הודעה על החמרה (מידע בטיחות)

תאריך: 20.3.2012

שם תכשיר באנגלית: Vancomycin 500mg, 1g/ vial

מספר רישום: 123 63 30297, 123 64 30298

שם בעל הרישום: ג'נמדיקס

השינויים בעלון שכוללים החמרות מסומנים על רקע צהוב

שינויים נוספים בעלון שאינן החמרות מסומנים באופן הבא: הוספה- בכחול, מחיקה- אדום עם קו חוצה.

עלון לרופא

פרטים על השינוי/ים המבוקש/ים		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
Precautions	Prolonged use of Vancomycine 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. In rare instances, there have been reports of pseudomembranous colitis, due to C. difficile, developing in patients who received intravenous Vancomycine.	The administration of vancomycin by intraperitoneal injection during continuous ambulatory peritoneal dialysis has been associated with a syndrome of chemical peritonitis. Prolonged use of Vancomycine 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. In rare instances, there have been reports of pseudomembranous colitis, due to ~~C.~~ Clostridium difficile, developing in patients who received intravenous Vancomycine. Vancomycin should be used with caution in patients with allergic reactions to teicoplanin, since crossed hypersensitivity reactions between vancomycin and teicoplanin have been reported. Anaesthetic induced myocardial depression may be enhanced by 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.

Concurrent or sequential systemic or topical use of other potentially neurotoxic or nephrotoxic drugs, such as amphotericin ~~3~~B, aminoglycosides (eg. gentamycin, streptomycin, neomycin, kanamycin, amikacin, tobramycin), bacitracin, polymixin B, colistin, viomycin or cisplatin, when indicated, requires careful monitoring. If vancomycin is administered during or directly after surgery, the effect (neuromuscular blockade) of muscle relaxants (such as succinylcholine) concurrently used can be enhanced and prolonged.	Concurrent or sequential systemic or topical use of other potentially neurotoxic or nephrotoxic drugs, such as amphotericin 3, aminoglycosides, bacitracin, polymixin B, colistin, viomycin or cisplatin, when indicated, requires careful monitoring.	**Interaction with other medicaments and other forms of interaction:**
Miscellaneous: Phlebitis, hypersensitivity reactions, anaphylaxis, stridor, nausea, chills, drug fever, decrease in blood pressure, thrombophlebitis, eosinophilia, rashes (including exfoliative dermatitis) and rare cases of vasculitis. Vancomycine has been associated with the bullous eruption disorders Stevens-Johnson syndrome, toxic epidermal necrolysis, exanthema and mucosal inflammation, Lyell's syndrome and linear IgA bullous dermatosis. If a bullous disorder is suspected, the drug should be discontinued and specialist dermatological assessment should be carried out.	*Miscellaneous*: Phlebitis, hypersensitivity reactions, anaphylaxis, nausea, chills, drug fever, eosinophilia, rashes (including exfoliative dermatitis) and rare cases of vasculitis. Vancomycine has been associated with the bullous eruption disorders Stevens-Johnson syndrome, toxic epidermal necrolysis and linear IgA bullous dermatosis. If a bullous disorder is suspected, the drug should be discontinued and specialist dermatological assessment should be carried out.	**Undesirable effects:**
Pharmacodynamic properties: ATC Code: J01 XA01 for intravenous use and A07 AA09 for oral use. Vancomycin is a tricyclic glycopeptide antibiotic derived from *Amycolatopsis orientalis*. The primary mode of action of vancomycin is inhibition of cell-wall synthesis. In addition, vancomycin may alter bacterial cell membrane permeability and RNA synthesis. There is no cross-resistance between vancomycin and other classes of antibiotics. EUCAST Clinical MIC Breakpoints The non-species related breakpoints for susceptible (S) and resistant (R) species are: S ≤4 mg/L and R >8 mg/L. For Staphylococcus spp. S ≤4 mg/L and R >8 mg/L For Enterococcus spp. S ≤4 mg/L and R >8 mg/L For Streptococcus ABCG S ≤4 mg/L and R >4 mg/L For *S. pneumoniae* S ≤4 mg/L and R >4 mg/L	**Pharmacodynamic properties:** Vancomycin is a glycopeptide antibiotic derived from Nocardia orientalis (formerly Streptomyces orientalis), and is active against many Gram-positive bacteria, including Staphylococcus aureus, Staph. epidermidis, alpha and beta haemolytic streptococci, group D streptococci, corynebacteria and clostridia.	**Pharmacologic al properties**

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable. Commonly susceptible species: **Gram-positive aerobes** *Enterococcus faecalis* *Staphylococcus aureus* Coagulase-negative staphyloccoci *Streptococcus group B* *Streptococcus group C* *Streptococcus group G* *Streptococcus pneumoniae* *Streptococcus pyogenes* Viridans streptococci Species for which acquired resistance may be a problem: Gram-positive aerobes *Enterococcus faecium* *Clostridium difficile* (e.g. toxigenic strains implicated in pseudomembranous colitis) is a target species for oral use where high intraluminal concentrations of vancomycin are achieved. ~~Vancomycin is a glycopeptide antibiotic derived from Nocardia orientalis (formerly Streptomyces orientalis), and is active against many Gram-positive bacteria, including Staphylococcus aureus, Staph. epidermidis, alpha and beta haemolytic streptococci, group D streptococci, corynebacteria and clostridia.~~		

Pharmacokinetic properties: Vancomycin is given intravenously for therapy of systemic infections. In subjects with normal renal function, multiple intravenous dosing of 1 g of vancomycin (15 mg/kg) infused over 60 minutes produces mean plasma concentrations of approximately 63 mg/L immediately after the completion of infusion, mean plasma concentrations of approximately 23 mg/L 2 hours after infusion. Mutiple dosing of 500 mg infused over 30 minutes produces mean plasma concentrations of about 49 mg/L at the completion of infusion, mean plasma concentrations of about 19 mg/L 2 hours after infusion, and mean plasma concentrations of about 10 mg/L 6 hours after infusion. The plasma concentrations during multiple dosing are similar to those after a single dose. The mean elimination half-life of vancomycin from the plasma is 4 to 6 hours in patients with normal renal function. About 75% of an administered dose of vancomycin is excreted in urine by glomerular filtration in the first 24 hours. Mean plasma clearance is about 0.058 L/kg/h, and mean renal clearance is about 0.048 L/kg/h. Renal vancomycin clearance is fairly constant and accounts for 70% to 80% of vancomycin elimination. The volume of distribution ranges from 0.39 to 0.97 L/kg. There is no apparent metabolism of the drug. Vancomycin is 55% protein bound as measured by ultrafiltration at vancomycin serum levels of 10 to 100 mg/L. After IV administration of vancomycin hydrochloride, inhibitory concentrations are present in pleural, pericardial, ascitic, atrial appendage tissue and synovial fluid, as well as urine and peritoneal fluid. Vancomycin does not readily penetrate the cerebrospinal fluid unless the meninges are inflamed. Renal dysfunction slows excretion of vancomycin. In anephric patients, the average half-life of elimination is 7.5 days. The total systemic and renal clearance of vancomycin may be reduced in the elderly due to the natural decrement of glomerular filtration.	**Pharmacokinetic properties:** **Distribution:** Using the parenteral route, the intravenous administration of a 1g dose produces a mean plasma concentration of 25mg/ml 2 hours post dose. At about 11 hours post dose the concentration is 3 to 12 g/ml. The plasma half- life varies greatly from one subject to the next (3 to 12 hours, mean=6 hours): At therapeutic concentrations, about 55% is bound to plasma proteins ; The distribution volume is 0.3 to 0.43 1/kg ; Vancomycin diffuses into pleural, synovial, peritoneal and fluids. In contrast it doses not diffuse into cerebrospinal fluid when the meninges are healthy, and concentrations are highly variable when the meninges is inflammed. **Biotransformation:** No metabolism of vancomycin occurs. **Excretion:** About 90% of the dose injected is excreted in urine in active form (including 75% within 24 hours).	

Vancomycin is not significantly absorbed from the normal gastro – intestinal tract and is therefore not effective by the oral route for infections other than staphylococcal enterocolitis and pseudomembranous colitis due to *Clostridium difficile*. 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. 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. ~~**Distribution:** Using the parenteral route, the intravenous administration of a 1g dose produces a mean plasma concentration of 25mg/ml 2 hours post dose. At about 11 hours post dose the concentration is 3 to 12 g/ml.~~ ~~The plasma half- life varies greatly from one subject to the next (3 to 12 hours, mean=6 hours): At therapeutic concentrations, about 55% is bound to plasma proteins ; The distribution volume is 0.3 to 0.43 1/kg ; Vancomycin diffuses into pleural, synovial, peritoneal and fluids. In contrast it doses not diffuse into cerebrospinal fluid when the meninges are healthy, and concentrations are highly variable when the meninges is inflammed.~~ ~~**Biotransformation:** No metabolism of vancomycin occurs.~~ ~~**Excretion:** About 90% of the dose injected is excreted in urine in active form (including 75% within 24 hours).~~		
Incompatibilities: Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds. It is inadvisable to combine vancomycin with drugs during infusion. Mixtures of solutions of vancomycin and beta-lactam antibiotics have been shown to be physically incompatible. The likelihood of precipitation	**Incompatibilities:** Vancomycin solution has a low pH that may cause chemical or physical instability when it is mixed with other compounds. It is inadvisable to combine vancomycin with drugs during infusion.	**Pharmaceutical Particulars**

increases with higher concentrations of vancomycin. It is recommended to adequately flush intravenous lines between administration of these antibiotics. It is also recommended to dilute solutions of vancomycin to 5 mg/mL or less. Although intravitreal injection is not an approved route of administration for vancomycin, precipitation has been reported after intravitreal injection of vancomycin and ceftazidime for endophthalmitis using different syringes and needles. The precipitates dissolved gradually, with complete clearing of the vitreous cavity over two months and with improvement of visual acuity. **Shelf life: 24 months.**		
Special precautions for storage: VANCOMYCIN MYLAN 500 MG: Store below 25°C. The solution reconstituted in water for injections may be **stored for 24 hours** between 2°C and 8°C. The solution diluted ~~with~~ using 0.9 % NaCl or 5 % glucose solution may be **stored for 24 hours** at between 2°C and 8°C. **NOTE:** The maximum storage time of the reconstituted and diluted solution is 24 hours. VANCOMYCIN MYLAN 1 G: Store below 25°C. The solution reconstituted ~~using~~ in water for injections may be **stored for 96 hours** at temperatures between 2°C and 8°C. The solution diluted ~~with~~ using 0.9 % NaCl or 5 % glucose solution may be **stored for 96 hours** at between 2°C and 8°C.	**Special precautions for storage:** VANCOMYCIN MYLAN 500 MG: Store below 25°C. The solution reconstituted may be **stored for 24 hours** between 2°C and 8°C. The solution diluted with 0.9 % NaCl or 5 % glucose solution may be **stored for 24 hours** at between 2°C and 8°C. **NOTE:** The maximum storage time of the reconstituted and diluted solution is 24 hours. VANCOMYCIN MYLAN 1 G: Store below 25°C. The solution reconstituted using water for injections may be **stored for 96 hours** at temperatures between 2°C and 8°C. The solution diluted with 0.9 % NaCl or 5 % glucose solution may be **stored for 96 hours** at between 2°C and 8°C.	