Fall 2019, Issue 11

# The Script

A Publication of the Department of Pharmacy, Norman Regional Health System

## Pharmacists are Back in the Emergency Room

By Lisa Dills-Zambrano, D.Ph.

Pharmacists are again keeping regular hours in the Porter and HealthPlex emergency departments. Each campus now has a full-time pharmacist available every day to assist in the medication reconciliation process. These clinical pharmacy specialists will also be available for questions, consults, and to anyone seeking a drug information specialist.

*From left to right: Alex Ehrhart, Danielle Trierweiler, and Justin Booth*

Pharmacy has not had a routine presence in the ER since 2010. Our pharmacists are excited and eager to provide our services to the important and fast-paced area of emergency medicine. Please feel free to involve them in any way possible.

Meet Your ER Clinical Pharmacy Specialists:

Justin Booth, Pharm.D., BCPS — Justin graduated from Southwestern Oklahoma State College of Pharmacy in 2013. He completed his residency at NRHS in 2014, has worked as a clinical pharmacy specialist since that time, and was pharmacist of the year for 2018. Justin will be the primary pharmacist for the Porter ER.

Alex Ehrhart, Pharm.D.—Alex graduated from Southwestern Oklahoma State College of Pharmacy in 2018. She completed her year-long residency with NRHS this past year. Alex will be one of two primary pharmacists rotating in the Healthplex ER.

Danielle Trierweiler, Pharm.D.—Danielle graduated from University of Wyoming College of Pharmacy in 2018. She recently completed her year-long residency with NRHS. Danielle will be the second of two primary pharmacist rotating in the Healthplex ER.

On the weekends other clinical pharmacy specialists from units across both campuses will be filling in to provide care, assist in the medication reconciliation process, and serve as drug information specialists.

ER Pharmacist Hours and Extensions

Porter: Daily 11 AM—7 PM, Ext. 7-7443

HPX: Mon-Fri 11 AM—7 PM, Weekends 7 AM—3 PM, Ext. 5-6772

## In This Issue:



**Please share your thoughts, comments and/or suggestions with us.**

Do you have an idea for a story? Is there information we can provide you?

All correspondence concerning *The Script* should be sent to:

**Christopher Brown, Pharm.D., BCPS**

**3300 HealthPlex Pkwy**

**Norman, OK 73072**

**cbrown@nrh-ok.com**

NORMAN REGIONAL Health System

# Direct Oral Anticoagulants in Obesity

By Katie Sullivan, Pharm.D.

Direct oral anticoagulants (DOACs) have been widely accepted since coming to the market due to their favorable efficacy and safety profile, and convenience of monitoring compared to warfarin. DOACs, which include the thrombin inhibitor dabigatran (Pradaxa), and factor Xa inhibitors rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Savaysa), and betrixaban (Bevyxxa) are generally used for treatment and prevention of venous thromboembolism (VTE) and for ischemic stroke prevention in patients with non-valvular atrial fibrillation. However, data is limited on the safety and efficacy of these agents in obese individuals. **In 2016, the International Society of Hemostasis and Thrombosis (ISHT) recommended to avoid use of DOACs in patients with a BMI of greater than 40 kg/m$^2$ OR weight greater than or equal to 120 kg.** This article discusses the reasons behind their recommendation and the available evidence since its release.

See table below for the evidence used by the ISHT in making its recommendation. The vast majority of data available are on patients with BMI greater than 35 kg/m$^2$ OR weight greater than or equal to 100 kg. Given the paucity of data on patients in larger weight categories the ISHT made its recommendation to avoid use of DOACs in patients with BMI of greater than 40 kg/m$^2$ OR weight greater than or equal to 120 kg.

**2016 ISHT Data Available for DOACs in Obesity**

| Medication | Study | Weight Categories | Number of Obese Patients (%) |
|---|---|---|---|
| Dabigatran (Pradaxa®) | RE-COVER I | ≥ 100 kg<br>BMI ≥ 35 | 502/2539 (20)<br>306/2539 (12) |
| | RE-COVER II | ≥ 100 kg<br>BMI ≥ 35 | 438/1280 (34.2)<br>302/1280 (23.6) |
| | RE-LY | ≥ 100 kg | 3099/18113 (17.1) |
| | RE-MEDY | ≥ 100 kg | 299/1430 (20.9) |
| | RE-SONATE | ≥ 100 kg | 122/681 (17.9) |
| Rivaroxaban (Xarelto®) | EINSTEIN DVT | > 100 kg | 245/1731 (14.2) |
| | EINSTEIN PE | > 100 kg | 345/2419 (14.3) |
| | EINSTEIN EXTENSION | > 100 kg | 85/602 (14.1) |
| | ROCKET-AF | > 90 kg<br>BMI > 35 | 2035/7131 (28.5)<br>972/7131 (13.6) |
| Apixaban (Eliquis®) | AMPLIFY | ≥ 100 kg<br>BMI > 35 | 522/2691 (19.4)<br>349/2691 (13.0) |
| | ARISTOTLE | None | |
| Edoxaban (Savaysa®) | ENGAGE AF TIMI 48 | None | |
| | HOKUSAI VTE > | 100 kg | 611/4118 (14.8) |

Since the 2016 ISHT guidance there have been a few studies released, mainly pharmacokinetic studies, but they too were lacking data in the morbidly obese. For example, one retrospective single-center study looked at apixaban, rivaroxaban, or dabigatran versus warfarin in 128 patients with atrial fibrillation/flutter and BMI greater than 40 kg/m$^2$ OR weight greater than 120 kg. The study found no difference in the rate of stroke/TIA or major bleeding, but dabigatran had numerically higher rates of stroke/TIA (Kido K, Ngorsuraches S. Comparing the efficacy and safety of DOACs with warfarin in the morbidly obese population with atrial fibrillation. Ann Pharmacotherapy.2019;53 (2):165-170). The applicability of this study is limited having a small sample size and being a single center retrospective study.

Overall, there is still a lack of robust clinical data supporting the use of DOACs in the morbidly obese (BMI of greater than 40 kg/m$^2$ OR weight greater than or equal to 120 kg). Therefore, pharmacists at Norman Regional utilize our surveillance software, Sentri7, to identify all patients on DOAC therapy. In the morbidly obese patients who are being initiated on a DOAC we contact the prescriber to discuss other potential options given each patient's specific comorbid conditions. Warfarin is typically the drug of choice in these patients as it can be titrated to a specific INR goal. However, patient compliance, price, concomitant drug -drug interactions, and more are all taken into account when making recommendations.

In general, further studies are needed to help elucidate the potential for DOAC use in the morbidly obese population. Until then warfarin will continue to be recommended in this population.

# Heparin Drips

By Alex Ehrhart, Pharm.D.

Heparin is a life-saving anticoagulant that is utilized in many different ways throughout our health system. However, with recent changes to the order sets, different rates, boluses, and weight limits varying for each order set it can be confusing. Picture this: a patient arrives on your floor after transferring from the emergency department. While you're receiving handoff they mention that the patient is on a heparin drip. At this point, you likely hear warning bells going off in your mind as heparin drips have been one of the most error prone medications in our health system. The purpose of this article is to clarify how to use each order set, discuss some new process changes, provide some pearls on use, and give the reader assurance they are appropriately titrating heparin.

**New heparin drip process changes:** There is one major change to the heparin drip order sets, which is to draw the baseline heparin anti-Xa level, but to NOT wait for the result to start the heparin drip and bolus. It's felt that starting the heparin drip as soon as possible will best serve our patients as it currently takes around 45 minutes to receive results. Along with this change the pharmacist and prescriber will be flagged in Meditech on order initiation to ensure the patient wasn't on a direct oral anticoagulant— apixaban (Eliquis®), rivaroxaban (Xarelto®), edoxaban (Savaysa®), betrixaban (Bevyxxa®), or dabigatran (Pradaxa®) - prior to starting heparin AND that the last dose wasn't taken LESS THAN 12 hours ago. If the baseline heparin anti-Xa level is elevated nursing will be called by lab with the result and if the level is greater than 0.7 IU/mL the prescriber should be notified for further orders.

**Obtain an accurate weight:** An accurate weight is essential for all heparin drips. Pharmacists, nurses, and other healthcare providers should ensure that the original weight is correct before starting a heparin drip. There have been instances where a patient's weight has been estimated at around 100 kg and later their actual weight is in the range of 65 to 75 kg. Differences this large are a safety concern as the patient's heparin drip would be initiated at a much faster rate than intended, increasing the patient's bleed risk. After an initial weight is verified in Meditech the weight is locked in on the medication order, and updating a patient's weight daily in Meditech will not effect the heparin order or the IV spreadsheet. It is important to remember not to change the weight in the pump after initiation of the infusion. An easy way to verify this is that the rate on the pump should match the rate in Meditech. This ensures that the correct weight is entered on the pump and on the medication order in Meditech.

**Low Intensity**: The low intensity order set should be used for patients with acute coronary syndrome, atrial fibrillation, high bleeding risk, continuous renal replacement therapy, status post thrombolytic, or ischemic stroke. The patient's actual body weight should be entered into the pump, unless the weight exceeds 83.2 kg – then use 83.2 kg as the pump weight. Boluses are calculated based on the patient's actual body weight. See chart on right for more details.

**High Intensity**: The high intensity order set should be used for patients with deep vein thrombosis, pulmonary embolism, or high risk of clot. The patient's actual body weight should be entered into the pump, unless the weight exceeds 111 kg – then use 111 kg as the pump weight. Boluses are calculated based on the patient's actual body weight. See chart on right for more details.

**Thrombolytic for Peripheral Arterial Occlusion**: Only cardiologists may order this order set and it should only be used in the ICU/CVICU after a patient has transferred to the floor from the catheterization lab. The patient's actual body weight should be entered into the pump, unless the weight exceeds 83.2 kg – then use 83.2 kg as the pump weight. This heparin drip is dosed sub-therapeutically (goal: 0.1 to 0.3 IU/mL) and given intra-arterially along with intra-arterial alteplase. If your patient is on this order set and it is not being given with intra-arterial alteplase, they are on the wrong order set. See chart above for more details.

**Heparin Drips**

| | Low Intensity | High Intensity | Thrombolytic for Peripheral Arterial Occlusion |
|---|---|---|---|
| Maximum Weight | *83.2 kg* | *111 kg* | *83.2 kg* |
| Starting Rate | *12 units/kg/hr* | *18 units/kg/hr* | *6 units/kg/hr* |
| Goal Heparin Anti-Xa Level | *0.3 to 0.7 IU/mL* | *0.3 to 0.7 IU/mL* | *0.1 to 0.3 IU/mL* |
| Titration | *Based on each specific order set, check anti-Xa levels every 6 hours until 2 consecutive anti-Xa levels at goal, then daily thereafter.* | | |
| New Process Changes | *New orders for heparin drips will now flag for the prescriber and pharmacist to check if patient was on apixaban (Eliquis®), rivaroxaban (Xarelto®), edoxaban (Savaysa®), betrixaban (Bevyxxa®), dabigatran (Pradaxa®), or another direct oral anticoagulant* ***AND*** *the last dose was taken LESS THAN 12 hours ago.* | | |
| | ***When starting a drip—draw and send the baseline heparin anti-Xa level, but do NOT wait for the result to start the heparin drip.*** | | |

In summary, appropriate timing of labs and titration are key to ensure our patients are receiving effective treatment. Remember, if your patient weighs more than the maximum weight on the specific order set, make sure the weight on the pump and on the Meditech order match. If not, please contact pharmacy to clarify. And as always, if you have questions at any time, please call the pharmacy for help!

# Critical Medication Shortages

By Donna Wilk, CPhT

| Medication | Action Plan |
|---|---|
| Acyclovir injection | Due to nationwide shortage acyclovir injection is being reserved for neonates; ganciclovir will be used for suspected HSV in adults. Manufacturers do not have an ETA at this time. Oral formulations are not affected at this time. |
| Amiodarone injection | Due to nationwide shortage 150mg bolus vials have been removed from crash carts. House supervisors and some Pyxis machines have stock for codes. Premix bolus and drip bags are not affected at this time. |
| Ampicillin/sulbactam injection | Product is intermittently on backorder. We have approximately 1 month supply of each strength. Please convert to a PO antibiotic whenever possible. We will continue to order additional stock as availability allows. |
| Aspirin suppositories | Due to nationwide shortage we have removed stock from all Pyxis machines to centralize stock in one location. We do still have a small supply on hand, however please use PO formulation whenever possible. |
| Cefazolin injection | Due to nationwide shortage we have removed all 2 gm premix bags from Pyxis machines except for MER and reserving that for heart carts and MER. Manufacturers report ETAs from August 2019 through March 2021. |
| Cefoxitin injection | Product is intermittently on backorder. We have approximately 1 month supply of each strength. Please convert to a PO antibiotic whenever possible. Manufacturers report ETAs from August 2019 through January 2020. |
| Dextrose 25% and 50% emergency syringes | Product remains on nationwide backorder. We still have stock on hand and are working with a secondary compounding pharmacy to obtain additional supply. Manufacturers report ETAs from August through December 2019. |
| Enoxaparin injection | Due to a breakout of African Swine Flu in China, there is a nationwide shortage on many injectable anticoagulant medications. We are closely monitoring the situation and have ordered additional stock in preparation. |
| Fondaparinux injection | Due to a breakout of African Swine Flu in China, there is a nationwide shortage on many injectable anticoagulant medications. We are closely monitoring the situation and have ordered additional stock in preparation. |
| Gentamicin ophthalmic ointment | Product is on nationwide backorder and we are OUT OF STOCK. Alternative option in stock is erythromycin ophthalmic ointment. Manufacturers do not have an ETA at this time. |
| Heparin injection (flushes, vials, and bags) | Due to a breakout of African Swine Flu in China, there is a nationwide shortage on many injectable anticoagulant medications. We are closely monitoring the situation and have ordered in additional stock in preparation. |
| Hydromorphone injection | Due to nationwide shortage on certain strengths, we will continue to stock only the 2mg formulation for all IV doses due to unavailability of the 1mg formulation. Please stay tuned for further updates in the coming weeks. |
| Hydroxyzine pamoate capsules | Product is intermittently on backorder. At this time our health system's primary stock for patient use is 25mg and 50mg capsules. In addition, we also have Atarax PO and Vistaril IM/IV in stock. |
| Hyoscyamine injection | Product remains on nationwide backorder. There are no other alternative options on the market, except PO/SL formulations. Mylan Institutional is the only manufacturer of the injectable formulation and they have no ETA at this time. |
| Levofloxacin ophthalmic solution | Product remains on nationwide backorder. Alternative options in stock are moxifloxacin, ciprofloxacin, and ofloxacin ophthalmic solutions. Akorn is the only manufacturer of levofloxacin ophthalmic drops and cannot provide an ETA at this time. |
| Losartan and losartan/ hydrochlorothiazide tablets | Due to discovery of NDMA (N-nitrosodimethylamine, a probable human carcinogen) in several angiotensin II receptor blocker (ARB) medications, there is a nationwide shortage on several ARBs. |
| Meperidine injection and oral formulations | Oral formulation of this medication has been removed from the market and no longer available. The injectable formulation is currently on nationwide backorder and our primary stock is 25mg vials. |
| Methyldopa and methyldopa/ hydrochlorothiazide tablets | On nationwide shortage and we are out of stock. Manufacturers are reporting ETA possibly in August 2019. |
| Midazolam injection | Product availability has worsened, however we were able to obtain a good supply of product. Manufacturers are reporting no ETA while some are reporting possible ETA of August 2020. |
| Mineral oil, sterile | Product has been removed from the market and no longer available to order. We have approximately 25 left in stock. |
| Morphine injection | Due to nationwide shortage of certain strengths, we will continue to stock only the 4mg formulation for all IV doses due to the unavailability of the 2mg formulation. Please stay tuned for further updates in the coming weeks. |
| Nicardipine injection | Due to nationwide shortage, we have removed premix drips from all Pyxis machines except procedural areas. For patient care floors nicardipine will be mixed by the pharmacy and sent up when demanded. |
| Sodium bicarbonate injection | Due to nationwide shortage on the prefilled emergency syringes, we are only stocking vials in the crash carts. House supervisors also have a small kit of vials as well for codes. Drips will only be compounded once nursing demands the dose.<br>Please demand dose 1 hour prior to when needed. Manufacturers report ETA from August to December 2019. |
| Talc, sterile | Product remains on backorder and we are out of stock. Possible alternatives in stock include: doxycycline powder for injection, bleomycin, iodine, and minocycline. At this time the manufacturers cannot provide an ETA. |

# New Prescribing Law for Treatment of Acute and Chronic Pain

By Danielle Trierweiler, Pharm.D.

Oklahoma legislature recently passed Senate Bill No. 1446 in attempts to address the opioid crisis. It was signed into law by Governor Mary Fallin and became effective November 1, 2018. This bill imposes new restrictions on physicians and healthcare providers on the prescribing of Schedule II opioid medications. The goal of this new law, as defined by the Centers for Disease Control, is to improve the way opioids are prescribed to ensure safe and efficacious use while reducing the risk of opioid use disorder, overdose, and death. **It is important to note that these requirements do not apply to patients receiving active treatment for cancer, hospice, palliative care, or residents of long-term care facilities.**

**Acute Pain:** Prior to prescribing an initial prescription, the practitioner must document a thorough medical and medication history; conduct and document a physical exam; and develop a treatment plan specific to the cause of pain. The practitioner must also review the prescription drug monitoring program (PDMP) which provides information on the fill history of controlled substances. For acute pain, the day supply must be limited to no more than a 7-day supply. If the patient is less than 18 years of age or pregnant, they must also enter into a pain-management agreement with the practitioner before being prescribed an initial prescription.

A subsequent prescription constituting no more than a 7-day supply may be issued provided that: it is deemed appropriate and necessary; the rationale for subsequent prescription is documented; and the subsequent prescription does not place the patient at undue risk of abuse, addiction, or diversion. If a third prescription is issued for acute pain, the patient must then enter into a pain-management agreement with the practitioner.

**Chronic Pain:** Chronic pain management is defined as greater than 3 months of continuous opioid therapy. All patients receiving chronic pain management with a Schedule II medication must enter into a pain-management agreement with the practitioner. The Senate Bill also mandates that the course of treatment be reviewed every 3 months. In addition, the practitioner must review the PDMP, monitor compliance with the agreement, and make reasonable efforts to stop use of controlled substances, reduce opioid doses, and trial other non-opioid pain modalities.

Two patient-provider agreements are available on Access Repository titled: “Patient-Provider Agreement Acute Pain Management Using Opioid Medications” and “Patient-Provider Agreement Chronic Pain Management Using Opioid Medications”. These documents are also available in Spanish.

# Pharmacy and Therapeutics Committee Update

| Drug | Labeled Indication | Usual Dose | Dosage and Strength | P&T Action |
|---|---|---|---|---|
| *Saccharomyces boulardii* (Florastor®) | Probiotic to promote normal bacterial flora of the intestinal tract. | 1 to 2 capsules twice daily | 250 mg capsules | Removed from formulary due to risk of fungemia |
| Fosfomycin (Monurol®) | Treatment of uncomplicated urinary tract infections (acute cystitis) in women due to susceptible strains of *Escherichia coli* and *Enterococcus faecalis.* | 3 gram as a single dose | 3 gram packet (orange flavor) | Added to formulary |
| Buprenorphine and Naloxone (Suboxone®) | Treatment of opioid dependence. | Dosage is adjusted to a level that maintains treatment and suppresses opioid withdrawal symptoms | 2 mg/0.5 mg and 4 mg/1 mg sublingual film | Added to formulary with restriction to home medication continuation only |

# How to Properly Dispose of Medicines

By Christopher Brown, Pharm.D., BCPS

Just about everything has expiration date, whether it be dairy, canned products, medications, or even frozen food. We don't drink expired milk, but often times we forget to check our own supply of medications. Why do medications have expiration dates, and how do you dispose of them once expired or no longer needed? Also, what should you do if you don't see an expiration date?

Medications lose their effectiveness over time, especially if they are stored in a warm, moist environment, like a bathroom medicine cabinet. Make sure your medications are stored in a cool, dry space to ensure the package expiration date remains valid. The expiration date the manufacturer places on the original container is the date at which the manufacturer can still guarantee the full potency and safety of the drug. In some uncommon cases, taking an expired medication can cause serious adverse effects. For instance, if you take tetracycline that has expired it can cause renal tubular acidosis.


Prescription bottles often have the expiration date on the label. Many over-the-counter (OTC) products and sample medication packets will have the expiration date printed on the label or stamped onto the package. If the medicine doesn't have an expiration date on it or you can't find it and you know it has been over a year since you purchased it, it is likely expired.

Previously, we were taught to flush medications down the toilet so that our loved ones and pets didn't ingest them by mistake. However, the Environmental Protection Agency (EPA) and Food and Drug Administration (FDA) no longer recommend this as flushed medicine can pass through water treatment facilities and ultimately end up in the community drinking water. Even drugs flushed where septic tanks are used can seep into the ground and make its way into our ground water.

The first choice for drug disposal recommended by the EPA is to dispose of prescription and OTC drugs through drug take-back events/programs. See table on the right for a list of take-back locations established by the Oklahoma Bureau of Narcotics (OBN) that are close to our health system.

If drug take-back is not an option the EPA recommends household disposal via the following steps:

1. Take drug(s) out of the original container.
2. Mix drug(s) with an undesirable substance, such as cat litter or used coffee grounds.
3. Put the mixture into a disposable container with a lid.
4. Conceal or remove any personal information on the empty containers.
5. Place the sealed container with the drug mixture into the trash.

**Pharmaceutical Take-Back Locations**

| Name | Address | City, State | Phone Number |
|---|---|---|---|
| Norman Police Department | 201 B West Gray | Norman, OK | (405) 366-5201 |
| Oklahoma University Police Department | 2775 Monitor Avenue | Norman, OK | (405) 325-2864 |
| Noble Police Department | 115 North 2nd Street | Noble, OK | (405) 872-9231 |
| Cleveland County Sheriff's Office | 2550 West Franklin Road | Norman, OK | (405) 701-8888 |
| Moore Police Department | 117 E. Main Street | Moore, OK | (405) 799-4357 |

For more drug take back locations, OBN has an Rx Disposal Boxes link on its website at www.ok.gov/obndd.

If you can't get to a drug take back location, the FDA recommends that some controlled dangerous substances be flushed due to their potential for abuse. For a list of these drugs see: www.fda.gov/media/85219/download.

**The Script** A Publication of the Department of Pharmacy

**Editor in Chief:**
**Christopher Brown, Pharm.D., BCPS**
Clinical Pharmacy Specialist

**Contributors:**
**Alex Ehrhart, Pharm.D.**
PGY1 Pharmacy Resident
**Carly Holmes, Pharm.D.**
Pharmacy Supervisor
**Katie Sullivan, Pharm.D.**
PGY1 Pharmacy Resident
**Lisa Dills-Zambrano, D.Ph.**
Clinical Pharmacist
**Danielle Trierweiler, Pharm.D.**
PGY1 Pharmacy Resident
**Lauren May, Pharm.D., BCPS**
Clinical Pharmacy Specialist
**Donna Wilk, CPhT**
Clinical Pharmacy Technician