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Critical Drug Shortages

On-going shortages and strategies to minimize the impact to patient care for drugs with limited availability

Shortage:	*Lidocaine, Bupivacaine injection with and without epinephrine*
Action:	*alternative concentrations, sizes*
Shortage:	*Acetazolamide injection*
Action:	*use oral route when possible*
Shortage:	*Injectable Multivitamins, Thiamine* **note: IV "banana bag" orders in Cerner will be temporarily unavailable*
Action:	*use oral route when possible*

In this Issue

If you have any questions or concerns, please contact the NMH Pharmacy Purchasing Department: 402-354-4337.

Vancomycin Dosing Using AUC Targets

The Infectious Disease Society of America (IDSA) and American Society of Health-System Pharmacists (ASHP) released new guidelines for dosing and monitoring vancomycin in 2020. The new guidelines recommend incorporating the area under the serum drug concentration-versus-time curve (AUC) to minimum inhibitory concentration (MIC) ratio to guide the dosing regimen in certain serious Staph aureus infections.

Under the 2009 guidelines, target vancomycin trough levels for treating serious S. *aureus* infections such as pneumonia and bacteremia were 15-20ug/mL. This serum level range served as a surrogate marker to obtain an estimated AUC/MIC ratio goal of 400-600. In many instances, troughs less than 15-20 are able to achieve AUC:MIC values of 400-600. The guidelines have found that achieving target AUC values of 400-600 results in less drug needing to be used thereby the risk of nephrotoxicity.

The pharmacy department, with the approval of the Medical Executive Committee, will begin using this new monitoring recommendation for adult patients at NMH/WH in March. The pharmacy will still be obtaining trough and/or random levels but, with the assistance of Bayesian PK software, will also be evaluating the calculated AUC when dosing patients with S. aureus pneumonia or bacteremia. Provider may notice instances where a lower trough may not necessarily result in a dose increase if the AUC/MIC is within the 400-600 range.

The vancomycin AUC/MIC goal has not been established or validated in less severe infections such as cellulitis, infections with methicillin sensitive S. aureus, coagulase-negative staff, or other organisms, or those with acute or chronic renal impairment. Serum level monitoring will continue to be the primary method of assessing the dosing regimen. However, looking into the future, this dosing/monitoring strategy may be expanded to other infections.

New FDA Labeling Changes: Warning about NSAID Use in Pregnancy

Previous prescribing information for non-steroidal anti-inflammatory drugs (NSAIDs) stated to withhold use in pregnancy after 30 weeks gestation due to the risk for premature closure of the ductus arteriosus. However, the FDA recently issued a warning statement to further caution patients on the risk of using these medications after 20 weeks gestation. This is due to the rare risk of NSAIDs causing oligohydramnios (low amniotic fluid levels) in the fetus. Given that the fetus produces the majority of amniotic fluid after about 20 weeks gestation, even short term use can lead to renal dysfunction and further complications in neonates.

If a provider deems that NSAID use is necessary between 20 and 30 weeks gestation, use should be limited to the lowest effective dose and shortest duration, and ultrasound monitoring of amniotic fluid is recommended if treatment extends beyond 48 hours. It is recommended to discontinue the NSAID if oligohydramnios is found, as this condition usually improves after discontinuation of the medication. It is important to note that one exception to this warning is the use of daily low-dose aspirin (81-162mg) in pregnancy, used to decrease the risk of preterm preeclampsia and low birth weight in patients with risk factors.

Health care providers frequently treating pregnant women generally know about the risk of oligohydramnios with these medications. This communication from the FDA is intended to more broadly educate other health care professionals and pregnant women, given the widespread use of this class of medications in both prescription and over the counter formulations. OTC and prescription labeling will be updated to add this information.

FDA Warnings: Xeljanz, Tranexamic Acid

Tofacitinib (Xeljanz®, Xeljanz XR®): FDA is alerting the public that preliminary results from a safety clinical trial show an increased risk of serious heart-related problems and cancer with the arthritis and ulcerative colitis medicine (tofacitinib) compared to tumor necrosis factor (TNF) inhibitors. FDA required the safety trial, which also investigated other potential risks including blood clots in the lungs and death. Those final results are not yet available. Health care professionals should consider the benefits and risks of tofacitinib when deciding whether to prescribe or continue patients on the medicine. Continue to follow the recommendations in the tofacitinib prescribing information.

Tranexamic Acid Injection: The FDA is alerting health care professionals about the risk of inadvertent intrathecal administration of tranexamic acid injection. Careful handling of tranexamic acid injection is important to prevent medication errors that could result in serious injury or death. Intrathecal administration of tranexamic acid injection may result in serious life-threatening injuries including seizures, cardiac arrhythmias, paraplegia, permanent neurological injury, and death. In most of the cases reported to FDA, tranexamic acid injection was erroneously administered instead of the intended intrathecal anesthetic (e.g., bupvicaine injection) for neuraxial anesthesia. Tranexamic acid injection, bupivacaine injection and other products used in the perioperative setting may have a similar appearance, such as similar vial cap color or packaging that may contribute to the mix-ups. Packaging will be updated as well as prescribing information detailing the risk of incorrect route administration

Reporting Vaccine Errors - VAERS

The Vaccine Adverse Event Reporting System (VAERS) is a national early warning system to detect possible safety problems in vaccines used in the United States. VAERS accepts and analyzes reports of adverse events (AEs) after a person has received a vaccination. Anyone can report an adverse event to VAERS, but healthcare professionals are required to report certain adverse events and encouraged to report any clinically significant event following vaccination in the VAERS system, even if they are not sure if vaccination caused the event. https://vaers.hhs.gov/

The following adverse events after COVID-19 vaccination should be reported to VAERS:

- Vaccine administration errors, whether or not associated with an adverse event (AE)
- Serious AEs regardless of causality. Serious AEs per FDA are defined as:
  1. Death;
  2. A life-threatening AE;
  3. Inpatient hospitalization or prolongation of existing hospitalization;
  4. A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions;
  5. A congenital anomaly/birth defect;
  6. An important medical event that based on appropriate medical judgement may jeopardize the individual and may require medical or surgical intervention to prevent one of the outcomes listed above.
- Cases of Multisystem Inflammatory Syndrome
- Cases of COVID-19 that result in hospitalization or death