



Shaukat Khanum Memorial Cancer Hospital and Research Center

Pharmacy Newsletter

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Clinical Pharmacy & Drug Information Center 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 Cap.** 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 consultant only)
12. **Sofosbuvir+Velpatasvir Tab.** Regular formulary item
13. **Immunoglobulin (IgG)** –Formulary status changed from Regular to Restricted Formulary item by cost.

American Society of Health System Pharmacist (ASHP) Post graduate Year-1(Pg-Y1) Residency Program at SKMCH & RC

Department of pharmaceutical services has been running residency program since 2012. Our resident pharmacists have contributed much in growth of pharmacy profession and for improved patient care. Now we have applied for American society of health system pharmacist (ASHP) accreditation of Pg-Y1 residency, which is a 12 month advance pharmacy practice experience. SKMCH&RC will be the first hospital in Southern Asia to have this program. This program will not only improve training of clinical pharmacists in the country but will also raise the standards of advance pharmacy practice. Residents in training will have hands on experience in direct patient care areas, practice foundation skills, teaching and communication skills. Available positions will be advertised in December each year. For further information and guidance you can email us or visit ASHP residency directory.

Anticancer Shortages: What else can be the option?

Anticancer drug shortages have always been troublesome for smooth processes in cancer therapeutics. Apart from global highlights, a recent commentary ⁽¹⁾ has just spotlighted this issue emerged in Pakistan. A sudden shortage of five vital drugs essential for the treatment of different malignancies created a state of uncertainty and regret among patients and healthcare providers. Agents like Vinblastine, Daunorubicin, Dacarbazine, Dactinomycin and MESNA, were on the top end of the shortage list and ultimately the shortages of these agents halted the treatment of diseases like sarcomas, lymphomas and leukemia. Although drug shortages in this case was non-availability of the active pharmaceutical ingredient at the manufacturer end, but drugs were not arranged from the other manufacturers as well. Why? The answer lies in the fact that only a single source is approved by (Drug Regulatory Authority of Pakistan) DRAP, which was fulfilling the requirement of chemotherapy of 0.174 million newly diagnosed patients of cancer for the year of 2018. In addition, there is no manufacturing of these agents at the local level within Pakistan. So in order to provide smooth and high level of anticancer treatments to the patients, manufacturing of these lifesaving agents at the local level within Pakistan and registration of other multiple resources by DRAP for import process as an alternative, are inevitable.

In 2019, drug shortages are further observed especially after declining the revised raised prices of medications by DRAP, followed by crisis in country economy, unstable dollar, which ultimately delays the availability of essential anticancer drugs imported as finished form.

Reference:

Elahi E, Andleeb S. Oncology Drug Shortages—What We Have Versus What We Expect to Have? A Critical Scenario of Pakistan. Journal of Pharmacy Technology. 2019;35(1):41-2.

FDA Updates on Medication Recall

Valsartan or losartan in combinations with amlodipine and hydrochlorothiazide (HCTZ) have been recalled from the market due to unacceptable amounts of N-Nitroso-N-methyl-4-aminobutyric acid (NMBA) found in the losartan active pharmaceutical ingredient (API).

Similarly 19 lots of all strength of losartan have been recalled from the market due to the detection of an impurity NMBA above the FDA's limit of 9.82 ppm. Based on the available information, the risk of developing cancer following long-term use of these product, could not be ruled out. Though to date, no reports of such adverse events following this recall, has been received.

On May 1, 2019, one lot of ketorolac (Toradol) injection have been recalled. This was a voluntary recall of ketorolac injection due to microbial growth detected during a routine simulation of the manufacturing process, though no batches of distributed product have been identified as actually containing microorganisms. To date, the company has not received reports of any adverse events associated with this issue.

Trastuzumab: Safety comparison between the Reference product and its Biosimilar

In 2018, SKMCH & RC introduced a biosimilar of trastuzumab (a monoclonal antibody, well known for its use in breast cancer). The tolerability of the biosimilar was compared with its reference product based on the number of adverse drug reactions reported by each drug.

A retrospective chart review revealed that from August 2018 to December 2018, 4 out of 160 patients presented with trastuzumab induced adverse drug reactions. Wherein, two cases (1.25%) showed cardiovascular toxicity after biosimilar infusion and the other two came out to be allergic reactions (1.25%) in response to reference product.

Cardiovascular events:

It was observed that about 90 (56.2%) patients received recently introduced biosimilar as a treatment for their cancer, out of which 2 (2.2%) patients demonstrated cardiovascular toxicity under the drug influence. Precisely, the patients suffered from dyspnoea and a significant drop in left ventricular ejection fraction (LVEF), hence presenting a clear picture of drug induced cardiomyopathy.

However, such adverse reactions may be the result of another chemotherapy doxorubicin, administered a few months before, but a drop in previously preserved LVEF was noticed as soon the patients were treated with the later. Thus, cardiovascular toxicity was assigned as the adverse effect of the biosimilar.

Cardiomyopathy	
Patient # 01	Patient # 02
LVEF dropped to 40% form 60%	LVEF dropped to 35% form 60%

Allergic Reaction:

Moreover, 70 (43.75%) patients received the reference product, out of which 2 (2.85%) cases were reported with drug induced-allergic reactions. In both cases, the patient developed fever and shivering during the administration, however managed conservatively.

Allergic Reaction	
Patient # 03	Patient # 04
Fever & shivering	Fever & Shivering

The frequency of both types of adverse reactions was much lower as compared to the frequencies reported in the individual monographs, i.e. $\geq 1/10$, of reference and biosimilar products, when Trastuzumab was used alone or in combination with chemotherapy in pivotal clinical trial and the post-marketing setting. The data infers that both the reference and the biosimilar products are well tolerated by the patients at our hospital, thus favouring the use of biosimilar Trastuzumab that is cost effective as well.

Epirubicin Vs Doxorubicin: Another way to treat DLBCL

A multi-centre study, published in Lancet haematology, recently, released the data from its phase 3 trial of anthracycline dose optimization in patients with diffuse large B cell lymphoma (DLBCL). The study, focused the substitution of Doxorubicin in chemotherapy protocol (R-CHOP50) with Epirubicin (R-CEOP70 or R-CEOP90), as the first-line treatment. Findings showed that use of Epirubicin with up to 70-90 mg/m² dosing, resulted in lesser proportion of patients with $\geq 10\%$ decline in left ventricular ejection fraction (LEVF), as a cause of long term cardiotoxicity as compared to (R-CHOP50). Yet, high-grade neutropenia was more prevalent among patients treated with Epirubicin 90mg/m² dosing, in comparison to other groups. In young patients, the 2-year progression-free survival with high dose Epirubicin in R-CEOP90 (88.8%), was considerably better compared with Doxorubicin in R-CHOP50 (75.9%) and Epirubicin in R-CEOP70 (77.4%). Epirubicin can be an alternative drug to Doxorubicin for the treatment of DLBCL. R-CEOP70 could be an option to R-CHOP50, with mild long-term cardiotoxicity in young patients, as per the published work.

Ref: Xu PP, Fu D, Li JY, Hu JD, Wang X, Zhou JF, Yu H, Zhao X, Huang YH, Jiang L, Liu F. Anthracycline dose optimisation in patients with diffuse large B-cell lymphoma: a multicentre, phase 3, randomised, controlled trial. The Lancet Haematology. 2019 Jun 1; 6(6):e328-37.

Dengvaxia: A new tool against Dengue virus

Being live and tetravalent vaccine for the prevention of dengue disease by serotypes 1 – 4, Dengvaxia got its approval by FDA on May 2019. It is approved for use in individuals 9 to 16 years of age with laboratory-confirmed previous dengue infection and living in endemic areas. Dengvaxia is supplied as a suspension for subcutaneous administration. The recommended dose is three doses (0.5 mL each) 6 months apart (at month 0, 6, and 12). Following administration, Dengvaxia elicits dengue-specific

immune responses against the four dengue virus serotypes. Most commonly observed side effects are injection site pain, malaise, headache and myalgia.

Reference:

Brady OJ, Gething PW, Bhatt S, Messina JP, Brownstein JS, Hoen AG et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis.* 2012; 6:e1760. doi:10.1371/journal.pntd.0001760.

Patient Assistance Program

Many patients in Pakistan are denied access to appropriate cancer care due to non-affordability of high cost medications. Considering this issue of cost, UNMOL, a patient assistance program has been introduced by Roche Pakistan.

UNMOL by Roche Pakistan

In “UNMOL” program patients may get assistance up-to a maximum of 50% of the complete therapy. This program is applicable on following medications only:

#	Medication (Brand)	Indigent Slots	Program offering for private patients
01	Trastuzumab (Herceptin)	08	Nil
02	Atezolizumab (Tecentriq)	Nil	
02	Obinutuzumab (Gazyva)		
03	Bevacizumab (Avastin)		
04	Pertuzumab (Perjeta)	04	<i>Note - Number of free vials are offered by company after financial assessment / doc review</i>
05	Rituximab (Ristova IV & Mabthera SC)	09	

(Please note, company is not offering any straight deal e.g. 1+1 etc.)

Process Flow private patients (Paying Status \geq 50%)

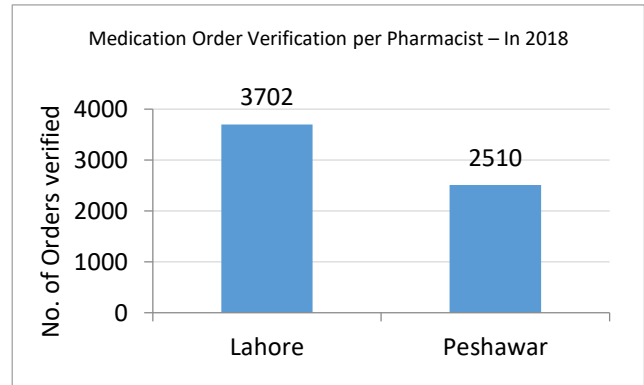
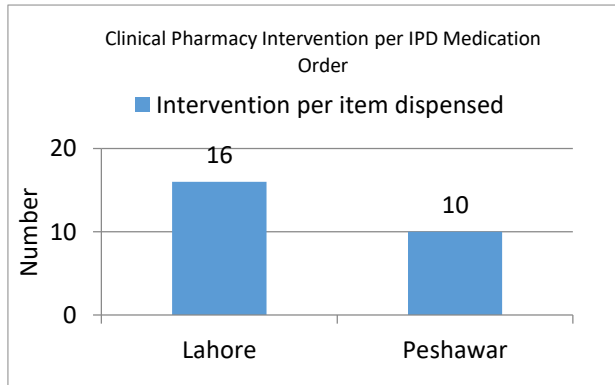
- Physician will share Prescription (restricted/ non-formulary form) with pharmacy.
- Pharmacy will share details of UNMOL program with patient / attendant and ask to submit documents required to proceed further.
- Company will evaluate each case and share the offering / support of free cycles/ vials etc.
- Estimated time of medication availability (3-4 weeks approx.)

Joint Commission International Accreditation (JCIA) – SKMCH Peshawar Chapter

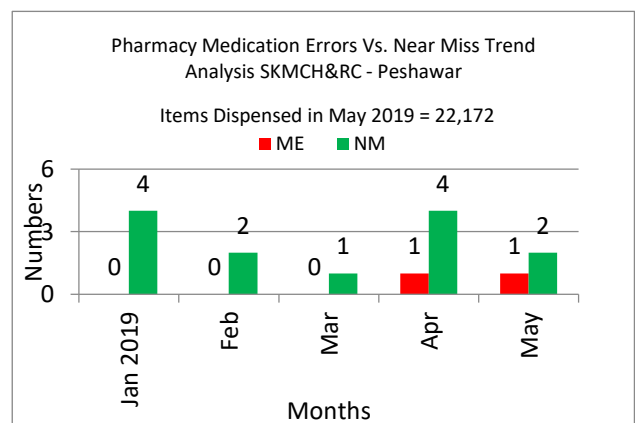
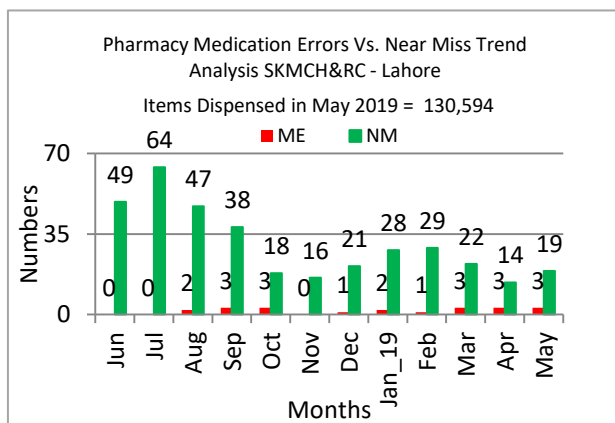
Document, what you do, and do, what you document. Yes! We are ready for the big one. In context of measures taken to prepare for Joint Commission International Accreditation (JCIA) at SKMCH&RC Peshawar, we have improved our attention to detail and through rigorous rounds of tracers, managers and supervisors have developed the eye that sees room for improvement and the vision that sets sky as the limit. Education, education and education. Daily evening meetings, tutorials and discussions, have improved the concept of patient safety and hence staff has become more comprehensive in their work to ensure it. Departments have come closer and communication gaps have been minimized. Not that all of this has been a walk in the garden; discussions, disagreements, conflicts that seemed un-resolving at times and emotional outbursts - we have had our fair share of twist in the tail.

At SKMCH&RC, we learn to empathize with our patients irrespective of their ability to pay, deciding preference only based on medical need – equity. With the standards of quality our policies define for patient care and thankless efforts put in from top to bottom of our institutional hierarchy, we are very hopeful to achieve this international certification. As we see the official countdown to the mega day, we stand strong, we stand confident, we stand together and irrespective of the outcome, our strife for excellence will keep moving ahead. Fingers crossed for the milestone!

Clinical Pharmacy Interventions Update



Medication Errors and Near Miss Update



Adverse Drug Reactions (ADR's) Update

