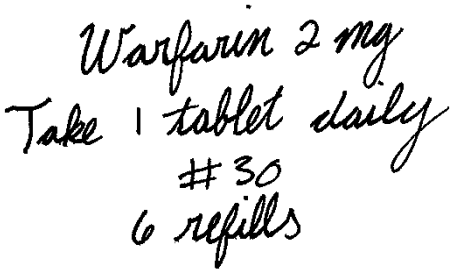
Technician Tutorial*:*
Safety Considerations With OTC Drugs

Over-the-counter medications (OTCs) are available without a prescription. When used according to the instructions on the label, OTCs can be used safely by most patients. However, some patients might be at risk for harm if they aren't given proper instructions. More specifically, some risks associated with OTCs include:

- Adverse events, including overdose
- Drug-disease interactions
- Drug-drug interactions
- Incorrect self-diagnosis
- Potential misuse and abuse of certain drugs

The number of OTC medications available has been increasing over the years. Year after year we see drugs that were once available with a prescription switching to be available over the counter. This is referred to as "Rx-to-OTC switch." For example, in the U.S., more than 700 products sold over the counter today use ingredients or dosage strengths only available by an Rx 30 years ago. One example of an Rx-to-OTC switch is the proton pump inhibitor omeprazole. This drug, which was once Rx-only, is now available over the counter in the U.S. (*Prilosec OTC*) and Canada (*Olex*). Another example is the steroid nasal spray for seasonal allergies, *Flonase* (fluticasone). This drug is now available over the counter in the U.S. and recently gained approval for an Rx-to-OTC switch in Canada. There have been talks for the past few years about making statins (cholesterol-lowering meds) and oral contraceptives available over the counter. While both drug classes are still Rx-only in both the U.S. and Canada, don't be surprised if you see changes in the future.

Technicians are on the front-lines of OTC medication purchasing. When helping patients at the pharmacy register, you likely often observe patients picking up prescriptions and buying OTC meds at the same time. By being aware of potential issues with OTCs, you can help pharmacists improve patient safety with OTC medications.



Mr. Allen is a 66-year-old patient who has been taking warfarin 2 mg once daily for the past 2 years. He takes warfarin to prevent blood clots due to his abnormal heart rhythm condition known as atrial fibrillation. He has run out of refills so he is at the pharmacy today to drop off this new prescription. He sounds very congested and sneezes several times while you chat. He tells you he thinks he is getting a cold. It's really busy in the pharmacy and Mr. Allen isn't in a rush to get his prescription. After you gather all of the information you need from him to make sure his profile is up-to-date, Mr. Allen leaves the pharmacy and promises to be back later.

Who determines if a drug can be made available without a prescription?

In the U.S., the FDA determines whether a drug can be available by prescription or if it could be sold over the counter. OTC drugs can either be Rx-to-OTC switches or they could be direct to OTC products. In both scenarios, applications for OTC drug approval must be submitted to the FDA. Manufacturers must provide studies that show the drug is safe and effective and that it can be used for self-care safely using the labeled instructions. In the case of generic OTCs, since the chemical entity has already been approved as an OTC, the manufacturer does not need to submit an application for approval. However, the manufacturer will need to label the product according to the approved OTC drug monograph on file with the FDA. FDA-approved OTC drug monographs typically list acceptable ingredients and required labeling information. For example, assume a company wanted to make an ibuprofen product. They wouldn't need to submit an application for approval since ibuprofen has already been approved as an OTC drug. However, the manufacturer would have to include required labeling information as outlined in ibuprofen's drug monograph on file with the FDA.

In Canada, Health Canada determines if a drug can be made available without a prescription. However, it's up to the individual provinces and territories to determine the conditions of sale of nonprescription drugs. Most provinces and territories determine the conditions of sale of OTC drugs based on recommendations made by the National Association of Pharmacy Regulatory Authorities (NAPRA). NAPRA recommends that products either be unscheduled (no restrictions) or that they be placed on one of three schedules (I, II, III), each reflecting a different level of restriction. Descriptions for the different levels are provided below:

- Schedule I – drugs that require a prescription for sale
- Schedule II – drugs that don't require a prescription, but do require pharmacist intervention; these drugs are to be kept away from public access within the pharmacy. Patients should not have the opportunity to self-select these products. Examples include omeprazole, loperamide (*Imodium*) marketed for pediatric use, insulin, and fluticasone nasal spray in a package size containing more than 120 metered sprays.
- Schedule III – drugs that don't require a prescription but can be risky in certain populations when used for self-care. These drugs must be placed in a "self-care" section of the pharmacy that is directly supervised by a pharmacist. Examples include cetirizine (*Zyrtec* [U.S.], *Reactine* [Canada]) marketed for pediatric use, acetaminophen in sustained-release formulations, and fluticasone nasal spray in a package size containing **no more** than 120 metered sprays.
- Unscheduled – nonprescription drugs that can be sold without professional supervision. Examples include loperamide marketed for adult use, cetirizine marketed for adult use, and acetaminophen in immediate-release formulations.

Unlike Canada, the U.S. doesn't have a formal system of classification for nonprescription drug sale restrictions. However, there are some restrictions for the sale of certain nonprescription drugs. For example, pseudoephedrine (*Sudafed*, etc) and ephedrine-containing products (*Bronkaid* [U.S.], etc) must be kept away from public access. These drugs must be kept behind the pharmacy counter and customers must present a valid ID to purchase them. There are quantity limits for what a person can buy in one day and in a 30-day period. There are also several documentation requirements. To learn more about these restrictions and requirements, review our CE, *Combating Methamphetamine Abuse*. Some states allow the nonprescription sale of codeine-containing cough syrups with no more than 200 mg of codeine per 100 mL. However, since this is a controlled substance, these products must be sold by the pharmacist, so they are also kept behind the counter. Similarly, in Canada there are certain codeine preparations which are exempted from the Controlled Drugs and Substances Act. Exempted codeine preparations include products containing codeine up to 8 mg per solid oral dosage form or 20 mg/30 mL of liquid, and two or more active non-narcotic ingredients (e.g., *Mersyndol*, *Robaxacet-8*, *Tylenol No. 1*). These drugs are considered "Schedule II" by NAPRA.

Keep in mind that in both the U.S. and Canada, dietary supplements such as herbal supplements, vitamins, minerals, and other nonprescription natural medicines aren't required to go through the same approval process as OTC drugs. They also aren't required to have the same type of labeling that will be described in the next section. Natural medicines only need to follow good manufacturing practices and follow restrictions to making truthful health claims on the label. For more information on dietary supplements, check out our clinical resource, *Tips for Dietary Supplement Users*.

How can I help patients navigate an OTC drug label?

The OTC drug label contains important information for patients to use the drug safely. Help patients navigate the OTC drug label by understanding the information it includes. In the U.S., the FDA requires manufacturers of OTC products to print what's called a "Drug Facts" label on the product packaging. The Drug Facts label must include:

- Active ingredient(s) and their purpose – this must include the amount of active ingredient per unit and the product category (such as antihistamine, antacid, cough suppressant, etc)
- Uses – symptoms or diseases the drug will treat or prevent
- Warnings – this is a very important section for safe medication use. It includes:
    - When the drug shouldn't be used
    - Conditions that may require advice from a healthcare provider before using the product
    - Drug interactions
    - Side effects
    - When to stop taking the drug and contact a healthcare provider
    - Pregnancy or breastfeeding precautions and guidance
    - Keeping the product out of children's reach
- Directions – for each age category this section includes how much drug to take, how to take it, how often to take it, and the maximum amount that can be taken in a day
- Other information – how to store the medication properly; depending on the product contents there may also be information required by the FDA on the amount of calcium, potassium, or sodium in the product. Since not all products contain these ingredients, this information will not appear on all OTCs.
- Inactive ingredients – substances such as colors, flavors, binders, etc. Use this section to help patients with allergies to dyes, foods, preservatives, etc.

FDA has an example you can use to familiarize yourself with the different sections of the Drug Facts label – http://www.fda.gov/drugs/resourcesforyou/consumers/ucm143551.htm.

Similarly, Canada recently published guidelines for a "Drug Facts" table which will include required key elements to be displayed in a standard format on the OTC drug label. Information that must be included are the brand and generic name, strength, dosage form, route of administration, warnings, population the drug is to be used in, and storage instructions. You can view examples of what these tables should look like here – http://www.hc-sc.gc.ca/dhp-mps/pubs/medeff/_guide/2016-label-package-practices-pratiques-etiquetage-emballage-non/index-eng.php#a2.4.4. Manufacturers bringing new products to the market will have to begin complying with these guidelines starting on June 13, 2017. Manufacturers with products already on the market will be required to comply with these guidelines by June 30, 2019.

When helping a patient who is purchasing an OTC med, advise them to make sure to review the warnings and directions sections before using it. Ask them if they have any questions for the pharmacist. Be on the lookout for multi-symptom products or patients purchasing multiple drugs for the same illness. For example, assume you are ringing up a patient who is purchasing three different cough and cold products. You should double check the active ingredients to make sure there isn't any ingredient duplication.

Overdoses can be a problem if patients don't pay attention to products that have the same ingredients, but different brand names. Be aware that OTC brand-name extensions can cause additional confusion and patient harm. To capitalize on name recognition and product loyalty, the manufacturer of a commonly recognized brand may market additional products using the same brand name, but with different ingredients and possibly a different indication. For example, *Advil PM* (U.S.) and *Advil Nighttime* (Canada) contain both ibuprofen and diphenhydramine. Patients may not realize that a product with *Advil* in the name would contain the same ingredient as *Benadryl* (diphenhydramine). If a patient also takes *Benadryl* at the same time for cold symptoms, they may end up taking too much diphenhydramine. Too much diphenhydramine can cause excessive drowsiness, dizziness, headache, etc. Checking the active ingredients on the label and encouraging patients to do so is very important.

A few hours later you are now helping patients who are picking up prescriptions. Mr. Allen shows up to pick up his warfarin prescription. He also has a couple boxes of OTC meds to start treating his cold, including ibuprofen and Benadryl *(diphenhydramine). You double check to make sure there aren't any extra, unexpected ingredients in these products by checking the "Active Ingredient" section of the Drug Facts. You ask Mr. Allen if he has taken any of these medications before and he says he usually takes acetaminophen for regular headaches but he ran out and he thought he would try something different for the sinus headache he has. He doesn't usually take* Benadryl *but he thinks he may have had it in the past. You remind Mr. Allen to read over the instructions and warnings on the label very carefully. He says he will and also asks if he could get a box of* Sudafed *(pseudoephedrine) too.*

What drug interactions should I be on the lookout for with OTC meds?

OTCs can be a concern for drug interactions. Be on the lookout for patients purchasing aspirin or NSAIDs (ibuprofen, naproxen, etc) and taking them with anticoagulants (warfarin, rivaroxaban [*Xarelto*], dabigatran (*Pradaxa*), etc) or antiplatelets (prasugrel [*Effient*], clopidogrel [*Plavix*], etc). Using aspirin or an NSAID can increase the risk of bleeding in patients taking anticoagulants and antiplatelets. But in some cases it may be appropriate for patients to be taking aspirin with one of these other blood thinners. The pharmacist can confirm if this is appropriate. NSAIDs can also increase the risk of bleeding in patients taking SSRIs (sertraline, paroxetine, etc).

The proton pump inhibitors omeprazole and lansoprazole (*Prevacid* [OTC in the U.S.]) are associated with several drug interactions. One example is the interaction between omeprazole and clopidogrel. Omeprazole may decrease the efficacy of clopidogrel in some patients, which can increase the risk for a heart attack in patients taking the drug to reduce this risk. Another potential interaction may be seen with omeprazole and methotrexate. In some patients, omeprazole can decrease the elimination of methotrexate leading to higher than expected levels of methotrexate. It's best to refer patients, especially elderly patients, purchasing proton pump inhibitors to the pharmacist for important instructions on appropriate use. Pharmacist involvement is required in Canada in provinces and territories that follow NAPRA since this is a Schedule II drug. Give patients purchasing OTC proton pump inhibitors our patient education handout, *What You Should Know About Proton Pump Inhibitors*.

ADHD meds (methylphenidate [*Ritalin*, *Concerta*], amphetamine mixed salts [*Adderall XR*], lisdexamfetamine [*Vyvanse*], etc) taken with pseudoephedrine-containing products can pose a problem for patients. Both drugs are stimulants so the risk of adverse effects on the heart such as fast heart rate and increased blood pressure are increased when taken together.

Antacids can interact with many meds through a few different mechanisms. For example, they can bind to some drugs and decrease their absorption. Examples of drugs impacted by this mechanism include bisphosphonates (alendronate [*Fosamax*], risedronate [*Actonel*], etc), fluoroquinolone antibiotics (ciprofloxacin, levofloxacin, etc), and tetracyclines (tetracycline, doxycycline, etc). Since antacids decrease the acidity of the stomach, they also interact with drugs that need an acidic or basic environment to be

absorbed. For example, this mechanism can decrease the absorption of drugs needing an acidic environment for absorption such as antifungals (ketoconazole, itraconazole [*Sporanox*], etc). To avoid these and other interactions with antacids, patients may be instructed to space out their antacid from affected drugs. You may have seen auxiliary labels telling patients to take their drug at least one to two hours before or two to four hours after antacids. It's important to include these on Rxs when appropriate.

Natural medicines purchased over the counter can also be a problem for people on certain drugs. For example, dong quai, garlic, ginkgo, saw palmetto, and yohimbine may all have antiplatelet effects. This means they should be avoided or used carefully with other antiplatelets and anticoagulants. Ginseng shouldn't be used with warfarin since it can decrease its efficacy. St. John's wort interacts with several drugs. For example, it can decrease the efficacy of amiodarone, amlodipine, digoxin, losartan, etc. Pay attention to patients purchasing melatonin and getting prescriptions for Rx sleep meds such as zolpidem and temazepam. These combos can cause excess sedation since melatonin also helps patients fall asleep. You can also ask patients purchasing melatonin if they use anything else to help them sleep to uncover potential issues.

As you go to grab the Sudafed *you start to think about potential issues with the OTC meds Mr. Allen is getting and the warfarin he is picking up. You remember that NSAIDs such as ibuprofen can be a problem with drugs that thin the blood, like warfarin. Once you make your way back to the register Mr. Allen, who was taking your recommendation about reviewing the Drug Facts label, asks you about the stomach bleeding warning for people on blood thinning meds located in the warnings section on the box of ibuprofen. You confirm that this can be a possible issue and let him know that the pharmacist can talk to him about alternatives.*

What problems can OTC drugs cause for patients with certain conditions?

NSAIDs can cause issues for patients with heart problems. NSAIDs seem to increase the risk of heart attack and stroke in some people, and can exacerbate high blood pressure and heart failure. Make a habit of asking customers purchasing OTC NSAIDs who the med is for if it isn't clear. A younger patient may be buying an NSAID for their older parent or grandparent. Older patients are more likely to have heart issues that can be negatively impacted by NSAIDs and should be referred to the pharmacist when purchasing OTC NSAIDs. Heart failure in particular is a condition that requires caution with NSAIDs. NSAIDs can cause sodium and water retention, which is already a problem in patients with heart failure. Other drugs that can cause a problem for patients with heart failure include drugs that contain high levels of sodium. Effervescent meds (meds that dissolve in water) such as *Alka Seltzer* and *Airborne* (U.S.) can contain large amounts of sodium and shouldn't be used by patients with heart failure. Look out for patients picking up prescriptions for heart failure meds such as digoxin, sacubitril/valsartan (*Entresto*), and ivabradine (*Corlanor*, [U.S.]) who are also buying an OTC NSAID or effervescent medication. Refer them to the pharmacist.

Some drugs such as NSAIDs and pseudoephedrine-containing products can be a problem for patients with diabetes. The issue is usually that these drugs throw off their glucose control. Patients may need to be instructed to monitor their blood glucose levels closely while taking these drugs. Or they may be advised to avoid them altogether. Refer patients picking up diabetes meds (metformin, insulin, etc) and purchasing nonprescription drugs such as NSAIDs, syrups (because of the potential sugar content), and pseudoephedrine to the pharmacist.

Patients with uncontrolled high blood pressure should use pseudoephedrine-containing products cautiously. If you see patients picking up a prescription for a high blood pressure med and buying pseudoephedrine, make sure you refer them to the pharmacist. The pharmacist will want to make sure their blood pressure is under control and that they are aware of the risks. Pseudoephedrine can cause increases in blood pressure, since it's a stimulant. Pseudoephedrine can also cause a problem for patients with diabetes, irregular

heartbeats, glaucoma, and more. All of these warnings are outlined on the Drug Facts label which you should remind patients to review prior to use.

Smoking cessation products such as nicotine patches or gum should be used cautiously in patients with a recent heart attack, heart rhythm problems, and pregnancy. This is because nicotine narrows the blood vessels causing issues for patients who already have reduced blood flow to the heart. Narrowing of blood vessels can also be a problem for pregnant women since the fetus needs an adequate supply of blood from the mother. However, it's generally thought that the benefits of stopping smoking outweigh the risks of nicotine replacement products. Regardless, refer pregnant patients and patients filling prescriptions for heart meds such as nitroglycerin, clopidogrel, amiodarone, sotalol, etc to the pharmacist if they are purchasing nicotine replacement products. Keep in mind you will want to refer all pregnant patients who you observe purchasing any OTC drug to the pharmacist. Many drugs don't have enough data in pregnancy to be considered completely safe. Pharmacists can explain the risks versus benefits of using OTC drugs during pregnancy.

First-generation antihistamines such as diphenhydramine, chlorpheniramine, clemastine (U.S.), etc are used to treat allergies or cold symptoms. These drugs can cause issues in older patients including drowsiness, dry mouth, difficulty urinating, constipation, and they can decrease the ability to think clearly and react quickly. Make sure to refer older patients who are purchasing first-generation antihistamines to the pharmacist.

Before you get the pharmacist involved to discuss the interaction between the ibuprofen and warfarin, you start to gather the information you need for the Sudafed *purchase. You ask Mr. Allen for his driver's license and start entering the required data into the computer. However, you stop what you are doing when you remember that pseudoephedrine-containing products can be an issue in people with heart rhythm problems. You know that Mr. Allen is taking warfarin because he has a heart rhythm disorder known as atrial fibrillation. You also start to think twice about the* Benadryl *considering Mr. Allen's age. You remember that this drug's side effects can be worse in older patients. You tell Mr. Allen that you are going to have the pharmacist come over to talk to him before you go any further.*

Which OTC meds have the potential to be misused and abused?

Nonprescription meds with a history of being misused and abused include pseudoephedrine and ephedrine-containing products, dextromethorphan (*Robitussin DM*), diphenhydramine, and loperamide. While pseudoephedrine and ephedrine-containing products have been placed behind the pharmacy counter to help address concerns of misuse and abuse, dextromethorphan, diphenhydramine, and loperamide are available for public access. In some U.S. states, the sale of dextromethorphan-containing products is limited to patients who are 18 years of age or older. This restriction was implemented because younger kids were abusing these drugs to get high. Dextromethorphan is used at therapeutic doses to help suppress bothersome coughs. At higher doses, it can cause euphoria and has been abused for this reason. Diphenhydramine is a first-generation antihistamine used to treat symptoms of colds and allergies and to help patients with insomnia. Diphenhydramine can increase euphoria when used with opioids and can cause hallucinations if taken at high doses. Loperamide, which is used to treat diarrhea, is nicknamed the "poor man's methadone." High doses of loperamide can lead to opioid-like effects. Abusers will take four or more times the maximum dose to get high. Abuse of loperamide can lead to irregular heart rhythm and death. Although loperamide abuse isn't new, it's becoming more common. Watch for frequent or unusually large quantity purchases of dextromethorphan, diphenhydramine, and/or loperamide and get the pharmacist involved when you suspect anything unusual.

How else can I help patients use OTC meds safely?

In addition to helping patients navigate the information on the OTC drug label, there are several things you can do to help patients use OTC medications safely.

Remind patients to store these medications away from children. Kids have been accidentally poisoned with OTC meds such as iron supplements and multivitamins containing iron. There are also reports of poisonings with acetaminophen and diphenhydramine. There are even reports of ingestion of OTC topical agents such as *Bengay* which contains methyl salicylate, a substance that is toxic to children when ingested.

Provide proper measuring devices for liquid OTCs if one isn't provided with the product. Household spoons aren't good for measuring doses. Patients should use the measuring device that comes with the product if possible. But if the product doesn't come with a device, provide a proper calibrated measuring device such as an oral syringe or dosing spoon or cup. Check the Drug Facts info for the recommended dose to determine the most appropriate measuring device to give. Try to choose a device that's a correct size for the patient to measure the dose just once. For example, if a dose is 15 mL, dispense a device that holds at least 15 mL. If you dispense one that holds only 5 mL, the patient has to measure the dose three separate times to get to 15 mL. Also, make sure that the dosing units on the device match the dosing units on the product's label.

Update patient profiles with information on OTC meds, vitamins, minerals, and herbal supplements. Gather this information when working on medication histories. Always ask patients who are dropping off prescriptions if they regularly take any OTCs, vitamins, minerals, or herbal supplements and enter these into the system. If you are ringing up OTC products for a patient who gets Rxs filled at your pharmacy, take the opportunity to add these meds into the patient profile. Pharmacists can use the information you enter into patient profiles to screen for drug interactions or other potential issues.

Keep an eye out for drug interactions when selling OTCs and Rxs in the same transaction. We already talked about a lot of important interactions to keep an eye out for. Get the pharmacist involved if you aren't sure about issues between an OTC and an Rx med a patient is getting.

Make sure to include any OTC-related auxiliary labels on prescription medications. For example, labels that instruct patients to separate their med from antacids or calcium supplements are important. Not following these instructions can lead to the drug not working as well as it should. Other examples of important auxiliary labels include those that warn patients not to take the drug with NSAIDs or aspirin (usually because of the increased risk of bleeding) and labels that warn patients not to take the drug with acetaminophen-containing products (usually to prevent against the duplication of this ingredient and the potential for overdose).

Get in the habit of asking patients if they would like to talk to the pharmacist about the OTC med they are purchasing. This is especially important for elderly patients who may be more susceptible to adverse drug events. Patients don't know what they don't know. Give them the opportunity to learn more about the medication from the pharmacist.

The pharmacist advises Mr. Allen to use acetaminophen instead of ibuprofen for his headache since it should also work for sinus headaches. She explains the risk of using Benadryl *and instead directs him to use a safer antihistamine like* Claritin *(loratadine). She recommends instead of using* Sudafed *to try a nasal saline spray first. If that doesn't work she says they can talk about* Sudafed *again, but it's best to avoid it since it could make his condition worse. Mr. Allen takes all of her recommendations and thanks you both for helping him navigate these safety risks. He tells you he had no idea OTC medications could cause issues; he just assumed they were all safe to use.*

What can I do to ensure safety with OTC meds in the hospital setting?

When taking medication histories in the hospital setting, be sure gather the same information on OTCs as you would Rx drugs. For example, be sure to document doses and how often the medication is taken; even for as needed meds. Also be sure to specify the exact versions of OTCs on med histories. Sometimes there

is confusion with the type of drug a brand name contains. To illustrate, in the U.S., *Pedia-Lax* chewable tabs contain magnesium hydroxide, *Pedia-Lax* liquid contains docusate, and *Pedia-Lax* suppositories contain glycerin.

When entering or filling orders, or even when documenting med histories, let the pharmacist know if you catch any duplications in therapy or drug interactions. Addressing duplicate ingredients is important to help prevent overdose. Patients might be doubling up on ingredients at home if they are getting the same OTC ingredient from multiple sources. There could also be issues in the hospital setting as well. For example, patients with orders for acetaminophen and an opioid-acetaminophen combo could end up getting too much acetaminophen.

Keep an eye out for OTC drug diversion since some of these could be misused and abused. Report frequent and unexpected inventory discrepancies involving pseudoephedrine and ephedrine-containing drugs, diphenhydramine, dextromethorphan, and loperamide to the pharmacist.

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