PHARMACY NEWSLETTER

Volume 3, Issue # 1, 2022

Issued by:

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1. Methotrexate Toxicity Management

Methotrexate (MTX) is a drug used in the treatment of various malignancies, early ectopic pregnancy, or chronic inflammatory diseases such as some types of carcinoma, rheumatoid arthritis, psoriasis, etc. Accidental poisoning with MTX is not a common condition and was rarely reported in the literature. Chronic MTX poisoning is more serious than acute toxicity and accompanies higher dermatologic, hematologic, and hepatic complications necessitating more aggressive treatments including administration of higher doses of leucovorin or bone marrow stimulants such as G-CSF. Please find below the MTX toxicity management plan. This may be attributable to the underlying diseases and features (including older ages) that predispose these patients to complications.

There are 3 key strategies to treating mtx toxicity in ADULT PATIENTS

1. Enhance renal elimination by giving intravenous fluids

(Fluid requirement= 175ml/hr

Urine Output= at least 60mL/hour

2. Alkalinizing the urine

(administer sodium bicarbonate by the intravenous route (the usual dose is **100 to 150 mEq** in a liter of dextrose 5% in water) to increase the urine pH to a target of **7.0 or higher)**

3. Bypass the blocked dihydrofolate reductase enzyme to restart the DNA synthesis process by giving folinic acid **(Leucovorin)**

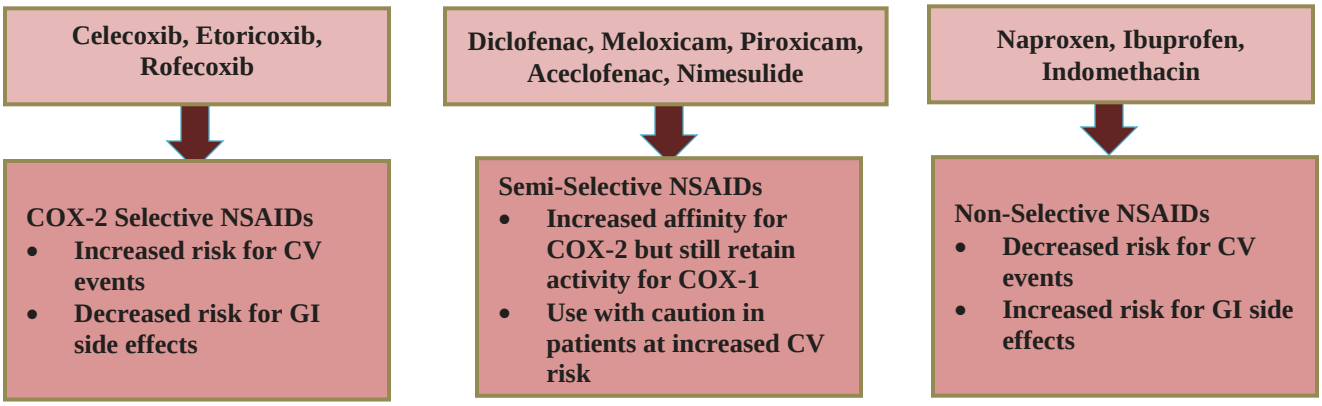
Dose =10mg/m2 (Usually 10 doses)

Do Not Take This Medicine Every Day!

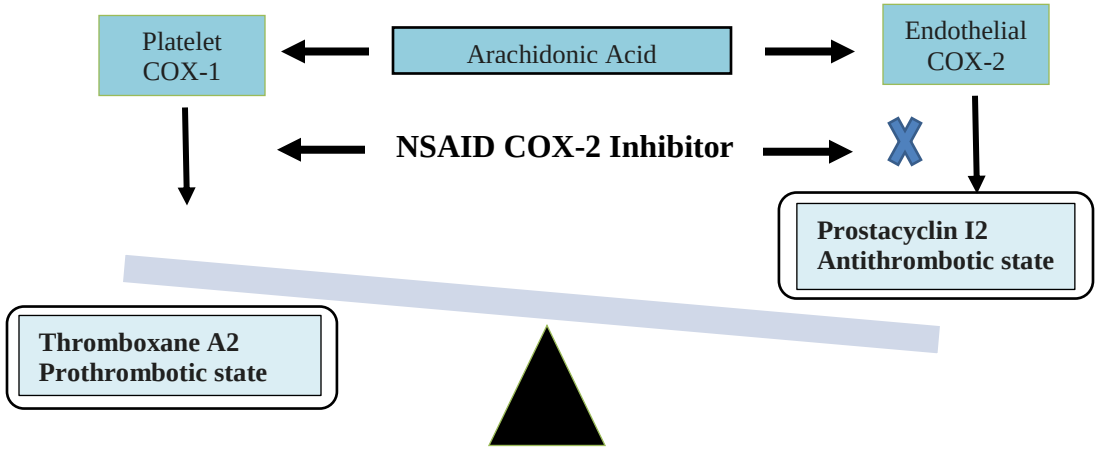
Deadly errors have happened when MTX was taken daily instead of just once a week. To treat conditions besides cancer, this medicine should be taken weekly, NOT daily. Weekly doses are taken as a single dose or divided into three smaller doses taken 12hours apart.

2. COX-2 inhibitor's induced Myocardial Infarction

- NSAIDs target both COX-1 and COX-2 but they have different selectivity for COX-1 and COX-2. COX-2 inhibitors are associated with an increased risk for myocardial infarction in patients having pre-existing cardiovascular disease.



- The Prostacyclin PG12 is produced by COX-2 activity, located in blood vessels and platelets, causes vasodilatation, and inhibits platelet aggregation. While, thromboxane (TXA2) produced by COX-1 activity, located in blood vessels and platelets, causes vasoconstriction and platelet aggregation. When there is a balanced effect of both PG12 & TXA_2, normal vascular homeostasis is maintained. However, when this balance is disturbed by COX-2 inhibition, vasoconstriction and platelet aggregation occur more. This ultimately leads to myocardial infarction.



3. Ceftriaxone- Restrictions In Neonates

Ceftriaxone competes with bilirubin for binding to human serum albumin. Therapeutic levels of ceftriaxone decrease the reserve albumin serum concentration in newborns by 39%*. This may may increase the risk of bilirubin encephalopathy in jaundiced premature newborns.

* Fink, S., Karp, W., & Robertson, A. (1987). Ceftriaxone effect on bilirubin-albumin binding. *Pediatrics*, *80*(6), 873-875.

Ceftriaxone should be avoided in infants younger than 28 days old if they are receiving or expected to receive Intravenous calcium-containing products because of resulting crystalline deposits in the lungs and kidneys leading to neonatal death.

Not for use in pre mature infants till 41 weeks of total age.
Consider restriction below 1 month of age

References: AAP (American Academy of Pediatrics), Nelson

4. Choice Of Infliximab As A Subcutaneous Dosage Form*

Infliximab is a monoclonal antibody (mAb) directed against tumor necrosis factor-alpha (TNF-α). TNF-α is a cytokine with multiple actions including mediation of inflammatory responses, modulation of the immune system, and the induction of apoptosis. Infliximab binds with high affinity to soluble and transmembrane forms of TNF-α and inhibits the functional activity of TNF-α.

*Extension of indication variation assessment report EMA/376884/2020

Dosing schedule of infliximab in differene indications

- **Rheumatoid arthritis: (in combination with methotrexate therapy:(SUBQ):** 120mg at 0, 1, 2, 3, and 4 weeks, then every 2 weeks thereafter
- **Ankylosing spondylitis:(SUBQ):** Maintenance therapy (begin 4 weeks following IV induction therapy of 2 IV Doses given 2 weeks apart): 120 mg once every 2 weeks
- **Plaque psoriasis: (SUBQ):** Maintenance therapy (begin 4 weeks following IV induction therapy of 2 IV Doses given 2 weeks apart): 120 mg once every 2 weeks

5. AWaRe Classification Of Antibiotics

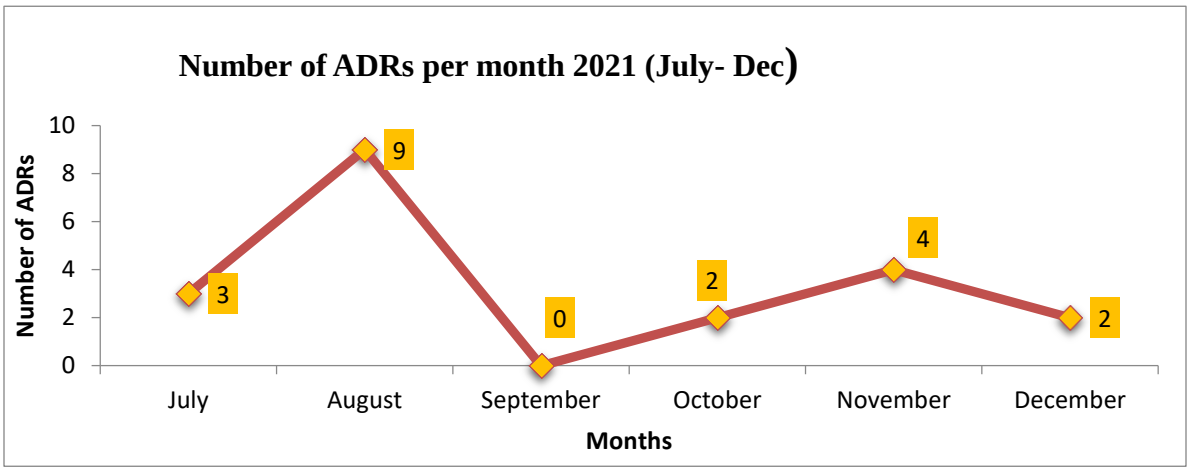
AWaRe classifies antibiotics into three stewardship groups: Access, Watch and Reserve, to emphasize the importance of their optimal uses and potential for antimicrobial resistance. The **AWaRe** Classification of antibiotics was developed in **2017** by the **WHO** Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts at local, national, and global levels. The **2021 update** of the AWaRe classification includes an additional 78 antibiotics not previously classified, bringing the total to 257 as follows.(**You can get the complete list of AwaRe classifications from the Pharmacy.**

WHO "AWaRe" Classification Of Antibiotics

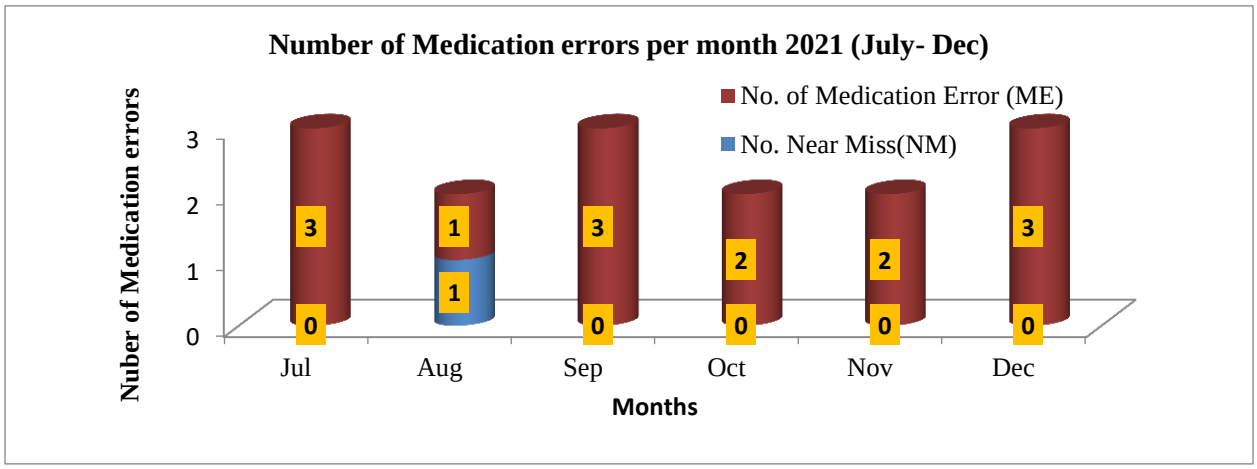
Access → **WAtch** → **REserve**

- **87 First-line antibiotics**
  Low resistance potential
  e.g Amoxicillin, Nitrofurantoin etc
- **141 Critically important antibiotics**
  High resistance Potential
  e.g Quinolones, Macrolides etc
- **29 Antibiotics for MDR organisms.**
  "Last Resort" antibiotics
  e.g. Polymixin, Tigecyline etc

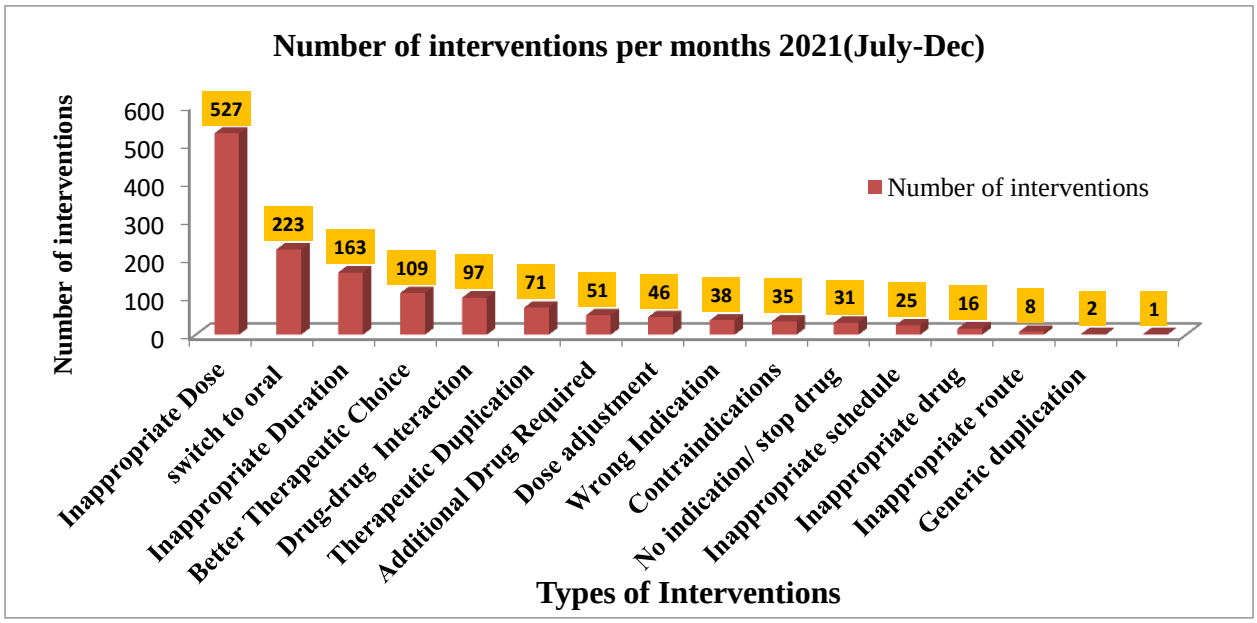
6. Adverse Drug Reaction (ADRs) Updates (July-Dec 2021)



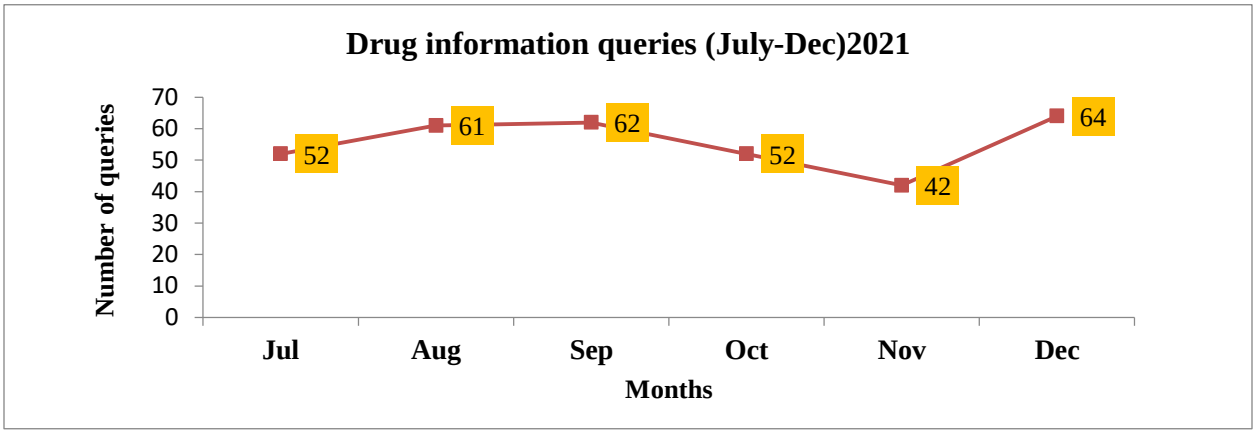
7. Near Miss and Medication Error Updates 2021 (July-Dec)



8. Clinical Pharmacy Interventions Updates (July-Dec 2021)



9. Drug Information Queries Responded (July– Dec 2021)



MED SAFETY WEEK CELEBRATION (1-7 November 2021)