Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vancocin Matrigel 250mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 250 mg vancomycin (as hydrochloride).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard capsule
Dark blue and grey capsules, imprinted with 3126 in red ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Vancomycin may be used orally for the treatment of staphylococcal enterocolitis and pseudomembranous colitis due to *Clostridium difficile*.

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

Intravenous administration may be used concomitantly if required.

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

4.2 Posology and method of administration

For oral administration.

Either the Matrigel capsules or the contents of the 500mg vial for parenteral administration may be used.

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

Children: The usual daily dose is 40mg/kg in three or four divided doses for 7 to 10 days. The total daily dosage should not exceed 2g.

Oral solution: The contents of the 500mg vial for parenteral administration may be used and either given to the patient to drink, or administered by nasogastric tube. Mix thoroughly to dissolve. Common flavouring syrups may be added to the solution at the time of administration to improve the taste.

4.3 Contraindications

Hypersensitivity to vancomycin.

4.4 Special warnings and precautions for use

Clinically significant serum concentrations have been reported in some patients who have taken multiple oral dosages of vancomycin for active *C. difficile* - induced pseudomembranous colitis. Therefore, monitoring of serum concentrations may be appropriate in these patients.

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 (see package insert accompanying the intravenous preparation).

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 aminoglycoside. 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 the overgrowth 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

Usage in 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 foetus 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. One infant, whose mother received vancomycin in the third trimester, experienced conductive hearing loss that was not attributable to vancomycin. Because vancomycin was administered only in the second and third trimesters, it is not known whether it causes foetal harm. Therefore vancomycin should be given to a pregnant woman only if clearly needed.

Usage in nursing mothers: Vancomycin hydrochloride is excreted in human milk. Caution should be exercised when vancomycin is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

None known.

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').

Nephrotoxicity: Rarely, renal failure, principally manifested by increased serum creatinine or blood urea concentrations, have been observed, especially in patients given large doses of intravenously administered vancomycin. Rare cases of interstitial nephritis have been reported. Most occurred in patients who were given aminoglycosides concomitantly or who had pre−existing kidney dysfunction. When vancomycin was discontinued, azotaemia resolved in most patients.

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. Vertigo, dizziness and tinnitus have been reported rarely.

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) have been reported rarely. Eosinophilia has been reported rarely.

Miscellaneous: Hypersensitivity reactions, anaphylaxis, chills, drug fever, hypotension, wheezing, dyspnoea, urticaria, pruritus, flushing of the upper body ("red neck" syndrome), pain, muscle spasm of the chest and back, nausea and rashes, including exfoliative dermatitis, Stevens−Johnson syndrome, toxic epidermal necrolysis and rare cases of vasculitis.

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

ATC Code: A07 AA09.

Vancomycin is a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis.* The bacterial action vancomycin results primarily from inhibition ofcell wall biosynthesis. In addition, vancomycin may alter bacterial cell membrane permeability and RNA synthesis. There is no cross resistance between vancomycin and other classes of antibiotics.

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

5.2 Pharmacokinetic properties

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.

Vancomycin is poorly absorbed from the gastro-intestinal tract. During multiple dosing of 250mg 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%.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber in addition to that summarised in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Contents
Macrogol 6000

Capsule Shell
Gelatin
Indigo Carmine (E132)
Red iron oxide (E172)
Black iron oxide (E172)
Titanium Dioxide (E171)

Printing Ink
Shellac
Soya Lecithin
Dimeticone
Red iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

AL/UPVC/Aclar blister packs of 20 capsules (2 strips of 10 capsules) and 28 capsules (4 strips of 7 capsules).

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Flynn Pharma Limited
Alton House
4 Herbert Street
Dublin 2

8 MARKETING AUTHORISATION NUMBER

PA1226/005/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 June 1986

Date of last renewal: 16 June 2006

10 DATE OF REVISION OF THE TEXT

March 2014