Shaukat Khanum Memorial Cancer Hospital and Research Center

Pharmacy Newsletter

Volume IX, Issue # 4, 2019

Issued By:

Drug Information Centre, SKMCH & RC

P&TC Updates:

Following drugs are approved by Pharmacy & Therapeutics Committee (P&TC) during 2019 SKMCH&RC:

1. **Etanercept Inj.** Regular formulary item
2. **Mycophenolate Tab & Inj.** Regular formulary item
3. **Anti-thymocyte globulin (ATG).** Regular formulary item
4. **Budesonide Oral Caps.** Regular formulary item
5. **Cis-atracurium Inj.** Restricted by service (Anaesthesia consultant only) – 20 patients / month
6. **Clonazepam Tab.** Regular formulary item
7. **Zolmitriptan Tab.** Restricted by service
8. **Abiraterone Tab.** Restricted by cost
9. **Pertuzumab Inj.** Regular formulary item (for indigent patients – 4 slots / month)
10. **Ketoprofen Patch.** Regular formulary item
11. **Empagliflozin Tab.** Restricted by service (Endocrinologist only)
12. **Sofosbuvir+Velpatasvir Tab.** Regular formulary item
13. **Immunoglobulin (IgG) Inj.** Formulary status changed from regular to restricted formulary item by cost.
14. **Arsenic Trioxide Inj.** Regular formulary item.
15. **Indomethacin Tablet 25mg.** Restricted by physicians Dr Khawaja Shehryar Nasir & Dr Attique-Ur-Rehman

International Pharmacy Practice Residency Program (IPPRP) by ASHP

Congratulations!!!

A long-awaited dream comes true!

Department of pharmaceutical services proudly announces American Society of Health- System Pharmacist (ASHP) accreditation under “International Pharmacy Practice Residency Program (IPPRP)”.
SKMCH is only the second non-US pharmacy residency program accredited by ASHP.
This milestone for sure will bring the pharmacy profession to the next level in the region - A proud moment for Pakistan. We have set a gold standard for other hospitals in Pakistan to step forward and contribute for the uplift of pharmacy profession in the region.

This was not possible without the utmost efforts of pharmacy team, continuous support and commitment by the hospital management.

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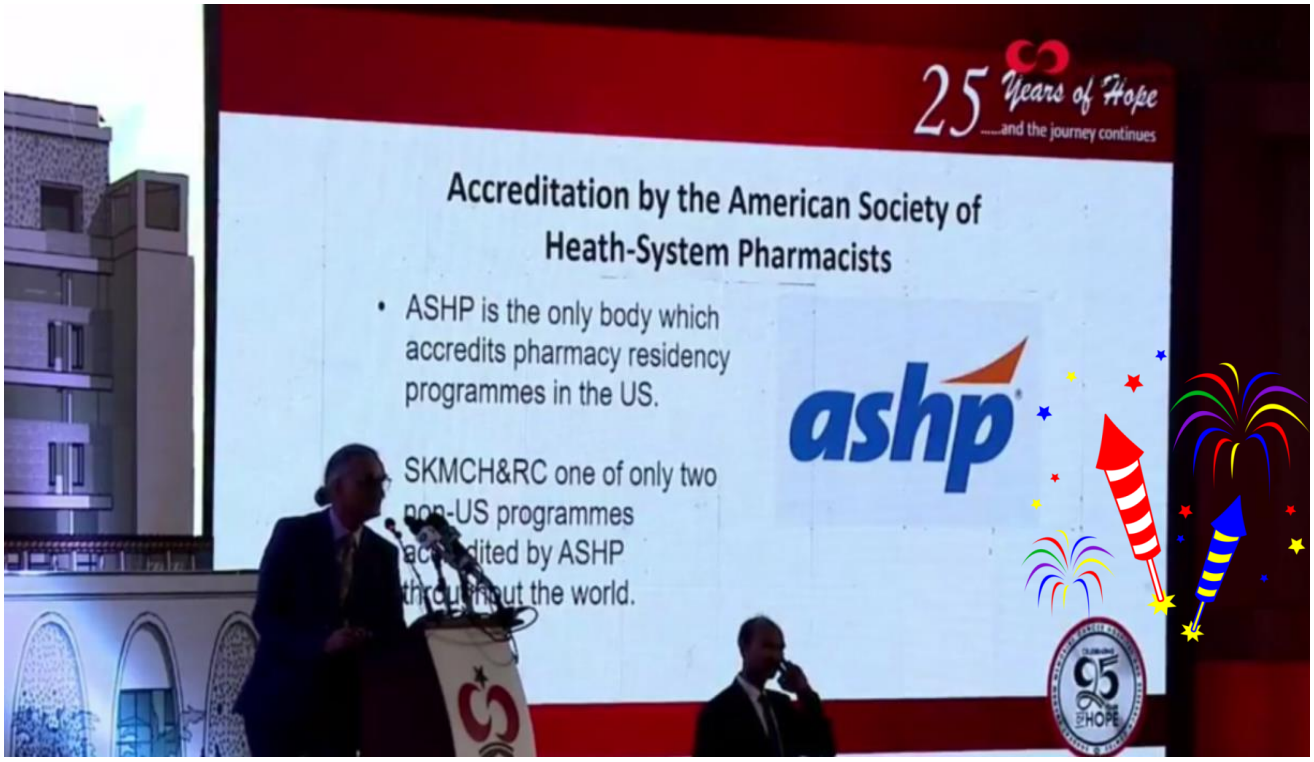


Carboplatin Dosing

Carboplatin dosing is calculated by using Calvert's Equation:

Calvert's Equation

Carboplatin Dose (mg) = **AUC (mg.min/ml) X [GFR(ml/min) + 25(ml/min)]**

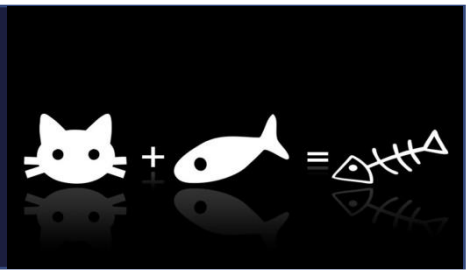
AUC: Area under the concentration curve, GFR: Glomerular filtration rate

*GFR estimated by calculated creatinine clearance (CrCl) using Cockcroft-Gault Equation (see below

Cockcroft-Gault Equation

CrCl (male; mL/min) = $\frac{(140 - \text{age in years}) \times (\text{weight in kg})}{72 \times \text{serum creatinine (mg/dL)}}$

CrCl (female; mL/min) = 0.85 x CrCl (male)



Maximum Carboplatin Dose

FDA has recommended that physicians consider capping the dose of carboplatin for desired exposure (AUC) to avoid potential toxicity due to overdosing. The maximum dose is based on a GFR estimate that is capped at 125 mL/min for patients with normal renal function.

Based on the Calvert's formula, the maximum doses can be calculated as:

Maximum Carboplatin Dose (mg) = Target AUC (mg·min/mL) x (125 mL/min + 25)

For a target AUC = 6, the maximum dose is 6 x 150 = 900 mg

For a target AUC = 5, the maximum dose is 5 x 150 = 750 mg

For a target AUC = 4, the maximum dose is 4 x 150 = 600 mg

Additional Considerations:

Overweight or obese patients (BMI ≥ 25 kg/m^2): Consider using an adjusted body weight.

ABW (kg) = IBW + 0.4 x (TBW – IBW)

ABW: Adjusted body weight, BMI: Body mass index, IBW: Ideal body weight, TBW: Total body weight

Patients with abnormally low serum creatinine (Cr), including elderly or cachectic patients: Consider using a minimum Cr. of 0.7 mg/dL to avoid over-estimation of CrCl.

Ref: NCCN Chemotherapy Order Templates (NCCN Templates)

In **Pediatric** patients, dosing may be based on either BSA (mg/m^2), weight (mg/kg), or a modified Calvert's formula calculation (mg); use extra precaution to verify dosing parameters and units of GFR/estimated CrCl during calculations, as errors can lead to significant over/under dosing. Some protocols suggest weight or age cut-offs for weight-based (mg/kg) dosing; refer to specific protocol.

Ref: Lexicomp, Carboplatin Monograph

Desensitization of Carboplatin

Carboplatin is a very useful cytotoxic drug against cancers, majorly ovarian and lung cancers, but there is high risk of developing hypersensitivity reactions. Desensitization protocols are a useful therapeutic strategy in patients with carboplatin hypersensitivity. In SKMCH & RC, we are using the following desensitization protocol.

Carboplatin Dose: Calvert's Formula
AUC used: Usually 5
Prepare 3 solutions:
A = 100th part of dose
B = 10th part of dose
C = Full dose
Diluent: 250 ml D5W
Pheniramine & hydrocortisone injection should be ready at bed site before starting infusion.

Table 1: Dose Preparation Protocol

Prepare 3 carboplatin dose dilutions:

Total Dose	500	Solution Concentration mg/ mL	Dose in each Solution (mg)
A	250	0.02	5
B	250	0.20	50
C	250	2.00	500

Table 2: Administration Protocol

Step	Solution	Rate (mL/Hr.)	Time(min)	Volume Infused, mL	Administered Dose	Cumulative Dose
1	A	2	15	0.5	0.01	0.010
2	A	5	15	1.25	0.025	0.035
3	A	10	15	2.5	0.05	0.085
4	A	20	15	5	0.1	0.185
5	B	5	15	1.25	0.25	0.435
6	B	10	15	2.5	0.5	0.935
7	B	20	15	5	1	1.935
8	B	40	15	10	2	3.935
9	C	10	15	2.5	5	8.935
10	C	20	15	5	10	18.935
11	C	40	15	10	20	38.935
12	C	60	230.5	230.5	461	499.935

If reaction occurs at any step, stop the infusion and administer pheniramine injection 10mg IV and hydrocortisone injection 100mg

ISMP Publishes Top 10 List of Medication Errors and Hazards

1. Selecting the wrong medication after entering the first few letters of the drug name
2. Daily instead of weekly oral methotrexate for non-oncologic conditions...
3. Errors and hazards due to look-alike labeling of manufacturers' products
4. Misheard drug orders or recommendations during verbal/telephone communication
5. Unsafe "overrides" with automated dispensing cabinets (ADCs).
6. Unsafe practices associated with IV push medications
7. Wrong route (intraspinal injection) errors with tranexamic acid
8. Unsafe labeling of prefilled syringes and infusions by 503b compounders
9. Unsafe use of syringes for vinca alkaloids
10. 1000 -fold overdoses with zinc.

ISMP Medication Safety Alert – Acute care newsletter

18th Shaukat Khanum Cancer Symposium - Oncology Pharmacy Session

The department of pharmaceutical services proudly presents highlights of the oncology pharmacy session held in the 18th annual symposium SKMCH & RC at Pearl Continental Hotel Lahore. It was a great learning opportunity involving valuable talks by renowned national and international speakers. Pharmacoeconomics dynamics of biosimilar drugs were the main theme of discussion during the session attended by pharmacists from a variety of institutions.






Upcoming Events:

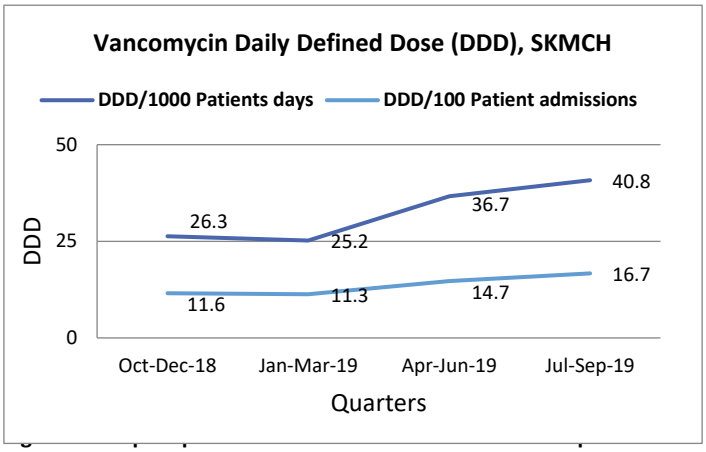
Impact of Culture Sampling Technique on Vancomycin consumption SKMCH&RC

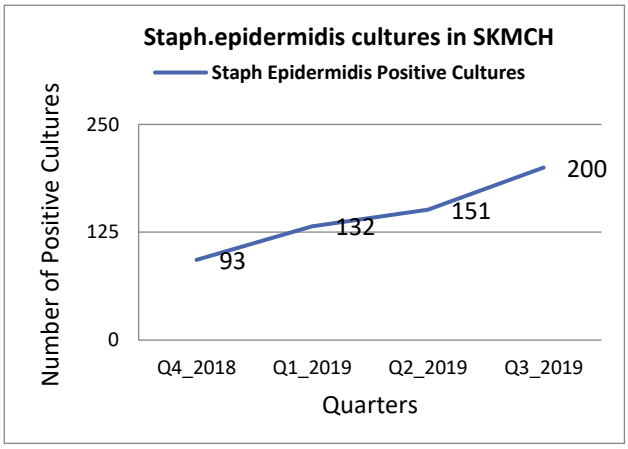
Over the span of last 2 quarters, we have faced an increase in Vancomycin consumption (as per our defined daily doses (DDD) per 1000 patient-days & DDD per 100 patient admissions trend). We analysed the possible causes behind the increased consumption through review of anti-biogram of all SKMCH Lahore patients. Just in last 4 quarters, 4th quarter 2018 and in 1st, 2nd and 3rd quarter 2019, we observed 93, 131, 151, and 200 isolates of S. epidermidis respectively.

S. epidermidis, is a gram-positive cocci bacterium, and is part of the normal human flora, typically prevalent in skin flora, and less commonly in mucosal flora. *S. epidermidis* is not usually pathogenic, and mostly considered as a contaminant in blood cultures. Nonetheless, whenever, gram positive cocci were reported in initial culture report, Vancomycin was initiated as a knee-jerk reaction. ID fellows had to approve Vancomycin for two to three days till final sensitivities. Unfortunately, in most cases, when culture turned out to be *S. epidermidis*, instead of methicillin resistant *S. aureus*, patients had received Vancomycin for 2 to 3 days.

On average, two-day therapy of **Vancomycin** costs around **Rs.5000/** and a tentative estimated cost, for treatment of 300-500 contaminant isolates of *S. epidermidis, per year* is around **Rs.1.5 to 2.5 million/.**

It's assumed that this rise in Vancomycin consumption is due to rise in *S. epidermidis* incidence. Hence, we point out a dire need for training of our staff in sampling technique, to reduce contaminants. It will have positive impact on the Cost of therapy and on patient health (considering high toxicity profile of vancomycin).





5-fluorouracil and Cardiotoxicity-Time to consider

5-fluorouracil is among the key chemotherapeutic agents used to treat gastrointestinal cancers. It is ranked second most common chemotherapeutic agent associated with cardiotoxicity after anthracyclines, involving acute coronary syndrome/myocardial infarction. A number of mechanisms are thought to be responsible for 5-FU related cardiotoxicity, but the two most likely contributors are:

- Ischemia
- Drug related myocardial toxicity.

Coronary vasospasm has historically been accepted to be the main contributor of myocardial ischemia.

Total three incidences of fatal cardiotoxicity have been reported in SKMCH & RC from 2018 to 2019, the details of which have been elaborated in the table below.

5-FU Induced Cardiomyopathy in SKMCH & RC Patients From 2018-2019							
Case	**Age/Sex**	**Disease**	**Co-Morbidity**	**5-FU Administration**	**Symptoms**	**ECG**	**Diagnosis**
1	52Y/F	Gall Bladder Cancer	DM, HTN	Continuous Infusion	Chest Pain, Chest Pressure	ST Elevation	5-FU induced Ischemia
2	51Y/F	Pancreatic Cancer	Nil	Continuous Infusion	Chest Pain, Epigastric Discomfort	ST Depression	5-FU induced NSTEMI
3	37Y/M	Duodenal Adenocarcinoma	Nil	Continuous Infusion	Chest Pain	ST Elevation	5-FU induced Coronary Vasospasm

5-Fu: 5 fluorouracil, DM: Diabetes mellitus, ECG: echocardiogram, HTN: hypertension, NSTEMI: Non-ST elevation myocardial infarction

Literature review showed that although history of pre-existing cardiac disease is a risk factor for cardiotoxicity, most patients who experience fluorouracil-induced cardiotoxicity have no previous cardiac problem. Continuous infusion is among other reasons contributing to cardiotoxicity.

In order to prevent such events, a reduced dose strategy and bolus infusions of 5-FU can be considered but such attempts may lead to therapeutic failure, and thus, not beneficial in all cases. Since, there is no definitive data supporting pre-treatment MUGA scan, echocardiography and dihydrogen pyrimidine dehydrogenase (DPD) analysis to assess and prevent cardiotoxicity, a pre-chemotherapy history and physical assessment is paramount.

All patients should have careful cardiac evaluation including an electrocardiography before, during and after 5-fluorouracil infusion, to identify any subclinical coronary artery disease or cardiomyopathies which may be exacerbated by 5-FU infusion.

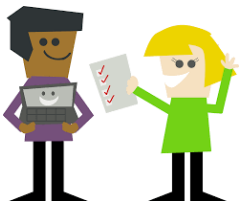
Sharing is Caring

SKMCH & RC believes in sharing the practices of pharmacy with pharmacist community. Shared are the highlights of a two weeks training session each on antibiotic stewardship program for clinical pharmacists from Ali Medical Centre Islamabad and Pakistan Institute of Kidney and Liver disease (PKLI).

Mr. Waqas Ali
Clinical Pharmacist, Ali Medical Center Islamabad

Mr. Mukarram Sajjad
Clinical Pharmacist, PKLI

Ms. Saadia Anum Raza
Clinical Pharmacist, PKLI



News & Updates:

Palonosetron registered in Pakistan

Second-generation 5-HT3 antagonist palonosetron, has recently been registered in Pakistan. It has a strong binding affinity for this receptor and used for the prevention of acute nausea and vomiting associated with initial and repeat courses of highly emetogenic cancer chemotherapy, in children aged 1 month to less than 17 years. When compared in randomized control trial in children, with first generation traditional 5-HT3 receptor antagonist i.e. ondansetron; complete response, defined as no vomiting, in acute (<24 h) and delayed (24 to 120 h) was observed in 88% and 88% of cases, respectively, for palonosetron versus 84% and 79% respectively, for ondansetron (P=0.42, 0.09 respectively) proving its efficacy during in the delayed phases. It has a prolonged duration of action but is associated with higher acquisition treatment costs as compared to ondansetron. It costs around approximately Rs.3000/- per vial as compared to ondansetron which costs around Rs.800/- per vial.

Adult Patients:
0.25mg IV as a single dose, 30 minutes prior to chemotherapy

Pediatric patients:
20mcg/kg/dose IV as a single dose (max: 1.5mg/dose) infused over 30 minutes prior to chemotherapy.

Neonates: Safety and efficacy have not been established.

Ref: Chaudhary, N. K., John, R. R., Boddu, D., Mahasampath, G., Nesadeepam, N., & Mathew, L. G. (2019). Palonosetron is a Better Choice Compared With Ondansetron for the Prevention of Chemotherapy-induced Nausea and Vomiting (CINV) in a Resource-limited Pediatric Oncology Center: Results From a Randomized Control Trial. *Journal of pediatric hematology/oncology*, *41*(4), 294-297.

Tramadol Dosing – Critical for patient safety

Tramadol, a racemic opioid, has potential role at step 2 of the analgesic ladder by WHO. Most of us are much familiar with its use and take its adverse effects into considerations while prescribing. When someone misses precautions or dose adjustment, it can lead to fatal toxicity.

A 19 years old male patient (weight 26 kg), known case of aplastic anemia, post allogenic stem cell transplant (3 years ago), presented in gastroenterology clinic with acute jaundice 9 days ago. Liver function was deranged for which liver biopsy was performed and patient was kept for post procedural monitoring. Patient was prescribed tramadol 100 mg for acute pain. Patient suffered respiratory depression following the dose. This tramadol dose appears correct for an adult patient; however, we need to consider the critical factors in such a patient:

Tramadol Adult Dose:
50-100mg q8h – q12h
Tramadol Pediatric Dose:
1-2mg/kg q8h – q12h

Monitoring Parameters:
- ✓ Liver Function Tests
- ✓ CrCl >30ml/minutes
- ✓ CNS disease

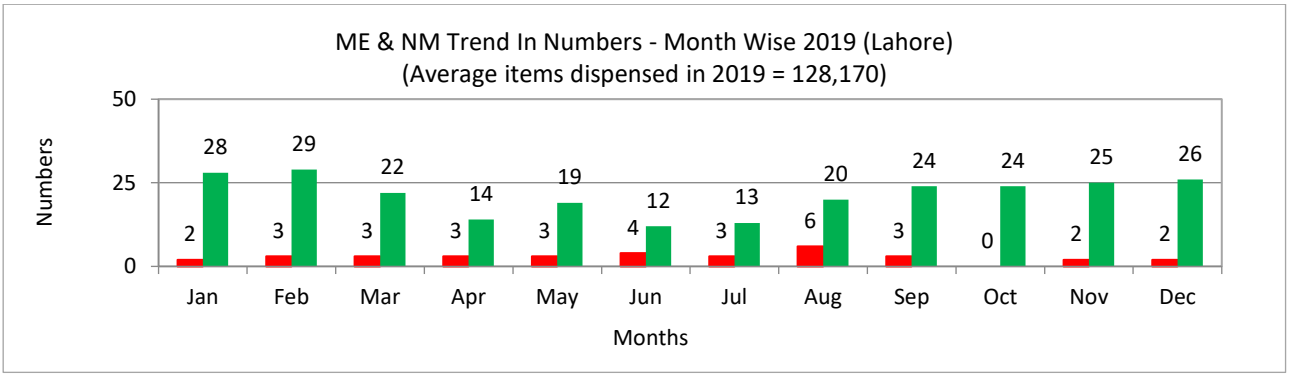
- Patient weighs 26 kg – this is a pediatric weight.
- Patient has grossly deranged liver functions – poor metabolism and overload is a major risk.
- Patient has marked renal impairment – poor chance of compensatory renal excretion.

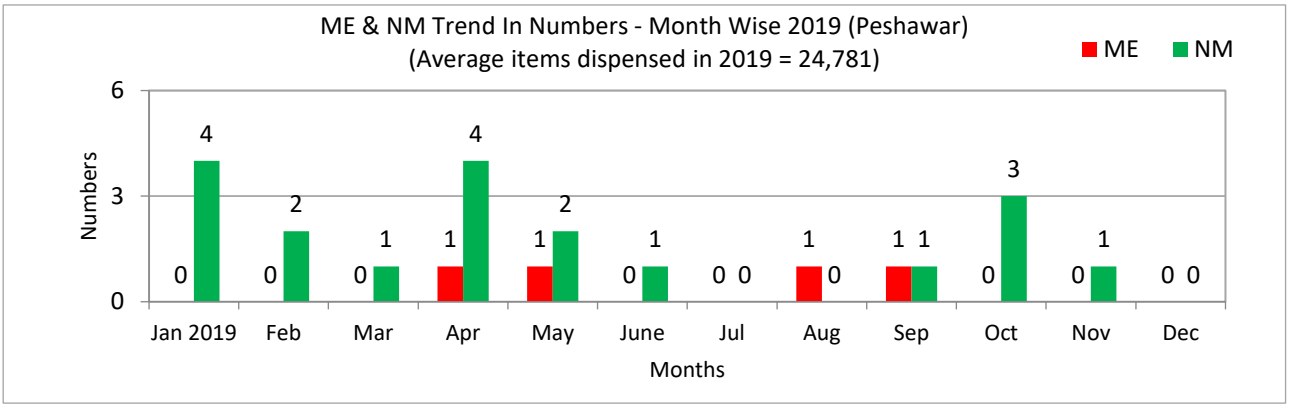
In debilitated patients there is greater risk of fatal respiratory depression with normal dosing of tramadol and it is suggested to use alternate analgesia in this case. Secondly patients with liver failure/liver cirrhosis should have the dose reduced to 50 % to avoid drug accumulation.

Ref: *Marcia L. Buck, Tramadol: Weighing the Risks in Children PEDIATRIC PHARMACOTHERAPY Volume 21 Number 10*

Adverse Drug Events 2019

Medication Error and Near Miss Reported





Adverse Drug Reaction Reported