**Technician Training Tutorial:**
Dispensing Oral Blood Thinners

**Warfarin** (*Coumadin, Jantoven-U.S., others*) is an oral “anticoagulant” blood thinner used to help prevent blood clots that can lead to problems such as heart attacks and strokes. Its name originates from the Wisconsin Alumni Research Foundation (WARF), which funded its development many years ago. Warfarin was actually used in the past as a rat poison and is structurally similar to many pesticides used today. Warfarin and other anticoagulant blood thinners work by blocking part of the thrombin system to prevent clots. This is one of the two parts of the clotting system in the body.

Patients on warfarin are constantly at risk for getting too much or too little of the drug. Pharmacists and technicians need to be extremely careful when dispensing warfarin since too much can increase the risk of fatal bleeding and too little warfarin can result in dangerous blood clots.

Prescribers monitor warfarin response with a laboratory test called an INR (international normalized ratio). INR results show the clotting ability of a patient’s blood, which gives an idea of whether the patient is getting too much or too little warfarin. INR testing is usually done at a lab or doctor’s office every few days or weekly when a patient first starts warfarin. It can be done monthly once a patient is on a stable dose of warfarin.

For a long time, warfarin was the only anticoagulant available that patients could take by mouth. However, in the past few years, several new oral anticoagulant blood thinners have come on the market. These can be used instead of warfarin and include **apixaban** (*Eliquis*), **dabigatran** (*Pradaxa*), and **rivaroxaban** (*Xarelto*). Dosing of these drugs is easier than for warfarin because they don’t require the same lab monitoring.

Other blood thinners are called “antiplatelet” drugs. These reduce the chance that platelets will stick together to form a clot. They’re most often used in situations such as after a patient has had a stent placed in his or her heart. Like warfarin is the hallmark anticoagulant, **aspirin** is the hallmark antiplatelet drug. Older antiplatelet agents include **cilostazol** (*Pletal-U.S. only*), **clopidogrel** (*Plavix*), **dipyridamole** (*Persantine, etc*), and **ticlopidine** (*Ticlid*). New antiplatelet drugs that have hit the market in the past few years include **prasugrel** (*Effient*) and **ticagrelor** (*Brilinta*).

Anticoagulants are more likely to cause bleeding than antiplatelets. In fact, anticoagulant blood thinners are actually considered high-alert medications, meaning errors with these meds are especially likely to lead to serious patient harm. Pharmacy technicians play an important role in making sure prescriptions for blood thinners are dispensed correctly.

*Mrs. Smith is a 79-year-old patient in your pharmacy. She has been a pharmacy customer for several years. She does not take many prescription medications, but she often purchases over-the-counter products. She presents with the following prescription for Coumadin 4 mg, one tablet, once daily.*
As Mrs. Smith hands you the prescription, you notice she is holding a bottle of garlic tablets and a bottle of generic ibuprofen that she wishes to purchase. Mrs. Smith likes to chat, and mentions that she just came from the local farmers’ market, where she purchased broccoli and Swiss chard.

What information should you ask for when a patient drops off an Rx for a blood thinner?

Some information such as allergies, date of birth, and address are commonly requested when patients drop off any prescription. Additional details can be helpful for patients taking blood thinners to identify those that may be at risk for bleeding or other problems.

For example, many common medications including antibiotics, thyroid hormones, medications for ulcers or heartburn, and cholesterol medications can interact with warfarin. Some of these medications make patients taking warfarin more likely to bleed. Others decrease warfarin’s effectiveness, making patients more likely to have a clot. There are also drug-drug interactions that can affect the new blood thinners. For example, the doses of apixaban and dabigatran must be reduced if a patient is taking ketoconazole, since ketoconazole can drastically increase their blood levels. And rivaroxaban should not be used with ketoconazole at all.

Rx and OTC nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and naproxen can increase the risk of bleeding with blood thinning meds. However, sometimes patients with certain conditions will actually take two antiplatelet drugs at the same time (dual antiplatelet therapy), such as aspirin plus clopidogrel, to get better effects.

Dietary supplements can also interact with blood thinners. Garlic might increase the risk of bleeding, especially when used with blood thinners.

Dietary factors can affect warfarin specifically. High protein diets (e.g., Atkins, South Beach) and foods high in vitamin K (mainly in dark green vegetables) can decrease warfarin’s effectiveness. Vitamin K may also be found in multivitamins, green tea, and soy products. Alcohol intake may also increase or decrease warfarin’s effects.

Ask patients presenting with a new or refill prescription for blood thinners if they take any dietary supplements or over-the-counter medications, follow any special diet, or take any prescription medications other than the ones they get at your pharmacy (e.g., samples from the prescriber or mail order prescriptions). Update patient profiles and provide this information to the pharmacist so he or she can screen for drug interactions and appropriately counsel the patient.

What should be considered when entering a prescription for a blood thinner into the computer?

Avoiding look-alike, sound-alike errors. Warfarin is available in nine different strengths, ranging from 1 mg to 10 mg. Some strengths can be easily confused with other similarly named medications. For example, prescriptions similar to the one shown above have been mistakenly confused and filled for “Avandia 4 mg” instead of “Coumadin 4 mg.” Be sure to clarify if you are unsure if a prescription is written for warfarin or a medication with a similar name. Asking the patient why he or she is taking the medicine can help. Using warfarin in a patient that does not need to take it can lead to toxicity or a fatal bleeding reaction.

Consider other look-alike sound-alike drug names, such as Pradaxa/Plavix and Plavix/Paxil.

Dosing and instructions. Watch out for decimal points and trailing zeros with warfarin prescriptions. A dose written for “1.0 mg” could easily be mistaken for “10 mg” and lead to a ten-fold overdose. In fact, it’s always a good idea to carefully examine any warfarin prescription written for more than 9 mg. Doses higher than 9 mg of warfarin are unusual and may result in serious bleeding if taken in error.
As mentioned, warfarin doses are often individualized and may change frequently so that prescribers can achieve a specific goal INR level to make sure it is working correctly. It is not uncommon for warfarin prescriptions to have complex instructions such as “Take one tablet on Monday, Wednesday, and Friday. Take one-half tablet on Tuesday, Thursday, Saturday, and Sunday.” These specific instructions allow prescribers to make dose changes in small increments without requiring the patient to get a new strength of the medication from the pharmacy. Alternatively, a prescriber may write the prescription instructions as “Use as directed,” allowing changes to be communicated directly to the patient without requiring a new prescription to be filled each time a dose change is made. However, this practice may not be allowed by some insurers and is generally frowned upon.

Pay special attention when entering dosing instructions for warfarin prescriptions into the computer. Make sure the prescription label reads exactly as it is written on the prescription. Additional label space may be required for detailed instructions.

Days’ supply. If a prescription for warfarin is written with instructions to “use as directed,” ask the patient how their doctor advised them to take warfarin. This information will allow you to estimate an accurate days’ supply for insurance purposes. Alert the pharmacist if the patient is unclear about the exact instructions so the prescriber can be contacted if needed to clarify the directions.

Apixaban, dabigatran (in Canada), and rivaroxaban are indicated to prevent clots after hip or knee replacements. Patients might only get short courses of these drugs with no refills such as 35 days’ worth of rivaroxaban for a hip replacement or 12 (U.S.) to 14 (Canada) days’ worth of rivaroxaban for a knee replacement.

Duplicate therapies. Patients may switch from warfarin to one of the new anticoagulants, or from one of the new anticoagulants to warfarin. Two of these anticoagulants should not be taken at the same time because this duplication could increase the risk of bleeding. Let the pharmacist know if you are not clear on which drug a patient should be taking. Make sure and zero out any refills remaining for the discontinued drug.

As mentioned, some patients will take two antiplatelets at the same time, or you may see an anticoagulant given with an antiplatelet. The most common combination is aspirin plus clopidogrel. Prasugrel and ticagrelor are actually indicated to be given in combination with aspirin. If you’re not sure, double check with the pharmacist to find out whether duplicate therapies with blood thinners are appropriate.

Generic substitution. There has been some controversy in the past about the use of generic forms of warfarin instead of the brand product. This stems from potential toxicities with warfarin and the concern that subtle product differences between brand and generic forms might mean big changes in effect or adverse events.

Generic warfarin is now commonly used in place of brand products. However, some prescribers may still prefer patients to start or remain on a brand warfarin product. Keep a close eye out for warfarin prescriptions marked as “Brand only,” “Do not substitute,” or “Dispense as written.” In these cases, the prescriber is indicating that the patient should receive a specific brand of warfarin. The appropriate product should be selected in the inventory list when entering the prescription into the computer and the DAW code changed if needed. DAW codes are a nationally recognized code set in the U.S. that is transmitted with the pharmacy claim to the insurance provider.

For the newer blood thinners, only brand name products are available.
Drug interaction alerts. It’s important to alert the pharmacist to any drug interaction warnings that come up for patients taking blood thinners. Computer generated drug interaction alerts are especially common when entering warfarin prescriptions because of the high number of potential drug interactions. You may encounter an alert when you are entering a prescription for a blood thinner OR entering another medication for a patient who is also taking a blood thinner. This is especially important if the interacting drugs are prescribed by two different physicians, since a prescriber may not be aware of medications a patient is taking from another prescriber. The pharmacist may need to discuss any potential interaction with the patient or contact the appropriate prescriber.

What should be considered when selecting a blood thinner from the shelf? Warfarin products are especially prone to mix-ups since there are so many different strengths. These are usually stored close to each other on pharmacy shelves, with at least one bottle of each of the nine strengths in both a brand and generic form kept in stock. Some doses are easily confused, for example, 1 mg and 10 mg or 2 mg and 2.5 mg. The bottles of different strengths also look similar, which can add to the potential for error.

To avoid a mix-up, make sure to pay close attention when you are pulling a warfarin product from the shelf to fill a prescription. Do not store the 1 mg and 10 mg strengths right next to each other. Instead store products in the order of increasing or decreasing strength to space 1 mg and 10 mg strengths as far apart as possible to help decrease the chance of a mix-up. It may also be helpful to write “1” and “10” with a marker directly on the bottle to indicate the strength. This written note will serve as an additional reminder to pharmacy staff and pharmacists of the warfarin strength when the bottles are pulled for filling a prescription. Make a habit of checking the strength indicated on the prescription and the label against the actual tablet when filling warfarin prescriptions. The strength in mg is indicated by a number on the tablet to help avoid errors. For example, warfarin 4 mg tabs have a large “4” on the tablet. Verify the NDC number or DIN on the label against the stock bottle as another double check.

It’s also a good idea to become familiar with the different colors of warfarin tablets. Each strength is supplied in a different color to help avoid potential errors. For example, Coumadin 1 mg and its generics are a bright pink color and Coumadin 10 mg and its generics are plain white. This coloring system can also help patients identify a potential error if they notice their tablet looks different than the one they have received in the past.

What auxiliary labels should be added to prescriptions for blood thinners? Check with your pharmacist about manually adding a sticker to prescriptions for blood thinners stating, “Do not take aspirin without the consent of your physician,” or a similar message if this does not automatically print on the prescription label. Although aspirin may occasionally be used with other blood thinners, it can also increase the risk of serious bleeding in some patients.

Apply a “take with food” label to rivaroxaban 15 mg and 20 mg strengths, since food helps improve absorption of the drug. Rivaroxaban 10 mg can be taken without regard to meals since its absorption is not affected by food.

In the U.S., remember to dispense a MedGuide with the following blood thinners: apixaban, clopidogrel, dabigatran, prasugrel, rivaroxaban, ticagrelor, and warfarin. Dabigatran, prasugrel, and ticagrelor must be dispensed and kept in their original containers to protect the drugs from moisture. The tablets should not be placed in other containers such as pillboxes. In the U.S., apply an auxiliary label to prescription bottles of dabigatran to let patients know to discard any remaining drug after the container has been opened for four months. In Canada, dabigatran is currently only available in blister packs.
Since warfarin is a new med for Mrs. Smith, the pharmacist takes some time to talk with her. She notices that Mrs. Smith is purchasing garlic and ibuprofen. She explains that both of these agents may increase the risk for bleeding in patients taking warfarin. The pharmacist suggests alternatives that will not increase the risk for bleeding, and Mrs. Smith agrees to try them. The pharmacist also reminds Mrs. Smith that it is important to keep her diet fairly consistent while she is taking warfarin.

**When should the pharmacist be alerted to a potential problem with a prescription for a blood thinner?**

Because of the potential for serious bleeding with blood thinners, pharmacists should be notified of any computer alerts such as drug-drug or drug-disease interactions that come up when entering these prescriptions. In addition, let pharmacists know about any patient reports of changes in diet, OTC medication, dietary supplements, etc. It is also helpful to make a note on the prescription and in the computer if patients report any significant changes in diet or alcohol intake; or any new prescriptions, OTC medicines, or herbal supplements.

Let the pharmacist know if you see a patient is getting late refills of any blood thinner. Late refills could signal a problem with adherence. Adherence to blood thinner regimens is very important, but patients must stick especially closely with their regimens of apixaban, dabigatran, or rivaroxaban. Skipping even a dose or two of these drugs can increase the risk for stroke in some patients. Manufacturers of these drugs will provide phone or email reminders to help patients stay on track. They may also provide assistance programs for patients who skip doses because they have trouble affording these meds. For example, apixaban has the Eliquis 360 Support, dabigatran has The New Housecall, and rivaroxaban has the Xarelto CarePath Support Program. Eligible patients will pay as little as $10/month for their Rx.

*Mrs. Smith presents to the pharmacy in three weeks with another prescription, this time for Coumadin 1 mg, one tablet, once daily.*

You notice that her prescription is written with a “trailing zero.” This prescription could be confused for 10 mg instead of 1 mg, resulting in a big overdose.

Since this is a new dose for Mrs. Smith, you let the pharmacist know. She thanks you and says that she will speak with Mrs. Smith. A few minutes later, you hear the pharmacist explaining the dose change to Mrs. Smith, and answering questions Mrs. Smith has about how her diet will affect her blood thinner.