Technician Training Tutorial:  
Safety Considerations with Opioids

Opioids as a drug class are considered to be high-alert drugs. This class includes codeine, methadone, oxycodone, etc. When a medication error involving an opioid occurs, the chance that the patient will be seriously harmed is generally higher than when an error occurs with a non-opioid drug. There is also a risk of serious harm when patients abuse or misuse opioids. Patients who take doses of opioids that are too high may experience a reduced level of alertness, increased sedation, and respiratory depression. This means that the patient’s breathing becomes slow, and he or she does not take in enough oxygen. The result can be death. In fact, deaths from opioid overdoses have tripled in the past 20 years. This Technician Training Tutorial provides important information to help you improve patient safety with opioids.

Mary Jones is a 55-year-old female patient. You know she has had multiple surgeries recently and can’t swallow any type of tablet or capsule. Her husband Ed comes in with her new Rx for liquid morphine. You tell him the wait will be about 30 minutes, and he says, “no problem.” He needed to grab a few items from the store anyway.

What types of problems can happen with prescriptions for opioids?

Drug allergies. Allergies to opioids are common. Plus, some opioids such as codeine and morphine cause reactions that mimic allergies (i.e., they cause the release of a substance in the body called histamine, which can lead to skin reactions such as flushing, itching, and hives). Opioids can also cause upset stomach, nausea, vomiting, etc., which a patient might report as an allergy, but are really side effects or intolerance.

If a patient reports an allergy to codeine, morphine, oxycodone, etc., ask about the specific reaction. Double-check with the pharmacist to find out if the reaction should be entered into the computer system as an allergy, or just noted as an intolerance. You don’t want a patient to get a drug that he or she is allergic to, but you also don’t want a drug to be unnecessarily avoided if it would truly help the patient without causing any serious problems.

Drug interactions. There are a number of important drug interactions with opioids. Methadone (Dolophine, Methadose [U.S.], Metadol [Canada]) is a good example to consider because it interacts with a lot of medications. If a patient takes other drugs that cause sedation, such as alprazolam (Xanax), diazepam (Valium), or even alcohol, this can increase the risk for respiratory depression with methadone. Drugs such as amiodarone (Cordarone, etc) and erythromycin, when taken with methadone, can increase the risk for dangerous irregular heartbeats. Certain drugs such as fluoxetine (Prozac, etc), fluvoxamine, and fluconazole (Diflucan, etc) can slow the elimination of methadone from the body. This can cause a buildup of methadone, which could lead to oversedation, slow breathing, etc.

The “black box” warning in the U.S. labeling for OxyContin (oxycodone) points out similar types of drug interactions for oxycodone. When a drug such as clarithromycin (Biaxin), ketoconazole (Nizoral), or ritonavir (Norvir, etc) is used by a patient who is also taking oxycodone, blood levels of oxycodone can increase and cause severe adverse effects. Other opioids that might be affected by these types of drug interactions include fentanyl (Duragesic, etc), hydrocodone (Lortab, etc [U.S.], Hycodan, etc [Canada]), and tramadol (Ultram, etc [U.S.], Ralivia, etc [Canada]).
If you get a drug interaction alert with an opioid, don’t bypass it. Make sure to let the pharmacist know, because these interactions can lead to very serious problems.

**Doses that are too high.** Since opioids can cause serious side effects like sedation and slow breathing, it’s important that patients who have not taken an opioid recently are started out on a relatively low dose. This way, they can build up tolerance to the side effects as the dose is increased to give them good control of their pain. When patients are started out on doses that are too high, there’s a chance that they will become too sedated and stop breathing. Some examples of starting doses in adults include Avinza (U.S.) 30 mg once daily, OxyContin (U.S.) 10 mg Q12H, and Opana ER (U.S.) 5 mg Q12H.

**Improper dosing interval.** Many opioids come in a controlled-release (long-acting) form. Some examples include the morphine formulations Avinza (U.S.), Kadian, and MS Contin, and the oxycodone formulation OxyContin. These are usually given either once daily or twice daily. If you see one of these formulations dosed more frequently, such as Q6H, Q4H, or PRN, alert the pharmacist. This could be an error, and could put the patient at risk for an overdose.

**Inappropriate use of certain drugs and/or dosage forms.** Some opioids are very potent, meaning that a very small dose can have very strong effects. These potent opioids should not be used in patients who have not been using opioids previously. An example of an opioid that should not be used in patients who have not been taking opioids already is fentanyl (all dosage forms). There’s a high risk that a patient who hasn’t built up tolerance to the side effects of opioids could become oversedated and have breathing problems. For outpatients who may not have someone around to check on them this is very dangerous. However, this isn’t necessarily applicable in the hospital, where patients are under close supervision.

Starting a patient out with an immediate-release (short-acting) opioid instead of a long-acting form is best. Starting with a short-acting opioid makes it easier and safer to find the appropriate dose that will control the patient’s pain. MS Contin, for example, is only recommended for patients who have already been on a short-acting opioid. The same is true for Exalgo (U.S.), a controlled-release form of hydromorphone.

The FDA is pushing for new labeling for long-acting opioids. This will include a warning saying that these products should only be used when options such as non-opioids or short-acting opioids don’t provide adequate pain relief.

**Multiple prescriptions with the same or similar ingredient.** Patients will often be prescribed more than one opioid formulation. When this is the case, there will usually be an Rx with a maintenance dose that is given around-the-clock, such as OxyContin 40 mg Q12H. There might also be an Rx for PRN use, for when the patient has breakthrough pain (i.e., pain that occurs before the next scheduled maintenance dose is due). An example of this would be oxycodone immediate-release 10 mg Q4H PRN. However, it is important to watch for inappropriate duplications from multiple products with the same or similar ingredients. If you get a “refill too soon” or “therapeutic duplication” flag with an opioid, let the pharmacist know. He or she may need to put in an override for patients who are getting more than one dosage form appropriately. Or the pharmacist may need to address an actual duplication that is not appropriate.

In the hospital, it’s also important to keep an eye out for opioids being given by different routes. For example, if a patient is getting an epidural infusion that contains an opioid such as fentanyl, or an intravenous infusion of an opioid such as morphine or hydromorphone, alert the pharmacist if you see additional orders for intravenous or oral opioids so that he or she can double-check the appropriateness of the orders.

A lot of opioids come in combinations with acetaminophen, such as Lortab (U.S.), Percocet, Tylenol #3, etc. It’s a good idea to make sure patients aren’t getting too much acetaminophen from these products, or from multiple sources of acetaminophen. In the U.S., the amount of acetaminophen per dosage unit (e.g., capsule, tablet) in prescription combo products is now capped at 325 mg. Most adult patients shouldn’t get more...
than 4000 mg of acetaminophen per day. Alert the pharmacist if you notice an Rx where a patient could potentially get more than 4000 mg of acetaminophen per day.

**Questionable prescriptions.** As mentioned, deaths from opioid overdoses have tripled in the past two decades. This is in part due to misuse of opioids, such as diversion. It’s important to watch for red flags that might indicate a prescription is inappropriate. However, it’s also important to keep in mind that many patients do use opioids appropriately to control pain, and that red flags aren’t absolute indicators of inappropriate prescriptions. Let the pharmacist know if you see any of the following red flags, so he or she can investigate further.

- Patients who ask to pay cash for controlled substances
- Patients who demand certain brands
- Patients with frequent prescriptions or prescriptions with large quantities
- Patients who aren’t local, or bring in prescriptions from prescribers who aren’t local
- Patients who are doctor or pharmacy shoppers
- Prescriptions that are incomplete
- Prescriptions that could potentially be altered or forged (e.g., different inks or handwriting used, a “too perfect” appearance, etc)

The pharmacist will likely take steps such as contacting the prescriber, checking your state’s prescription drug monitoring program (or provincial prescription or narcotic monitoring system in Canada), asking for the patient’s identification, validating the prescriber’s DEA number (or license number in Canada), etc. Remember to be discreet when these situations occur. You don’t want to make a patient who has a legitimate Rx for a legitimate reason feel embarrassed or self-conscious.

*You notice Mrs. Jones got an Rx for Percocet last month. However, she has been in the hospital for a couple of weeks, and the Rx for Percocet was entered into the computer far back enough so that you don’t get any type of flag for refilling too soon.*

**Are there special safety considerations when entering prescriptions for opioids into the computer system?**

Choose the right drug and dosage form. Be very careful when you select a drug on the computer screen. There are a number of look-alike, sound-alikes, such as oxymorphone and oxycodone, hydromorphone and hydrocodone, etc. Plus, as mentioned before, many opioids come in both an immediate-release and a controlled-release form, such as oxycodone immediate-release and OxyContin or Opana and Opana ER. It’s easy for mix-ups to happen. Pay special attention to prevent them.

Choose the right dose. This is especially applicable for liquid dosage forms. Some opioids, such as morphine oral liquid, come in different concentrations. Morphine oral liquid is available as 20 mg/5 mL, 10 mg/5 mL, and 20 mg/mL concentrations in the U.S. In Canada, it comes in even more strengths, and as high as 50 mg/mL. Methadone oral liquid comes as 1 mg/mL, 2 mg/mL (U.S. only), and 10 mg/mL. Mix-ups with these could lead to serious patient harm. Watch for confusion between mg and mL. If the dose is given in mL on an Rx, make sure the Rx also notes the concentration that you need to dispense. If not, ask the pharmacist to get clarification. If the handwriting on an Rx makes it hard to tell if the dose is given in mg or in mL, also have the pharmacist clarify. (Hopefully, with the new U.S. law allowing e-prescribing of controlled drugs, these problems will become less common.)

Note that in the U.S., fentanyl patches are now required to have the name of the product and the strength written on the patch in long-lasting ink, in a color that is clearly visible, to prevent accidental exposure to these products. This is being considered in Canada as well.
As you are entering Mrs. Jones’s Rx, you look for the morphine liquid in the computer system. You notice that there is both a 20 mg/5 mL concentration and a 20 mg/mL concentration. From the Rx, it’s not clear which one you should choose. Does the prescriber want each dose to be 20 mg, which would be 5 mL of the 20 mg/5 mL solution? Or does he want each dose to be 5 mL of the 20 mg/mL solution, which would be 100 mg per dose? You ask the pharmacist if he could clarify it for you. He calls the prescriber to double-check on Mrs. Jones’s dose.

As it turns out, the prescriber wanted Mrs. Jones to have 20 mg per dose, so the correct concentration to be dispensed is 20 mg/5 mL. You consider that if you had chosen the more concentrated formulation, Mrs. Jones would have gotten five times more morphine than she was intended to take.

Are there special considerations when filling prescriptions for opioids?

Counting and documentation. Most opioid drugs are classified as Schedule II controlled substances in the U.S. The role of the technician in preparing prescriptions for opioids may vary depending on the practice and the supervising pharmacist. Some pharmacists prefer to personally count and verify these prescriptions to ensure that they can account for each tablet, capsule, etc. In other practices, pharmacists ask technicians to pull the drug from the shelf and perform a first count, while the pharmacist double counts the technician and personally records the amount of drug dispensed in a logbook. Check with your pharmacist if you are unsure about your role in handling controlled substances in your pharmacy.

As you can see, this Technician Training Tutorial mainly focuses on patient safety considerations with opioids. We have another Technician Training Tutorial with info on the U.S. legal requirements for dispensing scheduled drugs (e.g., refills, days’ supply, etc) and tips such as how to check a DEA number. It’s called Scheduled Drugs.

Are there special considerations when labeling opioid prescriptions or other information that can be provided to help improve patient safety?

Clear directions for use. Make sure the directions for use are very clear on the Rx label, so the patient doesn’t get confused and take too much or too little of the drug. Provide a dosing cup or oral syringe with liquids to help patients measure an accurate dose. Some liquid meds, such as the morphine oral liquid made by Roxane in the U.S., come with their own oral syringes. There are instructions for using these in Roxane’s MedGuide.

Auxiliary labels. Always include a label to let the patient know that his or her Rx can cause sedation. If possible, a warning to avoid drinking alcohol should also be included. Alcohol can increase the risk for sedation with opioids, but it can also cause dangerously high blood levels of some controlled-release opioids, such as Avinza, Embeda (U.S.), and Opana ER. Also, be sure to include a label warning that the drug must be kept out of reach of children.

In the hospital, you’ll want to make sure that opioids have labels showing that they are high-alert drugs. Do this according to your pharmacy’s policy.

Safekeeping of drugs. Believe it or not, patients who take opioids are at high risk of having them stolen, even by family members or friends. It’s a good idea for patients to keep these prescriptions in a safe (and childproof) place, and not to advertise to others that they are taking these meds. It is unfortunate, but opioids are worth a lot of money on the street, which might make them a tempting item to an individual with less than honorable intentions.

Disposal. Proper disposal of opioids is very important for keeping them away from children and pets. The best option is for the patient to bring these to a take-back program. Otherwise, it’s generally best not to put these types of meds in household trash and to flush them down the toilet instead. (Note that flushing of
meds is not recommended by Health Canada. In Canada take-back programs are more readily available. However, product labeling for some opioids in Canada [e.g., Duragesic MAT] does recommend disposal by flushing.) A discarded fentanyl patch, for example, might still contain enough drug to seriously harm or even cause the death of a child or small animal. When fentanyl patches are discarded, they should be folded in half, so the sticky side sticks together, and then flushed down the toilet. A partially used dose of Actiq (oral transmucosal fentanyl citrate [U.S.]) might recommend disposal by flushing. A discarded fentanyl patch, for example, might still contain enough drug to seriously harm or even cause the death of a child or small animal. When fentanyl patches are discarded, they should be folded in half, so the sticky side sticks together, and then flushed down the toilet. A partially used dose of Actiq (oral transmucosal fentanyl citrate [U.S.]) might look like a lollipop, which could be tempting for children. These should be run under warm water until the drug is completely dissolved, and then the empty plastic stick should be thrown in the garbage, out of reach of children and pets. We have a handout for U.S. patients with more information, Medication Disposal Guide.

MedGuides (U.S. only). Not all opioids have MedGuides, but some do. These can provide patients with important information about safety risks with opioids, such as how to use the drugs and signs of dangerous side effects.

Opioids that have MedGuides include Actiq, Duragesic, Embeda, Exalgo, Fentora, morphine oral solutions, and OxyContin. Opioids that are combined with an NSAID like ibuprofen (e.g., Combunox) also require a MedGuide. You can access these, and any other available MedGuides, on our website, Drug Products with Medication Guides. Remember that for outpatients, these MedGuides must be dispensed the first time you fill an Rx and with every refill as well.

The pharmacist places the correct amount of morphine 20 mg/5 mL solution into an amber bottle. You apply the Rx label, and also add an auxiliary label stating that the medication may cause drowsiness, and to keep out of reach of children. For good measure, you double-check that the cap is a childproof one. You print out the MedGuide for morphine oral solution, and also place an oral syringe with the Rx, which is ready to be checked by the pharmacist.