SCHEDULING STATUS: **S4**

1. NAME OF THE MEDICINE

MYLAN VANCOMYCIN 500 mg (Powder for solution for Infusion)

MYLAN VANCOMYCIN 1 g (Powder for solution for Infusion)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **MYLAN VANCOMYCIN 500 mg** vial contains sterile vancomycin hydrochloride equivalent to 500 mg of vancomycin base per 10 ml of reconstituted solution.

Each **MYLAN VANCOMYCIN 1 g** vial contains sterile vancomycin hydrochloride equivalent to 1 g of vancomycin base per 20 ml of reconstituted solution.

Sugar free

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for infusion.

White to almost white or slightly pink or yellow freeze-dried powder.

After reconstitution a solution is obtained with a pH between 2,8 – 4,5.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

MYLAN VANCOMYCIN is indicated in the treatment of methicillin-resistant (β-lactam-resistant) systemic staphylococcal infections. It is also indicated in the treatment of serious staphylococcal infections in penicillin-allergic patients or in patients who have failed to respond to the penicillin derivatives and/or cephalosporins.

MYLAN VANCOMYCIN is indicated in patients with serious infections caused by vancomycin-sensitive organisms that are resistant to other antimicrobial medicines, including penicillin derivatives and/or cephalosporins.

MYLAN VANCOMYCIN is indicated for initial treatment when methicillin-resistant staphylococci are suspected, however, once sensitivity data are available, treatment should be adjusted accordingly.

MYLAN VANCOMYCIN is indicated in the treatment of staphylococcal endocarditis.

It may be indicated in the treatment of serious infections due to staphylococci resistant to methicillin. When staphylococcal infections are localised and purulent, antibiotics are used as adjuncts to appropriate surgical measures.

In penicillin-allergic patients, **MYLAN VANCOMYCIN** is indicated alone or in combination with an aminoglycoside for endocarditis caused by *S. viridans* or *S. bovis*.

For the treatment of endocarditis caused by enterococci (e.g. *E. faecalis*), **MYLAN VANCOMYCIN** should be used in combination with an aminoglycoside.

Specimens for bacteriologic cultures should be obtained in order to isolate and identify causative organisms and to determine their susceptibilities to **MYLAN VANCOMYCIN**.

The parenteral form of **MYLAN VANCOMYCIN** may be administered orally for treatment of staphylococcal enterocolitis and antibiotic-associated pseudomembranous colitis produced by *C. difficile*. The parenteral administration of **MYLAN VANCOMYCIN** alone is of unproven benefit for

these indications.

MYLAN VANCOMYCIN is not effective by the oral route for other types of infections.

4.2 Posology and method of administration

Posology

Patients with normal renal function:

Adults: The usual daily intravenous dose is 2 g divided either as 500 mg every 6 hours or 1 g every 12 hours.

For oral administration:

The usual adult total daily dosage for antibiotic-associated pseudomembranous colitis produced by *C. difficile* is 500 mg to 2 g given in three or four divided doses for 7 to 10 days. The total daily dosage in children is 40 mg/kg of body mass in three or four divided doses. The total daily dosage should not exceed 2 g.

Special populations:

Patients with impaired renal function:

Dosage adjustment must be made in these patients. **MYLAN VANCOMYCIN** serum concentration should be measured in order to optimise treatment, especially in seriously ill patients with changing renal function.

The following dosage calculations may be used for renally impaired and elderly patients, with appropriate monitoring of serum concentrations:

Creatinine Clearance (ml/min)	***MYLAN VANCOMYCIN Dose (mg/24 hours)***

100	1 545
90	1 390
80	1 235
70	1 080
60	925
50	770
40	620
30	465
20	310
10	155

The initial dose should be no less than 15 mg/kg, even in patients with mild to moderate renal insufficiency and functionally anephric patients.

Paediatric population:

Children: The total daily intravenous dose, calculated on the basis of 40 mg/kg of body mass, can be divided and incorporated into the child's 24-hour fluid requirement.

Infants and neonates: The initial dose of 15 mg/kg is suggested, followed by 10 mg/kg every 12 hours in the first week of life and every 8 hours thereafter until one month of age. Close monitoring of serum **MYLAN VANCOMYCIN** concentration is warranted.

Method of administration

Intermittent intravenous infusion:

This is the preferred method of administration.

Each dose should be administered at a rate of no more than 500 mg per half-hour.

When reconstituted in water, it is a clear solution, free from visible particles.

For instructions on reconstitution and dilution before administration, see section 6.6.

Oral administration:

The reconstituted solutions containing 500 mg and 1000 mg of vancomycin can be diluted in 30 ml of water and given to the patient to drink. Common flavouring syrups should be added to the solution to disguise the taste for oral administration.

For instructions on reconstitution see section 6.6.

4.3 Contraindications

Hypersensitivity to vancomycin hydrochloride or to any of the excipients listed in section 6.1.

MYLAN VANCOMYCIN should not be administered intramuscularly due to the risk of necrosis at the site of administration.

4.4 Special warnings and precautions for use

Infusion-related reactions

MYLAN VANCOMYCIN should not be given intramuscularly, and care should be taken when it is given intravenously to avoid extravasation, because of the risk of tissue necrosis. **MYLAN VANCOMYCIN** should be administered in a diluted solution at a rate of no more than 500 mg per half-hour to avoid rapid-infusion-related reactions such as "red man syndrome", characterised by chills or fever, fainting, rapid heartbeat, hives, hypotension, itching of skin, nausea or vomiting, rash or redness of face, base of neck, upper body, back and arms (see sections 4.2 and 4.8). Stopping the infusion usually results in a prompt cessation of these reactions. The frequency of infusion-related reactions (hypotension, flushing, erythema, urticaria and pruritus) increases with the concomitant administration of anaesthetic medicines (see section 4.5). This may be reduced by administering **MYLAN VANCOMYCIN** by infusion over at least 60 minutes, before anaesthetic induction.

Pseudomembranous enterocolitis

Pseudomembranous colitis has been reported with many broad spectrum antibiotics, including **MYLAN VANCOMYCIN**; therefore, it is important to consider its diagnosis in patients who develop diarrhoea in association with its use. Such colitis may be life-threatening and appropriate measures should be taken, including discontinuation of treatment. Anti-diarrhoeic medicines should not be given.

Nephrotoxicity

Dosage of **MYLAN VANCOMYCIN** should be adjusted for patients with renal dysfunction, including anuria, as the possibility of developing toxic effects is much higher in the presence of prolonged high blood concentrations. The risk of toxicity is increased by high blood concentrations or prolonged treatment.

It should be noted that the total systemic and renal clearances of vancomycin are reduced in the elderly. When patients with underlying renal dysfunction or those patients receiving concomitant treatment with an aminoglycoside (or other nephrotoxic medicines) are being treated, serial monitoring of renal function should be performed, as the risk for the development of adverse reactions is greater if renal impairment is present. Serial tests of auditory function may be helpful in order to minimise the risk of ototoxicity.

Hypersensitivity reactions

Serious and occasionally fatal hypersensitivity reactions are possible. In case of hypersensitivity reactions, treatment with **MYLAN VANCOMYCIN** must be discontinued immediately and adequate emergency measures must be initiated.

In patients receiving **MYLAN VANCOMYCIN** over a longer-term period or concurrently with other medicines which may cause neutropenia or agranulocytosis, the leukocyte count should be

monitored at regular intervals. All patients receiving **MYLAN VANCOMYCIN** should have periodic haematologic studies, urine analysis, liver, and renal function tests.

MYLAN VANCOMYCIN should be used with caution in patients with allergic reactions to teicoplanin, since cross hypersensitivity, including fatal anaphylactic shock, may occur.

Spectrum of antibacterial activity

MYLAN VANCOMYCIN has a spectrum of antibacterial activity limited to gram-positive organisms. It is not suitable for use as a single medicine for the treatment of some types of infections unless the pathogen is already documented and known to be susceptible or there is a high suspicion that the most likely pathogen(s) would be suitable for treatment with **MYLAN VANCOMYCIN**. The rational use of **MYLAN VANCOMYCIN** should take into account the bacterial spectrum of activity, the safety profile and the suitability of standard antibacterial treatment to treat the individual patient.

Ototoxicity

Ototoxicity, which may be transitory or permanent (see section 4.8) has been reported in patients with prior deafness, who have received excessive intravenous doses, or who receive concomitant treatment with another ototoxic medicine such as an aminoglycoside. **MYLAN VANCOMYCIN** should also be avoided in patients with previous hearing loss. 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.

The elderly are particularly susceptible to auditory damage. Monitoring of vestibular and auditory function in the elderly should be carried out during and after treatment. Concurrent or sequential use of other ototoxic medicines should be avoided.

Severe cutaneous adverse reactions (SCARs)

Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with **MYLAN VANCOMYCIN** treatment (see section 4.8). Most of these reactions occurred within a few days and up to 8 weeks after commencing treatment with **MYLAN VANCOMYCIN**.

At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, **MYLAN VANCOMYCIN** should be withdrawn immediately and an alternative treatment considered. If the patient has developed a SCAR with the use of **MYLAN VANCOMYCIN**, treatment with **MYLAN VANCOMYCIN** must not be restarted at any time.

Administration site related reactions

Pain and thrombophlebitis may occur in many patients receiving intravenous **MYLAN VANCOMYCIN** and are occasionally severe. The frequency and severity of thrombophlebitis can be minimised by administering the medicine slowly as a dilute solution (see section 4.2) and by changing the sites of infusion regularly.

The efficacy and safety of **MYLAN VANCOMYCIN** has not been established for the intrathecal, intralumbar and intraventricular routes of administration.

Interactions with anaesthetic medicines

Anaesthetic induced myocardial depression may be enhanced by **MYLAN VANCOMYCIN**. During anaesthesia, doses must be well diluted and administered slowly with close cardiac monitoring. Position changes should be delayed until the infusion is completed to allow for postural adjustment (see section 4.5).

Superinfection

Prolonged use of **MYLAN VANCOMYCIN** may result in the overgrowth of non-susceptible organisms. Careful observation of the patient is essential. If superinfection occurs during treatment, appropriate measures should be taken.

Eye disorders

MYLAN VANCOMYCIN is not authorised for intracameral or intravitreal use, including prophylaxis of endophthalmitis. Haemorrhagic occlusive retinal vasculitis (HORV), including permanent loss of vision, have been observed in individual cases following intracameral or intravitreal use of **MYLAN VANCOMYCIN** during or after cataract surgery.

Use in the elderly

The natural decrement of glomerular filtration with increasing age may lead to elevated **MYLAN VANCOMYCIN** serum concentrations if dosage is not adjusted (see section 4.2).

Paediatric population

The current intravenous dosing recommendations for the paediatric population, in particular for children below 12 years of age, may lead to sub-therapeutic vancomycin levels in a substantial number of children. However, the safety of increased **MYLAN VANCOMYCIN** dosing has not been properly assessed and higher doses than 60 mg/kg/day cannot be generally recommended. **MYLAN VANCOMYCIN** should be used with particular care in premature neonates and young infants, because of their renal immaturity and the possible increase in the serum concentration of vancomycin. The blood concentrations of vancomycin should therefore be monitored carefully in these children. Concomitant administration of **MYLAN VANCOMYCIN** and anaesthetic medicines has been associated with erythema and histamine-like flushing in children. Similarly, concomitant use with nephrotoxic medicines such as aminoglycoside antibiotics, NSAIDs (e.g. ibuprofen for

closure of patent ductus arteriosus) or amphotericin B is associated with an increased risk of nephrotoxicity (see section 4.5) and therefore more frequent monitoring of vancomycin serum levels and renal function is indicated.

Oral administration

Intravenous administration of **MYLAN VANCOMYCIN** is not effective for the treatment of *Clostridium difficile* infection. **MYLAN VANCOMYCIN** should be administered orally for this indication. Testing for *Clostridium difficile* colonisation or toxin is not recommended in children younger than 1 year due to high rate of asymptomatic colonisation unless severe diarrhoea is present in infants with risk factors for stasis such as Hirschsprung disease, operated anal atresia or other severe motility disorders. Alternative aetiologies should always be sought and *Clostridium difficile* enterocolitis be proven.

Potential for systemic absorption

Absorption may be enhanced in patients with inflammatory disorders of the intestinal mucosa or with *Clostridium difficile* induced pseudomembranous colitis. These patients may be at risk for the development of adverse reactions, especially if there is a concomitant renal impairment. The greater the renal impairment, the greater the risk of developing the adverse reactions associated with the parenteral administration of **MYLAN VANCOMYCIN**. Monitoring of serum vancomycin concentrations of patients with inflammatory disorders of the intestinal mucosa should be performed.

Interactions with anti-motility medicines and proton pump inhibitors

Anti-motility medicines should be avoided and proton pump inhibitor use should be reconsidered.

4.5 Interaction with other medicines and other forms of interaction

Other ototoxic or nephrotoxic medicines, such as the aminoglycosides, amphotericin B,

streptomycin, neomycin, gentamycin, kanamycin, amikacin, tobramycin, viomycin, bacitracin, polymyxins, colistin, cisplatin and loop diuretics, markedly increase the risk of toxicity and should be given concomitantly (concurrent or sequential systemic or topical administration) with **MYLAN VANCOMYCIN** only with great caution.

Vancomycin may increase neuromuscular blockade produced by medicines such as suxamethonium and vecuronium.

Concomitant administration of **MYLAN VANCOMYCIN** and anaesthetic medicines has been associated with erythema, histamine-like flushing and anaphylactoid reactions.

There have been reports that the frequency of infusion-related events increases with the concomitant administration of anaesthetic medicines. Infusion-related events may be minimised by the administration of vancomycin as a 60-minute infusion prior to anaesthetic induction. When administered during anaesthesia, doses must be diluted to 5 mg/ml or less and administered slowly with close cardiac monitoring. Position changes should be delayed until the infusion is completed to allow for postural adjustment.

Oral administration:

Consideration should be given to discontinuing proton pump inhibitors and anti-motility medicines in line with local guidelines for *Clostridium Difficile* infection.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Breastfeeding

Vancomycin is excreted in human milk. Safety in breastfeeding women has not been established.

4.7 Effects on ability to drive and use machines

MYLAN VANCOMYCIN causes dizziness which may affect the ability to drive and use machines.

4.8 Undesirable effects

a) Summary of the safety profile

The most common adverse reactions are phlebitis, pseudo-allergic reactions and flushing of the upper body (“redneck syndrome") in connection with too rapid intravenous infusion of **MYLAN VANCOMYCIN**.

The absorption of vancomycin from the gastrointestinal tract is negligible. However, in severe inflammation of the intestinal mucosa, especially in combination with renal insufficiency, adverse reactions that occur when **MYLAN VANCOMYCIN** is administered parenterally may appear.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalised exanthematous pustulosis (AGEP) have been reported in association with **MYLAN VANCOMYCIN** treatment (see section 4.4).

b) Tabulated summary of adverse reactions

Infections and Infestations
Frequency unknown: Overgrowth of non-susceptible organisms, super-infections
Blood and lymphatic system disorders
Less frequent: Agranulocytosis, eosinophilia, pancytopenia, reversible neutropenia,

thrombocytopenia
Immune system disorders
Less frequent: Hypersensitivity reactions, anaphylactic reactions
Ear and labyrinth disorders
Less frequent: Vertigo, dizziness, hearing loss, tinnitus
Frequency unknown: Ototoxicity
Cardiac disorders
Less frequent: Cardiac arrest
Vascular disorders
Frequent: Hypotension
Less frequent: Vasculitis
Respiratory, thoracic and mediastinal disorders
Frequent: Dyspnoea, stridor
Gastrointestinal disorders
Less frequent: Nausea, pseudomembranous enterocolitis
Frequency unknown: Inflammatory disorders of the intestinal mucosa, vomiting, diarrhoea
Skin and subcutaneous tissue disorders
Frequent: Flushing of the upper body ("red man syndrome"), exanthema and

mucosal inflammation, pruritus, urticaria
Less frequent: Linear lgA bullous dermatosis, Stevens-Johnson syndrome, rashes (including exfoliative dermatitis), toxic epidermal necrolysis (TEN)
Frequency unknown: Eosinophilia and systemic symptoms (DRESS syndrome), AGEP (Acute Generalised Exanthematous Pustulosis)
Renal and urinary disorders
Frequent: Renal insufficiency manifested primarily by increased serum creatinine and serum urea
Less frequent: Interstitial nephritis, acute renal failure
Frequency unknown: Nephrotoxicity, acute tubular necrosis
General disorders and administrative site conditions
Frequent: Phlebitis, redness of the upper body and face
Less frequent: Shivering, pain and muscle spasm of the chest and back muscles, medicine fever
Frequency unknown: Chills

c) Description of selected adverse reactions

Reversible neutropenia usually starting one week or more after onset of intravenous treatment or after total dose of more than 25 g.

During or shortly after rapid infusion, anaphylactic/anaphylactoid reactions including wheezing may occur. The reactions abate when administration is stopped, generally between 20 minutes and 2 hours.

MYLAN VANCOMYCIN should be infused slowly (see sections 4.2 and 4.4). Necrosis may occur

after intramuscular injection.

Tinnitus, possibly preceding onset of deafness, should be regarded as an indication to discontinue treatment.

Ototoxicity has primarily been reported in patients given high doses, or in those on concomitant treatment with other ototoxic medicines like aminoglycoside, or in those who had a pre-existing reduction in kidney function or hearing.

d) Paediatric population

The safety profile is generally consistent among children and adult patients. Nephrotoxicity has been described in children, usually in association with other nephrotoxic medicines such as aminoglycosides.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Supportive care is advised, with maintenance of glomerular filtration. **MYLAN VANCOMYCIN** is poorly removed by dialysis. Haemoperfusion may be of limited benefit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.1.1 Broad and Medium Spectrum Antibiotics

ATC code: J01 XA01 for intravenous use and A07 AA09 for oral use.

Vancomycin is a glycopeptides antibiotic with primarily bactericidal action against a variety of gram-positive bacteria. The bactericidal action of vancomycin results primarily from inhibition of cell-wall biosynthesis. In addition, vancomycin alters bacterial cell membrane permeability and RNA synthesis.

Microbiology:

Vancomycin is active against gram-positive bacteria:

- *Staphylococcus aureus* (including heterogeneous methicillin-resistant strains)
- *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains)
- *Streptococcus pyogenes*
- *Streptococcus pneumoniae*
- *Streptococcus agalactiae*
- *Viridans* group of streptococci
- *Streptococcus bovis*
- Enterococci (e.g. *Enterococcus faecalis* [formerly *Streptococcus faecalis*]) – provided **MYLAN VANCOMYCIN** is used in combination with aminoglycosides
- *Clostridium difficile* (e.g. toxigenic strains implicated in pseudomembranous enterocolitis)
- Diphtheroids

Inherently resistant

All gram-negative bacteria

Gram-positive aerobic species

Erysipelothrix rhusiopathiae,

Heteroferrnentative Lactobacillus,

Leuconostoc spp,

Pediococcus spp.

Anaerobic species

Clostridium innocuum

Vancomycin is not active *in vitro* against gram-negative bacilli, mycobacteria, or fungi. *In vitro* sensitivity does not imply *in vivo* activity.

5.2 Pharmacokinetic properties:

Absorption

Vancomycin is given intravenously for systemic disease indications, as it is poorly absorbed by the oral route.

Distribution

Vancomycin is about 30 % bound to plasma proteins. The volume of distribution is about 60L/1,73 m^2 body surface. Vancomycin diffuses readily across the placenta and is distributed into cord blood. In non-inflamed meninges, vancomycin passes the blood-brain barrier only to a low extent.

Biotransformation

There is very little metabolism of vancomycin. After parenteral administration it is excreted almost completely as microbiologically active substance (approx. 75-90 % within 24 hours) through glomerular filtration via the kidneys.

Elimination

It has a serum elimination half-life of about 4 to 6 hours. Vancomycin is excreted unchanged by the kidneys, with 80 to 90 % of the dose excreted unchanged within 24 hours.

Linearity/non-linearity

Vancomycin concentration generally increases proportionally with increasing dose. Plasma concentrations during multiple dose administration are similar to those after the administration of a single dose.

Characteristics in specific groups of patients

Renal impairment

Vancomycin is primarily cleared by glomerular filtration. In patients with impaired renal function the terminal elimination half-life of vancomycin is prolonged and the total body clearance is reduced. Subsequently, optimal dose should be calculated in line with dosing recommendations provided in section 4.2.

Hepatic impairment

Vancomycin pharmacokinetics is not altered in patients with hepatic impairment.

Pregnant Women

Significantly increased doses may be required to achieve therapeutic serum concentrations in pregnant women.

Overweight patients

Vancomycin distribution may be altered in overweight patients due to increases in volume of distribution, in renal clearance and possible changes in plasma protein binding. In these sub populations vancomycin serum concentration was found higher than expected in male healthy adults (see section 4.2).

Paediatric population

Vancomycin PK has shown wide inter-individual variability in preterm and term neonates. In neonates, after intravenous administration, vancomycin volume of distribution varies between 0,38 and 0,97 L/kg, similar to adult values, while clearance varies between 0,63 and 1,4 ml/kg/min. Half-life varies between 3,5 and 10 h and is longer than in adults, reflecting the usual lower values for clearance in the neonate. In infants and older children, the volume of distribution ranges between 0,26-1,05 L/kg while clearance varies between 0,33-1,87 ml/kg/min.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (if necessary to adjust pH) and water for injection.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

MYLAN VANCOMYCIN 500 mg: 36 months

MYLAN VANCOMYCIN 1 g: 24 months

6.4 Special precautions for storage

Before reconstitution*:* Store at or below 25 °C.

After reconstitution: With water for injection: Store at 2 – 8 °C or below 25 °C for up to 24 hours.

After dilution: With either 5 % glucose or 0,9 % sodium chloride: Store at 2 – 8 °C or below 25 °C for up to 24 hours.

6.5 Nature and contents of container

MYLAN VANCOMYCIN 500 mg (Powder for solution for Infusion): 10 ml type II clear glass vials sealed with dark grey bromobutyl rubber stoppers and over sealed with aluminium flip-off caps are supplied in packs of 1 or 10.

MYLAN VANCOMYCIN 1 g (Powder for solution for Infusion): 20 ml type II clear glass vials sealed

with dark grey bromobutyl rubber stoppers and over sealed with aluminium flip-off caps are supplied in packs of 1 or 10.

The vials are packed into an outer carton.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Preparation of the reconstituted solution and final diluted Solution for infusion:

MYLAN VANCOMYCIN 500 mg: Dissolve the powder in 10 ml of sterile water for injection. The reconstituted solution containing 500 mg of **MYLAN VANCOMYCIN** must be diluted with at least 100 ml of diluent.

MYLAN VANCOMYCIN 1 g: Dissolve the powder in 20 ml of sterile water for injection. The reconstituted solution containing 1 g of **MYLAN VANCOMYCIN** must be diluted with at least 200 ml of diluent.

Appearance of reconstituted solution: When reconstituted in water, it is a clear solution, free from visible particles.

Oral Administration:

The contents of vials for parenteral administration may be used. The reconstituted solutions (as instructed above) containing 500 mg and 1000 mg of vancomycin can be diluted in 30 ml of water and given to the patient to drink. Common flavouring syrups should be added to the solution to disguise the taste for oral administration.

Compatible fluids/diluents:

MYLAN VANCOMYCIN reconstituted in water for injection and diluted either in 5 % glucose or 0,9 % sodium chloride may be stored at 25 °C for 48 hours or in a refrigerator (2 to 8 °C) for 96 hours without significant loss of potency.

Vancomycin solution has a low pH and may cause physical instability of other compounds.

Parenteral medicines should be inspected visually for particulate matter and discolouration prior to administration, whenever solution or container permits.

DISCARD ANY UNUSED SOLUTION.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Mylan (Pty) Ltd

Building 6, Greenstone Hill Office Park

Emerald Boulevard

MODDERFONTEIN, 1645

Republic of South Africa

8. REGISTRATION NUMBER(S)

MYLAN VANCOMYCIN 500 mg: 41/20.1.1/0571

MYLAN VANCOMYCIN 1 g: 41/20.1.1/0572

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

04 December 2009

10. DATE OF REVISION OF THE TEXT

To be confirmed