Tabba Heart Institute

VOLUME IV

2024 PHARMA CONNECT

TABLE OF CONTENTS

1 **Role of Spironolactone in management of Ascites in cirrhosis**
Submitted by Areeba Nayab | Clinical Pharmacist

2 **Protecting Heart Rhythms: Pharmacists role in QTC-Safe Medications**
Submitted by Nehal Nadir | Clinical Pharmacist

3 **IDSA Update 2024: Antibiotic Treatment Regimen for Bloodstream Infections can safely be cut by half**

4 **Enteral Feeding in critically ill Adult**
Submitted by Palwashay Iqbal | Sterile Area Pharmacist

5 **Actual Case Scenario**
Phenytoin-Induced Thrombocytopenia in a Female Patient
WHO Casuality Assessment on Phenytoin induced Thrombocytopenia

6 **Formulary Inclusion**

7 **Clinical Pharmacy pearls**
Submitted by Nehal Nadir | Clinical Pharmacist

8 **FDA's black box warning for Febuxostat and its Cardiovascular risks**
Submitted by Umme Hani | Outpatient Pharmacist

9 **"BRIDGE TO CARE"**
A pharmacist significant role in suggesting alternative brands during drug shortages
Submitted by Rabiya Mazhar | Inpatient Pharmacy

10 **IV Fluids and Opportunity to Improve Labels**
Submitted by Palwashay Iqbal | Sterile Area Pharmacist

11 **FDA Update: Approval of Respiratory syncytial virus (RSV) vaccine**
Submitted by Syed Sarwat Jabeen | Outpatient Pharmacist

12 **POCT (Point of care Testing) INR devices Status**

13 **Impact of Accurate Weight Assessment in Critical Care**
Submitted by Rabia Sami | Trainee Pharmacist batch 2024

Role of Spironolactone in management of Ascites in Cirrhosis

Submitted by Areeba Nayab | Clinical Pharmacist

Ascites is one of the major complications of liver cirrhosis & is associated with a poor prognosis. It is important to distinguish noncirrhotic from cirrhotic causes of ascites to guide therapy in patients with noncirrhotic ascites. Mild to moderate ascites is treated by salt restriction and diuretic therapy. The diuretic of choice is spironolactone. Tense ascites is treated by paracentesis, followed by albumin infusion and diuretic therapy.

Mechanism of Spironolactone in Ascites

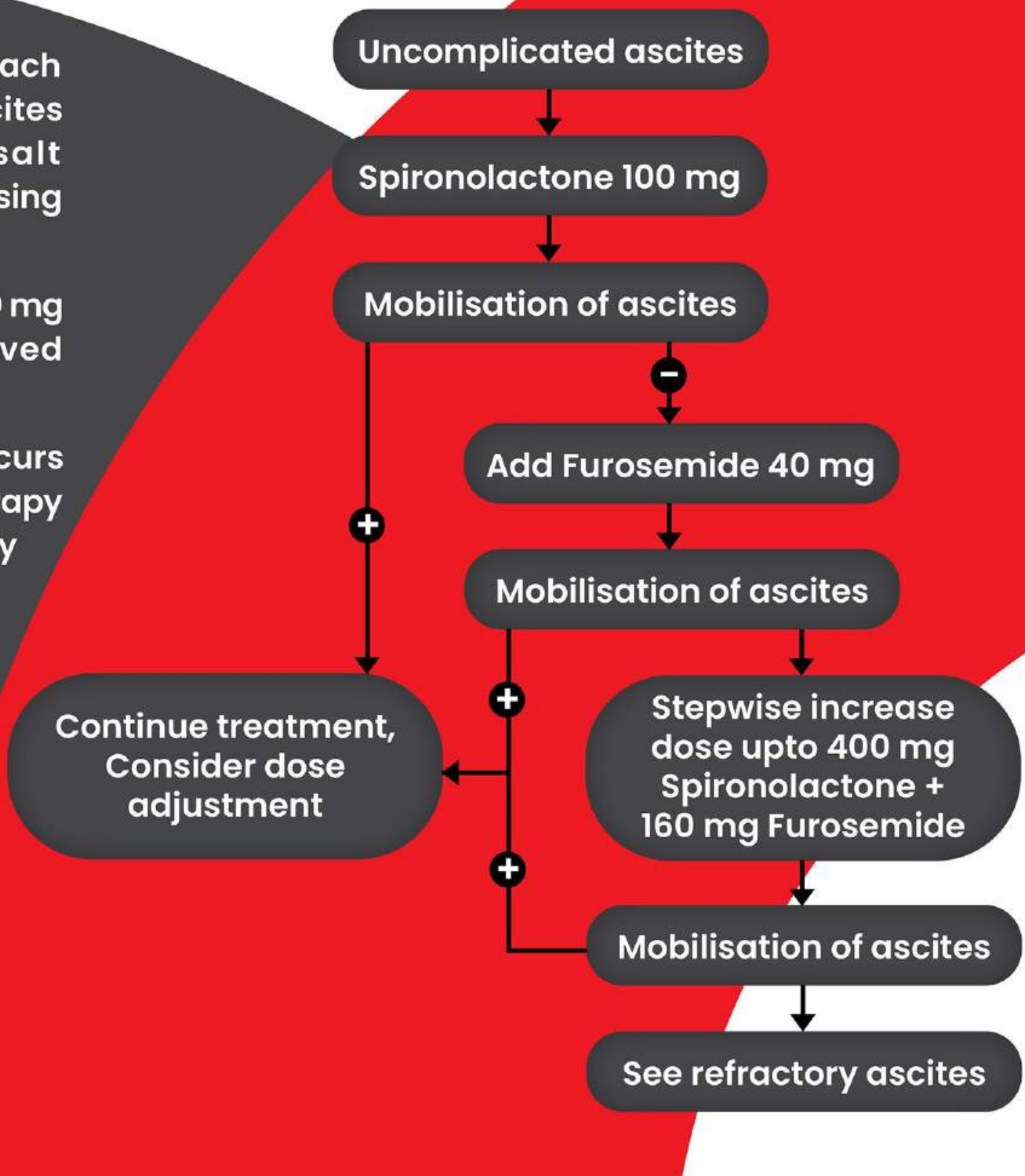
The activation of the renin-aldosterone-angiotensin-system in patients with liver cirrhosis causes hyperaldosteronism and increased reabsorption of sodium along the distal tubule. Therefore, aldosterone antagonists like spironolactone are considered the diuretics of choice.

Patients with mild to moderate ascites are treated with a monotherapy of spironolactone. The starting dose is 100-200 mg/d. A monotherapy with a loop diuretic like furosemide is less effective compared to spironolactone and is not recommended. If the response to 200 mg spironolactone within the first two weeks is not sufficient, furosemide with an initial dose of 20-40 mg/d is added. If necessary, the spironolactone dose is increased stepwise up to 400 mg/d and the furosemide dose is increased up to 160 mg/d.

Generally, a "stepped care" approach is used in the management of ascites starting with modest dietary salt restriction, together with an increasing dose of spironolactone.

Furosemide is only added when 400 mg of spironolactone alone has proved ineffective.

Following paracentesis, ascites recurs in the majority (93%) if diuretic therapy is not reinstituted but recurs in only 18% of patients treated with spironolactone.



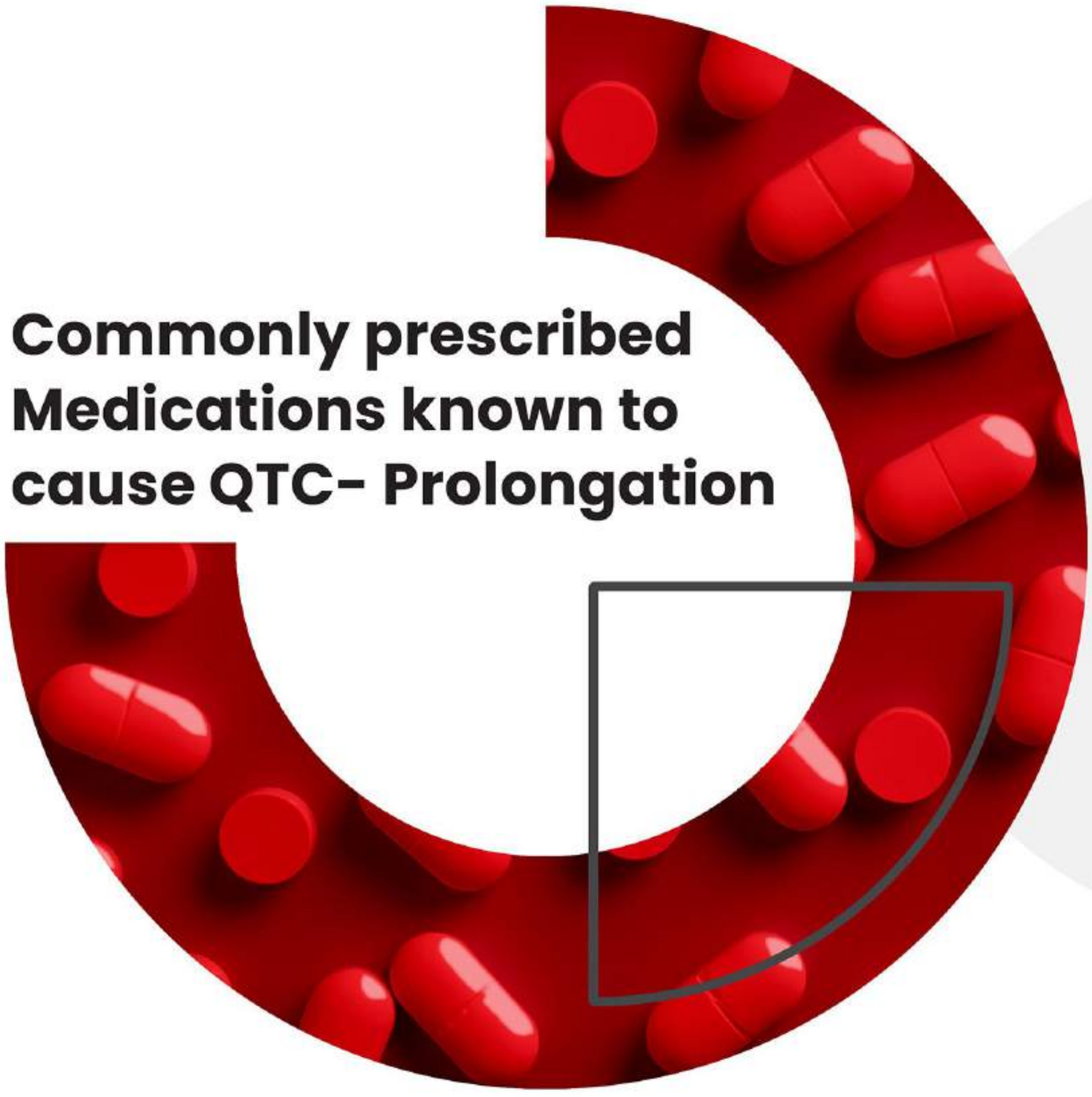
References

- Campra JL, Reynolds TB. Effectiveness of high-dose spironolactone therapy in patients with chronic liver disease and relatively refractory ascites. Am JDig Dis. 1978 Nov;23(11): 1025-30. doi: 10.1007/BF01263103. PMID: 31086.
- https://www.wjgnet.com/1007-9327/full/v17/i10/1237

Protecting Heart Rhythms: Pharmacists role in QTC-Safe medications

Submitted by Nehal Nadir | Clinical Pharmacist

Pharmacists ensure cardiac safety by managing QTC-prolonging medications, monitoring interactions, also ECG checks Collaborating with healthcare teams, counseling patients on adherence. Their expertise prevents arrhythmias and supports effective treatment.

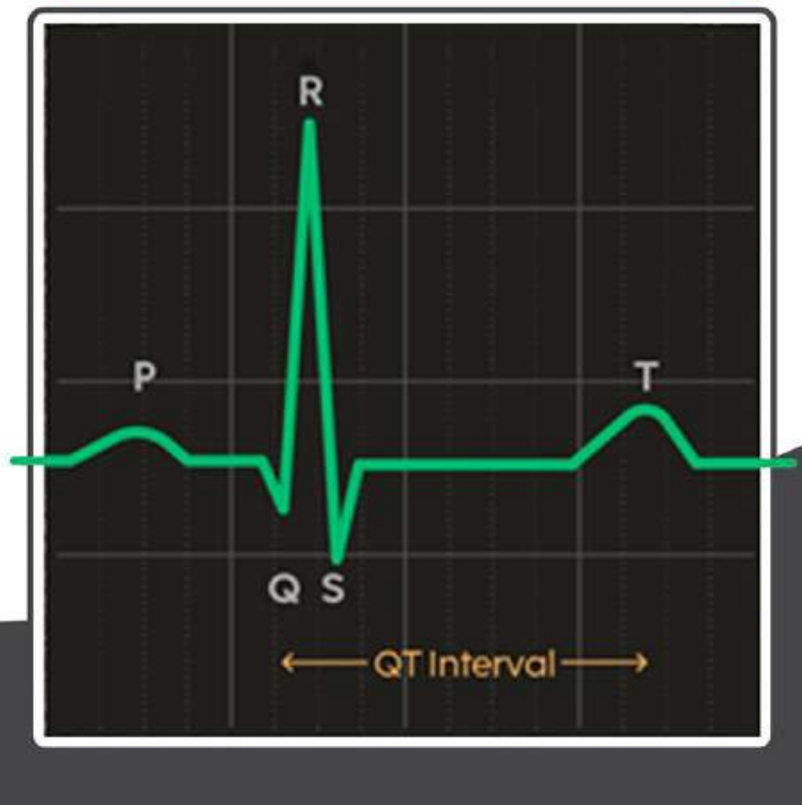


Commonly prescribed Medications known to cause QTC- Prolongation

- **Anti-anginal drugs**
  e.g. Ranolazine
- **Anti-psychotic**
  e.g. Haloperidol
- **Fluoroquinolones**
  e.g. Moxifloxacin
- **Anti-arrhythmic drugs**
  e.g. Amiodarone
- **HT3 antagonist**
  e.g. Ondansetron
- **Macrolides**
  e.g. Azithromycin
- **Azole-antifungals**
  e.g. Fluconazole
- **H2-receptor antagonists**
  e.g. Famotidine
- **Muscle Relaxers**
  e.g. Tizanidine

Normal QT

Long QT Syndrome



References
- https://pmc.ncbi.nlm.nih.gov/articles/PMC8698549/

IDSA Update 2024:

Antibiotic Treatment Regimen for Bloodstream Infections can safely be cut by half

7 days treatment is effective

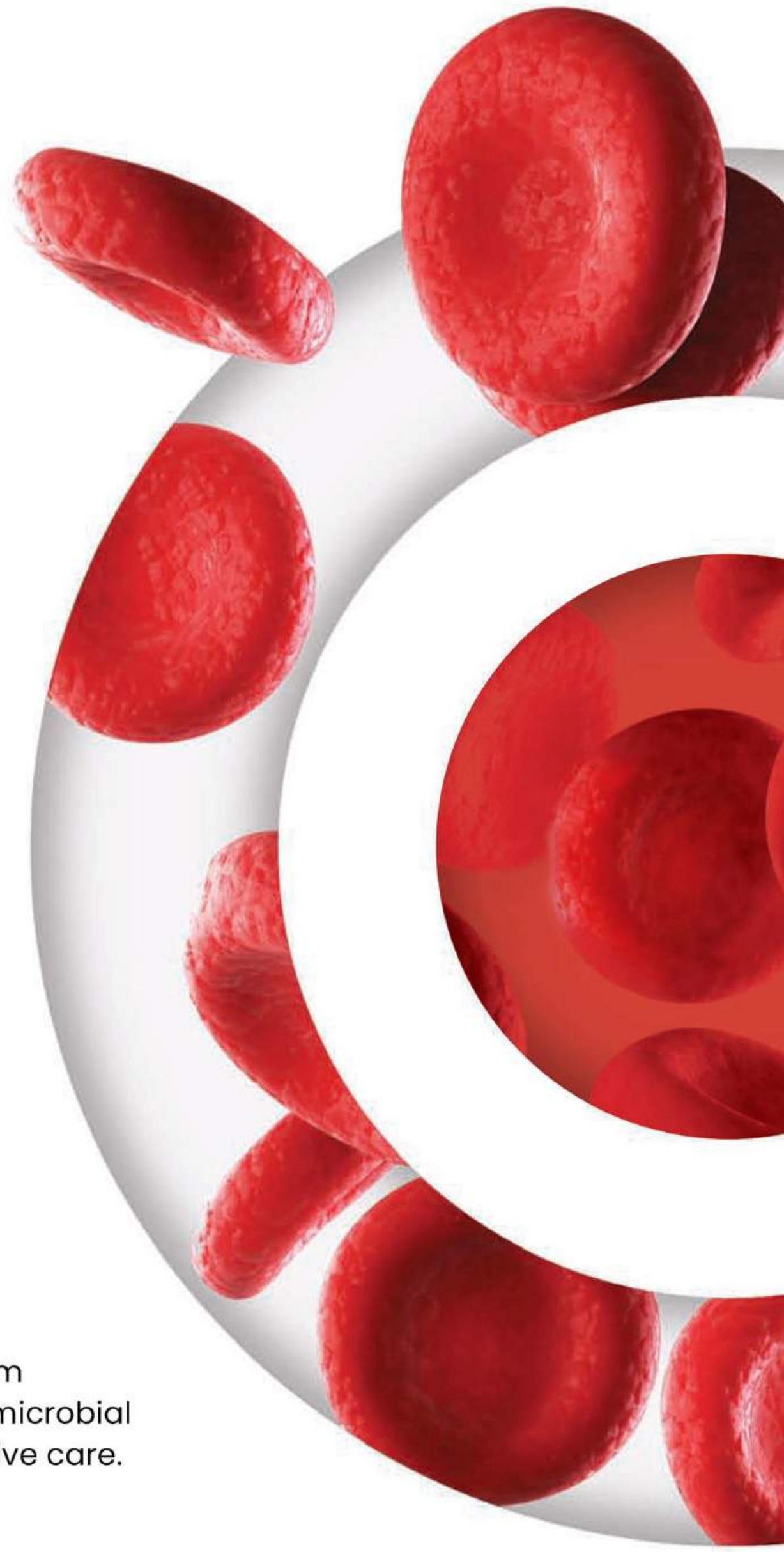
Treating hospitalized patients with bloodstream infections with antibiotics for seven days is just as effective as a 14-day treatment regimen.

90 days mortality rate

Both treatment durations demonstrated similar 90-days mortality rates during the study period.

Antimicrobial resistance & Cost effective

Shorter antibiotic treatment courses for bloodstream infections may help limit the growing threat of antimicrobial resistance in addition to reducing the cost of effective care.



A seven-day course of antibiotics for hospitalized patients with bloodstream infections is just as effective as a 14-day course, according to new findings presented at IDWeek 2024.

Enteral Feeding in Critically ill adults

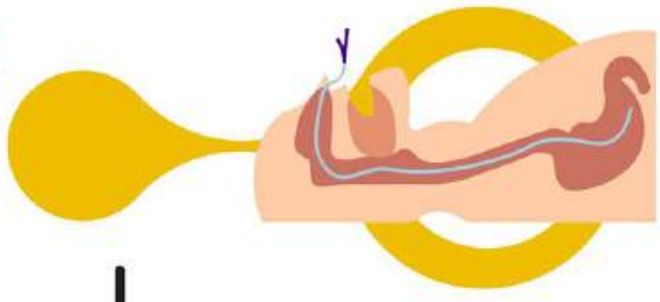
Submitted by Palwashay Iqdbal | Sterile Area Pharmacist

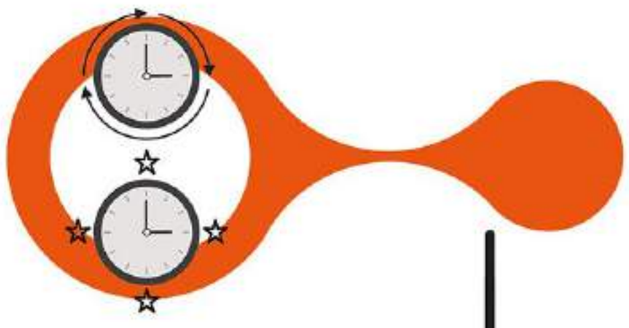
09 Recommendations

about Enteral feeding in Critically ill adults

RECOMMENDATION 1
In the absence of contraindications, enternal nutrition should be initiated upon admission to the ICU.

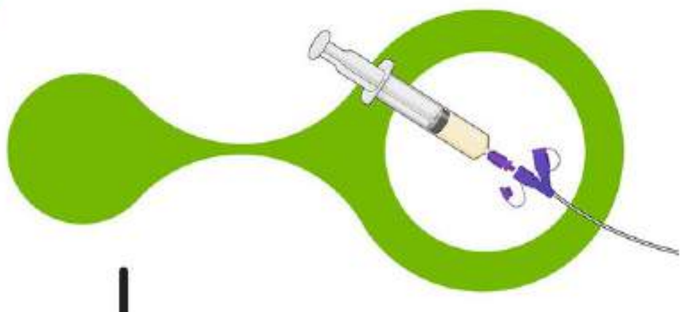
RECOMMENDATION 2
Early enteral nutrition via the gastric route is more beneficial than delaying feeding while awaiting small bowel access.

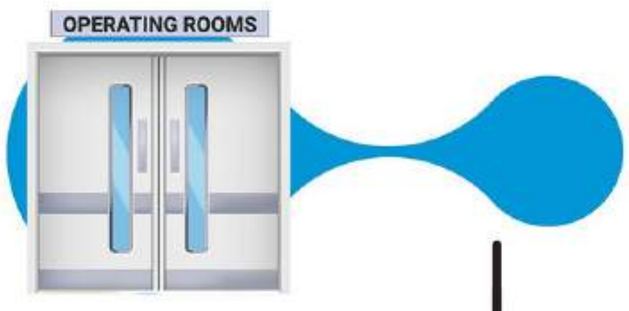




RECOMMENDATION 3
Both intermittent enteral nutrition and continuous enteral nutrition are appropriate in most ICU patients.

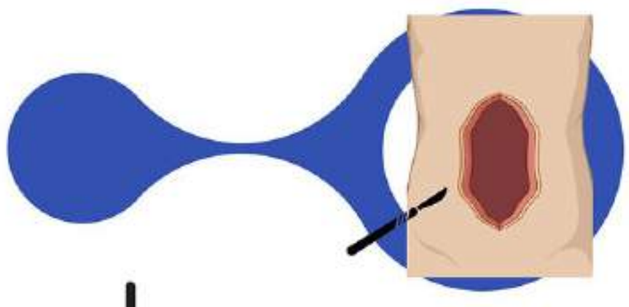
RECOMMENDATION 4
Gastric residual volumes should no longer be measured. Physical examination, monitoring for nausea/ vomiting, evaluating for regular bowel movements and reviewing abdominal radiologic films should be used to monitor feeding tolerance.

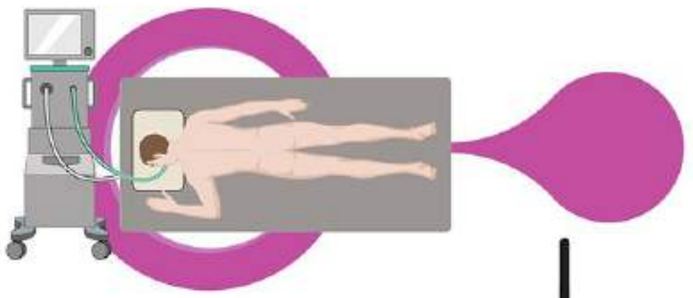




RECOMMENDATION 5
In patients with secure airways, enteral nutrition only needs to be held for abdominal surgeries, thoracic surgeries or surgeries in the prone position.

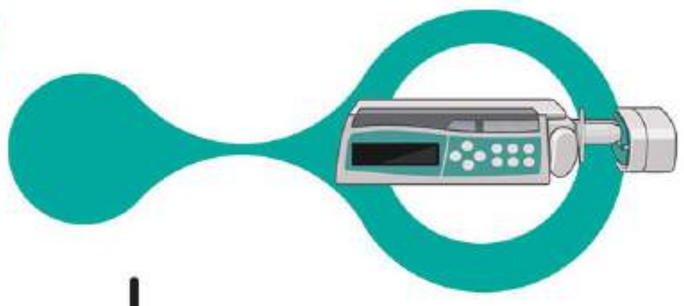
RECOMMENDATION 6
Enteral nutrition shoulld be resumed within 24 hours of abdominal surgery unless there is evidence of continued obstruction of the GI tract, bowel discontinuity, bowel ischemia or ongoing peritonitis. Patients with open abdomens can be safely fed in the absence of bowel injury.

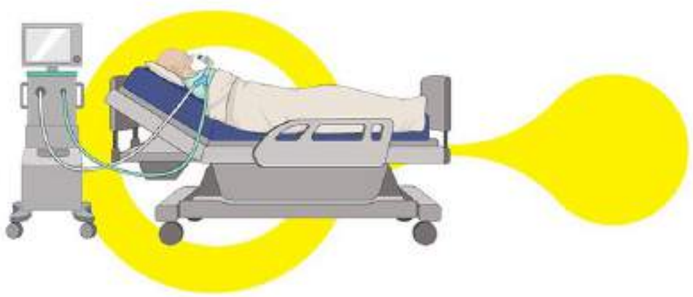




RECOMMENDATION 7
Early enteral nutrition can be safely initiated in proned and paralyzed patients.

RECOMMENDATION 8
In patients requiring moderate dose vasopressors, enteral nutrition should be started with gradual advancement.



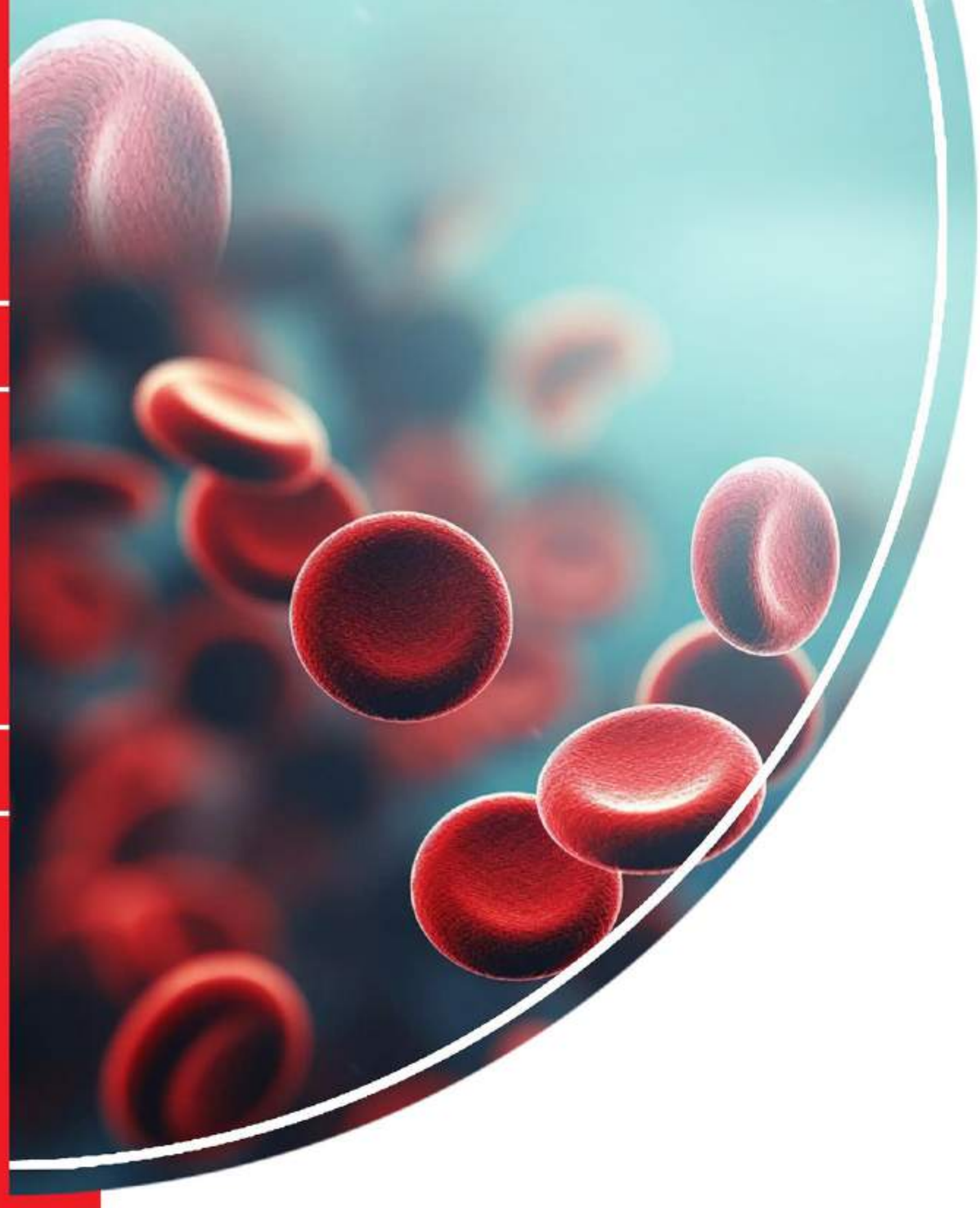


RECOMMENDATION 9
Continuing enteral nutrition prior to extubation may optimize nutrition without an adverse impact on extubation success.

References
- https://www.sciencedirect.com/science/article/pii/S2161831324001790?via%3Dihub

Actual Case Scenario

Phenytoin-Induced Thrombocytopenia in a Female Patient



Chief Complaint

A female patient presented to the emergency department with complaints of drowsiness, lack of appetite and cough since the morning.

History of presenting Illness

According to the patient's son, she had been started on meropenem earlier that day as prescribed by her physician. Following this, her oxygen saturation began to drop, prompting the family to bring her to the hospital.

Associated Symptoms

- No history of chest pain
- No paroxysmal nocturnal dyspnea (PND) or orthopnea
- No high-grade fever reported at home

Past Medical History

Known history of seizures, managed with **phenytoin** at home.

Laboratory Investigations

Platelet Count: Initial: 89,000/µL. Subsequent drop to 59,000/µL.

Other laboratory parameters:
No significant abnormalities noted.

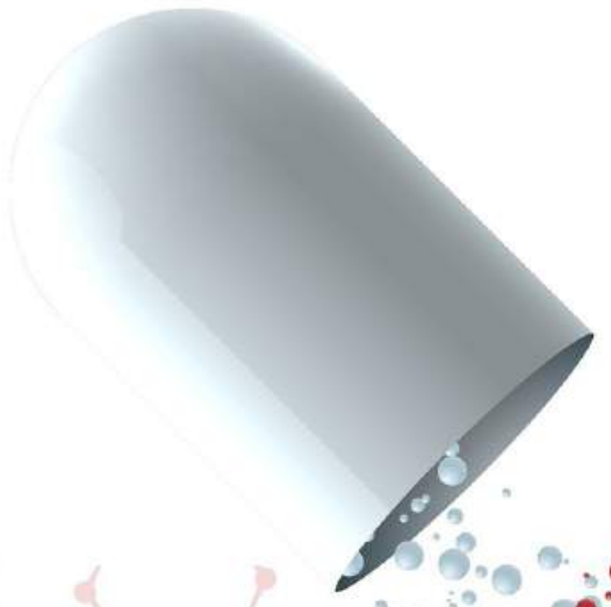
WHO Casuality Assessment on Phenytoin induced Thrombocytopenia

Using the WHO causality assessment framework, the relationship between phenytoin and the adverse event (thrombocytopenia) can be analyzed as follows:

CASUALITY TERM	ASSESSMENT CRITERIA
Certain	The temporal relationship aligns with known phenytoin-induced thrombocytopenia (1–90 days after administration). Platelet counts began to recover after phenytoin discontinuation. No alternative cause (e.g., infection or another drug) was identified. Rechallenge was not conducted due to the seriousness of the reaction. Thus, it meets many criteria, but the lack of rechallenge evidence prevents this classification.
Probable / Likely	Temporal relationship and improvement post-discontinuation strongly suggest phenytoin as the cause. No evidence of other causes, such as sepsis, autoimmune conditions or bone marrow disorders.
Possible	While plausible, the detailed evaluation ruled out significant alternative causes, making this classification less appropriate.

Reference
https://pmc.ncbi.nlm.nih.gov/articles/PMC11186397/#:~:text=Thrombocytopenia%20is%20a%20serious%20adverse,is%20drug%2Dinduced%20immune%20thrombocytopenia

Formulary Inclusion



GENERIC NAME	REASON FOR INCLUSION	KEY BENEFITS
Semaglutide	Addressing the need for better management of type 2 diabetes and obesity.	Improves glycemic control, supports weight reduction and offers cardiovascular protection.
Inclisiran	Meeting the demand for advanced lipid-lowering therapies for high cardiovascular risk patients.	Reduces LDL cholesterol with twice-yearly dosing, enhancing patient adherence & outcomes.
Finerenone	Improving care for diabetic kidney disease and chronic heart failure patients.	Provides renal-protective and cardio protective effects for high-risk populations.
Dronedarone	Offering a safer antiarrhythmic option for managing non-permanent atrial fibrillation.	Reduces cardiovascular events and hospitalizations while maintaining rhythm control.
Bempedoic Acid	Expanding lipid management options for statin-intolerant patients.	Lowers LDL cholesterol effectively, ensuring a more inclusive approach to hyperlipidemia treatment.

Clinical Pharmacy Pearls

From Common Use to Careful Monitoring:
Category D interaction

Submitted by Nehal Nadir | Clinical Pharmacist

DRUG - DRUG INTERACTION | **Amiodarone and Loratadine**

RISK OF INTERACTIONS

The combination of amiodarone and loratadine increases the risk of QT prolongation and potentially life-threatening Torsades de Pointes.

CLINICAL RECOMMENDATIONS

The amiodarone-loratadine interaction is a Category D risk, warranting therapy modification. Avoid combining them when possible, opting for safer alternatives like cetirizine or fexofenadine.

DRUG - DRUG INTERACTION | **Febuxostat and Rosuvastatin**

RISK OF INTERACTIONS

Co-administration of febuxostat and rosuvastatin increases rosuvastatin levels via BCRP inhibition, heightening the risk of myopathy and rhabdomyolysis.

CLINICAL RECOMMENDATIONS

Limit rosuvastatin to 20 mg daily when combined with febuxostat, monitor for toxicity signs and consider alternative statins like atorvastatin or pravastatin to avoid interactions.

Respiratory Syncytial Virus (RSV) Vaccine

Submitted by Syeda Sarwat Jabeen | Outpatient Pharmacist

Abstract

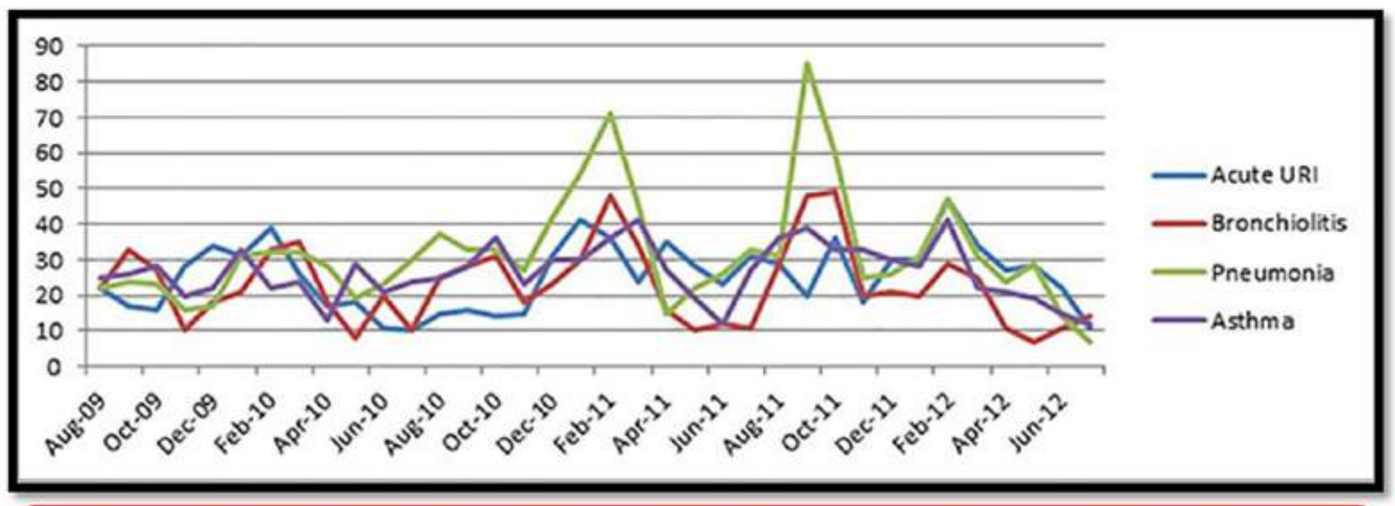
Respiratory syncytial virus is highly contagious virus affecting young children, older adults, immunocompromised individuals & pregnant women are at high risk. RSV causes severe respiratory illnesses, including bronchiolities, URT infection and pneumonia.

According to WHO, RSV is responsible for 2.1 million hospitalizations worldwide annually.

Arexvy (Pfizer), Abrysvo (GSK), Nuvaxovid (Novavax) are newly FDA approved RSV vaccines that offer protection for high-risk groups

Introduction

A three years prospective study was conducted at the Aga Khan University hospital in Karachi, a city of 20 million in south Pakistan, from August 2009 to June 2012.



Monthly number of cases for each diagnosis among the total admissions at Aga Khan University Karachi

The proportion of RSV cases in various months varied from

2% to 43%

The cases started increasing in the month of July (14%) reaching the peak (43%) in September and then slowly declining reaching to 8% in the month of December.

RSV Vaccines Approved by FDA in 2022:

Arexvy(Pfizer) Nuvaxovid (Novavax)
For adults 60+ years

Abrysvo (GSK)
for pregnant women to protect newborns

Other candidates
Multiple RSV vaccines in various stages of clinical development

Description

Arexvy (Pfizer) Effectiveness against severe RSV-related illness

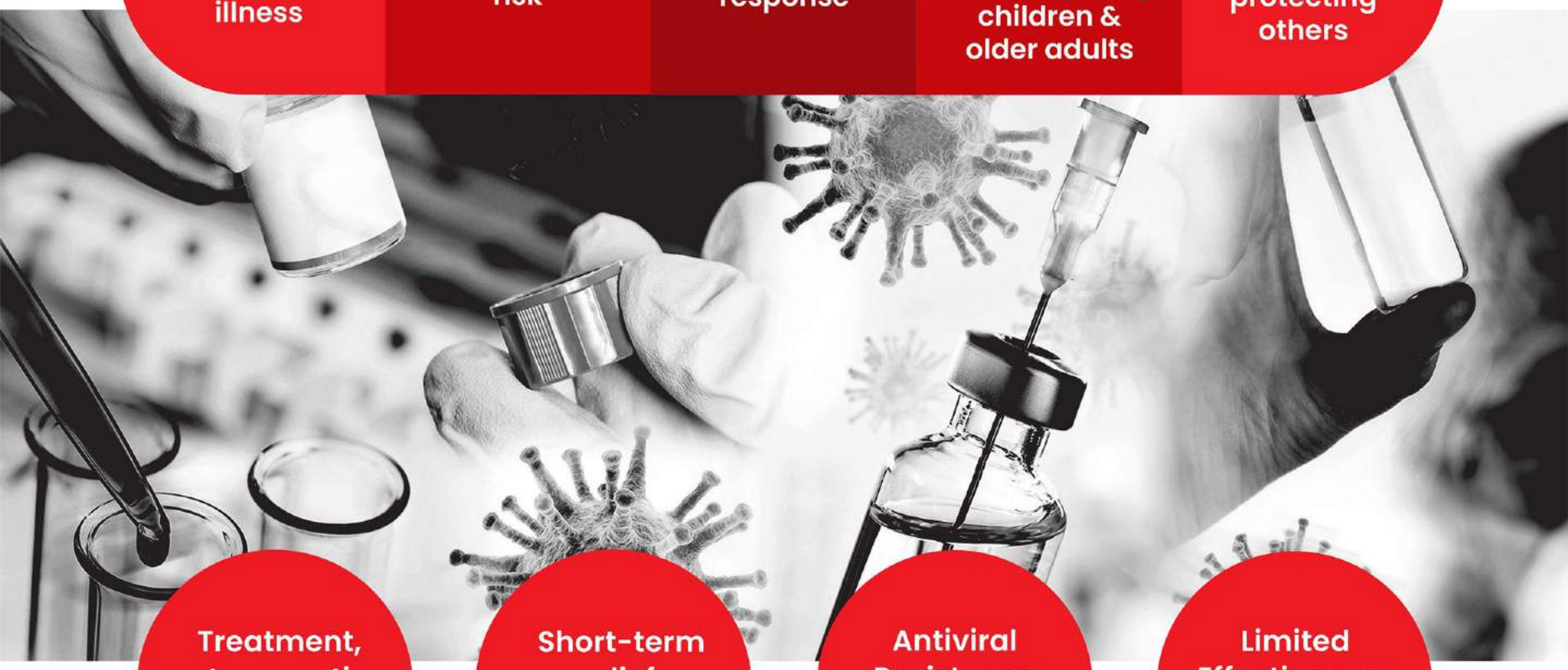
Abrysvo (GSK) Effectiveness against RSV-related hospitalization

Drawbacks

Pain | Redness | Headache | Swelling at injection site | Fatigue

Vaccine Benefits

- Protection against severe RSV-related illness
- Reduced hospitalization risk
- Enhanced immune response
- It protects vulnerable populations, such as young children & older adults
- Vaccines decrease the spread of RSV, protecting others



Medicine Limitation

- Treatment, not prevention
- Short-term relief
- Antiviral Resistance
- Limited Effectiveness

Why both are needed

Treatment for vulnerable populations:

Medicines are crucial e.g. immunocompromised individuals

Vaccines + Medicine:

For severe cases or high-risk individuals.

Precaution & Conclusion

- Monitor allergic reactions and severe side effects.
- Practicing good hygiene.
- Maintaining physical distancing.

References

https://www.nhs.uk/vaccinations/rsv-vaccine/ •

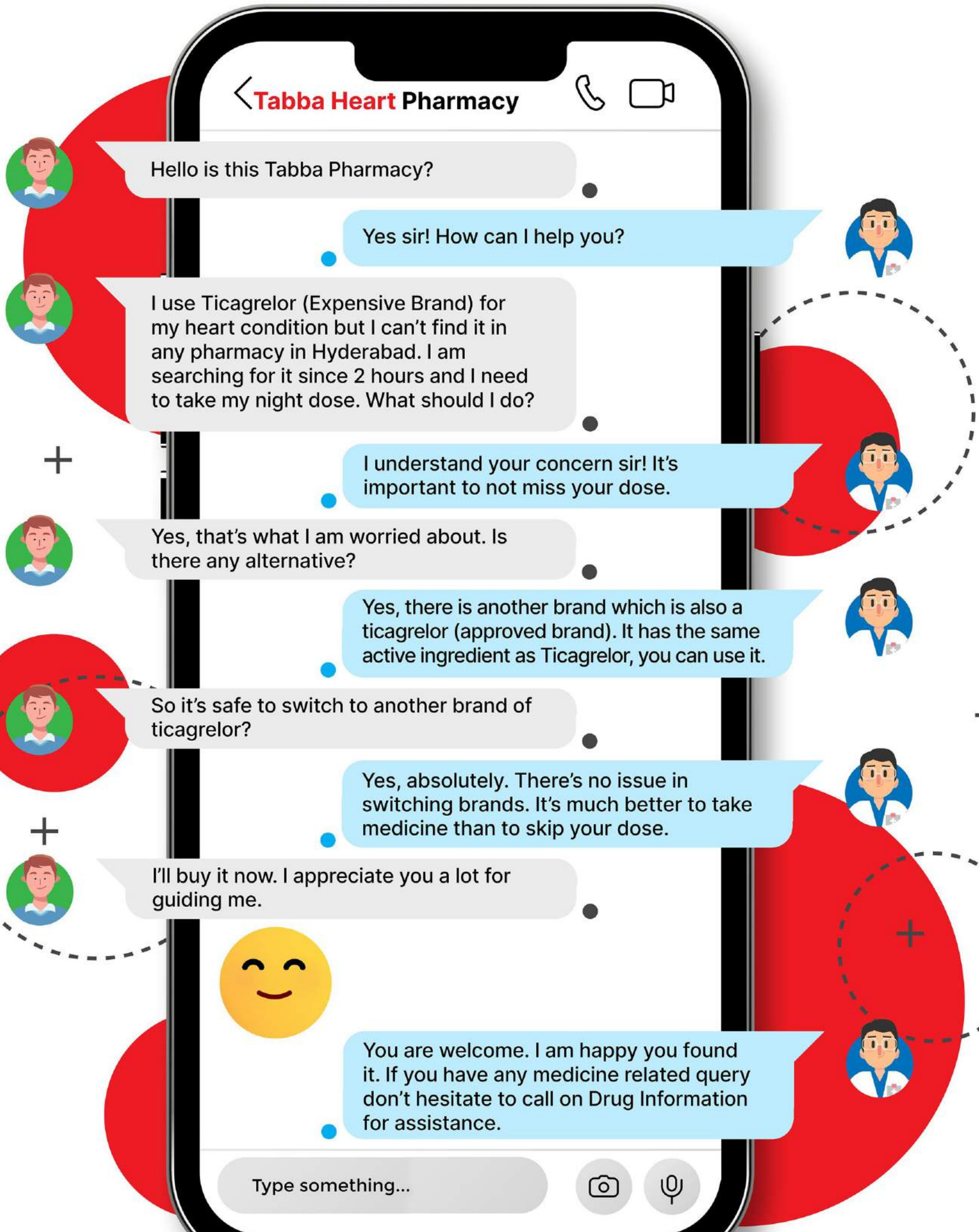
https://www.cdc.gov/rsv/vaccines/older-adults.html •

https://pmc.ncbi.nlm.nih.gov/articles/PMC5805860/#:~:text=The%20proportion%20of%20RSV%20cases,in%20the%20month%20of%20December. •

Bridge to Care

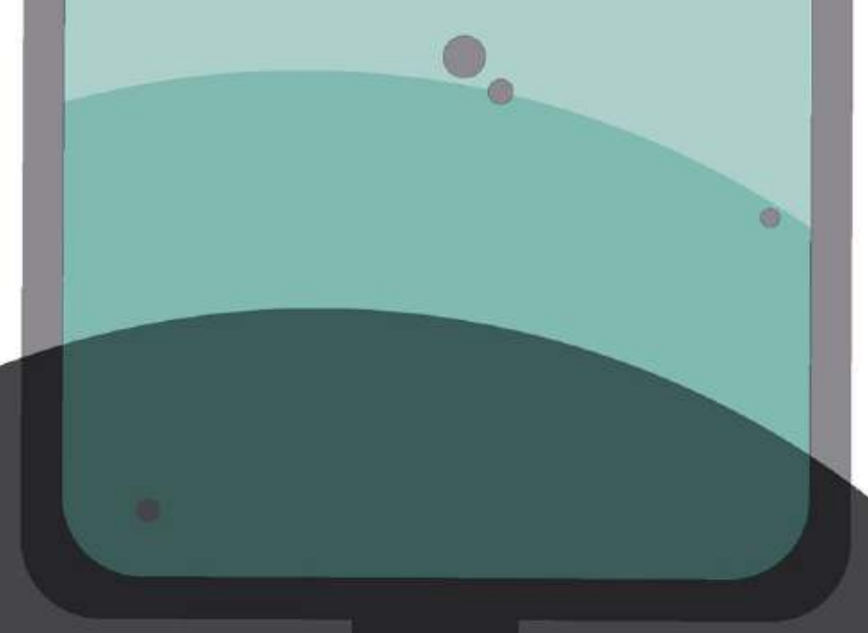
A Pharmacist significant role in suggesting Alternative Brands during drug shortages

Submitted by Rabiya Mazhar | Inpatient Pharmacist



IV Fluids and Opportunity to Improve Labels

Submitted by Palwashay Iqbal | Sterile Area Pharmacist



Intravenous (IV) fluids are frequently used when providing health care. Although IV fluids may be viewed as having low risk their improper use can cause serious harm.

Understanding the risks, benefits and proper use of these solutions is paramount for patient safety. Specifically, unintentional administration of a fluid that is hypotonic or becomes hypotonic in vivo, can result in harm or death, especially in at-risk populations such as children. There is opportunity to improve product labels so that potential risks and proper use are better understood.

Two related but distinct properties of IV fluids are

- Osmolality
- Tonicity

Fluid tonicity, in particular, plays a key role in regulating intracellular & extracellular fluid. Infusion of an IV fluid of inappropriate tonicity can lead to clinically significant electrolyte disturbances.The authors of a recent paper identified a number of Canadian IV fluid products that are initially hypertonic or isotonic and are labelled as such on the bag and in their respective product monographs, but become hypotonic when infused. Examples of such fluids are dextrose 10% & dextrose 5% in water. Once such fluids have been administered, the dextrose is metabolized, leaving free water, which is hypotonic and contributes to hyponatremia. The authors noted that current labelling of these IV fluids can lead to misunderstanding.

Given the reports of IV fluid-related errors and the potential ambiguity and confusion related to labelling of some IV fluid bags, ISMP Canada suggests the development of a good practices guide for the labelling and packaging of IV solutions-similar to the guides that exist for the labelling and packaging of prescription and nonprescription drugs.

Such a guide would include the following considerations:

- Provision of space for additive medication labels
- Use of machine-readable coding to support correct selection of prescribed solutions
- Removal of non-essential information
- Prominence of critical information

References

- Manderville JR, More KM, Tennankore K. Misunderstandings about tonicity and osmolality can lead to patient harm. Can J Hosp Pharm. 2023;76(4):324-6.
- Reducing the risk of hospital-acquired hyponatremia: intravenous fluid management and monitoring. ISMP Can Saf Bull. 2024 [cited 2024 Jun 18];24(6):1-6. Available from: https://ismpcanada.ca/bulletin/reducing-the-risk-of-hospital-acquired-hyponatremia-intravenous-fluid-management-and-monitoring/

FDA's Black Box warning for Febuxostat and its Cardiovascular Risks

Submitted by Umme Hani | Outpatient Pharmacist

Introduction

On February 21, 2019, the U.S. Food & Drug Administration (FDA) issued a significant safety communication regarding Febuxostat, a medication prescribed for the treatment of gout in adults. This communication highlighted an increased risk of death associated with Febuxostat compared to another commonly used gout medication, allopurinol. The FDA's decision was based on an in-depth review of data from a safety clinical trial, revealing elevated risks of heart-related deaths and deaths from all causes among patients taking Febuxostat.

As a result, the FDA mandated the inclusion of a Black Box warning along with a new patient Medication Guide. Additionally, the approved use of Febuxostat was limited to specific patient populations who have not responded effectively to allopurinol or have experienced severe side effects.

Background Information

Febuxostat, approved by the FDA in 2009, functions by reducing uric acid levels in the blood, thereby alleviating symptoms of gout—a form of arthritis characterized by sudden attacks of joint pain, swelling, and redness caused by uric acid buildup. Despite the chronic nature of gout and its prevalence affecting millions of adults in the U.S., treatment options remain limited, necessitating the need for effective medications.

Implications for Patients

Patients prescribed febuxostat are advised to inform their healthcare providers about any history of heart problems or stroke and to carefully weigh the benefits & risks associated with its use. Additionally, patients are urged to seek immediate medical attention if they experience symptoms such as chest pain, shortness of breath, rapid or irregular heartbeat, numbness or weakness on one side of the body, dizziness, trouble speaking or sudden severe headache while taking febuxostat. It is emphasized that discontinuing febuxostat without consulting a healthcare professional may exacerbate gout symptoms.

Implications for Healthcare Providers

Healthcare providers are encouraged to reserve the use of Febuxostat for patients who have failed to respond to or cannot tolerate allopurinol. Providers should counsel patients about the cardiovascular risks associated with Febuxostat and advise prompt medical attention if concerning symptoms arise.

Conclusion

The FDA's decision to issue a Black Box Warning for Febuxostat (Febuxostat) underscores the importance of vigilant monitoring of medication safety and the need for informed decision-making by both healthcare providers and patients.

This development highlights the ongoing efforts to enhance medication safety and underscores the significance of post-market surveillance in identifying potential risks associated with pharmaceutical products.

References

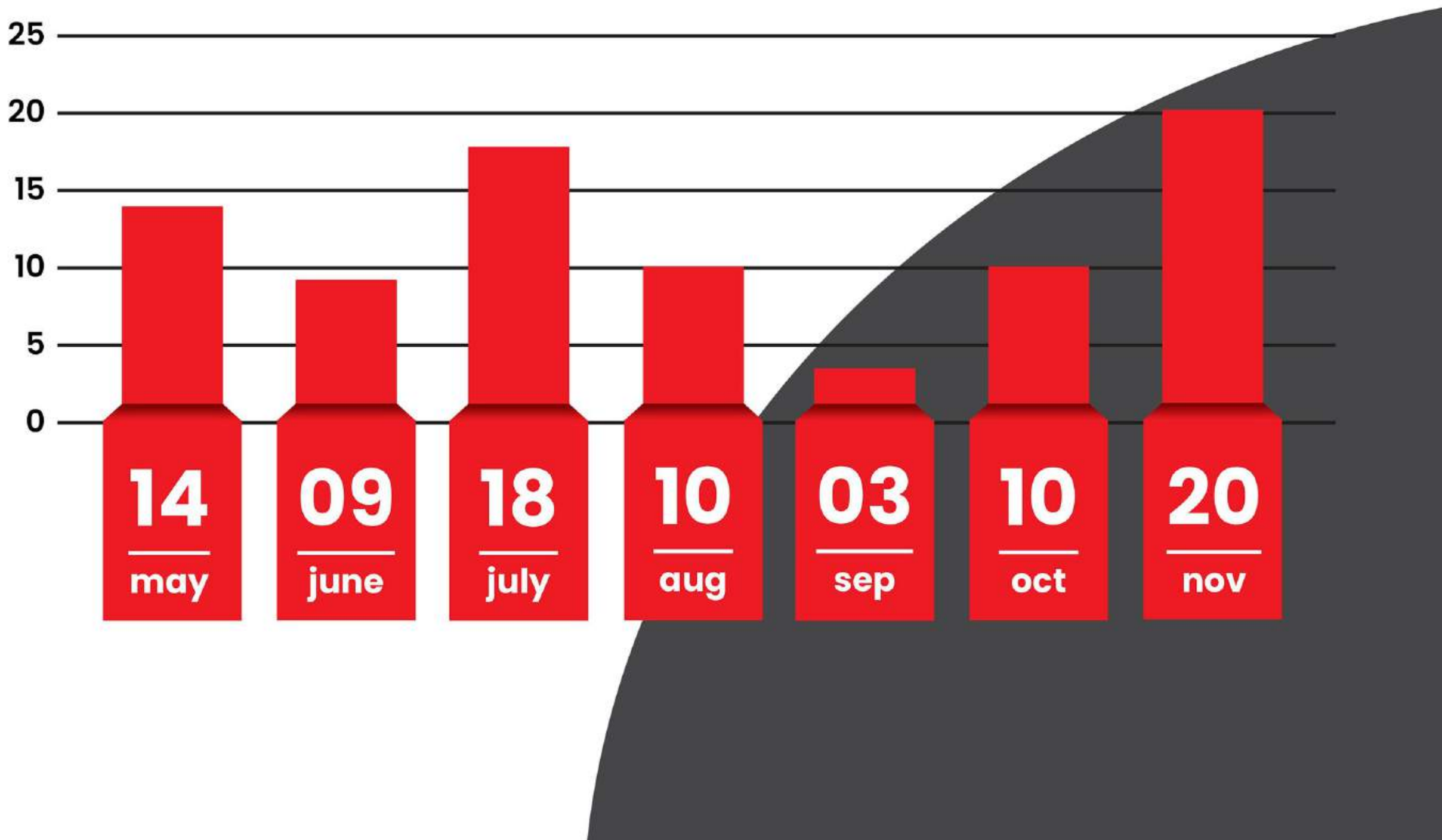
- https://www.fda.gov/drugs/drug-safety-and-availability/fda-adds-boxed-warning-increased-risk-death-gout-medicine-Febuxostat-febuxostat
- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6858030/
- https://pubmed.ncbi.nlm.nih.gov/29527974/

POCT (Point of care Testing): INR devices given to Mechanical Valve Patients from last 6 months at Tabba Heart Institute

This includes hands-on demonstrations and explanations of how to perform a test and how to interpret results.

Pharmacists assess each patient's capability to use the device safely and guide them on troubleshooting common issues.

They also ensure patients understand how to manage abnormal INR results & when to seek further medical help.



Impact of Accurate Weight Assessment in Critical Care

Submitted by Rabia Sami | Trainee Pharmacist Batch 2024

Optimizing Antibiotic Dosing, Nutritional Needs and Medication Adjustments

Accurate weight assessment is a cornerstone of effective patient management in critical care settings. Weight influences a broad spectrum of clinical decisions, including the dosing of antibiotics, tailoring nutritional needs, and making precise medication adjustments to maintain therapeutic efficacy & safety. However, reliance on estimated, inappropriate or outdated weight measurements can lead to suboptimal dosing which risks treatment failure, to overdosing, which can cause toxicity or several other adverse effects, particularly in patients with fluctuating weights due to fluid shifts, obesity, or cachexia.

However Ideal Body Weight (IBW) is an estimation of the weight a person should ideally have based on their height, gender, and body frame. It is often used in medical contexts to standardize dosages or treatments, especially for medications that are affected by body size. IBW does not account for variations like muscle mass or fat distribution but provides a reference for assessing the need for weight-based treatment.

In patients with obesity or extreme weight differences from normal body mass, using actual body weight (ABW) in CrCl calculations may overestimate renal function. For such patients, adjusted body weight (AdjBW) is often used to avoid overestimating drug clearance. Similarly weight plays a crucial role in determining the hepati clearance particularly for medicines metabolized by liver & influence the overall assessment of liver function & how drugs should be dosed in patients with liver impairment.

Key areas where weight estimation plays a crucial role include:

1 Medication Dosing

- **Antibiotics:** Antibiotics such as vancomycin and aminoglycosides require weight-based dosing to achieve precise therapeutic levels, minimizing the risk of toxicity or resistance.
- **Anticoagulants:** Dosing of heparin and enoxaparin depends on weight to prevent clotting and bleeding complications.
- Other drugs including phenytoin, digoxin etc. require careful dosing according to patients weight.

2 Weight is critical for determining caloric and protein needs, guiding enteral or parenteral nutrition and also influences Total parental nutrition calculations (TPN). Incorrect weight estimates can lead to overfeeding or malnutrition.

3 Its also used to calculate fluid resuscitation needs & avoid complications like pulmonary edema.

4 Accurate weight is necessary to determine the ultrafiltration rate in dialysis or hemofiltration.

5 During Mechanical Ventilation predicted body weight (PBW) is used for tidal volume calculations to prevent ventilator-induced lung injury.

6 Weight is crucial in emergencies for dosing drugs like epinephrine, amiodarone or lidocaine. In pediatric cases, defibrillation energy levels depend on weight.

7 Approximation of weight is critical in neonates and children for all interventions with accurate measurements essential due to their smaller tolerance for errors.

8 In patients with altered physiology, such as obesity or ascites, choosing the correct weight (actual, ideal, or adjusted) is crucial for optimizing drug pharmacokinetics and ensuring effective dosing.

Case Scenario

In a community-based incident, a child was seen in a medical clinic for a sore throat. A throat swab was obtained on the initial visit and a positive culture result was reported 2 days later. Clinic staff contacted the parents to obtain allergy information & the child's weight. The mother reported that the child had no allergies and that her weight was "18" pounds.

This information was passed on to the physician, who prescribed amoxicillin at a dose based on a weight of 18 pounds. Five days later the child returned to the clinic with a persistent fever & sore throat, requiring additional treatment. Before an alternative antibiotic was prescribed, the physician weighed the patient and it was determined that she weighed 40 pounds (18 kg).

The physician's assumption that the weight initially provided by the mother was in pounds led to underdoing of the initial antibiotic.

Pharma Gallery

Tabba Heart Institute

2024 Platinum Performance Achievement Award
Chest Pain – MI Registry
NCDR

Center for Patient Safety

The 1st Hospital in Pakistan Recognized by American College of Cardiology with Platinum Achievement Award and Certified for WHO's Patient Safety & Friendly Hospital Framework

UKAS MANAGEMENT SYSTEMS 0045

ISO 9001:2015, ISO 14001:2015 & ISO 45001:2018 CERTIFIED