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## News & Noteworthy:

### Fluoroquinolones – More Harm than Good?

*by Stanley Moy, Antimicrobial Stewardship Pharmacist, and Eric Ocheretyaner, Pharmacy Practice Resident*

Fluoroquinolones are a class of antibiotics that have a broad spectrum of activity and can be utilized to treat a variety of different infections. Several fluoroquinolones have been withdrawn from the market after approval due to severe adverse effects. In 2008, the Food and Drug Administration (FDA) released safety warnings about tendon rupture and tendinitis and again in 2013 for peripheral neuropathy, prompting the inclusion of a black box warning.<sup>1,2</sup> Despite these warnings, fluoroquinolones are still commonly prescribed antibiotics in the community. Fluoroquinolones are also associated with causing exacerbations of myasthenia gravis, hallucinations, photosensitivity, QTc prolongation, and hypo/hyperglycemia. As a result, this class of antibiotics has been closely monitored for toxicity.

On May 12, 2016, the FDA released a safety announcement, "...the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment options." The serious side effects prompting the FDA warning involve the tendons, muscles, joints, nerves, and central nervous system.<sup>3</sup> The proposed mechanism for tendon rupture is a direct

*(Continued on page 2)*

## Pharmacy & Therapeutics Committee Updates

*by Eric Ocheretyaner, Pharmacy Practice Resident*

During the second quarter of 2016, several policies and protocols were approved or updated and several changes were made to the hospital formulary.

The committee approved guidelines for the use of cangrelor (brand name Kengreal®) in the Cardiac Catheterization Laboratory. For inpatient use, safety monitoring parameters were also approved in the setting of high-dose hydromorphone (Dilaudid®) use, including provisions for monitoring vital signs, oxygen saturation, and urine output. In addition, medication administration times for inpatient orders were approved to be restandardized.

Two cost-containment measures were also approved by the committee. First, a hypercalcemia treatment guideline was approved to reduce the inappropriate use of calcitonin (Miacalcin®). Costing more than \$2000 per 200-unit vial, calcitonin orders now require recommendation from Hematology or Endocrinology Services. Secondly, the committee approved a change in formulary insulin from insulin aspart (NovoLog®) and insulin regular (Novolin® R) to insulin lispro (Humalog®) and insulin regular (Humulin® R), respectively. As the Humulin products are available in 3-mL vials rather than 10-mL vials, the change in formulary can result in reduced wastage and several thousand dollars in cost-savings per year.

Other changes to the hospital formulary include addition of sugammadex (Bridion®) with restrictions to Anesthesia and the Emergency Department, indomethacin suppositories (Indocin®), normal saline flush syringes (SwabFlush® syringes), and active leptospermum honey (Medihoney®). (Read more about Medihoney® on page 2.) Finally, tacrolimus extended-release (Astagraf XL®) was removed from hospital formulary.

## New Drug Primer: Active Leptospermum Honey (Medihoney®)

by Eric Ocheretyaner, Pharmacy Practice Resident

Active leptospermum honey (ALH) is a medical grade honey for the management of wounds and burns. Utilizing its high osmotic potential, it increases outflow of fluid to the wound surface, thus helping the body promote debridement of necrotic tissue. The low pH of ALH helps to lower the pH at the wound site, which has been shown to have wound healing benefits.

### Indications:

- ◆ Diabetic foot ulcers
- ◆ Leg ulcers (venous stasis, arterial, and leg ulcers of mixed etiology)
- ◆ Pressure ulcers / sores (partial and full thickness)
- ◆ First- and second-degree partial thickness burns
- ◆ Donor sites, and traumatic and surgical wounds

### Contraindications:

- ◆ Third-degree burns
- ◆ Known sensitivity to honey or any component of the product, including algae or seaweed
- ◆ To control heavy bleeding

### Adverse Reactions:

- ◆ Allergic site reactions, pain, stinging

### Hospital Formulary Restrictions:

- ◆ None

## Fluoroquinolones - More Harm than Good?

(Continued from page 1)

effect of the fluoroquinolones on the quantity and quality of collagen fibrils due to up-regulation of matrix metalloproteinases, which may then lead to tendon rupture and possibly aortic dissection and aneurysm, as well as retinal detachment.<sup>4</sup>

Furthermore, from an antimicrobial stewardship perspective, fluoroquinolones cause a significant amount of "collateral damage." Collateral damage refers to ecologic adverse effects of antibiotics, especially the selection of drug-resistant organisms. Fluoroquinolones have been linked to an increased risk of methicillin-resistant *S. aureus* (MRSA), *C. difficile*, and drug-resistant gram-negative infections. Less noticeably, resistance to fluoroquinolones has increased for most bacteria due to overuse.<sup>5</sup>

### References:

<sup>1</sup><http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm126085.htm>. Last updated August 15, 2013.

<sup>2</sup><http://www.fda.gov/Drugs/DrugSafety/ucm365050.htm>. Last updated January 16, 2016.

<sup>3</sup><http://www.fda.gov/Drugs/DrugSafety/ucm500143.htm>. Last updated May 12, 2106.

<sup>4</sup>Daneman N, et al. *BMJ Open* 2015;5:e010077 doi:10.1136/bmjopen-2015-010077.

<sup>5</sup>Paterson DL. *Clin Infect Dis*. 2004;38 Suppl 4:S341-5.

## Drug Shortage Updates

by Eric Ocheretyaner, Pharmacy Practice Resident

Drug shortages are a commonly encountered problem amongst health-care settings. It is important to disseminate this information in a timely manner. At our institution, the Pharmacy Department will make this knowledge readily available to prescribers on the 1<sup>st</sup> and 15<sup>th</sup> of every month utilizing the flyer shown below.

CRITICAL SHORTAGES	URGENT SHORTAGES
Substitution protocols or restrictions in place. Consider alternatives.	Current supplies meeting demands. Consider alternatives.
<ul style="list-style-type: none"> <li>▪ <b>Penicillin G benzathine (Bicillin-LA®)</b> <ul style="list-style-type: none"> <li>▪ Restricted to pregnant patients</li> </ul> </li> <li>▪ <b>Alternative:</b> Doxycycline</li> <li>▪ <b>Docusate Oral Solution</b> <ul style="list-style-type: none"> <li>▪ CDC recommended removal due to concerns related to <i>Burkholderia cepacia</i> infections</li> </ul> </li> <li>▪ <b>Alternatives:</b> Docusate capsules, Senna solution/tablets, Polyethylene glycol (Miralax®) solution</li> </ul>	<ul style="list-style-type: none"> <li>▪ <b>Piperacillin/tazobactam (Zosyn®) 2.25-gram vials</b> <ul style="list-style-type: none"> <li>▪ Sufficient supply</li> </ul> </li> <li>▪ <b>Dopamine 40 mg/mL and 80 mg/mL vials</b> <ul style="list-style-type: none"> <li>▪ Utilized to compound 1600 mg/250 mL preparation for pediatric and fluid restricted patients</li> </ul> </li> </ul>

## Pharmacy Focus: Biosimilars – The New “Generics”

by Eric Ocheretyaner, Pharmacy Practice Resident

“Biosimilars” is a new terminology that has recently entered the pharmaceutical world to describe products that may be used interchangeably with current biological products on the market. The pathway to create biosimilars was outlined in the Affordable Care Act (signed in March 2010) under the subtitle of the Biologics Price Competition and Innovation Act (BCPI Act) of 2009. Despite the availability of biosimilars in the European Union market since 2006,<sup>1</sup> the first biosimilar launched in the United States, filgrastim-sndz (brand name Zarxio<sup>®</sup>), was not approved until 2015.<sup>2</sup>

“Biologics” are complex molecules derived from living organisms or cells of living organisms (such as yeast, bacteria, or animals) that are far more complex than standard chemical drug moieties. Examples include erythropoietin (Epogen<sup>®</sup>, Procrit<sup>®</sup>) and rituximab (Rituxan<sup>®</sup>). The complexity and size of biologics creates difficulty in creating a traditional “generic” that would be structurally identical to the reference product. The FDA defines a biosimilar as a biological product that has “data [to] show that, among other things, the product is ‘highly similar’ to an already-approved biological product ... and has no clinically meaningful differences in terms of safety and effectiveness.”<sup>3</sup> FDA approval of a biosimilar to be interchangeable with the reference biologic product requires the manufacturer to demonstrate that the biosimilar produces the same clinical effect and that risks associated with switching between biologic and biosimilar are would be no greater than potential risks of continued use of the biologic alone.<sup>3</sup> Similar to generics, once approved as interchangeable to brand and legend drugs, biosimilars inherit the same FDA-approved indications as the reference product.<sup>4</sup>

### References:

<sup>1</sup> Lucio SD, et al. Am J Health Syst Pharm 2013;70(22):2004-2017.

<sup>2</sup> Zarxio<sup>®</sup> (filgrastim-sndz) [package insert]. Princeton, NJ: Sandoz Inc. August 2015.

<sup>3</sup> <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm241719.htm>. Updated May 10, 2016.

<sup>4</sup> Weise M, et al. Nature Biotechnology 2011;29(8):690-693.

Featured  
patient-  
care  
question

### Nurses Want To Know ...

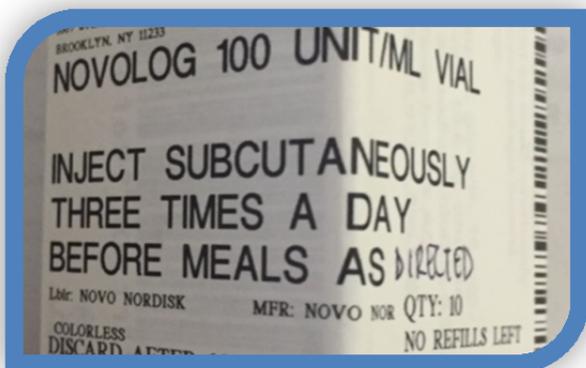
**Q: Why does the pharmacy send vials of medication to the floors? Doesn't the pharmacy mix IVs?**

**A:** In general, the Pharmacy Department dispenses intravenous compounds (or IV admixtures) in ready-to-use form as premixed or compounded IV bags. However, a number of medications must be used within a very short period of time, if not immediately, due to limited stability in solution. At University Hospital of Brooklyn, short stability is defined as medications that are stable for 4 hours or less from the time the medication is mixed with an IV diluent. Common short stability drugs include ampicillin and sulfamethoxazole-trimethoprim (Bactrim<sup>®</sup>). When mixing these drugs, practice aseptic technique in clean areas and wipe rubber stoppers and IV bag ports with an alcohol pad prior to puncture with a needle.

## Spotlight on Safety: Taking Medications “As Directed”

by LilyAnn Jeu, Medication Safety/Internal Medicine Clinical Pharmacist

Can you spot what's wrong with this prescription label?



When 76-year old RG was discharged from University Hospital in January 2016, he probably did not expect to return to the hospital one day after a nearly month-long stay at a skilled nursing facility.

Upon discharge from the nursing facility, RG was prescribed insulin aspart (NovoLog<sup>®</sup>). Without a clear dose on the label, RG's son administered 100 units of the rapid-acting insulin as the patient's very first dose of insulin. Within 4 - 5 hours, RG became very jittery and was sweating profusely. EMS brought RG to the Emergency Department, where multiple fingerstick blood glucose readings were less than 20 mg/dL. RG was treated with Dextrose 50% boluses and recovered from severe hypoglycemia with no permanent harm.

Further assessment by the admitting team found RG's hemoglobin A<sub>1c</sub> to be 6.2%, and thus the insulin was discontinued. Interview of the patient and son also revealed that the family had never been counseled about the appropriate dose or the need for insulin. At least for this family, “As Directed” actually meant “Never said it.” Electronically submitted prescriptions today will mandate the dose field to be completed on the prescription; however, communication and patient education are still essential component for the safe use of medications.

## Clinical Pearls: Enoxaparin Treatment Doses in Obesity

By Ishtiaq Chowdhury, PharmD Candidate

For most patients, weight-based treatment doses of enoxaparin (Lovenox®) generally achieve target anti-factor Xa levels without the need for laboratory monitoring.<sup>1</sup> However, although some studies have shown that capping doses in obese patients to avoid over-anticoagulation may result in failure to achieve targeted levels, few studies have included patients with total body weights above 140 kg.<sup>2,3</sup>

To examine the impact of enoxaparin doses on bleeding risk in larger patients, Lee et al.<sup>4</sup> assessed anti-Xa levels among adults with a body-mass index (BMI) > 40 mg/kg<sup>2</sup> or body weight > 150 kg following a course of enoxaparin 1 mg/kg twice daily. Targeting 0.5 - 1.1 units/mL, 50.5% of 99 patients (weighing 99-249 kg) had a therapeutic level, 14.1% (weighing 78-244 kg) subtherapeutic, and 35.4% (weighing 103 - 249 kg) suprathereapeutic up to 2.0 units/mL. No bleeding events were recorded, and no differences in major bleeding or transfusion were observed.

Similarly, among patients with BMIs > 30 mg/kg<sup>2</sup>, Bazinet and colleagues<sup>5</sup> observed that 60% of patients treated with enoxaparin 1.5 mg/kg once daily (n= 30/60; weighing 66 -136 kg) achieved target anti-Xa levels (1.0 - 2.0 units/mL), while 45% of patients treated with enoxaparin 1 mg/kg twice daily (n = 23/51; weighing 63-159 kg) achieved target levels (0.5-1.1 units/mL). Meanwhile, the once-daily regimen tended to result in subtherapeutic levels (37% of patients), while the twice-daily regimen tended to result in suprathereapeutic levels (53% of patients).

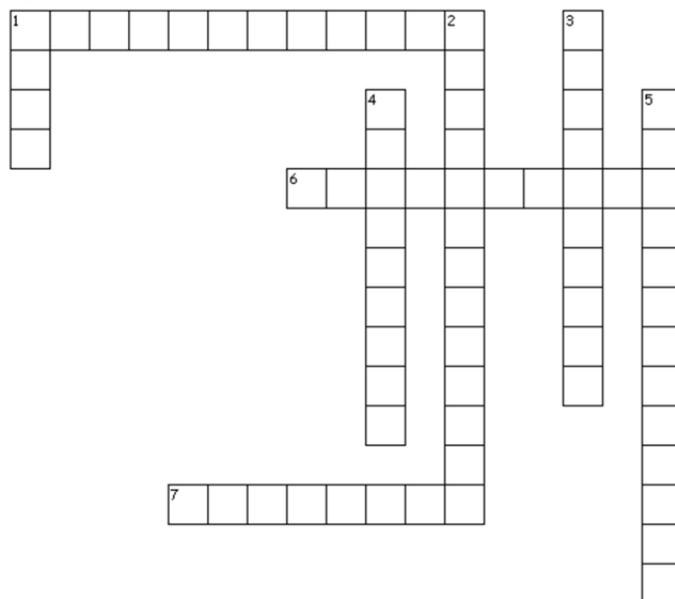
These studies<sup>4,5</sup> suggest weight-based enoxaparin dosing using total body weight does not consistently result in suprathereapeutic anti-Xa levels, even among (morbidly) obese patients or patients weighing more than 240 kg. Instead, adjustment of enoxaparin dose based on anti-Xa levels is still recommended, and a once-daily regimen of enoxaparin should be used cautiously in obese patients due to greater potential for initially subtherapeutic anti-factor Xa levels prior to adjustments.

### References:

- Garcia DA, et al. *CHEST* 2012;141(2)(Suppl):e24S-e34S.
- Nutescu EA, et al. *Ann Pharmacother* 2009;43:1064-83.
- Thomson P, et al. *Can J Hosp Pharm* 2009;62(5):367-374.
- Lee Y, et al. *Pharmacotherapy* 2015;35(11):1007-1015.
- Bazinet A, et al. *Thrombosis Res* 2005;116(1):41-50.

## Crossword Puzzle: Infectious Diseases

by Sana Sohail, PharmD Candidate



### Across

- The first-line treatment of *Pneumocystis jiroveci* pneumonia is dosed on its \_\_\_\_\_ component.
- \_\_\_\_\_ is commonly used for MRSA and requires monitoring of trough drug levels.
- This fourth-generation cephalosporin has anti-pseudomonal activity.

### Down

- Beta lactams efficacy is based on \_\_\_\_\_ dependent killing.
- First line for mild to moderate *Clostridium difficile*
- This is the drug of choice for syphilis.
- This antibiotic is used for vancomycin-resistant organisms and has excellent oral bioavailability.
- Aminoglycoside efficacy is based on a \_\_\_\_\_ dependent killing.

### Answers to Crossword Puzzle:

- Across:** 1. Trimethoprim 6. Vancomycin 7. Cefepime  
**Down:** 1. Time 2. Metronidazole 3. Penicillin  
 4. Linezolid 5. Concentration



### Team Tip of the Day Discharge Counseling Pharmacist

If you would like to request a consult for medication counseling, please page the

Discharge Counseling Pharmacist

at (917) 219-9855.

