Xarelto® Lawsuits and You

What is Xarelto®?
The generic name for Xarelto® is rivaroxaban. Xarelto® is a medication used to stop your blood from clotting.

Why am I on Xarelto®?
You are on this medication because your healthcare provider thinks you are at an increased risk of stroke, heart attack, or clot.

Why are people suing Xarelto®?
Many people feel that Bayer and Johnson & Johnson, the manufacturers of Xarelto®, did not do a good job warning people about the risks of taking Xarelto®.

What are the risks of taking Xarelto®?
Since Xarelto® prevents your blood from clotting, people on Xarelto® are at an increased risk of bleeding.

There is no way to reverse the effects of Xarelto®. So if you have a major bleed for any reason, there is no way to slow it down other than blood transfusions.

If I am on Xarelto® is there anything I can do to reduce the risks?
Yes, take your medications as your healthcare provider has instructed. You also need to watch out for signs and symptoms of bleeding or clotting.

Signs of Bleeding:
♦ Easy bruising
♦ Blood in urine or stools
♦ Bloody noses which don’t stop bleeding
♦ Excessive bleeding of the gums

Signs of Clotting:
♦ Redness, swelling, pain, and heat in an arm or leg
♦ Sudden vision changes in one eye
♦ Weakness on one side of body
♦ Sudden onset of sharp chest pain
If you notice any of these signs or symptoms contact your doctor immediately.

Are there alternatives to Xarelto®?
Yes, there are various new oral anticoagulants (NOACs) currently approved by the FDA. However, they may not be safer than Xarelto®.

The current standard of treatment is warfarin, which has been used since the 1950s.

You should talk to your healthcare provider and determine which anticoagulant will best fit your needs.

By Doua Vang, PharmD Candidate

REFERENCES:
Afrezza® (inhaled insulin human) is a fast-acting insulin that you take with meals to help control blood sugar levels. It is the only approved inhaled insulin currently available. Afrezza® reaches full effect in 12-15 minutes. It can be used for both type 1 and type 2 diabetes.

Each Afrezza® box comes with two inhalers that will each last 15 days. Make sure that you store the inhaler in a cool, dry place and do not ever wash it.

The dose of insulin you use will decide what color and quantity of cartridges you use. See the conversion table for help converting your current mealtime insulin dose to Afrezza®.

**Storage of unopened foil packages:**
- Store in refrigerator for up to 1 month
- If not refrigerated then packages are only good for 10 days
- Throw away after expiration date

**Storage of opened foil packages:**
- Store at room temperature
- Use opened packages within 3 days
- Before use, make sure cartridge has been at room temperature for at least 10 minutes

**Side Effects of Afrezza®:**

- **Long-Term Lung Disease:** Afrezza® can cause a decline in lung function. Do not use Afrezza® if you have a chronic lung disease like asthma or COPD (chronic obstructive pulmonary disease).
- **Low Blood Sugar:** Afrezza®, like all insulins, can cause low blood sugar. This can cause life threatening seizures and other problems. Checking blood sugar levels after meals can help eliminate this problem and gain better control of HbA1c.
- **Allergic Reaction:** Severe allergic reactions can occur while taking Afrezza®. If a reaction does occur, stop taking Afrezza® immediately and call your doctor.

**Fluid Retention:** Taking medications like Actos® (pioglitazone) or Avandia® (rosiglitazone) along with Afrezza® can cause fluid retention to occur. If left unchecked, this can cause or worsen heart failure symptoms. Contact your doctor if you have shortness of breath or swelling in your legs or face.

**By Haiden Mohl, PharmD Candidate**

**REFERENCES:**
How to Administer Afrezza®

Step 1: Select the cartridge for your dose
- If your Afrezza® dose is 4 units, use 1 blue cartridge
- If your Afrezza® dose is 8 units, use 1 green cartridge
- If your Afrezza® dose is 12 units, use 1 yellow cartridge
- Multiple cartridges are required for doses exceeding 12 units

Step 2: Load a cartridge
- Open inhaler
  Holding the inhaler level, lift the white mouthpiece to a vertical position
- Load cartridge
  Place cartridge into the inhaler, making sure it lies flat in inhaler
- Keep inhaler level
  Do not turn upside down, shake, or drop, as this could cause a loss of insulin
- Close inhaler
  Lower the mouthpiece to close the inhaler

Step 3: Inhale insulin
- Exhale
  Remove mouthpiece cover, hold the inhaler away from your mouth and exhale fully
- Position inhaler
  Keeping your head and inhaler level, place the mouthpiece in your mouth, then lift the inhaler down toward your chin
- Inhale deeply and hold breath
  With your mouth closed around the mouthpiece, inhale deeply and hold your breath as long as is comfortable before exhaling

Step 4: Remove cartridge and discard
- Put the mouthpiece cover back onto the inhaler
- Open the inhaler by lifting the white mouthpiece
- Remove the cartridge from the purple base
- Dispose of cartridge in your regular household trash
- Repeat as necessary

The Afrezza® inhaler can be used for up to 15 days from the date of first use. After 15 days of use, the inhaler must be discarded and replaced with a new inhaler.

Mepolizumab (cont.)

Naloxone References
What is naloxone used for?
Naloxone is a non-prescription medication that is used to treat opioid overdose.

How does naloxone work?
Taking too many opioids may cause someone to stop breathing or even lead to death. These effects can become worse when opioids are taken with alcohol or other medications that make people sleepy.

Naloxone helps prevent a person from having life-threatening opioid overdoses by binding to the same parts of the brain as opioid medications. Once bound, Naloxone reverses the effects of opioid medications and allows a person to breathe.

Naloxone works for about 20 to 90 minutes. Call 9-1-1 after administration of naloxone.

<table>
<thead>
<tr>
<th>Signs of an overdose:</th>
<th>Drugs Reversed by Naloxone</th>
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<tbody>
<tr>
<td>♦ Very small or “pinpoint” pupils</td>
<td>Buprenorphine</td>
</tr>
<tr>
<td>♦ Slowed or shallow breathing</td>
<td>Butrans®, Subutex®, Buprenex®</td>
</tr>
<tr>
<td>♦ Blue lips</td>
<td>Codeine</td>
</tr>
<tr>
<td>♦ Limp body</td>
<td>Fentanyl</td>
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<tr>
<td>♦ Pale face</td>
<td>Hydromorphone</td>
</tr>
<tr>
<td>♦ Unconsciousness or failure to respond to loud noises</td>
<td>Methadone</td>
</tr>
<tr>
<td>♦ Deep snoring or gurgling</td>
<td>Hydromorphone</td>
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<tr>
<td></td>
<td>Morphine</td>
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<td></td>
<td>Oxycodone</td>
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<td>Tramadol</td>
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⇒ Naloxone can also reverse heroin overdoses.

Side effects of naloxone:
♦ Nausea or vomiting
♦ Hot sweats
♦ Hallucinations or agitation
♦ Violent behavior

How to Administer Intranasal Naloxone:

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<tbody>
<tr>
<td>Step 1</td>
<td>Step 2</td>
<td>Step 3</td>
<td>Step 4</td>
<td>Step 5</td>
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<tr>
<td>Call 9-1-1</td>
<td>Remove yellow and red caps. Screw together the nasal applicator and the needle-less syringe top.</td>
<td>Screw the naloxone capsule onto the applicator. Refer to diagram for instructions.</td>
<td>Tilt the person’s head back and spray half the medication in one nostril and half the medication in the other nostril.</td>
<td>If the person does not respond or get better within 3 to 5 minutes. Give a second dose.</td>
</tr>
</tbody>
</table>

How to Give Nasal Spray Naloxone:

1. Pull or pry off yellow caps.
2. Pry off red cap.
3. Gently screw capsule of naloxone into barrel of syringe.
4. Insert white cone into nostril; give a short, vigorous push on end of capsule to spray naloxone into nose; one half of the capsule into each nostril.
5. Push to spray.
6. If no reaction in 2-5 minutes, give the second dose.

Image at right from: http://www.familyrecoverspecialists.com/naloxone-emergency-treatment-for-opioid-overdose/

By Valerie Naudett, PharmD Candidate

References on Page 3
Veltassa® (patiromer) is approved for the treatment of hyperkalemia. Patiromer increases the excretion of potassium by binding potassium in the gastrointestinal (GI) tract. Bound potassium is eliminated in the feces and is not systemically absorbed. The anti-absorption effects of patiromer do not occur until approximately 7 hours after ingestion. Therefore, patiromer should not be used to treat life-threatening potassium levels.

Previously, sodium polystyrene sulfonate was the only approved treatment for hyperkalemia. GI adverse drug events, horrible taste, and a possibility of GI necrosis prevent long-term use of sodium polystyrene sulfonate. Furthermore, sodium polystyrene sulfonate may lead to an undesirable sodium load, which is problematic for disease states such as hypertension and heart failure.

Patiromer does not increase sodium levels, so it is a potential long-term solution for patients with hyperkalemia due to medications that inhibit the RAAS system, which are needed to manage common disease states such as hypertension, diabetes, liver failure, and heart failure.

A majority (76%) of patients achieved target serum potassium levels after 4 weeks of treatment with patiromer. Patients in this study had hyperkalemia and chronic kidney disease (CKD) and were taking at least one renin-angiotensin-aldosterone system (RAAS) inhibitor. Participants received either patiromer 8.4 g/day or 16.8 g/day, based on baseline serum potassium. Patiromer doses were titrated to achieve target serum potassium levels for 4 weeks. After 4 weeks, patients with baseline serum potassium levels ≥5.5 mEq/L were randomized to manage potassium levels either by continuing patiromer or by adjusting RAAS inhibitor doses for 8 weeks. More patients who managed their potassium levels with adjustment of RAAS inhibitor therapy had at least one episode of hyperkalemia (60% compared to 15% in the patiromer group; p<0.001).

In patients with diabetes and CKD, patiromer lowered potassium levels within the first week of therapy. In this 52-week study, patients were treated with a RAAS inhibitor with or without spironolactone. Patients received 1 of 3 daily patiromer doses (8.4 g, 16.8 g, or 25.2 g) based on baseline potassium levels. Most patients with mild hyperkalemia and at least 77% of patients with moderate hyperkalemia achieved target potassium levels during the study. Potassium levels increased by the third day after discontinuation of patiromer at the end of the study.

The most common adverse events reported during clinical trials were related to the GI tract. Hypomagnesemia also occurred more frequently with patiromer compared to placebo.

The starting dose of patiromer is 8.4 g (1 packet) once daily. The daily dose should be increased by 8.4 g at ≥1 week intervals to achieve target serum potassium levels. The maximum patiromer dose is 25.2 g (3 packets) once daily. Patiromer should be taken with food, but the powder should not be added to food for administration.

Patiromer binds to oral medications, which may lead to decreased absorption and lack of efficacy. Therefore, patiromer must be administered 6 hours apart from concurrent oral medications.

By Luke Schonsberg, PharmD Candidate

REFERENCES:

Kybella® (deoxycholic acid) for Submental Fat Loss

In April 2015, the FDA approved Kybella® (deoxycholic acid) injection to reduce submental fat (SMF), the fat found beneath the chin.

This treatment provides a non-surgical option for patients looking to lessen unwanted submental fat. Before now, liposuction or a face-lift represented the only efficacious options available. SMF appears in many people, even those with a low BMI, hinting at a genetic link. The body naturally produces deoxycholic acid as a secondary bile salt; Kybella® is a non-human and non-animal form of deoxycholic acid. When injected into submental fat, deoxycholic acid breaks down fat cell membranes and destroys fat cells. The body’s natural inflammatory response then removes the debris. When injected correctly, Kybella® only targets fat cells, and leaves non-adipose tissue alone. Physicians inject Kybella® 0.2 mL subcutaneously 1 cm apart in a grid on the submental fat beneath the chin (see photo to right). Patients may receive a maximum of 50 injections in one treatment, or 10 mL (2 mg) and may have as many as six treatments spaced out by a month. Kybella® comes in a 2mL (10 mg/mL) bottle intended for single patient use.

Researchers conducted a randomized, placebo-controlled study of patients with moderate to severe SMF (n = 360). Patients were randomized into three groups: 1 or 2 mg/cm², or placebo injected in a grid pattern into their submental fat. The study required that patients be dissatisfied with their SMF appearance, have a BMI ≤ 30 kg/m², have no previous SMF treatment, and have no plans to start a weight loss program. Patients received up to four treatments about 1 month apart, then reported 12 weeks later for follow-up. Researchers stopped or delayed treatment for patients with early efficacy, insufficient SMF, or adverse events. Patients included in the study received at least one treatment. 90.6% of participants completed the study, and 81.4% completed all four treatments. At the check-in, 12 weeks after final treatment, 29.3%, 68.3%, and 64.8% of people were satisfied with their appearance of face and chin in the placebo, 1 mg/cm², and 2 mg/cm² groups, respectively. The study also measured SMF with the Clinician-Reported Submental Fat Rating Scale (CR-SMFRS). At the end of the study, patients treated with Kybella® improved by ≥ 1 point (58.3% and 62.3% for 1 and 2 mg/cm², respectively) while 34.5% placebo patients improved the same amount.

The most common treatment-emergent adverse events included burning at injection site, swelling, bruising, and induration. Pain from injection was the most common reason why patients withdrew from the study. The only side effect that did not completely resolve by the 3-month follow-up was a nerve injury from injection in one patient. This patient experienced an asymmetrical smile that eventually resolved without further complications.

While the phase III trial included mostly women (72.0%), the procedure has gained popularity among businessmen hoping to improve their professional appearance. RealSelf, a Web site that allows users to rate cosmetic procedures, gives Kybella® a 100% rating from 56 reviews and cites $1,525 as the average cost. Other sources estimate the total cost to be around $2,000 for the whole treatment.

Overall, Kybella® provides a safe, effective, non-surgical method to remove unwanted submental fat.

REFERENCES:

By Halley Lopez, PharmD Candidate

Nucala® (mepolizumab) for Asthma

Nucala® (mepolizumab) is a newly approved (November 4, 2015) medication for the treatment of severe asthma. The FDA approved mepolizumab for poorly-controlled asthma patients 12 years of age or older. Mepolizumab is approved for use with currently prescribed medications in patients with chronic exacerbations.1,2

Mepolizumab, a humanized monoclonal antibody, decreases eosinophilia via interleukin (IL)-5. IL-5, a key regulator of immunity, attracts and activates eosinophils, which are key players in asthma. Historically classified as an eosinophil colony-stimulating factor, mepolizumab binds to soluble IL-5, blocking its ability to bind and activate eosinophils. The binding site for mepolizumab has been mapped to the region on IL-5 that interacts with its receptor.3

Three major clinical trials were key in the approval of mepolizumab.5-7 The first was a multicenter, double-blind, placebo-controlled trial (DREAM) that evaluated the efficacy of mepolizumab.5 In the DREAM trial, 621 patients were randomized to one of three intravenous mepolizumab doses (75 mg, 250 mg, or 750 mg) or placebo. Patients received study medication every 4 weeks for 13 doses. While all three mepolizumab doses resulted in significant decreases in asthma exacerbations, the 75 mg dose was better than the 250 mg dose (48% vs. 39%) and comparable to 750 mg dose (48% vs. 52%).5 The second study compared the 75 mg IV mepolizumab dose with a 100 mg subcutaneous dose and found comparable reductions in asthma exacerbations (47% and 53%, respectively; p<0.001 for both).6 Finally, the last study assessed the effect of 100 mg subcutaneous mepolizumab on oral glucocorticoid use.7 Not only did oral glucocorticoid use decrease with mepolizumab use, but the asthma exacerbation rate was also reduced by 32% compared to placebo.7

The approved dosing of mepolizumab is 100 mg injected subcutaneously every 4 weeks using a 1 mL polypropylene disposable syringe.2 The drug is administered by a trained professional under direct medical supervision. Injections should be administered in the upper arm, thigh, or abdomen.2

In general, mepolizumab is well-tolerated; however, a few adverse effects were reported with mepolizumab more often than with placebo in the clinical trials. A herpes zoster infection occurred in a few patients, suggesting that varicella vaccination should be given prior to starting mepolizumab, if appropriate.2 In addition, because of the decrease in eosinophils with mepolizumab, there is an increased risk of parasitic (Helminth) infections. Pre-existing Helminth infections should be treated before starting mepolizumab. There is always the potential for immediate or delayed hypersensitivity reactions. Mepolizumab is NOT indicated for treatment of acute asthma symptoms.2

By Chris Migliaccio, PharmD Candidate

REFERENCES: