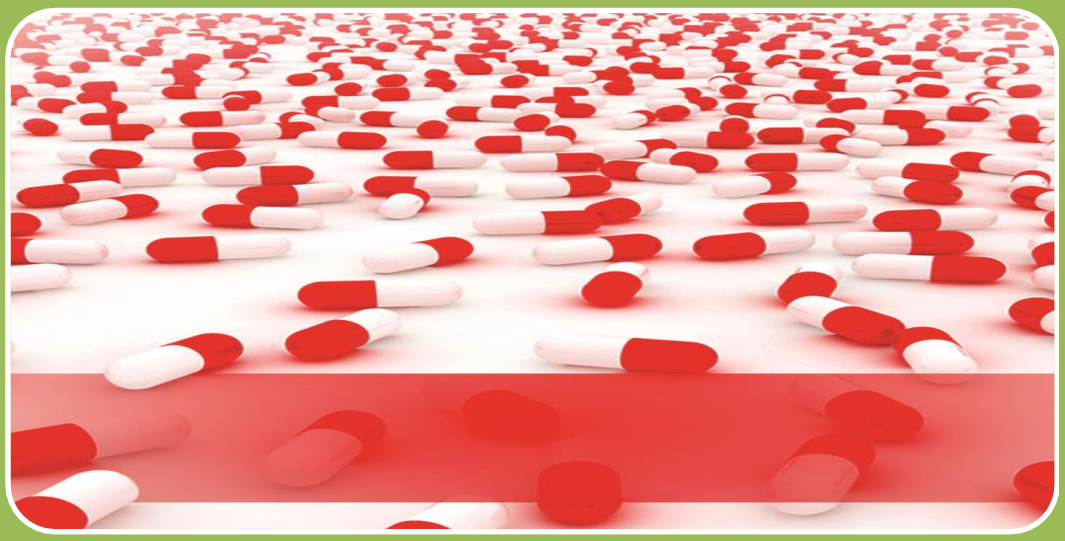
HAYATABAD MEDICAL COMLPEX

CLINICAL PHARMACY NEWSLETTER

Vol-1, Issue-1



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VOl-1, Issue-1

KEY POINTS:

1.The practice of clinical pharmacy
2.Amphotericin-B and Colistin dosing and dilution
3.Carbapenem sparing strategy for ESBL infections

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INTRODUCTION TO CLINICAL PHARMACY SERVICES:

The Clinical Pharmacy Services aimed at providing patient centered approach to the effective use of drugs. The clinical pharmacy is headed by Lead Clinical Pharmacist with expertise in antimicrobial therapeutics. All clinicians are welcomed to approach the department for any patient care related activities relevant to drugs in general and antibiotics in specific. The scope of services includes but is not limited to:

1. Selection of patient specific drug dosages
2. Optimization of dose and duration
3. Pharmacovigilance activities
4. Drug dilution protocols
5. Patient counseling in complex medication regimen

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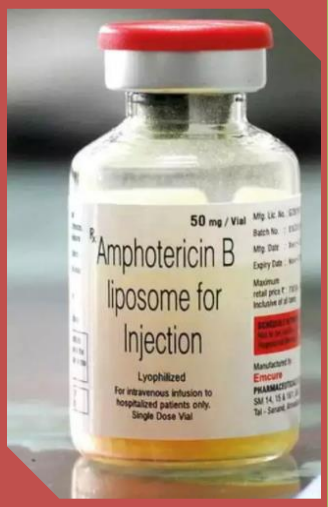

AMPHOTERICIN FORMULATIONS

DO NOT CONFUSE LIPOSOMAL WITH LYPHOLIZED, THEY ARE NOT THE SAME!

Amphotericin-B is type of antifungal belong to polyene class. Three types of amphotericin-B formulations are available:

Amphotericin-B deoxycholate; the conventional form with heightened toxicity profile

Amphotericin-B Lipid complex; newer formulation with favorable safety profile

Liposomal Amphotericin-B; newer formulation with most favorable safety profile

Tissue uptake of amphotercin is dependent on its size and permeability across the membranes. Small size molecules have penetration into a wide range of organs; hence the toxicity increases in a dose dependent manner. Owing to the extensive toxic profile of this precious drug, two new formulations were developed with an aim to lessen the toxicity profile and increasing the efficacy in terms of modified dosing regimen. These were the lipid complex and liposomal.

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AMPHOTERICIN DOSING AND DILUTIONS

Amphotericin B deoxycholate (Conventional)	
Test dose	1 mg IV infused over 20 -30 minutes.
Load dose	0.25 mg-0.5 mg /kg IV infused over 2-6 hrs.
Maintenance dose	0.25 mg- 1mg/kg IV Qday or up to 1.5 mg /kg IV Qod(may increase up to 0.25 mg increment/day.
Amphotericin B liposomal	
Initial dose	1 mg/kg per day, increasing up to 3-5 mg/kg /day
Empiric therapy	3 mg/kg/day
Confirmed Infection	5mg/kg/day
Neonates	1-5 mg/kg/day
Total dose for therapy	2.5-3 gm.
Dilution, Compatibility and Administration:	
Reconstitution	Add 12 ml sterile water for injection to 50 mg vial
Resulting concentration	4 mg/ml
IV compatibility	5 % dextrose solution.
IV incompatibility	Fluids containing NaCl other electrolytes and bacteriostatic agents.
Further dilution	Add reconstituted solution to 5% dextrose solution to provide final concentration to 1-2mg/ml.
Administration	IV infusion: Infuse over 2-6 hours. Flush the line before and after infusion with Buffered Glucose 5% (if available from pharmacy) or Glucose 5% Do not use sodium chloride – causes precipitation
Monitoring Parameters:	
Serum Electrolytes (Na^+, K^+, Mg^{2+})	0-2-4-6 days then every week if no derangement observed.
Serum creatinine	0-2-4-6 days then every week if not derangement observed
Full blood count	0-3-7 days then every week if no derangement observed
Infusion related reactions	Occurs during first infusion and is dependent on rate of infusion

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INTRAVENOUS COLISTIMETHATE (COLISTIN/POLYMYXIN E) PRESCRIBING GUIDELINES

1 Vial = 1 MU = 80mg CMS = 30mg Colistin base (CB)

Indications for use	➢ Antibacterial for the treatment of proven urinary tract infections due to susceptible gram-negative bacilli including ***E. coli*, *Klebsiella* sp, *Pseudomonas* sp, *Acinetobacter* sp** lacking susceptibility to all cefepime or ceftazidime, imipenem or meropenem, piperacillin-tazobactam, and ciprofloxacin. ➢ VAP ➢ HAP ❖ **DO NOT USE IN**: *Burkholderia cepacia, Serratia marcescens, Moraxella catarrhalis, Proteus spp, Providencia spp, and Morganella morganii.*
Place in Therapy	Use in combination with either a carbapenems, tigecycline, or rifampicin for multiresistant gram negative infections
Dosage	➢ Colistimethate sodium (CMS) is an inactive pro-drug of colistin base (CB) hydrolysed to colistin base (CB) in the body. ➢ Prescribed dose must be expressed in terms of MU. ➢ No dose adjustment is required for patients with mild, moderate or severe hepatic impairment.
Duration of therapy	➢ Duration should be based on bacterial cultures and the patient's clinical response. ➢ In general, therapy should continue for at least 5 days after the last negative blood culture.
Monitoring requirements Safety Effectiveness	➢ Daily electrolytes and urea, full blood count,Scr, urine output. ➢ Daily blood cultures until negative if bacteraemic. ➢ Signs and symptoms of neuromuscular blockade (i.e. depressed respiration, muscle weakness, apnoea). ➢ **Effectiveness is determined by clinical response and bacterial cultures**
Contraindications	➢ Myasthenia Gravis ➢ Porphyria

Recommended adult dosages of IV colistin (CMS) in critically-ill patients.

Formula for calculating maintenance dose: Cssavg x (1.5 x CrCl + 30) (Cssavg = 2 mg/L)

If CrCl is >80 mL/min, there is a risk of under dosing (due to increased clearance of CMS before being converted to colistin).

Normal renal function:	**Loading dose**: 12 million units (*All Patient categories REGARDLESS OF RENAL FUNCTION*) **Then**: 3 million units every 8 hours OR: 4.5 million units every 12 hours
Renal impairment:	
• CrCl* 40-60 ml/min	2 million units every 12 hours
• CrCl* 10-40 ml/min	2 million units every 24 hours
• CrCl* <10ml/min	1.5 million units every 36 hours
Renal replacement therapy:	
Haemodialysis	As per CrCl*, with an additional 2 million units after dialysis

CVVHD**	Dosing as for normal renal function
*Creatinine clearance (CrCL) based on Cockcroft-Gault equation; **Continuous veno-venous hemodialysis	

Recommended Pediatrics dosages for colistin (CMS)

Dosage based on Colistimethate Sodium (CMS)	
Neonates	50 000 - 75 000 U/kg/day in three divided dosages.
Infants and children	75 000 - 150 000 U/kg/day in three divided dosages.
Inhalation CMS	<40kg: 500 000 U (0.5MU) every 12 hours > 40kg: 1 000 000 U (1MU) every 12 hours

Colistin (CMS) reconstitution outline information

Dosage	Final volume	Diluent	Infusion time
12 MU loading doses	100 ml	NS/D5W	60 minutes
3 MU 8 hourly	50-100 ml	NS/D5W	15-30 minutes
4.5 MU 12 hourly	50-100 ml	NS/D5W	15-30 minutes
❖ *Cannot be stored once mixed – therefore discard any unused portion.*			

The Dosing of Aerosolized Colistin

Body weight	Dosing recommendations
<40kg	0.5MU 12-hourly
>40kg	1MU 12-hourly
Recurrent/severe pulmonary infections	2MU 08-hourly
❖ *Cannot be stored once mixed – therefore discard any unused portion.*	

Can piperacillin/tazobactam be used as a carbapenem-sparing strategy for extended-spectrum beta-lactamase (ESBL) infections?!

Extended-spectrum beta-lactamase (ESBL) production is a subtype of enzymatic deactivation that confers resistance to many penicillins, cephalosporins (except the cephamycins), and the monobactams.ESBL-producingEnterobacteriaceae
(e.g., *Proteus* species, *Escherichia coli*, and *Klebsiella* spp (AKA, the "PEcK" organisms) are encountered all too commonly in clinical practice today. Carbapenems (e.g., meropenem) are generally considered the drugs of choice for carbapenem-susceptible ESBL-producing isolates. However, it is possible for an ESBL producer to have other resistance mechanisms conferring simultaneous carbapenem resistance.

Piperacillin is a ureidopenicillin that is susceptible to hydrolytic cleavage and inactivation by bacterial penicillinases and ESBLs. The addition of the beta-lactamase inhibitor tazobactam expands the activity of piperacillin alone, allowing it to overcome enzymatic cleavage by some beta-lactamases. Tazobactam inhibits ESBL enzymes, and ESBL-producing bacteria are frequently susceptible to beta-lactam/beta-lactamase inhibitors *in vitro*. Given its ability to retain activity when many other drugs do not, piperacillin/tazobactam (PZT, Zosyn) may provide a carbapenem-sparing treatment for ESBLs.

The issue ends here.

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