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ISMP An ECRI Affiliate

Community/Ambulatory Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Prevent age-related mix-ups of the COVID-19 vaccines

Since the US Food and Drug Administration (FDA) authorized emergency use of the pediatric Pfizer-BioNTech coronavirus disease 2019 (COVID-19) vaccine for children ages 5 through 11 on October 29, 2021, ISMP has received numerous reports of mix-ups between the pediatric formulation and the formulation for individuals 12 years or older. The majority of the mix-ups occurred in outpatient or ambulatory care settings such as public health clinics, community pharmacies, physician practice offices, and outpatient clinics. The errors have resulted in wrong doses for both children ages 5 to 11 years (over- and underdoses) and 12 years or older (underdoses).

The Pediatric Vaccine

The pediatric formulation (10 mcg per 0.2 mL after dilution) of the Pfizer-BioNTech COVID-19 vaccines is NOT interchangeable with the 30 mcg per 0.3 mL formulation for patients 12 years and older. The pediatric formulation is supplied in a multiple-dose vial with an orange border on the label and an orange cap (the formulation for individuals 12 years and older has a purple cap). The pediatric formulation must be diluted with 1.3 mL of 0.9% sodium chloride prior to use to prepare 10 doses of 0.2 mL (10 mcg). The label states: "Age 5y to < 12y" (**Figure 1**), but this is not as prominent as "**DILUTE PRIOR TO USE**" and could be missed. Surprisingly, the dose in mcg is not listed on the label, which would have been helpful in differentiating this product from the 30 mcg/0.3 mL formulations for patients 12 years and older. ISMP believes FDA should require this information on the label.

Figure 1. The vaccine vial label (above) for ages 5 through 11 years has an orange border, and the vial (right) has an orange cap.

While different color caps on the Pfizer-BioNTech COVID-19 vaccines might help prevent some mix-ups, once the cap is removed and discarded, doses may be prepared one at a time rather than all at once, which will render the cap color irrelevant. Also, it is unlikely that the vial will accompany prepared syringes, so the vial label cannot be verified by those administering the vaccine or parents/patients receiving the vaccine.

Events Reported to ISMP

Fourteen reports submitted to ISMP described cases of underdosing in which children ages 12 years and older received doses appropriate for 5- to 11-year-old children (10 mcg/0.2 mL rather than 30 mcg/0.3 mL). In some of these cases, those administering the vaccine were unaware of the proper dose for 12-year-old children. In other reports, the patient's age was not correctly identified prior to administration.

Nurse was getting the COVID-19 vaccine for a 12-year-old for a second dose. Vaccine was brought to the nurse by the inventory nurse from another area of the clinic for administration. The vaccine was labeled with 0.2 mL pediatric COVID. The inventory

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SAFETY briefs

Concern over look-alike tablets with nearly identical tablet codes. A pharmacist checking a patient's medication containers discovered two brown, round tablets that had nearly identical tablet codes, "I2" and "I-2." The pharmacist searched to learn whether these look-alike tablets were the same medication, but he found that they were different medications—amitriptyline and ibuprofen (**Figure 1**).

Figure 1: Similar tablet codes appear on amitriptyline ("I2") supplied by Accord Healthcare and ibuprofen ("I-2") supplied by Major Pharmaceuticals.

The medication with the "I2" imprint was identified as amitriptyline hydrochloride 25 mg, a tricyclic antidepressant, while the tablet marked "I-2" was ibuprofen 200 mg. It is not difficult to imagine the danger of product misidentification. For example, a patient brought to the emergency department with a tricyclic antidepressant overdose, which is associated with severe cardiovascular, anticholinergic, and central nervous system effects, may be treated incorrectly if it is thought the patient took an overdose of a nonsteroidal anti-inflammatory drug. ISMP will be contacting to Accord Healthcare and Major Pharmaceuticals to address these look-alike safety concerns.

ISMP has reached out to the US Food and Drug Administration (FDA) to report this look-alike tablet code concern, as we have previously when presented with other situations where oral dosage forms are difficult to properly identify due to similar or seemingly identical medication identifiers. For example, in our August 2021

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nurse had to return to another area to bring back the EUA [Emergency Use Authorization] for 5-11 year old children, the COVID card and v-safe material previously forgotten. The administering nurse was not very familiar with the dosing for COVID therefore, did not realize it was a pediatric dose instead of an adult dose. The administering nurse indicated she did not receive the information for the vaccine either.

The vaccinator accidentally administered the pediatric dose (0.2 mL) of the Pfizer-BioNTech COVID-19 vaccine to a 12-year-old patient. The vaccinator had just administered a pediatric dose to the patient's sibling who was age 5-11 years. The family assumed they both needed the same dose, but the 12-year-old really needed the adult dose (0.3 mL). There was also a language barrier. In the future we recommend the vaccinator taking their time to verify all information before administration takes place.

Twelve-year-old client was administered pediatric dose (0.2 mL) of Pfizer-BioNTech COVID-19 vaccine. Client paperwork was incorrectly labeled by non-clinical staff. Clinician failed to notice that paperwork was incorrectly labeled, and that client had turned 12 and should have received an adult dose. Clinician documented that client received an adult dose. Event was discovered during pharmacy reconciliation. Leadership reached out to the family to check in on the youth and provide CDC [Centers for Disease Control and Prevention] guidance.

Patient was checked in and Pfizer-BioNTech COVID-19 pediatric vaccine 0.2 mL was administered. After administration, it was disclosed that the patient was 13, and not in the 5-11 age bracket. The father of the patient stated that he scheduled the appointment deliberately so that she would have the lower dose to avoid severe side effects.

In twelve reports, 5- to 11-year-old children received a higher dose intended for individuals 12 years and older. Similar to the wrong dose errors involving children 12 years and older, failure to correctly identify or verify the patient's age contributed to these events. In one case, those administering the vaccine had not yet been made aware that a pediatric formulation existed and that the dose was different for individuals 12 years and older. So, the children were given 30 mcg/0.3 mL of the Pfizer-BioNTech COVID-19 vaccine in error. In another case, a pharmacy used the strategy to place the letter "P" (for "Pfizer") on the syringe labels for the **COMIRNATY** vaccine, the brand FDA-approved Pfizer-BioNTech COVID-19 vaccine for ages 16 and older, to differentiate them from the pharmacy-prepared Moderna vaccine syringes. However, the "P" was mistaken to indicate "pediatric." Another reason attributed to some of the mix-ups was high patient volumes.

The medical assistant accidently vaccinated an 11-year-old patient with Pfizer-BioNTech COVID-19 vaccine 0.3 mL instead of Pfizer-BioNTech COVID-19 vaccine 0.2 mL, due to not double checking the age or verifying with the provider. The doctor and the parent were made aware of the error. The child was well under supervision, was released to go home, and is to call office if parent has any questions. We will start labeling

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issue, we discussed a case involving tablet misidentification between topiramate 50 mg and tra**ZOD**one 50 mg tablets. In the February 2020 issue, we discussed potential harm from tablet mix-ups due to similar-looking indapamide 2.5 mg and spironolactone 25 mg tablets.

While the Code of Federal Regulations (CFR § 206.10) requires code imprints, it does not mention specific instructions to ensure tablets and associated markings are not similar. We have asked FDA to explore working with legislators to modify the CFR. At one point, USP explored the development and promotion of standardized imprint coding for solid oral dosage forms. USP members agreed that the current system for identifying oral dosage forms needed improvement. However, this effort was abandoned due to cost considerations and uncertainty regarding the optimal solution to this concern.

It is important to mention that the National Library of Medicine's (NLM) Pillbox program, which included images and drug identification data, was retired in January 2021 (www.ismp.org/ext/806). This program should no longer be used for pill identification. While DailyMed provides official drug labeling, which often includes a description of the medication in the *How Supplied* section, images of many container labels, and sometimes images of tablets and capsules, it is not designed to search and identify medications based on the tablet markings. Some commercial referential drug information products do provide tablet identification search functionality, so check with your drug information vendor to determine if their product has this functionality. However, we hope FDA will work to improve data sources and capability for the public to identify drug products.

FDA communication on the accuracy of ENFit low dose tip syringes. A recent US Food and Drug Administration (FDA) communication to patients and healthcare providers (www.ismp.org/ext/798) mentioned the potential for overdoses, under certain conditions, when using ENFit low dose tip (LDT) syringes (between 0.5 mL and 6 mL). This can happen if the

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COVID-19 syringes and color coding storage units as purple and orange to match our vials.

Our system was down, so all documents were written by hand. The MA [medical assistant] did not catch that the patient was only 9 years old. The patient's DOB [date of birth] was written on top, and the MA assumed that year of DOB was the patient's age. The patient was brought in by mom. Vaccine that was drawn and administered was Pfizer-BioNTech 0.3 [mL]. The patient waited for the 15 minutes. Mom stated that the patient was doing fine, checked out with the front staff, and picked up vaccine card. The MA did not catch the error until she entered into the system once it came back up.

We administered an adult Pfizer dose for the COVID-19 vaccine (Comirnaty) to a pediatric patient. The adult doses were already drawn up with a red "P" label on the syringe. Our pediatric doses are labeled with a blue "PED." However, at the time of administration there were no blue "PED" drawn up. When administering the vaccine, the administrator saw the Red "P" and thought that it was the one for pediatrics. As a result, the adult dose was given to the child.

Child and mother presented for COVID vaccine. Both vaccines were on the table, and both labeled. Child was given adult Pfizer vaccine and dosage.

Events Reported in the Media

Wrong dose and formulation errors are also being reported in the news media. In at least a couple of these incidents, the 30 mcg/0.3 mL Pfizer-BioNTech vaccine (intended for individuals 12 years and older) was used but was thought to be acceptable for children ages 5 to 11 years if only 10 mcg was given, either as 0.1 mL of the 30 mcg/0.3 mL vaccine (10 mcg), or by diluting the 10 mcg dose in a syringe to 0.2 mL. One hundred twelve children ages 5 to 11 years (www.ismp.org/ext/814) in one report and 25 children ages 5 to 11 (www.ismp.org/ext/815) in another report appear to have received their vaccine in this manner. Neither method would be correct, though, since the pediatric vaccine is specifically formulated to be more diluted to ensure accurate measurement. Withdrawing 0.1 mL in a 1 mL syringe will result in an inaccurate volume, as it is recommended that no less than 20% of the nominal syringe capacity is measured to limit instrumental error. Also, if a needle different from the one used for drawing up the vaccine is used for administration, some of the 0.1 mL dose would likely be lost to dead space in the needle. If a 0.1 mL dose is drawn up and the same needle and syringe are used to draw up a 0.9% sodium chloride diluent, the vaccine initially in any dead space of the needle and syringe hub would be drawn into the syringe as it is pulled back to withdraw the diluent. Depending on how evenly the vaccine is distributed in the syringe, this could result in either too much or too little vaccine reaching the patient upon injection.

ISMP also received a report in which a hospital requested numerous physician offices to schedule 5- to 11-year-old children for the Pfizer-BioNTech 30 mcg/0.3 mL vaccine because the vials were expiring soon, with the misunderstanding that 10 mcg doses could be prepared from that formulation for the younger children. However, ISMP was unable to confirm if any doses were actually administered in this manner.

The media has also reported that some parents have expressed vaccine hesitancy after hearing about COVID-19 vaccine errors (www.ismp.org/ext/804). We certainly do not want mix-ups between these vaccine formulations to raise concerns even more.

Safe Practice Recommendations. Implement these safety strategies during the multistep vaccination process to avoid mix-ups between the pediatric (5-11 years) and adult (12 years and older) COVID-19 vaccines:

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user does not clear the moat area around the syringe tip (**Figure 1**) before administering a medication. Liquid medications can enter the moat area when the syringe is dipped into a liquid medication without using a syringe filling adapter such as an ENFit cap or medication straw. If fluid or air bubbles enter the moat area, the tip of the syringe should be tapped or flicked to eliminate the fluid or air bubbles before administering the medication. ISMP believes that the overdose risk is mainly with oral liquid medications that enter the moat area, especially with tiny doses used for pediatric patients.

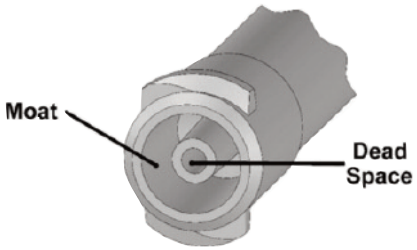

Figure 1. Liquid medications that enter the moat area of an ENFit low dose tip (LDT) syringe under certain conditions may lead to an overdose if not cleared.

While the FDA's analysis has identified a potential for overdose using ENFit LDT syringes, no patient injuries have been reported. However, serious patient injuries and deaths have been reported due to misconnections (www.ismp.org/ext/799). Therefore, FDA continues to recommend the use of enteral devices and syringes that reduce the risk of misconnections, including ENFit LDT syringes.

HIGH-ALERT

More on fluorouracil and pets. The November 2020 newsletter issue drew attention to the importance of keeping medicines, particularly toxic ones such as fluorouracil cream, away from pets. Exposure often happens when a pet licks the owner's skin where the medication was applied or chews the fluorouracil container. The medicine is extremely toxic to dogs and cats and can be fatal. ISMP has asked the US Food and Drug Administration (FDA), USP, and major drug information vendors to prominently include warnings on labels and in patient instructions. However, the problem is not just with topicals.

A patient was receiving intravenous (IV) fluorouracil via an elastomeric pump at home. His 3-month-old dog (about 3

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Segregate storage. Segregate and store these in refrigerators and freezers that are organized and properly labeled. Store the adult (12 years and older) and pediatric COVID-19 vaccines apart from one another, such as in separate labeled plastic bins.

Scan the barcode. During the production and/or verification phase of the dispensing process, use barcode scanning whenever possible to verify that the correct product has been retrieved. Ideally, prior to administration, barcode scanning should again confirm the correct vaccine.

Label the syringes. Make it a policy to clearly label all individual syringes containing vaccines. To facilitate proper labeling, print labels for each patient or provide vaccine preparers with strips of preprinted labels that differentiate adult and pediatric doses.

Separate the vaccines. Only bring the intended and labeled vaccine syringe(s) for one patient into the vaccination area at a time.

Verify the patient's age. At the pharmacy counter or when checking in a patient to receive a vaccine, ask the patient to provide at least two patient identifiers—their full name and date of birth. Repeat this process immediately prior to vaccine administration. For pediatric patients, also verify the patient's actual age with the parent or caregiver and be sure to ask which vaccine(s) they have requested.

Involve the patient/parent in the checking process. Involve the parent or patient in verifying the vaccine by reading the label to confirm the correct vaccine.

Document lot number/expiration date. Document the vaccine lot number and expiration date (or date of manufacture) prior to vaccine administration. Then, document administration afterwards in the patient's profile, on vaccination records, and via state or other immunization registries.

Provide staffing support. Schedule vaccines for a dedicated block of time each day and ensure adequate staffing. Ideally, staff should not be expected to accomplish both vaccine administration and regular dispensing functions simultaneously. Explore the use of qualified and trained volunteers to assist in the vaccination process (as was done initially when the COVID-19 vaccines first became available) to relieve some of the stress associated with professional staffing shortages.

Report vaccine errors. Report all vaccine errors internally and to the FDA/CDC Vaccine Adverse Event Reporting System (VAERS, https://vaers.hhs.gov/), which is mandatory for COVID-19 vaccine errors under an EUA. ISMP also asks providers to report vaccine errors to the ***ISMP National Vaccine Errors Reporting Program*** (VERP; www.ismp.org/VERP). Additional vaccine information can be found at: www.cvdvaccine-us.com and in the latest vaccine *Fact Sheets* (www.ismp.org/ext/803, www.ismp.org/ext/813).

If you would like to subscribe to this newsletter, visit: www.ismp.org/node/126

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Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E), or visit www.ismp.org/report-medication-error. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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pounds) chewed through the chemotherapy line and ingested the medication. The patient was lying in bed when the puppy jumped up and retreated under the blanket. After 30 minutes, the patient noticed that the bed felt wet and realized that the puppy had bitten into his chemotherapy line. Just a few mL of the infusion will kill a dog (Dorman DC, Coddington KA, Richardson RC. 5-fluorouracil toxicosis in the dog. *J Vet Intern Med*. 1990;4[5]:254-7). Sadly, the puppy died.

Counsel patients about the toxicity of fluorouracil in pets, including how to ensure pets do not accidentally ingest the medication. This can be done by keeping pets away from chemotherapy lines, keeping the medications out of reach, and ensuring that pets do not lick the medication on a patient's skin if the medication is applied topically. These steps can also be applied to other medications that are potentially toxic to animals.

Special Announcements

Register for the virtual CHEERS AWARDS Celebration!

Please join ISMP on Tuesday evening, **December 7, 2021**, at 6:00 p.m. ET, for our **virtual** 24th Annual CHEERS AWARDS. We will be honoring a group of healthcare leaders who have left their footprint on medication safety by developing best practices and programs that prevent medication errors and protect patients. To register for the free event, please visit: www.ismp.org/node/25790.

Help support ISMP during our only fundraising event!

You can honor this year's CHEERS AWARDS winners by attending the virtual awards celebration, purchasing raffle tickets for a variety of high-end prizes, and/or making a donation. With your support, ISMP can continue on our path to promote safe medication use in all healthcare settings. To purchase raffle tickets, please visit: www.ismp.org/ext/790. To make a donation, please visit: www.ismp.org/node/25784.