



Shaukat Khanum Memorial Cancer Hospital and Research Center

Pharmacy Newsletter

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The Team

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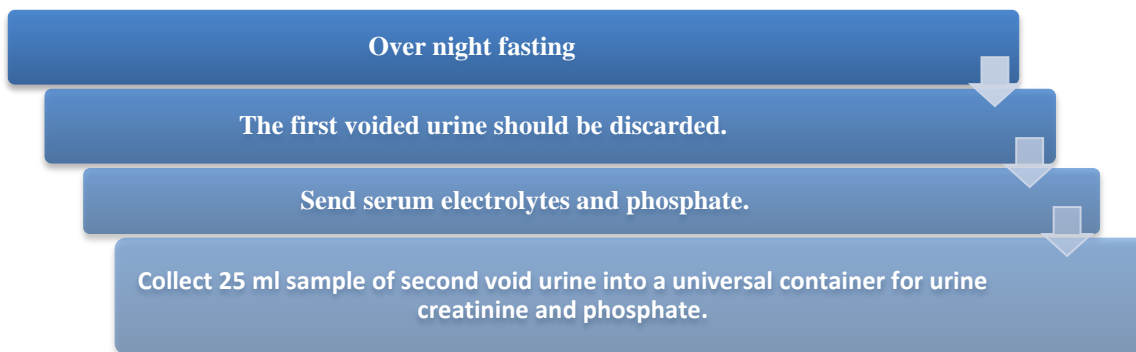
P& TC UPDATES:

New formulary additions

- 1. Daclatasvir 80mg Tablet:** Regular formulary drug.
- 2. Absolute alcohol Injection:** Regular formulary drug.
- 3. Sustagen school 6 plus:** Regular formulary drug.
- 4. Avibactam + Ceftazidime inj.** Restricted by service (ID consultant only)
 - Carbapenem resistant gram negative (Pseudomonas and Enterobacteracea) culture/s.
 - Colistin use is unfavourable due to :
 - Compromised renal function (CrCl < 60 ml/min)
 - Nephrotoxicity –serum creatinine increased $\geq 50\%$ from the baseline.
 - Nephrotoxicity – creatinine clearance decreased $\geq 25\%$
- 5. Temozolamide capsules.** Only for grade-III oligodendroglioma, 1p/19 q deletion positive

IFOSFAMIDE DOSING BASED ON FRACTIONAL EXCRETION OF PHOSPHORUS:

Procedure:



Calculations:

1. Calculate the ratio of phosphate clearance to Creatinine clearance (C_p/C_{Cr})

$$C_p/C_{Cr} = \frac{\text{Serum Creatinine} \times \text{Urine Phosphate}}{\text{Urine Creatinine} \times \text{Serum Phosphate}}$$

(This ratio is normally less than 0.15 and is often elevated in primary hyperparathyroidism).

2. Subtract this fraction from 1.0 to give the fractional tubular reabsorption of phosphate (TRP).

$$TRP = 1 - \frac{\text{Serum Creatinine} \times \text{Urine Phosphate}}{\text{Urine Creatinine} \times \text{Serum Phosphate}}$$

3. If TRP is ≤ 0.86 then phosphate reabsorption is maximal and there is a linear relationship between plasma phosphate concentration and excretion and Tmp/GFR which is calculated by:

$$TmP/GFR = TRP \times \text{serum phosphate}$$

4. If TRP is > 0.86 relationship between plasma phosphate concentration and excretion is curvilinear and Tmp/GFR is defined as follows:

$$TmP/GFR = a \times \text{serum phosphate}$$

$$\text{Where ; } a = \frac{0.3 \times TRP}{1 - (0.8 \times TRP)}$$

Adjustment of Ifosfamide:

Classify toxicity as grade 0/1, 2 or 3/4 and adjust Ifosfamide dose as indicated if either GFR or (TmP/GFR) or HCO₃ is reduced.

Toxicity grade	GFR (ml/min/1.73m ²)	Tp/Crea (TmP/GFR) (mmol/l)	HCO ₃ (mmol/l)	Action
Grade 0/1	≥ 60	≥ 1.00	≥ 17	Continue Ifosfamide dose 100%
Grade 2	40-59	0.8-0.99	14-16.9	Reduce Ifosfamide dose by 30%
Grade 3/4	≤ 40	≤ 0.80	≤ 14	Use cyclophosphamide instead

Ref: *Journal of Nature Microbiology.*

NEWS AND UPDATES:

TAMOXIFEN AND SSRI_s ANTIDEPRESSANT

Paroxetine and fluoxetine are no good drugs to use if your patient is on tamoxifen. Antidepressants are often co-prescribed with tamoxifen for extended periods, in part because depression often coexists with breast cancer and in part to offset vasomotor symptoms induced by tamoxifen. As a prodrug, tamoxifen requires conversion to active metabolites, the most important of which is endoxifen. This process is influenced by cytochrome-P450 isoenzyme 2D6 (CYP2D6). Some selective serotonin reuptake inhibitors (SSRIs) but not others inhibit CYP2D6, conceivably attenuating or even abolishing the benefits of tamoxifen. The consequences are delayed by years and manifest simply as treatment failure, undermining causal attribution at the patient level. SSRIs that inhibit CYP2D6 are paroxetine and fluoxetine whereas SSRIs that do not inhibit CYP2D6 are citalopram, escitalopram, fluvoxamine and sertraline and hence can be options for patients on concurrent therapy.

Ref: <http://www.bmj.com/content/354/bmj.i5309>

LONG TERM USE OF ACETAMINOPHEN AND NSAID_s LINKED TO HEARING LOSS IN ADULTS

A study recently circulated in American Journal of Epidemiology states that regular, long term utilization of NSAIDs (excluding Aspirin) and acetaminophen might have been connected with somewhat higher risk of hearing loss for ladies. Results were calculated from the data acquired from Nurses' Health Study which is one of the largest long-term epidemiological studies on risk factors for chronic diseases in women. It is essential to remember the general wellbeing part of this on a public level. More data and further reviews are required before patients could be directed to keep away from these items totally. Such studies fortify the need to guarantee patients are instructed about appropriate signs for use and additional potential unfriendly impacts, for example, hearing misfortune.

Ref: 2017 American Pharmacists Association. Published by Elsevier Inc.

STATINS-GOOD OR BAD?

Statins are the most commonly used drugs to lower cholesterol levels in human body and are also among the most widely prescribed drugs. They are mostly prescribed to patients having high LDL and triglyceride levels with an aim to prevent any cardiac or related events, but there are some serious risks related to statins use including muscle pain, liver toxicity, memory loss and development of type 2 diabetes. Clinical trials have shown a 27% increased risk of diabetes type 2 with use of statins (especially high dose statins). Use of statins in patients with any cardiac issues or related events is justified and is beneficial for patients but their prophylactic use in patients with high cholesterol level may not be justified as adverse effects outweigh the expected benefits. Dietary management may be a better option in such patients.

Ref: <http://dev.center4research.org/statins-lower-cholesterol-will-reduce-risk-heart-attacks-strokes/>

U.S FDA APPROVED RIBOCICLIB MARCH 13, 2017

FDA approved ribociclib (*KISQALI, Novartis Pharmaceuticals Corp.*), a cyclin-dependent kinase 4/6 inhibitor, in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. Ribociclib 600mg or placebo was administered orally once daily for 21 consecutive days, followed by 7 days off, with Letrozole 2.5mg administered OD for 28 days. Common ADRs in 20% patients were neutropenia, fatigue, diarrhea, nausea, leukopenia, alopecia, vomiting constipation, headache, backache and prolonged QT interval in a concentration dependent manner. Recommended starting dose is 600mg PO OD with or without food for 21 consecutive days followed by 7 days off treatment. Novartis has priced 28-day supply of the 600-mg dose at \$10,950. The same duration supply of the 400-mg dose will cost \$8,760, and the 200-mg dose will be available at \$4,380. The drug is un-registered in Pakistan as yet.

Ref: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm546438.htm>

VACCINE FOR DIABETES TYPE 1 ENTERS PHASE 2 CLINICAL TRIAL

FDA has approved Vaccine for diabetes type 1 to enter 2nd phase of clinical trials. Researchers have been working on BCG and have found it useful in killing abnormal T-cells that attack pancreatic beta-cells. During trials on mice, vaccine, along with killing abnormal T-cells, has also proved to help in regeneration of beta-cells and improvement in insulin release. The planned phase II trials will include 150 patients aged 18 to 60 years. Patients must have low but detectable levels of insulin secretion to meet inclusion criteria. It's going to be a five year trial in which 1st two doses (BCG or placebo) will be administered four weeks apart followed by annual vaccination for next four years. Success in phase 2 trials will pave way for more extensive phase 3 trials. Success in future studies will be a great breakthrough for patients in initial phases of type 1 diabetes.

Ref: <https://diabetesresearchconnection.org/fda-approves-the-second-phase-of-dr-denise-faustmans-clinical-testing-of-a-type-1-diabetes-vaccine/>

FDA APPROVES NEW DRUG TO TREAT MULTIPLE SCLEROSIS

On March 28, 2017 the U.S. FDA approved ocrelizumab (Ocrevus) to treat adult patients with relapsing forms of multiple sclerosis (MS) and primary progressive multiple sclerosis (PPMS). This is the first drug approved by the FDA for PPMS. Ocrelizumab is an intravenous infusion with efficacy for the treatment of relapsing forms of MS in two clinical trials (n=1,656) treated for 96 weeks. Both studies compared ocrelizumab to another MS drug, Rebif (interferon beta-1a). Patients receiving ocrelizumab had reduced relapse rates and reduced worsening of disability compared to Rebif. In a study of PPMS (n=732) treated for at least 120 weeks, those receiving ocrelizumab showed a longer time to the worsening of disability compared to placebo. Ocrelizumab should not be used in patients with active hepatitis B infection or a history of life-threatening infusion-related reactions to ocrelizumab. Ocrelizumab must be dispensed with a patient medication guide that describes important information about the drug's uses and risks. Ocrelizumab treatment for patients with active infections should be delayed. Vaccination with live or live attenuated vaccines is not recommended in patients receiving the drug. Ocrelizumab can cause infusion-related reactions, may increase the risk for malignancies, particularly breast cancer, can cause upper respiratory tract infections, skin infection, and lower respiratory tract infection. The drug is a recent addition to the international medicine market and is unregistered in Pakistan.

Ref: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm549325.htm>

FDA APPROVES NEW ECZEMA DRUG

On March 28, 2017 U.S. FDA approved dupilumab (Dupixent) injection an interleukin-4 (IL-4) receptor alpha subunit (IL-4R) inhibitor to treat adults with moderate-to-severe eczema (atopic dermatitis). Dupilumab is intended for patients whose eczema is not controlled adequately by topical therapies, or those for whom topical therapies are not advisable. Dupilumab can be used with or without topical corticosteroids. The safety and efficacy of Dupilumab were established in three placebo-controlled clinical trials n=2,119 adult participants with moderate-to-severe atopic dermatitis not adequately controlled by topical medication(s). Overall, participants who received dupilumab achieved greater response, defined as clear or almost clear skin, and experienced a reduction in itch after 16 weeks of treatment. The most common side effects include injection site reactions; cold sores in the mouth or on the lips; and eye and eyelid inflammation, including redness, swelling and itching. The drug is a recent addition to the international medicine market and is unregistered in Pakistan.

Ref: <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm549078.htm>