# **Pharmacy Newsletter**

Department of Pharmaceutical services is pleased to resume pharmacy newsletter, a quarterly publication aimed to provide the latest information on most economical, therapeutically effective utilization of prescription medications, formulary update and to provide current drug information to health care professionals at SKMCH & RC. The aim of the newsletter is to share therapeutic knowledge with the healthcare providers and to provide an insight into our services. We look forward to your input and participation.

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Volume IV, Issue # 1, 2014

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## Updates

#### **Pre-medications to Amphotericin – No longer Needed**

As reported by Johnson, *et al*; 2010, empiric pre-medications for infusion related adverse effects associated with the use of amphotericin B cannot be routinely advocated. Instead, patients should be treated for the symptoms as they first arise and pre-medications should be used for subsequent amphotericin B infusion.

#### Penicillin Allergy – Make sure is it really an allergy

In-accurate allergy diagnosis may adversely affect health care utilization and quality. Studies say that 95% of the cases with penicillin allergy history are not actually allergic. It is related to longer hospital stay, methicillin-resistant Staphylococcus aureus and Vancomycin resistant enterococcus infections. Antibiotic costs for patients reporting with penicillin allergy are 63% higher than for those who do not report being allergic to penicillin. The gold standard for diagnosing penicillin allergy is skin testing with appropriate major and minor penicillin reagents and controls. Testing for penicillin allergy may result in cost savings, improved patient care and fewer drug resistant bacteria.

#### Rituximab – Risk of Hepatitis B reactivation & usage in population with high risk of HCV infestation

Egyptian Pharmaceutical Vigilance Center has issued information on the risk of hepatitis B reactivation with rituximab and its usage in population known to bear a high potential risk of hepatitis C virus infestation. It is now recommended that HBV screening be performed in all patients before the initiation of treatment with rituximab in all indications, and that patients with positive HBV serology should consult with a liver disease specialist before start of treatment.

### CARBOPLATIN DESENSITIZATION

#### By Sidrah Andleeb

Allergic reactions to Carboplatin are IgE / Mast cell mediated. They are dose as well as infusion related and are more frequent with subsequent cycles. De-sensitization is an encouraging approach for administering Carboplatin to patients showing allergic reaction. It comprises three steps: Skin testing, intra-dermal testing and de-sensitization

Skin Test

Positive control histamine: 1 ml Negative control: NS 0.9% 1ml

Carboplatin: 10mg/ml (1ml) solution

Indicators for positive test

Wheal about 50% in size for that of histamine wheal and 3 mm or more in size of the saline injection area. If negative proceed to intra dermal test.

Intra-dermal test

Carboplatin concentration 0.1mg/ml

Volume to give 0.02ml

Observe for 15 min.

Increase concentration 10

Observe for 15 min and so on

till maximal concentration of 10mg/ml

Positive test: if wheal

#### **De-sensitization**

- 6hr, 12 steps
- Be prepared. Keep following at bed-side
- \*Epinephrine
- \*Anti-histamine
- \*Broncho-dilators
- \*Supplemental oxygen
- Use following for premedication 30 min before infusion:

\*H1 receptor blocker (e.g. Dimenhydrinate)

#### **De-sensitization Protocol**

Carboplatin Dose: Calvert's Formula

AUC used: Usually 5 Prepare 3 solutions:

 $A = 100^{th} \text{ part of dose}$  $B = 10^{th} \text{ part of dose}$ 

C = Dose Diluent: 250 cc D5W

**Table1: Dose preparation protocol** 

Total Dose	500mg	Solution Concentration	Dose in each Solution (mg)
Α	250ml	0.02mg/ml	5
В	250ml	0.2mg/ml	50
С	250ml	2mg/ml	500

**Table 2: Administration protocol** 

Step	Solution	Rate (ml/hr)	Time ( min)	Administer ed Dose	Cumulative Dose
1	Α	2	15	0.01	0.01
2	Α	5	15	0.025	0.035
3	Α	10	15	0.05	0.085
4	Α	20	15	0.1	0.185
5	В	5	15	0.25	0.435
6	В	10	15	0.5	0.935
7	В	20	15	1	1.935
8	В	40	15	2	3.935
9	С	10	15	5	8.935
10	С	20	15	10	18.935
11	С	40	15	20	38.935
12	С	75	185	461	500

## COLISTIN, COLISTIMETHATE SODIUM (KNOWN AS POLYMYXIN E)

By Mariam Nawaz

#### COLISTIN

Loading dose:

For all patients' categories: Adult

Loading dose = Colistin target x = 2.0x body weigh (kg)

Dose of Colistin: **Based on CMS base:** 2.5 – 5 /mg/kg/day **Based on salt:** 6.67 – 13.3 mg/kg/day

Maintenance dose to be given 12 h after the loading dose:

Creatinine clearance	Target
80	5mg/kg/day
57-79	2.5-3mg/kg in 2 divided doses
30-49	2.5mg/kg/day in 1-2 divided doses
10-29	1.5mg/kg/day every 36 hours

Patients not on renal replacement:

Daily dose of CMS = Colistin target x(1.50x CrCl + 30)

Patients on interm	ittent hemodialysis	Patients on continuous renal replacement
Daily dose of CMS on a non-HD day to achieve 1mg/liter Colistin Cmax target: 30mg	Supplemental dose of CMS on HD day: add 50% to the daily maintenance dose to be administered during the last hour of HD session. Twice daily dosing is recommended.	Daily dose of CMA to achieve mg/liter Colistin Cmax target: 192mg. dose may be given 8-12 hours.

Colistimethate	Colistimethate	Colistin base
sodium(IU)	sodium(mg)	activity (CBA) (mg)
12 500	1	0.4
150 000	12	5
1 000 000	80	34
4 500 000	360	150
9 000 000	720	300



#### Alemtuzumab to be re-named & re-launched

Sanofi has withdrawn its leukemia therapy Alemtuzumab (Campath) from the U.S. market to relaunch it under the name Lemtrada at a lower dose to treat relapsing-remitting multiple sclerosis. The withdrawal from the commercial market is designed to prevent the off-label use of the drug in multiple sclerosis.

#### US FDA approves Pomalidomide for advanced multiple myeloma

The US FDA has approved Pomalidomide (Pomalyst) to treat patients with multiple myeloma whose disease has progressed after being treated with other cancer drugs. Pomalyst is a pill that modulates the body's immune system to destroy cancerous cells and inhibit their growth. It is intended for patients who have received at least two prior therapies, including Lenalidomide and Bortezomib, and whose disease did not respond to treatment and progressed within 60 days of the last treatment (relapsed and refractory).

#### **Crofelemer - A new antidiarrheal for HIV+ patients**

Crofelemer, derived from the red sap of the Croton lechleri, is the second ever drug of Botanical origin that has been approved by US FDA. It is indicated to relieve Diarrhea in HIV positive patients. The recommended oral dose is 125mg twice a day. The expected side effects may include nausea, upper respiratory tract infections & lung inflammation.

#### Dalbavancin gets approval for ABSSSI

A novel second generation lipoglycopeptide antibiotic, dalbavancin is approved by FDA in May, 2014 for acute bacterial skin and skin structure infections (ABSSSI). As an intravenous preparation, dalbavancin has shown activity against Staphylococcus aureus (methicillin resistant as well as methicillin sensitive species) and Streptococcus pyogenes. The drug has been provided with Qualified Infectious Disease Product status as it has both antibacterial and anti-fungal activity and has shown good response in life threatening skin infections during phase III trial.

#### **Ledipasvir + Sofosbuvir (Harvoni)**

Harvoni for chronic hepatitis C genotype 1 infection, the first regimen that does not require administration with interferon or ribavirin has been approved by FDA. Ledipasvir is NS5A inhibitor and sofosbuvir is NS5B polymerase inhibitor. Dose is 1 tablet po once daily for 8 to 24 weeks. No renal or hepatic dose adjustments are required.

#### Metformin

Metformin (MET) shows promise as anti-tuberculosis drug. It is reported that the anti-diabetic drug MET reduces the intracellular growth of *Mycobacterium tuberculosis* (*Mtb*) in an AMPK (adenosine monophosphate–activated protein kinase)–dependent manner. MET controls the growth of drug-resistant *Mtb* strains, increases production of mitochondrial reactive oxygen species, and facilitates phagosome-lysosome fusion. In two separate human cohorts, MET treatment was associated with improved control of *Mtb* infection and decreased disease severity, a promising candidate host-adjunctive therapy for improving the effective treatment of TB.