Nepal Medical College Pvt. Ltd & Teaching Hospital

Antimicrobial Stewardship Team in ICU

Antimicrobial stewardship Director: Dr. Saurav Pradhan, MD,DM (Critical care Medicine)

Antimicrobial stewardship coordinator: Dr. Anup Raj Upreti, PharmD,MAD-ID (Certified)

Members:

1. Dr. Abashesh Bhandari, MD (Gastroenterologist)
2. Dr. Manish Oli, MD (Anesthesia & Critical Care)
3. Dr. Sarobar Upadhya, MD (Anesthesia & Critical Care)
4. Dr. Rishav Sharma, MD (Anesthesia & Critical Care)

S.N	Antimicrobial Agents	Daily Dose	Dose modification with CrCl (ml/min)	Remarks
1.	Amoxicillin sodium-Clavulanate potassium	IV: 1000/200 mg q8h	IV: CrCl: 10-30: 1000/200 mg initial dose followed by 500/100 mg q12h CrCl< 10: 1000/200 mg initial dose followed by 500/100 mg q24h	❖ Person with infectious mononucleosis i.e Epstein-Barr Virus (EBV) are likely to develop rash. It is not a permanent allergy ❖ In patients with true Amoxicillin allergy, increased risk to cross allergenicity with cephalosporins having an identical side chain. ❖ Hepatoxicity linked to clavulanic acid. Amoxicillin-clavulanate is the most common cause 13-23% of drug-induced cholestatic liver injury. ❖ Major drug interaction: Concomitant administration with Allopurinol increases frequency of rash.
2.	Ampicillin & Sulbactum	IV: 1.5-3 gm q6h **For serious Gram negative bacilli**: 3 gm (2gm amp + 1gm sulb) over 30 min q6h **Ventilator associated pneumonia (VAP) due to *Acinetobacter:*** 9 gm (6 gm amp + 3 gm sulb) IV over 4 hrs and repeat q8h as a part of combination therapy. (Eur J of Pharm Sci	CrCl: 30-50: 3 gm q8h CrCl: 10-49: 3 gm q12h CrCl <10: 3 gm q24h	❖ A maculopapular rash occur (not urticarial), not true penicillin allergy, in 65-100% patients with infectious mono, 90% with chronic lymphocytic leukemia, and 15-20 % with allopurinol therapy. ❖ The Sulbactum component has useful activity against Acineobacter Baumannii.

		2019;136;104940) Do not use monotherapy for fear of resistance		
3.	Azithromycin	IV: 500 mg q24h Enteric fever: 20mg/kg/day Oral: 500 mg q24h Enteric fever: 20mg/kg/day	None	❖ Macrolides prolong QT intervals and must be used with caution.
4.	Aztreonam	IV: 1 g IV q8h Systemic infection (moderate severity): 1-2 gm IV q8-12h Systemic infection (severe or life threatening severity): 2 gm iv q6-8h Pseudomonas infections: 2 gm iv q6-8h	CrCl 10-30: 1-2 gm IV q12h CrCl <10: 1-2 gm IV q24h	❖ With exception of ceftazidime, no cross allergenicity with other beta-lactam antibiotics ❖ It has no activity against gram positive ❖ ESBL producing bacteria inactivate aztreonam.
5.	Amikacin	IV: Once Daily Dose: 15 mg/kg q24h Multiple Daily Dose: 7.5mg/kg q12h	For Once Daily Dose: CrCl 60-80: 12 mg/kg q24h CrCl 40-59: 7.5 mg/kg q24h CrCl 30-39: 4mg/kg q24h CrCl 20-29: 7.5 mg/kg q48h CrCl 10-19: 4 mg/kg q48h	❖ Aminoglycosides require oxygen to be active and thus are less effective in anaerobic environment such as an abscess or infected bone ❖ Aminoglycosides have decreased activity in low-pH environments such as respiratory secretions or abscesses

<table>
<tr>
<td></td>
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<td></td>
<td>CrCl 0-9: 3 mg/kg q72h and After hemodialysis

For Multiple Daily Dose:
CrCl 10-50: 7.5mg/kg q24h
CrCl <10: 7.5mg/kg q48h</td>
<td>❖ When dosing Aminoglycosides use IBW(Ideal Body Weight)
❖ All aminoglycosides have potential to cause tubular necrosis and renal failure, deafness due to cochlear toxicity, vertigo due to damage to vestibule organs and rare neuromuscular blockade.
❖ Risk of Nephrotoxicity increases with concomitant administration of Nephrotoxic drugs such as vancomycin, cyclosporine, Amphotericin B.
❖ Aminoglycosides are concentration dependent and therefore are more effective if given at longer intervals and with higher doses.
❖ IV dose should be infused over 60 minutes to avoid neuromuscular blockade</td>
</tr>
<tr>
<td>6.</td>
<td>Cefepime</td>
<td>IV:
1-2 gm q8-12h

For Neutropenic Fever (Absolute Neutrophil Count (ANC) is ≤500: 2g q 8h

Continous infusion Dose:
Intial dose of 15mg/kg IV over 30 minutes and then immediately begin Continuous infusion:
If CrCl> 60 ml/min: 6gm iv over 24hr
If CrCl 30-60 ml/min: : 4gm iv over 24hr</td>
<td>
<table>
<tr><th>CrCl</th><th>Intraabdominal Infection</th><th>Febrile neutropenia</th></tr>
<tr><td>>60</td><td>2 gm q12h</td><td>2 gm q8h</td></tr>
<tr><td>30-60</td><td>2 gm q24h</td><td>2 gm q12h</td></tr>
<tr><td>11-29</td><td>1 gm q24h</td><td>2 gm q24h</td></tr>
<tr><td><11</td><td>500 mg q24h</td><td>1 gm q24h</td></tr>
</table>
Obesity:
Modest dose increase: 2gm IV q8h
</td>
<td>❖ FDA safety warning: Risk of non-convulsive status epilepticus.
❖ Cefepime can competitively inhibit the major CNS inhibitory neurotransmitter GABA
❖ Nephrotoxicity risk increases with concomitant aminoglycosides
❖ High dose may cause encephalopathy if creatinine clearance is reduced.
❖ The probability of target attainment is similar for doses of 2g IV q8h and 1g IV q6h, both at a desired probability of ≥90%, up to the susceptibility breakpoint of 8 mg/L and both regimens are superior to 2g IV q12h . (Lodise TP, et al. Pharmacotherapy. 2006; 26: 1320-32.)</td>
</tr>
</table>

		If CrCl 11-29 ml/min: : 2gm iv over 24hr (J Antimicrob Chemother 57:1017,2006; Am J Health Syst Pharm 68:319,2011.)		
7.	Cefoperazone -sulbactam	IV: 1-2 gm q12h	IV CrCl 15-30: 1 gm q12h CrCl <15 : 500 mg q12h	❖ May increase PT/INR ❖ Administration of ethanol may lead to a reaction with flushing,sweating,headache, tachycardia. ❖ Pharmaceutical preparations: Cefoperazone 0.5gm+sulbactam0.5gm Cefoperazone 1gm+sulbactam 1gm (Daily dose of sulbactam should not exceed 4 gm)
8.	Ceftazidime	IV: 1-2 gm q8-12h Continous infusion Dose: Intial dose of 15mg/kg IV over 30 minutes and then immediately begin Continuous infusion: If CrCl> 60 ml/min: 6gm iv over 24hr If CrCl 31-50 ml/min: : 4gm iv over 24hr If CrCl 11-29 ml/min: : 2gm iv over 24hr (Int J Antimicrob Agents 17:497, 2001; Antimicrob Agents Chemother 49:3550, 2005; Infection 37 : 418,	CrCl 31-50: 1-2 gm q12h CrCl 16-30: 1-2 gm q24h CrCl 6-15 : 1 gm q24h CrCl <5 : 1gm q48h	❖ Side chain of Ceftazidime and Aztreonam are the same; cross-allerginicity reported ❖ Caftazidime is a 3rd generation cephalosporins with activity against p.aeruginosa ❖ Rash: increased susceptibility to sunburn observed

		2009.)		
9.	Ceftriaxone	IV: 1-2 gm q24 or divided equally and given twice a day. Or 500mg IV bolus followed by 2gm as continuous infusion (J Antimicrob Chemother 59:285, 2007) For Meningitis: 2gm IV q12h	Not needed	❖ Notably lack activity against Listeria sp, enterococci, MRSA, P.aeruginosa and B. fagilis ❖ Contraindication in hyperbilirubinemia. Crystallization of ceftriaxone in the gallbladder can occur. Pseudocholelithiasis secondary to sludge in glabladder by ultrasound (50%), symptomatic (9%) (N Engl J Med 322:1821,1990). More likely with ceftriaxone≥ 2 gm/day and with patient on total parenteral nutrition and not eating. (Ann Intern Med 115:712, 1991) ❖ Drug Induced immune thrombocytopenia (J Thrombosis & Haemostasis 2012,11:169) ❖ Coadministration of ceftriaxone and IV calcium containing product like
10	Cefotaxime	IV: Life-threatening infections and Meningitis: 2gm IV q4h Intra-abdominal infection: 1-2 gm IV q6-8h (with metronidazole) SBP: 2gm IV q8h	CrCl>10-50: 2 gm q12h CrCl<10 : 2 gm q24h	❖ Most Penicillin-resistant pneumococci and N.meningitidis are susceptible to cefotaxime. Listeria is resistant ❖
11	Cefazolin	IV: 1-2 gm q8h	CrCl>10-50:1- 2 gm q12h CrCl<10 : 1-2 gm q24h	❖ Major use is for surgical prophylaxis ❖ Cefazolin does not share side chains with any other beta-lactam antibiotic. Hence,

				risk of cross allerginicity in patients with allergy to a penicillin, another cephalosporin, a carbapenem or aztreonam is extremely low. Nonehteless, in patients with documented anaphylactic shock to another beta-lactam and a pressing need for cefazolin, cefazolin administration should only be conducted in medical facility equipped to handle acute anaphylaxis. (J allergy Clin Immunol.2015;136:685; Clinic Rev Allerg Immunol 2014;47:46)
12	Clindamycin	IV:400-900 mg q8h (max 4.8gm/day)	Not needed	❖ To avoid neuromuscular blockade, donot exceed infusion rate 30mg/min. ❖ Use in caution in patient receiving musculoskeletal blocking agents. ❖ Can cause severe C.difficile toxin mediated colitis ❖ Reversible neutropenia, thrombocytopenia and eosinophilia ❖ Clindamycin activity against B.fragilis has been declining and rates of resistance world-wide approach 60%. (Clin Infect Dis. 2014; 59:698-705)
13	Ciprofloxacin	IV: 400mg q8-12h	CrCl 5-29: 400mg q18-24h	❖ Concomitant administration with tizanidine is contraindicated.(Clin Pharmacol Ther. 2004;76(6):598-606.) ❖ Avoid Co-administration with antiarrhythmics (Class IA/III) ❖ In randomized study of critically ill patients, use of Ciprofloxacin associated with a reduction in the absolute platelet

				count.(PLoS 8(11):e81477,2013) Thrombocytopenia believed due to drug – induced immune thrombocytopenia (J Thrombosis& Haemostasis 11:169,2012)
14	Colistin (Polymixin E)	Dosing as Colistimethate sodium (CMS) Loading dose: 9 million unit CMS followed by 4.5 million unit q12h The first maintenance dose should be given 12 hours later Inhalation Therapy: 50-75mg CBA(1mg CBA= 30,000 IU CMS) in 3-4 ml saline via vibrating mesh nebulizer 2-3 times/day. Intraventricular/Intrathecal dose: 10mg/day for several weeks; Intrathecal dose often combined with IV dosing. (Consult Clinical pharmacist to avoid confusion)	Dosing as Colistimethate sodium (CMS) CrCl 30-50: 3MIU q12h CrCl 10-30: 2.5MIU q12h CrCl <10 : 1.5MIU q12h	❖ For all indication other than UTI and ad adjuvant inhalation therapy for pneumonia caused by MDR gram negative bacilli, Polymixin B is preferred over Colistin because of equivalent efficacy, faster attainment of target serum concentrations, less inter-patient variability in pharmacokinetics, no dose adjustment for renal impairment and lower risk of renal toxicity (Antimicrob Ag Chemother 60: 2443, 2016, Antimicrob Agts Chemother 2017:61:e02319-16) ❖ Colistin is formulated as a prodrug, colistimethate sodium (CMS). Product vials may be labeled as international unit (IU) or mg of prodrug or mg of colistin base activity (CBA) of active drug. To avoid dosing error read product labels carefully! Conversion: 1mg CBA= 30,000 IU CMS 33 mg CBA = 1,000,000 IU CMS
15	Imipenem-cilastatin	IV: 500mh q6 or 1gm q8h For bacterial species with intermediate susceptibility	CrCl 30-59: 300mg q6h OR 500mg q8h For species with intermediate susceptibility: 500mg q6h CrCl 15-29: 200mg q6h OR 500mg q12h	❖ Seizure risk is greater than for other carbapenems ❖ Increased potential for seizure if recommended doses are exceeded in

		1 gm IV q6h For infection due to P. aeruginosa 3-4gm/day divided q8h or q6h	For species with intermediate susceptibility: 500mg q12h	patients with CrCl <20ml/min. ❖ Concomitant administration of valporic acid , decreases valporic acid concentration. ❖ Cilastin prevents both renal toxicity and hydrolysis of impenem by renal tubular enzymes.
16	Meropenem	IV: 1 gm q8h Can infuse rapidly over 3-5 mintues in an urgent situation Prolonged Infusion: If CrCl≥50: 2gm (over 3hr) q8h If CrCl 30-49: 1gm (over 3hr) q8h If CrCl 10-29: 1gm (over 3hr) q12h Meningitis dose Upto 2gm IV q8h. To help overcome low level of CSF penetration, infuse each dose over 4 hrs. (Antimicrob Agts Chemother 2016;60:6619) For Critically ill patients consider loading dose of 2gm.	CrCl 25-50: 1gm q12h CrCl 10-25: 1gm q12h CrCl <10 : 0.5 gm q24h	❖ Seizure risk lower than for imipenem ❖ Meropenem may reduce serum valporic acid concentration; levels should be monitored ❖ In patient with penicillin allergy, 11% had allergic reaction after imipenem or Meropenem ❖ Probability of target steady state concentration attainment is similar for doses of 1g IV q8h and 500mg IV q6h (both at the desired probability of ≥90%), up to an MIC of 2 mg/L. (Li C, et al. J Clin Pharmacol. 2006;4610:1171-8. Lodise TP, et al. Pharmacotherapy. 2006;269:1320-32.)
17	Piperacillin	IV:	CrCl>40 :3.375 q6h	❖ Piperacillin plus tazobactum is a

	sodium & Tazobactum	4.5 g q8h over 30 minutes Anti-pseudomonal dosing: 4.5 g IV q6h over 30 minutes Prolonged Infusion: 4.5 gm IV over 30 minutes, then 3.375 gm (over 4hours) q8h CrCl>20ml/min: 4.5 gm IV over 30 minutes, then 3.375 gm (over 4hours) q8h CrCl<20ml/min: 4.5 gm IV over 30 minutes, then 3.375 gm (over 4hours) q12h * Consult Clinical pharmacist to avoid confusion regarding preparation of 3.375gm)	CrCl 20-40: 2.25 q6h CrCl <20 : 2.25 q8h Anti-pseudomonal dosing: CrCl>40 :4.5 q6h CrCl 20-40: 3.375 q6h CrCl <20 : 2.25 q6h	monosodium salt of piperacillin and tazobactum and contains a total of 2.79mEq (64mg) of Na+ per gram of piperacilin in the combination product. 1 vial (4.5 g of piperacillin – tazobactum has 12mEq of sodium >275 mg of sodium).This should be considered when one is treating patient requiring restricted salt intake. ❖ Infusion line dead space was identified as a potential source of piperacillin/ tazobactam underdosing when administered via extended infusion. To ensure patients receive a minimum of 3.375 gm over four hours, a 4.5 gm IV dose will be utilized and dispensed in a volume of 100 mL. (Considering dead space of 20ml) ❖ Concurrent administration of Methotrexate increases concentration of Methotrexate. Avoid or monitor this therapy
18	Vancomycin	IV: Loading dose : 25-30mg/kg (especially in septic shock patients) Max dose 2gm Then Maintenance dose :15-20mg/kg q8-12h Continuous infusion:	Loading dose 25mkg/kg then CrCl>50-100: 15-20 mg/kg q12h CrCl 20-49: 15-20 mg/kg q24h CrCl <20 : 15-20 mg/kg q48h	❖ Individual dose ≥1 gm should be infused over 1.5 – 2 hrs ❖ "Red man" syndrome: consequence of rapid infusion of vancomycin with a non specific histamine release ❖ Drug induced Neutropenia/ Drug induced immune Thrombocytopenia ❖ Dose Dependent Nephrotoxicity ❖ Dose mg/day: 15.4mg * CrCl ❖ Infusion rate should not exceed

		Loading dose 15-20 mg/kg over 30-60 minutes, then 30mg/kg (over 24hr) daily Give first maintenance dose 12, 24 or 48 hours after start of loading dose or consult clinical pharmacist		10mg/min. ❖ Consider Therapeutic Drug monitoring. Check trough levels, target 15-20µg/ml.
19	Polymyxin B	IV: Loading dose : 25000IU/kg as 2 hr IV infusion Maintenance dose: Then 12 hours later start 15000IU/kg as a 1 hour IV infusion. Repeat q12h. Meningitis, Intrathecal Dose: 50,000 IU once daily for 3-4 days then every alternate day for ≥ 2 weeks	No dosage adjustment for renal impairement	❖ Polymyxin B is not recommended for ihalation therapy due to potential for damage to lung epithelial cells. ❖ Polymyxin B is not excreted by the kidneys.Hence, Polymyxin B should be avoided in treatment of UTIs. ❖ There is lower patient to patient variability in pharmacokinetic with polymyxin B than colistin. ❖ Colistin associated with higher rates of renal failure than polymyxin B (Antimicrob Agts Chemother 61:e02319-19,2017) ❖ Polymyxin B has activity against multidrug-resistant aerobic gram negative bacilli, e.g P.aeruginosa, Acinetobacter baumanni and carbapenemase producing E.coli and klebsiella pneumonia. Note that Serratia species, Proteus species, Providencia species, Morganella species and Burkholderia cepacia are intrinsically resistant to polymyxins. ❖ The standard unit of dosage for polymyxin B is the international unit (IU):

				10,000 IU = 1mg.
20	Teicoplanin	IV: Complicated Skin and Soft tissue infection, pneumonia, complicated UTI Loading Dose: 6mg/kg q12h for first 3 doses followed by 6mg/kg q24h Usual dose: 400mg IV 12 hourly for 3 dose then 400mg OD For severe Illness: 12mg/kg q12h for first 3 doses followed by 12mg/kg q24h	CrCl 30-80: Load as usual then 6mg/kg q48h CrCl < 30: Load as usual then 6mg/kg q72h	❖ Red neck syndrome less common than vancomycin ❖ CSF/Blood penetration negligible ❖ It has activity against particularly for MRSA, E.faecalis, S.epidermidis, Viridans Strep.
21	Tigecycline	IV: Loading dose: 100mg IV initially then 50mg IV q12h For Hospital acquired infection, severe illness, Acinetobacter,VAP: Loading dose: 200mg IV initially then 100mg IV q12h Hepatic adjustment dose: With severe hepatic impairement (Child Pugh Category C), initial dose of	No dosage adjustment for renal impairement	❖ No activity against P.aeruginosa ❖ Like other tetracycline, may cause photosensitivity, pseudotumor cerebi, pancreatitis, a catabolic sate (elevated BUN). (Clin Infect Dis 45:136,2007). Tetracycline, Minocycline & Tigecycline associated with acute pancreatitis. (Int J Antimicrob Agents 34:486,2009)

<table>
<tr><td></td><td></td><td>100mg IV then 25 mg IV q12h.</td><td></td><td></td></tr>
<tr><td>22</td><td>Levofloxacin</td><td>IV:
750mg OD</td><td>CrCl 20-49 750mg q48h
CrCl <20 75omg once then 500mg q48h</td><td>❖ Levofloxacin is the L enantiomer of Ofloxacin.
❖ Any fluroquinolones may exacerbate muscle weakness in patients with myasthenia gravis.
❖ For oral therapy avoid concomitant exposure to multivalent cations (Ca, Fe, Al, Mg, Zn) in diary products, multivitamins, antacids.</td></tr>
<tr><td>23</td><td>Gentamicin</td><td>IV:
Multiple Daily Dose:
2mg/kg load then 1.7-2mg/kg q8h

Once Daily Dose:
5.1mg/kg q24h (7mg/kg q24 if crtically ill)
Renal dose adjustment for once daily dose:<table><tr><td>CrCl</td><td>Dose</td></tr><tr><td>>80</td><td>5.1 q24h</td></tr><tr><td>60-80</td><td>4 q24h</td></tr><tr><td>40-60</td><td>3.5 q24h</td></tr><tr><td>30-40</td><td>2.5 q24h</td></tr><tr><td>20-30</td><td>4 q48h</td></tr><tr><td>10-20</td><td>3 q48h</td></tr><tr><td>0-10</td><td>2 q72h</td></tr></table></td><td>CrCl>50-89: 1.7-2mg/kg q12h
CrCl 10-49 : 1.7-2mg/kg q24h
CrCl<10 : 1.7-2mg/kg q48h</td><td>❖ Exclusion criteria for once daily dose
Age < 13
- Burns > 20%
- Ascites
- Synergistic dosing for gram-positive infections (e.g. endocarditis)
- History of ototoxicity
- Pregnancy</td></tr>
<tr><td colspan="5">Antifungal</td></tr>
<tr><td>1</td><td>Fluconazole</td><td>IV:
Loading dose :12 mg/kg</td><td>CrCl <50 : 50% reduction in dose</td><td>❖ Antimcorbial Spectrum:
Candida albicans,Candida dubliniensis,</td></tr>
</table>

		IV stat Maintenance dose :6 mg/kg/day Usual Dose: 800mg followed by 400mg q24h		Candida parapsilosis, Candida tropicalis, Candida guilliermondii, Crytpococcus neoformans, Coccidioides immitis ❖ Monitor for Drug interactions
2	Amphotericin B conventional amphotericin or amphotericin deoxycholate)	0.5-1.0 mg/kg/day q24h, depending on infection being treated (Max Dose: 1.5 mg/kg/day Or 80 mg)	Not required	❖ Dilution should be done in electrolyte free D5W. Avoid NS for dilution. ❖ Infusion is usually over 4+ hours ❖ Major concern is nephrotoxicity. Manifest initially by Kaliuresis and hypokalemia then fall in serum bicarbonate (may proceed to renal tubular acidosis), decrease renal erythropoietin and anemia and rising BUN/serum creatinine. Hypomagnesia may occur. Can reduce risk of renal injury by a pre-post infusion hydration with 500ml saline (if clinical status allow salt load), avoidance of nephrotoxins eg radiocontrast, aminoglycosides, cis-platinum, use of lipid preparation of amphotericin B.
3	Voriconazole	IV: Loading dose:6mg/kg q12h for 2 doses Maintenance dose : 4mg/kg q12h	CrCl<50 : Accumulation of IV vehicle (Cyclodextrin) results, switch to oral drug (Normal dose) or discontinue	❖ Voriconazole is a triazole (trifluorinated) with activity against Aspergillus Sp. Including Amphotericin B resistant strains of A. terreus.Active Vs candida Sp. (including krusei), Fusarium Sp. And various molds. ❖ In patientsw with CrCl<50ml/min, the drug should be given orally not IV, since the intravenous vehicle SBECD (Sulfobutylether-β cyclodextrin) may accumulate.

				❖ With prolonged use, fluoride in drug can cause a painful periostitis. (Clin Infect Dis 59: 1237,2014)
4	Caspofungin	IV: Loading Dose: 70 mg on day 1 followed by Maintainance Dose: 50mg q24h	None	❖ Inactive against Cryptococcus, trichosporon and molds other then Aspergillus ❖ Not compatible with Dextrose containing solution ❖ Recent PK study finds only a small reduction in clearance in cirrhotic patients with moderate or severe hepatic insufficiency and recommends no dosage adjustment . (J Antimicrob Chemother 2018;73(9):2493-2496)
5	Anidulafungin	IV: Loading Dose: 200 mg on day 1 followed by Maintainance Dose: 100mg /day	None	❖ Inactive against Cryptococcus, trichosporon and molds other then Aspergillus ❖ No drug in CSF or urine
6	Micafungin	IV: 100mg q24h Candida esophagitis: 150mg q24h	None	❖ Inactive against Cryptococcus, trichosporon and molds other then Aspergillus ❖ No drug in CSF or urine
AntiViral				
1	Oseltamivir	PO: 75mg q12h Chemoprophylaxis 75mg once daily	Crcl 30-60 : 30mg PO q12h CrCl 11-30 : 30mg PO q24h CrCl <10 : 30mg after each dialysis	❖ For patients who are severely ill with influenza, consideration was given to use Oseltamivir at higher doses (150mg q12h). However, in prospective study no additional benefit of higher-dose oseltamivir treatment in adults hospitalized with influenza A was

<table>
<tr><td></td><td></td><td></td><td></td><td>observed, but an improved virologic response in influenza B. (Clin Infect Dis 2013 Dec;57(11):1511-9)
❖ In immunocompromised patients, evidence that clinically relevant flu virus replication beyond 5 days. Hence, clinical judgement guides use of oseltamalavir beyond 5 days. Especially true in critically ill who often have concomitant bacterial pneumonia. (Infect Dis cli N Am 27:157,2013)</td></tr>
<tr><td>2</td><td>Acyclovir</td><td>Genital herpes simplex (HSV), first episode : 400mg PO q8h

Varicella zoster : 800mg PO 5 times a day

Serious HSV/VZV infections (e.g. CNS infections) : 5-12.5mg/kg IV q8h</td><td><table>
<tr><td>Crcl >90</td><td>5-12.5 mg/kg IV q8h</td><td>200 mg PO 5 */day</td><td>400 mg PO q12h</td><td>800 mg PO 5 */day</td></tr>
<tr><td>50-90</td><td>5-12.5 mg/kg IV q8h</td><td>200 mg PO 5 */day</td><td>400 mg PO q12h</td><td>800 mg PO 5 */day</td></tr>
<tr><td>10-50</td><td>>25 5-12.5 mg/kg IV q12</td><td>200 mg PO 5 */day</td><td>400 mg PO q12h</td><td>>25: 800 mg PO 5 */day</td></tr>
</table></td><td>❖ It is used to treat herpes virus infections but not cytomegalovirus infections.
❖ Rapid IV infusion can cause increased serum creatinine. Administer doses over at least one hour.
❖ With high dose may crystallize in renal tubules leading to obstructive uropathy (rapid infusion, dehydration, renal insufficiency and increase dose increase risk)</td></tr>
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10-25: 5-12.5 mg/kg IV q24h</td><td></td><td></td><td>10-25: 800 mg po q8h</td></tr>
<tr><td><10</td><td>2.5-6.25 mg/kg IV q 24h</td><td>200 mg PO q12h</td><td>200 mg PO q12h</td><td>800 mg po q12h</td></tr>
</table></td><td></td></tr>
<tr><td>3.</td><td>Ganciclovir</td><td>Induction Dose:
5 mg/kg IV q12h
Maintenance Dose:
5 mg/kg IV q24h or 6mg/kg 5 times a week or 1000mg PO tid</td><td><table>
<tr><td>CrCl</td><td>Induction Dose:</td><td>Maintenance Dose</td></tr>
<tr><td>70-90</td><td>5 mg/kg IV q12h</td><td>2.5-5 mg/kg IV q24h</td></tr>
<tr><td>50-69</td><td>2.5 mg/kg IV q12h</td><td>2.5-5 mg/kg IV q24h</td></tr>
<tr><td>25-49</td><td>2.5 mg/kg IV q24h</td><td>0.625-1.25 mg/kg IV q24h</td></tr>
<tr><td>10-24</td><td>1.25 mg/kg IV q24h</td><td>0.625-1.25 mg/kg IV q24h</td></tr>
</table></td><td></td><td>❖ It is used for cytomegalovirus (CMV) infections. It also has activity against other herpes viruses, although it is rarely used for these infections.</td></tr>
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<tr><td></td><td></td><td></td><td><table><tr><td><10</td><td>1.25mg/kg 3 times a week</td><td>0.625mg/kg 3 times a week</td></tr></table></td><td></td></tr>
<tr><td>4.</td><td>Valacyclovir</td><td><table><tr><td>Oral Herpes (non-HIV) (Cold sore, fever blister)</td><td>2000mg PO q12h for 1 day</td></tr><tr><td>Primary Genital Herpes (non-HIV)</td><td>1000mg PO q12h for 7-10 days</td></tr><tr><td>Recurrent Genital Herpes (non-HIV)</td><td>500mg PO q12h for 3 days or 1000mg PO once daily for 5 days.</td></tr><tr><td>Genital Herpes Chronic Supression (non-HIV)</td><td>1000mg PO q24h</td></tr><tr><td>Herpes Zoster (Shingles) (non-HIV)</td><td>1000mg PO q8h for 7-10 days</td></tr><tr><td colspan="2">Dose for adult patients immunocompromised (HIV)</td></tr><tr><td>Recurrent Genital Herpes (HIV)</td><td>1000mg PO q12h for 5-10 days</td></tr></table></td><td><table><tr><td>CrCl</td><td>Dose</td></tr><tr><td>>50-90</td><td>1000mg q8h</td></tr><tr><td>10-50</td><td>1000mg q12-24h</td></tr><tr><td><10</td><td>500mg q24h</td></tr></table></td><td>❖ It is an ester of the prodrug Acyclovir that is well absorbed. Used in treatment of Herpes virus infections: Herpes simplex (HSV) and Varicella Zoster (VZV), but not cytomegalovirus.
❖ Bioavailability is 3-5 times greater than Acyclovir
❖ Neurotoxicity: manifest as hallucinations, death delusions and involuntary movements. Result of high serum levels as a failure of dose reduction in patients with renal insufficiency. (Am J Med 128:692,2015)
❖ The recommended dose for immunocompetent adults with varicella or herpes zoster is 1000 mg three times daily for 7 days. (Gnann Jr. JW. Antiviral therapy of varicella-zoster virus infections. In: Arvin A, Campadelli-Fiume G, Mocarski E, et al., editors. Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis. Cambridge: Cambridge University Press; 2007. Chapter 65.)</td></tr>
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		Genital Herpes Chronic Supression (HIV)	500mg PO q12h			