therefore, monitoring of serum concentrations may be appropriate in these patients. The risk may be increased in patients with impaired renal function.
- Some patients with inflammatory disorders of the intestinal mucosa may have significant systemic absorption of vancomycin and, therefore, may be at risk for the development of adverse reactions associated with the parenteral administration of vancomycin. The risk is greater in patients with renal impairment. It should be noted that the total systemic and renal clearances of vancomycin are reduced in the elderly.
- Ototoxicity has occurred in patients receiving vancomycin. It may be transient or permanent. It has been reported mostly in patients who have been given excessive intravenous doses, have an underlying hearing loss, or are receiving concomitant therapy with an ototoxic agent such as an amino glycoside. Serial tests of auditory function may be helpful in order to minimise the risk of ototoxicity.
- When treating patients with underlying renal dysfunction or patients receiving concomitant therapy with an aminoglycoside, serial monitoring of renal function should be performed.
- Prolonged use of vancomycin may result in growth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent and/or sequential systemic or topical use of other potentially ototoxic and/or nephrotoxic drugs requires careful monitoring.

4.6 Fertility, pregnancy and lactation

Pregnancy

Teratology studies have been performed at 5 times the human dose in rats and 3 times the human dose in rabbits, and have revealed no evidence of harm to the fetus due to vancomycin.

In a controlled clinical study, the potential ototoxic and nephrotoxic effects of vancomycin hydrochloride on infants were evaluated when the drug was administered to pregnant women for serious staphylococcal infections complicating intravenous drug abuse. Vancomycin hydrochloride was found in cord blood.

No sensorineural hearing loss or nephrotoxicity attributable to vancomycin was noted. Vancomycin was administered only in the second and third trimesters; hence it is not known whether it causes fetal harm.

Consequently, vancomycin should only be given in pregnancy if clearly needed and after a careful benefit-risk assessment.

Breast-feeding

Vancomycin is secreted in breast milk and should therefore only be used during breast-feeding if other antibiotics have failed. In breast-fed infants, disorders of the intestinal flora with diarrhoea, fungus infection and possibly sensitisation may occur. It is recommended to stop breast-feeding during vancomycin treatment. Risks of systemic effects in premature and young neonates exposed to vancomycin in breast milk cannot be excluded due to relatively high intestinal permeability and immature elimination functions of these infants.

Fertility

Animal studies regarding effects on fertility are not available.

4.7 Effects on ability to drive and use machines

Vancomycin has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Since vancomycin is not usually significantly absorbed from the gastro-intestinal tract, the toxicity encountered with parenteral therapy is unlikely to occur after oral administration (but see 'Precautions').

The list below mentions the adverse reactions reported with vancomycin, ranked under the following frequency classification:

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).

Blood and lymphatic system disorders	
Rare	Haematological (Reversible

	neutropenia, usually starting one week or more after onset of *intravenous* therapy or after a total dose of more than 25g, Neutropenia appears to be promptly reversible when vancomycin is discontinued.)
	Thrombocytopenia and reversible agranulocytosis (granulocyte count less than 500/mm^3)
	Eosinophilia
Ear and labyrinth disorders	
Uncommon	Ototoxicity (Hearing loss associated with intravenously administered vancomycin has been reported. Most of these patients had kidney dysfunction, pre-existing hearing loss, or concomitant treatment with an ototoxic drug.)
Rare	Vertigo, dizziness, tinnitus
Vascular disorders	
Rare	Hypotension
Gastrointestinal disorders	
Uncommon	Nausea
Skin and subcutaneous tissue disorders	
Uncommon	Rash, Pruritus
Rare	Flushing of the upper body ("Red neck syndrome"), Urticaria, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Exfoliative dermatitis, Vasculitis, Wheezing, Dyspnoea
Musculoskeletal and connective tissue disorders	
Rare	Muscle spasm of the chest and back
Renal and urinary disorders	
Rare	Nephrotoxicity (Renal failure, principally manifested by increased serum creatinine or blood urea concentrations, has been observed, especially in patients given large doses of intravenously administered vancomycin.)
	Interstitial nephritis (most cases occurred in patients who were given aminoglycosides concomitantly or who had pre-existing kidney dysfunction. When vancomycin was discontinued, azotaemia resolved in most patients.)
General disorders and administration site conditions	

Uncommon	Hypersensitivity reactions, Drug fever

Rare	Anaphylaxis, Pain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Treatment of Overdosage

Supportive care is advised, with maintenance of glomerular filtration. Vancomycin is poorly removed by dialysis. Haemofiltration and haemoperfusion with Amberlite resin XAD-4 have been reported to be of limited benefit.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-intestinal infections, antibiotics, ATC code: A07AA09

Mechanism of action

Vancomycin is a tricyclic glycopeptide antibiotic derived from Amycolatopsis orientalis. The bacterial action of vancomycin results primarily from inhibition of cell-wall biosynthesis. In addition, vancomycin may alter bacterial cell membrane permeability and RNA synthesis.

Orally administered vancomycin is active against C. difficile (e.g. toxigenic strains implicated in pseudomembranous enterocolitis). It is also active against staphylococci, including Staphylococcus aureus. Vancomycin is not active in vitro against Gram-negative bacilli, mycobacteria or fungi.

Sensitivity

The prevalence of resistance may vary geographically and over time. Local information regarding resistance is desirable, in particular, when treating severe infections. This information only provides an approximate guideline about the possibility of microorganisms being sensitive to vancomycin.

Commonly susceptible species
Gram-positive, aerobic
Staphylococcus aureus (incl.methicillin resistant strains)*
Staphylococcus epidermidis (incl.methicillin resistant strains)*

Gram-positive, anaerobic

*Clostridium difficile**
*Clostridium sp.**
Inherently resistant organisms
Gram-positive, aerobic
Mycobacteria
Gram-negative
Gram-negative bacilli
Other microorganisms
Fungi

*Clinical efficacy has been demonstrated for susceptible isolates in registered clinical indications

5.2 Pharmacokinetic properties

Absorption

Vancomycin is poorly absorbed from the gastro-intestinal tract. During multiple dosing of 250 mg every 8 hours for 7 doses, faecal concentrations of vancomycin, in volunteers, exceeded 100mg/kg in the majority of samples.

No blood concentrations were detected and urinary recovery did not exceed 0.76%

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.

Elimination

Administration of vancomycin oral solution, 2 g daily for 16 days to anephric patients with no inflammatory bowel disease, gave serum levels of <0.66 μg/ml. With doses of 2 g daily, concentration of 3,100 mg/kg can be found in the faeces and levels of <1 μg/ml can be found in the serum of patients with normal renal function who have pseudomembranous colitis.

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 a carcinogenic potential are not available. In teratogenicity studies, where rats and rabbits received doses approximately corresponding to the human dose based on body surface (mg/m^2), no direct or indirect teratogenic effects were observed.

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Polyethylene glycol (Macrogol) 6000

Capsule cap and body:

Gelatin

Colorants:

Iron oxide Yellow (E172)

Iron oxide Red (E172)

Titanium dioxide (E171)

Iron Oxide Black (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

21 months.

6.4 Special precautions for storage

Do not store above 25 ° C.

6.5 Nature and contents of container

AL-PVC/PE/Aclar blister packs of 20 capsules or 28 capsules or 30 capsules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

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

7 MARKETING AUTHORISATION HOLDER

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Trading as: Co-pharma

8 MARKETING AUTHORISATION NUMBER(S)

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03/12/2014

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19.05.2016