A NEWSLETTER BY DEPARTMENT OF PHARMACY—SIH

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Inside this issue

EID MUBARAK

Olanzapine for anorexia nervosa

Sana Akhter (Inpatient Pharmacist)

Anorexia nervosa, often referred to simply as anorexia, is an eating disorder, characterized by low weight, food restriction, fear of gaining weight, and a strong desire to be thin. Standard treatment for anorexia nervosa consists of nutritional rehabilitation and psychotherapy. In addition, accumulating evidence from observational studies suggests that augmentation with pharmacotherapy, particularly antipsychotic olanzapine modestly enhances weight gain. So add-on treatment with Olanzapine 2.5 mg to 10 mg per day is now suggested.

Olanzapine has been more widely studied for treatment of anorexia nervosa than any other antipsychotic, and multiple randomized trials suggest that olanzapine may help restore weight. In addition, the drug is generally well tolerated, with no indication of the adverse metabolic effects frequently observed when olanzapine is prescribed for other disorders.

Source: Uptodate online (April 2019)

Ticagrelor an Antiplatelet with possible use as an Antibiotic:

Fatima Ashfaq Butt (Clinical Pharmacist, ID/Transplant)

Ticagrelor in conventional Antiplatelet dosages affect Antibiotic-Resistant Gram-Positive Bacteria without selecting for resistant mutants. Ticagrelor and its metabolite AR-C124910 had bactericidal activity against all gram-positive strains tested, including drug-resistant strains glycopeptide intermediate S aureus (GISA), MRSE, MRSA, and VRE. At minimal bactericidal concentration, Ticagrelor was superior to Vancomycin, with rapid killing of late-exponential-phase cultures of MRSA Bactericidal activity was similar to the bactericidal cyclic lipopeptide Daptomycin, recently introduced against resistant strains of S aureus. A subminimal bactericidal concentration of Ticagrelor (10 µg/mL) combined with Vancomycin (4 µg/mL) killed approximately 50% of the initial MRSA inoculum, depicting synergistic activity. Ticagrelor also increased the bactericidal activity of Rifampicin, Ciprofloxacin, and Vancomycin in a disk diffusion assay. It displayed bactericidal activity against MRSE and VRE, with superiority over Vancomycin for killing MRSE. At 24 hours, its ability to kill MRSE and VRE was similar to Daptomycin.

Source: JAMA Cardiol, May 8, 2019

The ICU-Induced Delirium and use of Dexmedetomidine

Sundus Maria (Clinical Pharmacist, ICU)

The ICU-induced delirium-a sudden and intense confusional state that includes hallucinations, delusions, and paranoia is experienced by almost 80% of the critically ill patients. The terrifying and long lasting delirium is a massive public health problem that is often overlooked. Patients in ICU go through a lot, from invasive ventilation and catheter changes to fever spikes and dialysis. The lack of sleep due to agitation and anxiety as well as the beeps and alarms coming off from different machines lead to the "alarm fatigue". These effects even haunt the patients long after their discharge often leading to PTSD.

Various *non pharmacological strategies* such as mobilization and light therapy help to some extent. Almost all of the patients in the ICU receive continuous infusions of *benzodiazepines and opioid analgesics* to combat anxiety, delirium and pain. Multiple studies have shown that although good pain management reduces the chances of delirium, benzodiazepines and narcotics actually worsen cognition and exacerbate the problem, causing a paradoxical increase in agitation as the sedative effects wear off. Traditional heavy sedation should be avoided and used only when necessary.

Newer agent such as *Dexmedetomidine* is preferred to benzodiazepines due to lower incidence of delirium; it has sedative, amnestic and mild analgesic effects. It produces a unique sedative state in patients similar to normal sleep as arousal is maintained, despite deep levels of sedation. Patient can be aroused without discontinuing the infusion and when awake, patients are able to follow commands. When arousal is no longer required , patient returns to prior state of sedation, This makes Dexmedetomidine an appealing sedative for weaning patients from ventilation.

Reference: https://annalsofintensivecare.springeropen.com/articles/10.1186/s13613-018-0437-z

The Ultimate drug class to lower LDL the PCSK9 Inhibitors

Bakhtawar Raza Chohan (Take Home/Discharge Pharmacist)

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protein that's made in the liver. Research has shown that people with high levels of PCSK9 tend to have high cholesterol throughout their lives and develop heart disease early. On the other hand, people with low levels of PCSK9 tend to have low cholesterol and a lower risk of heart disease. These are the monoclonal antibodies. Three of PCSK9 Inhibitors are discovered until yet are Alirocumab , Evolocumab ,and Bococizumab In clinical studies, they have lowered cholesterol levels by more than half. Early research shows they could prevent strokes and heart attacks too. They can also be safely used alongside other cholesterol lowering treatments such as statins.

According to new **2018 American College of Cardiology/American Heart Association cholesterol guidelines** "For the very high-risk patient with ASCVD and LDL-C ≥70 mg/dL despite maximal statin therapy, Ezetimibe is the preferred initial agent (Class IIa; Level of Evidence B), and PCSK9 inhibitors (Class IIa; Level of Evidence A) are a reasonable option only if the patient is already prescribed statin and Ezetimibe (Class I; Level of Evidence B)."

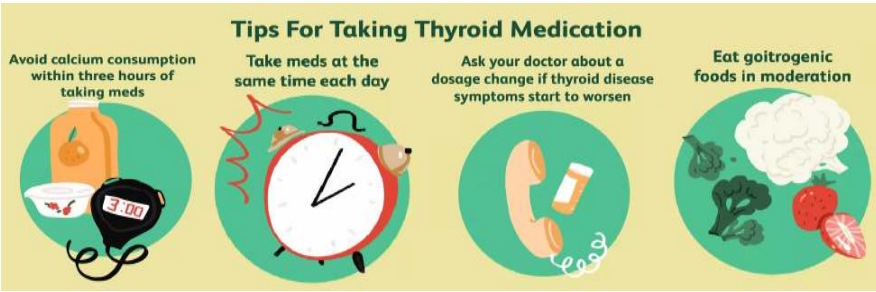
In 2015, **US-FDA** approved once every two week subcutaneous injections of Evolocumab and Alirocumab for LDL lowering as they are comparatively more efficient.

Possible side effect of the PCSK9 inhibitors are

- Flu-like symptoms such as cold, nausea, back and joint pain
- Soreness or itchiness at site of the injection
- Muscle pain

	LDL	HDL	TG
Statins	↓ 18-55 %	↑ 5-15 %	↓ 7-30 %
Bile acid sequestrants	↓ 15- 30 %	↑ 3-5 %	↑ 0-10%
Nicotinic acid	↓ 5- 25 %	↑ 15-35 %	↓ 20-50%
Fibric acids	↓ 5- 20 %	↑ 10-20 %	↓ 20-50%
Ezetimibe	↓ 13 – 20 %	↑ 3-5 %	↓ 5-11 %
Omega-3 fatty acids	↓ 8– 12 %	↑ 5- 7 %	↓ 19-44%
PCSK9 Inhibitors	↓ 40-72 %	↑ 0-10 %	↓ 0-17%

Reference: https://www.heartuk.org.uk/getting-treatment/pcsk9-inhibitors, https://www.ahajournals.org/doi/pdf/10.1161/circulationaha.118.038629



- Thyroid tests are to be repeated every 6 weeks or as advised by doctor
- Immediately inform doctor if you get pregnant in order to adjust the dose
- Do not switch brands of Thyroxin unless advised by your doctor or pharmacist .
- Must inform if you are taking antidepressants (SSRIs/ TCA), heart burn drugs (PPIs/antacids) or blood thinner

Drug Information Service

Use of Silver Sulfadiazine Cream during pregnancy:

Rehan Anjum (Clinical Pharmacist ICU)

When it comes to topical preparations we usually consider them safe to be used during pregnancy. Drugs may be safe but this may not hold true during entire pregnancy or during various trimesters. Silver sulfadiazine has FDA pregnancy category B (safe). Silver sulfadiazine topical is not expected to harm an unborn baby, however, **this medicine can cause serious medical problems in a newborn and should not be used during late pregnancy and in neonates less than 2 months** as it may cause **kernicterus** in neonates by displacing bilirubin from plasma albumin.

How to apply Silver Sulfadiazine?

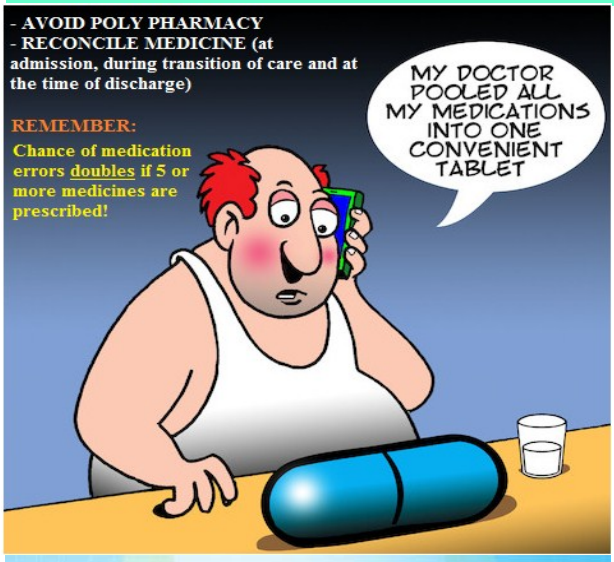
- Do not use this medicine in larger amounts or for longer than recommended.
- Wash your hands before and after applying silver sulfadiazine cream.
- The person applying silver sulfadiazine to burn wounds should wear sterile disposable gloves.
- Take care to keep the treatment area as clean as possible to prevent further infection.
- Apply enough silver sulfadiazine to cover the affected area evenly

Reference: https://reference.medscape.com/drug/silvadene-thermazene-silver-sulfadiazine-343477

CAUTION

Cautious to use Silver Sulfadiazine:

- G6PD deficiency
- Renal and hepatic impairment
- Hematological disease, leukopenia, thrombocytopenia
- Sulfonamides hypersensitivity
- Porphyria
- Breast feeding



Name new high alert medicines recently included in hospital formulary?

Ans:
- Cis-Atracurium
- Fentanyl Patches

"The art of medicine consist in amusing the patient while nature cures the disease"
Voltaire

Ruxolitinib (Jakafi ®) approved for steroid refractory acute graft versus host disease

Anum Farooq Butt (Clinical Pharmacist Oncology)

FDA approved Ruxolitinib (JAKAFI, Incyte Corporation) for steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older.

Approval was based on an open-label, single-arm, multicenter study of Ruxolitinib (n = 49) in steroid-refractory acute GVHD Grades 2 to 4 (Mount Sinai Acute GVHD International Consortium criteria) occurring after allogeneic hematopoietic stem cell transplantation. Ruxolitinib was administered at 5 mg twice daily, and the dose could be increased to 10 mg twice daily after 3 days in the absence of toxicity.

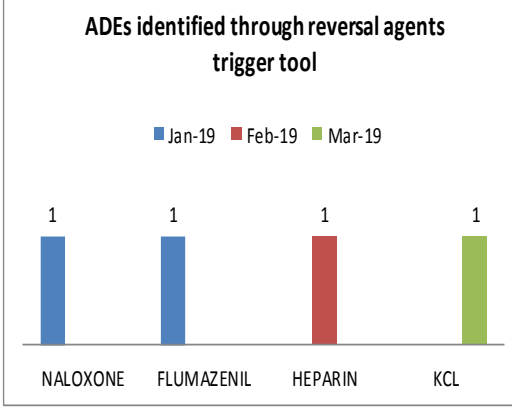
The trial's primary endpoints were day-28 overall response rate (ORR) defined as complete response, very good partial response, or partial response by Center for International Blood and Marrow Transplant Research criteria, and the response duration. Day-28 ORR was 100% for Grade 2 GVHD, 40.7% for Grade 3 GVHD, and 44.4% for Grade 4 GVHD.

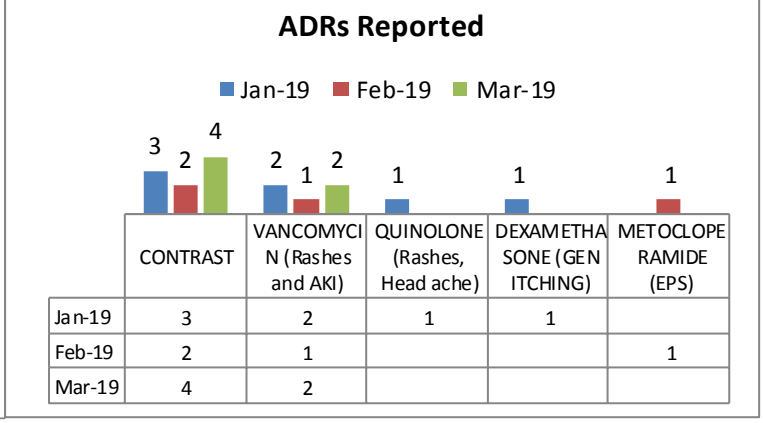
The median response duration, calculated from day-28 response to progression, new salvage therapy for acute GVHD, or death from any cause (with progression being defined as worsening by one stage in any organ without improvement in other organs in comparison to prior response assessment) was 16 days (95% CI: 9, 83), and the median time from day-28 response to either death or need for new therapy for acute GVHD (additional salvage therapy or increase in steroids) was 173 days (95% CI 66, NE).

In acute GVHD, the most common hematologic adverse reactions (incidence > 50%) are anemia, thrombocytopenia, and neutropenia. The most common nonhematologic adverse reactions (incidence > 50%) are infections and edema.

Reference:
https://www.ajmc.com/newsroom/fda-approves-ruxolitinib-for-steroidrefractory-acute-graftversushost-disease

Formulary updates			(Visit Shifa Intranet Home Page, Medication Updates for details)
Brand	**Generic**	**Class**	**Indications**
Somno tab	Melatonin	Nutraceutical	Insomnia, sleep disturbances, Jet lag
Empozin +/-M, XengluMet tab	Empagliflozin+/- Metformin	Anti diabetic	SGLT2 Inhibitor, reduces renal glucose re absorption, promoting its excretion
Ocrevus inj	Ocrelizumab	Monoclonal antibody	Multiple sclerosis
Mabthera SC	Rituximab	Monoclonal antibody	Anti Cancer, now in subcutaneous injection form
Paridopa tab	Levo/Carbidopa + Entacapone	Anti Parkinson	Addition of COMT inhibitor Entacapone increases the concentration of Levodopa peripherally and in brain
Fentanyl patch	Fentanyl	Opioid analgesic	Managing severe pain in patients chronically using opioids to control pain
Combihale neb	Ipratopium + Salbutamol	Bronchodilator	Acute Asthma, bronchospasm
Midodrine Tab	Midodrine	Alpha$_1$-agonist	Orthostatic or dialysis induced hypotension, sparing vasopressors in ICU





	CONTRAST	VANCOMYCIN (Rashes and AKI)	QUINOLONE (Rashes, Head ache)	DEXAMETHASONE (GEN ITCHING)	METOCLOPERAMIDE (EPS)
Jan-19	3	2	1	1	
Feb-19	2	1			1
Mar-19	4	2			

Remember, Reporting ADRs especially for new drugs is important for patient safety. Report ADR via **ADR hot-line 3977** or send the filled ADR form to pharmacy

PRESCRIBING:

* Ensure that correct MR# or patient is selected
* Orders are correctly transcribed from patient file to MOAR (Online)
* Check relevant labs (e.g. INR with anticoagulant, C/S with Antibiotics etc)
* Do not ignore dose/duplication or other system alerts
* Write orders completely and legibly

DISPENSING:

* Ensure that correct MR# or patient is selected
* **R3** (Read the label Thrice): Read drug label, then drug (name & strength) and then again match with label after filling
* Don't be distracted while order entry and final checking
* If filler and checker is same staff, then never check medicine in same go as it is filled

ADMINISTRATION:

* Identify patient correctly
* Never borrow medicine of other patient
* Double check High alert medicine (Rate, concentration and dose)
* Never ignore pharmacy instructions (read the label)

And, Involve and Educate Patients

Looking for Your Valuable Feedback

We want to bring to you valuable, updated and interesting information via Pharmacy Newsletter, so please spare some time to provide feedback in the form of comments or suggestions. Its your newsletter and with your help we'll make it better!

*Kindly send us your **comments/suggestions** via email at : **drug.information@shifa.com.pk***