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ISMP An ECRI Affiliate

Community/Ambulatory Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Analysis of transdermal medication patch errors uncovers a "patchwork" of safety challenges

PROBLEM: A recent cluster of error reports associated with transdermal medication patches submitted to the ISMP National Medication Errors Reporting Program (ISMP MERP) led us to look back a few years at all transdermal patch error reports submitted to the ISMP MERP to identify contributing factors and make recommendations to avoid errors with this type of drug delivery system. A transdermal patch is a medicated adhesive patch placed on intact skin to provide regular, controlled release of medication doses into the bloodstream through the skin. Transdermal patches are used to deliver a wide variety of pharmaceuticals, including medications used for smoking cessation, motion sickness, hormone replacement therapy, hormonal contraception, hypertension, angina, pain, depression, overactive bladder, and Alzheimer's disease.

Our analysis included more than 50 reports associated with 12 different transdermal medication patches submitted to the ISMP MERP within the past 4 years. During analysis, four reports were excluded because the contributing factors were not unique to medication patch delivery systems (e.g., wrong patient). Patches most frequently involved in reported errors included fenta**NYL** (n = 16), clo**NID**ine (n = 10), scopolamine (n = 7), and estradiol (n = 6). While ISMP has repeatedly published reports of errors associated with transdermal patches, we now provide details about the error types we discovered during our recent analysis of patch errors.

Errors in the Frequency of Patch Application or Removal

ISMP received 10 reports associated with an error in the frequency of patch application or removal. Four of these errors involved estradiol patches. Depending on the brand or formulation, estradiol patches are applied either twice a week (**ALORA**, **DOTTI**, **LYLLANA**, **MINIVELLE**, **VIVELLE-DOT**, generics) or once a week (**CLIMARA**, **MENOSTAR**, generics). In two of the cases, a weekly estradiol patch was prescribed, but a twice weekly formulation was dispensed with directions to apply one patch weekly, which resulted in underdoses. In another case, a physician prescribed a twice weekly estradiol patch with directions to change the patch weekly, also resulting in an underdose. In the fourth event, a prescriber ordered a twice weekly estradiol patch, but the pharmacy dispensed a weekly patch with directions to apply the patch twice weekly. Some dispensing errors continued for several refills. In some cases, the manufacturers' outer carton did not clearly specify if the patch was to be applied weekly or twice weekly.

Three of the 10 frequency errors involved dispensing fenta**NYL** patches with the wrong directions for application, sometimes due to a transcription error in the pharmacy. Another error in this category involved misinterpretation of a consultant's note to "Increase Clonidine patch to TTS-2 to mitigate ketamine side effects and help with opioid withdrawal symptoms." The physician interpreted the "TTS-2" to mean Tuesday, Thursday, and Saturday, and did not know that "TTS-2" was the nomenclature used for the 0.2 mg/24 hour **CATAPRES-TTS-2** (transdermal therapeutic system) brand of clo**NID**ine patches, which should only be applied weekly. We also received two error reports associated with removing a patch at the wrong time—one involving

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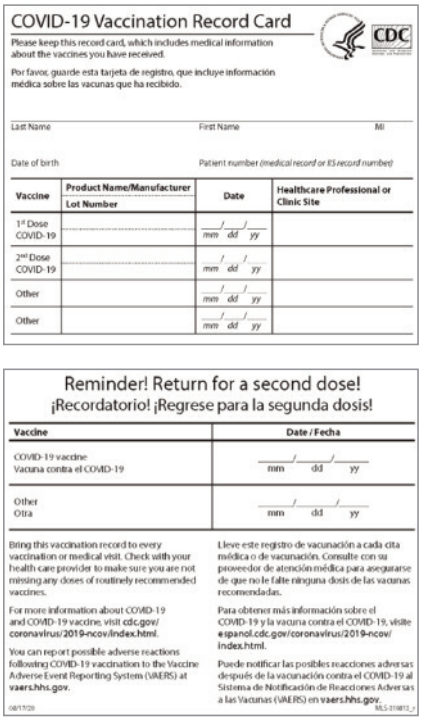
SAFETY briefs

Vaccine card incorrect for single-dose COVID-19 vaccine. When an organization received its first shipment of the single-dose Janssen coronavirus disease 2019 (COVID-19) vaccine, the accompanying supplies included COVID-19 Vaccination Record Cards that reference a two-dose vaccine series (**Figure 1**). The cards have the US Department of Health and Human Services (HHS) and the Centers for Disease Control and Prevention (CDC) logos in the



COVID-19 Vaccination Record Card

Please keep this record card, which includes medical information about the vaccines you have received.

Por favor, guarde esta tarjeta de registro, que incluye información médica sobre las vacunas que ha recibido.

Last Name | First Name | MI

Date of birth | Patient number (medical record or IIS record number)

Vaccine	Product Name/Manufacturer Lot Number	Date	Healthcare Professional or Clinic Site
1st Dose COVID-19		mm dd yy	
2nd Dose COVID-19		mm dd yy	
Other		mm dd yy	
Other		mm dd yy	

Reminder! Return for a second dose!
¡Recordatorio! ¡Regrese para la segunda dosis!

Vaccine	Date / Fecha
COVID-19 vaccine Vacuna contra el COVID-19	mm dd yy
Other Otra	mm dd yy

Bring this vaccination record to every vaccination or medical visit. Check with your health care provider to make sure you are not missing any doses of routinely recommended vaccines.

For more information about COVID-19 and COVID-19 vaccine, visit cdc.gov/coronavirus/2019-ncov/index.html.

You can report possible adverse reactions following COVID-19 vaccination to the Vaccine Adverse Event Reporting System (VAERS) at vaers.hhs.gov.

Lleve este registro de vacunación a cada cita médica o de vacunación. Consulte con su proveedor de atención médica para asegurarse de que no le falte ninguna dosis de las vacunas recomendadas.

Para obtener más información sobre el COVID-19 y la vacuna contra el COVID-19, visite espanol.cdc.gov/coronavirus/2019-ncov/index.html.

Puede notificar las posibles reacciones adversas después de la vacunación contra el COVID-19 al Sistema de Notificación de Reacciones Adversas a las Vacunas (VAERS) en vaers.hhs.gov.

Figure 1. COVID-19 Vaccination Record Cards accompanying the Janssen single-dose vaccine incorrectly call for two doses (front of card, top) and advises patients to return for a second dose (back of card, bottom).

upper right corner. All vaccination sites also receive these cards with the Moderna and Pfizer-BioNTech vaccines, which require two doses. The front of the card provides space to document the product name, manufacturer, and lot number of both the first and second vaccine doses.

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the removal of a fenta**NYL** patch instead of a lidocaine patch after 12 hours, and the other involving the removal of a nitroglycerin patch after 24 hours instead of after 12-14 hours.

Lack of Awareness of Patches on the Patient's/Resident's Skin

ISMP received seven reports associated with practitioners failing to identify patches on the patient's or resident's skin (which had been applied prior to admission), not removing an old patch when applying a new patch, and/or finding multiple patches on patients that had been left on longer than prescribed. Five of these events involved fenta**NYL** patches. In one case, two patches were found on an unexpectedly somnolent patient during rounds. In another case, three 100 mcg/hour fenta**NYL** patches were found on an over-sedated patient with respiratory depression. One health system reported an increase in reports of patients with an applied fenta**NYL** patch that was missed upon admission and not found on their skin until days later. We have also received reports of finding multiple nicotine patches and rivastigmine (**EXELON**) patches (used for Alzheimer's) on patients during their admission. Because many patches are clear or beige, they might easily be missed on the skin of some patients, especially during transitions of care.

Dose Confusion Due to Labeling

ISMP received seven error reports related to confusing the dose expression on the label of scopolamine patches. In the most recent report received just last month, a pharmacy technician noticed that the dose listed on the carton and inner patch pouches of the Perrigo brand of scopolamine patches (1 mg/3 days) (**Figure 1**, left) did not match the dose (1.5 mg/3 days) listed in the organization's computer systems. On the back of the Perrigo scopolamine carton, the technician noticed that the patch contains 1.3 mg of scopolamine base but only delivers 1 mg over 3 days. When examining other scopolamine patch products, the technician found that many have changed to a 1 mg/3 days dose expression, while others still display the dose as 1.5 mg (**Figure 1**, right), even though each patch only delivers 1 mg over 3 days.

Figure 1. Scopolamine transdermal system from Perrigo (left) expresses the dose as 1 mg/3 days, while **TRANSDERM SCŌP** (scopolamine) from Sandoz (right) expresses the dose as 1.5 mg, although the patch delivers 1 mg over 3 days.

This label confusion has led to prescribing, dispensing, and administration errors. In one reported event, a prescriber ordered 1 mg of a 1.5 mg/3 days patch (0.667 of the patch), and the nurse cut off one-third of the dispensed patch before applying the other two-thirds of the patch on the patient. Scopolamine patches should not be cut. In another case, a prescriber ordered a 1.5 mg scopolamine patch for a patient, and the pharmacy dispensed 1½ patches. Serious toxic effects are possible with a scopolamine overdose.

According to the US Food and Drug Administration (FDA), transdermal scopolamine product labeling should be standardized at the nominal delivery rate of 1 mg/3 days. Based on the recent reports we received in 2021, there might be a few products that have not yet transitioned to the newer dose expression (1 mg/3 days) on container labels. Or, some products with the older label (1.5 mg) may still be in circulation.

Inappropriate Patch Prescribing

ISMP received six reports of inappropriate prescribing of fenta**NYL** patches. In an August 2020 newsletter article, we described examples of fenta**NYL** patches inappropriately prescribed for opioid-naïve patients discharged from the emergency depart-

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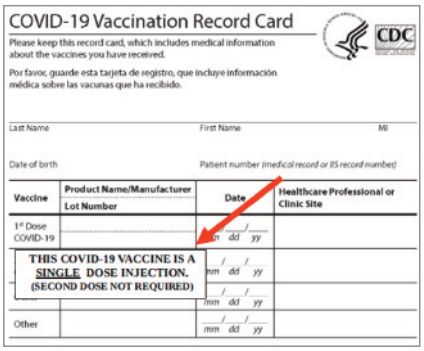
The back of the card includes a reminder to return for a second dose, which appears in both English and Spanish. Since the Janssen vaccine is only a single-dose vaccine, this may cause confusion and lead patients to seek an unnecessary second dose.

The organization submitted an inquiry to the CDC and so did ISMP. The CDC noted that it is not presently considering an update to the card for the Janssen vaccine. The organization is now affixing labels on the cards for use with the Janssen vaccine to note that a second dose is not required (**Figure 2**). They also cover the statement on the back of the card about returning for a second dose.


COVID-19 Vaccination Record Card

Please keep this record card, which includes medical information about the vaccines you have received.

Por favor, guarde esta tarjeta de registro, que incluye información médica sobre las vacunas que ha recibido.

CDC

Last Name | First Name | MI

Date of birth | Patient number (medical record or IIS record number)

Vaccine	Product Name/Manufacturer Lot Number	Date	Healthcare Professional or Clinic Site
1st Dose COVID-19		mm dd yy	
THIS COVID-19 VACCINE IS A SINGLE DOSE INJECTION. (SECOND DOSE NOT REQUIRED)		mm dd yy	
		mm dd yy	
Other		mm dd yy	

Figure 2. One organization affixes a label to each card handed to patients who receive the Janssen single-dose COVID-19 vaccine, indicating that only a single dose is needed.

Practitioners should educate patients receiving the Janssen vaccine, emphasizing that a second dose is not needed. This is reinforced in the *Fact Sheet for Recipients and Caregivers*, which should be given to the vaccine recipient. This is similar to guidance that is recommended when a subsequent vaccine dose is not needed. For example, state vaccination record cards often include spaces for the dates of 4 doses of the Hib (*Haemophilus influenzae* type b) vaccine, but the child may only need 3 doses based on the age the doses were given or the product administered.

Beware of COVID-19 vaccines sold online. We recently became aware that empty coronavirus disease 2019 (COVID-19) vaccine vials and cartons may be available for purchase online through retailers like eBay (**Figure 1**, page 3). Although the event reported to ISMP was with the Moderna COVID-19 vaccine, empty con-

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ment (ED) to treat acute pain or due to an "allergy" to codeine that was only a minor drug intolerance. Prescribing information recommends fenta**NYL** patches only be used in opioid-tolerant patients for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment. Since then, we have received three more error reports associated with inappropriate prescribing of fenta**NYL** patches to opioid-naïve patients in long-term care (LTC) facilities. Reliance on product labeling and practitioner education alone will not do enough to solve this life-threatening problem.

Wrong Dose Dispensing Errors

ISMP received six reports of dispensing the wrong dose of patches that are available in more than one strength. We previously published one of these errors in our September 2020 newsletter. An order for 50 mcg/hour fenta**NYL** patches included "72 hours" for the duration of patch application. The "72" was mistaken as the strength, leading to erroneous dispensing of a 75 mcg/hour instead of the intended 50 mcg/hour fenta**NYL** patch. Including the duration of controlled drug delivery (i.e., 72 hours) in the order and the drug description field contributed to this dispensing error. In another event, a technician filling an order for rivastigmine patches 9.5 mg/24 hour for a LTC resident prepared 13.3 mg/24 hour patches and failed to notice the error because he bypassed the usual barcode scanning process. The pharmacist verifying the product did not notice a discrepancy between the 13.3 mg/24 hour patches and the image of the 9.5 mg/24 hour patches on the computer screen and dispensed the patches. The remaining event reports did not include information regarding the primary causes of the wrong dose dispensing errors.

Patch Cover Applied without the Medication Patch

ISMP received five reports of applying a clo**NID**ine patch adhesive cover directly to the skin, without first applying the clo**NID**ine patch. In one case, only the adhesive cover was retrieved from the carton and applied; in all other cases, the active medication patch was accidentally discarded. The errors contributed to uncontrolled blood pressure. In an ***FDA AdviseERR*** published in our March 2019 newsletter, FDA described reports they had received regarding *patients* and *caregivers* who had applied only the adhesive cover to the skin. The clo**NID**ine transdermal system (Catapres-TTS) is packaged in a carton containing individually labeled pouches of four clo**NID**ine patches and four adhesive covers. Once removed from the pouches, the clo**NID**ine patch is a different size, shape, and color than the adhesive cover, but the patch and cover do not specify which is which. Application of the adhesive cover is optional; the cover should be applied directly over the clo**NID**ine patch *only* if the patch begins to separate from the skin.

Wrong Patch Prescribed Due to Similar Ingredients

Recently we received a report about a patch error we have not previously described. A pharmacist noticed that a hormone replacement therapy drug, **COMBIPATCH** (estradiol and norethindrone), had been prescribed for a 20-year-old woman. Because CombiPatch is typically used to treat vasomotor symptoms associated with menopause, the pharmacist contacted the prescriber to ask whether he had instead intended to prescribe the hormonal contraceptive patch, **XULANE** (ethinyl estradiol and norelgestromin), for the young woman. The prescriber confirmed that he had selected the wrong patch and prescribed the intended product, Xulane.

After a second, similar prescribing error was made, the pharmacist investigated further and found that the same error had occurred with several different prescribers. Because there are so many hormonal contraceptives with similar ingredients, most prescribers had searched for "patch" and then selected the product with ingredients consistent with a contraceptive patch. However, the only hormonal "patch" available for selection in the facility's default electronic medical record drug list was CombiPatch.

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tainers of COVID-19 vaccines from other manufacturers may be for sale online as well. With the authentic, empty vials and cartons available online, the concern is that these products may land in the wrong hands and can be easily filled with unknown substances and resold as the real vaccine. Since early in the pandemic, the World Health Organization (WHO) and the US Food and Drug Administration (FDA) have warned about counterfeit vaccines and treatment products sold online around the entire world (www.ismp.org/ext/664; www.ismp.org/ext/413).

Figure 1. Empty Moderna COVID-19 vaccine vials (top) and cartons (bottom) for sale online.

A recent newscast in Pennsylvania featured a community pharmacist expressing his concern about the proper disposal of empty COVID-19 vaccine vials (www.ismp.org/ext/665). The pharmacist reported that the Healthcare Distribution Alliance (HDA) recommends that empty COVID-19 vaccine vials be destroyed to prevent unauthorized manipulations. It is important to remember that COVID-19 vaccines are currently being distributed by the federal government at no cost to the consumer, so any COVID-19 vaccines or treatments for sale online cannot be trusted as an authentic product. As healthcare facilities around the world continue to provide millions of COVID-19 vaccines per day, please be cautious of how you dispose of empty vaccine vials and cartons.

Dosing error with Entresto. A dispensing error occurred when a pharmacist misinterpreted a prescription for **ENTRESTO**, a product used to treat heart failure that contains sacubitril and valsartan in different amounts (i.e., 24 mg/26 mg, 49 mg/51 mg,

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Miscellaneous Concerns and Errors

ISMP also received numerous reports of miscellaneous concerns and errors associated with patches, including a drug interaction between a clo**NID**ine patch and a tricyclic antidepressant; a complaint about an estradiol patch that would not adhere to the skin; two reports of patches placed on skin that was not intact; two barcode issues (now resolved); and two reports of unsecured fenta**NYL** patch disposal that could allow diversion, abuse, or accidental poisoning by children who might chew or stick the patches on their skin.

SAFE PRACTICE RECOMMENDATIONS: Managing patients receiving medication patches can be challenging given the variety of strengths and dosing intervals. To prevent errors with patches, consider the following recommendations, many of which are specific to the unique contributing factors associated with patch errors:

Patch Prescribing and Pharmacist Order Verification

All Patches

- Collect a medication history from each patient. Use scripted questions or prompts to help identify all medications and substances that may not be readily identified by patients. Specifically question patients regarding the use of any type of patch.
- Verify the indication and assess the appropriateness of patch use for each patient.
- Within electronic prescribing systems, create medication patch order sentences that include the appropriate application frequency.
- Consider allowing the entry of ONLY the appropriate application frequencies. For example, only allow entry of the frequency of fenta**NYL** patch application every 72 hours or every 48 hours, not every 24 hours.

Specific Patches

- **Estradiol:** Include brand names when prescribing estradiol patches since they have different application frequencies. If it is unclear which product is to be dispensed, the pharmacist should verify the prescription with the prescriber.
- **FentaNYL:** Do not include the duration of medication delivery in the patch drug description field (which could be confused as the dose). The patient's dosing instructions should communicate the frequency of changing the patch.
- **Hormone replacement therapy:** Consider requiring documentation of the indication when prescribing these patches.
- **Opioid:** Enhance clinical decision support with pain-related order sets that are specific to patients' opioid tolerance and prevent the ordering of fenta**NYL** patches for opioid-naïve patients with acute pain.
- **Opioid:** Default prescribing systems to the lowest initial starting dose and frequency.

Patch Dispensing

All Patches

- Employ barcode scanning during the dispensing process to ensure correct product selection.
- Identify which patches can be safely cut and which cannot. Share the information with the pharmacy staff and the staff at LTC facilities you service. Include this information on the medication administration record (MAR).

Specific Patches

- **CloNIDine:** For LTC residents, consider dispensing the medication patch and adhesive cover in a ziplock bag with a label explaining the two components of the product.

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and 97 mg/103 mg). The prescription listed the strength as 100 mg, which the patient was supposed to take twice daily. However, none of the three available strengths of Entresto includes a 100 mg strength. The pharmacist dispensed what he thought was closest to the strength prescribed, the 97 mg/103 mg product, and instructed the patient to take the medication twice daily.

A few months later, the patient's physician increased the dose to 200 mg twice daily, and the pharmacist dispensed the 97 mg/103 mg strength with instructions to take 2 tablets twice daily. However, that dose soon led the patient to experience severe side effects, including intense lethargy and hypotension. At that point, the pharmacist discovered the patient had received twice the intended dose due to a dispensing error. The prescriber had added the dosage amounts of the two ingredients together in the original prescription, so Entresto 49 mg/51 mg (100 mg total) was the original intended dose (**Figure 1**). Even though the product label lists the ingredients separately, the package insert suggests that dosing in clinical trials was based on the total amount of both components of Entresto; sacubitril and valsartan 24 mg/26 mg, 49 mg/51 mg, and 97 mg/103 mg were referred to as 50 mg, 100 mg, and 200 mg, respectively. Also, instructions for preparing a suspension from eight 49 mg/51 mg tablets indicates the final concentration in terms of the combined strengths of the ingredients, 800 mg/200 mL.

Figure 1. A pharmacist dispensed Entresto 97 mg/103 mg (top), thinking the strengths were closest to the 100 mg strength prescribed. However, the prescriber intended for the patient to receive the 49 mg/51 mg strength (49 + 51 = 100) (bottom).

Such confusion by the pharmacist is easy to understand. Most combination tablets in the US are prescribed according to the strengths of each respective drug, not the

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- **Opioid:** Confirm the patient's opioid status (naïve versus tolerant) prior to dispensing patches appropriate only for opioid-tolerant patients.
- **Scopolamine:** Purchase and dispense scopolamine patches that have a newer 1 mg/3 days dose expression. For LTC facilities, be sure MARs express the drug delivery rate of 1 mg/3 days.

Patch Administration/Removal

All Patches

- Place prompts on LTC MARs to document the location of all medication patches applied and link all entries for medication patches to an order for removal at the appropriate interval.
- Provide LTC nurses with a documentation prompt each shift to verify placement of each medication patch and to record the location, if necessary.
- Work with LTC facilities to ensure they have secure waste disposal systems for patches containing controlled substances.

Specific Patches

- **CloNIDine:** Consider building an MAR note to remind LTC nurses to apply the medication patch and not just the cover. If the adhesive cover is used over the medication patch, it is best for nurses to label the adhesive cover with the drug name, strength, and date, *before* applying it.

Patient/Caregiver Education

All Patches

- Encourage patients to keep an up-to-date record of all their medications (including any patches and over-the-counter products) and to share this list at each encounter with their healthcare providers. Explore ways to assist patients to maintain such a list, such as providing them with a current medication list at each encounter.
- Provide verbal and written education to patients/caregivers on the use of patches (e.g., when to remove and replace the patch), including how to establish a system (e.g., calendar or alarm reminders) for the appropriate cadence of patch application and removal. Discuss any related safety concerns and error potential. Always verify the patient's understanding of the information. (For an ISMP fenta**NYL** patch consumer leaflet, visit: www.ismp.org/ext/653.)
- Remind patients/caregivers to read the accompanying leaflet or *Patient Instructions* (often found in the manufacturer's carton) before using the patches.
- Teach patients and caregivers to safely discard used or unneeded patches according to guidance in the product's prescribing information. For example, a fenta**NYL** patch should be disposed by folding the sticky side together and flushing it down the toilet.

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Report medication and vaccine errors to ISMP: Call 1-800-FAIL-SAF(E), or visit our website at: 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.

Editors: Michael J. Gaunt, PharmD; Michael Cohen, RPh, MS, ScD (hon), DPS (hon); Judy Smetzer, BSN, RN, FISMP; Ann Shastay, MSN, RN, AOCN. ISMP, 200 Lakeside Drive, Suite 200, Horsham, PA 19044. Email: ismpinfo@ismp.org; Tel: 215-947-7797; Fax: 215-914-1492.

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total strength of all active ingredients. For example, the anti-Parkinson's drug **SINEMET** (carbidopa and levodopa) lists the ingredients separately on the label and in the package insert, and the drug is prescribed according to the strengths of each respective drug (i.e., Sinemet 10 mg/100 mg, Sinemet 25 mg/100 mg), not the combined total of both drugs. Entresto product labeling mentions dosing both in terms of individual ingredient strengths as well as the total mg dose of the two ingredients added together. Ideally, the way strengths are expressed for multi-ingredient products and how these drugs are prescribed should be standardized to prevent confusion. For now, please inform prescribers and pharmacy staff about this potential for error. An alert in prescribing and dispensing software may be warranted. If there is uncertainty as to which strength was ordered, the pharmacist should contact the prescriber.

ASPEN-ISMP error reporting project. For more than 10 years, ISMP and the American Society for Parenteral and Enteral Nutrition (ASPEN) have worked collaboratively to educate clinicians about the benefits of reporting errors involving nutrition support therapy and associated devices. Our goals are to learn about the underlying causes of these errors, publish and present the findings, and foster national initiatives that address risk reduction for nutrition support. To report errors involving nutrition support, please visit our error-reporting page (www.ismp.org/report-medication-error). For more information about the project, please visit the ASPEN-ISMP project site at: www.ismp.org/ext/645.

Special Announcement

Attend an ISMP MSI workshop

Do not miss a unique opportunity to learn how to establish a comprehensive medication safety program. Register for one of the virtual ***ISMP Medication Safety Intensive (MSI)*** workshops in 2021. The 2-day workshops will be offered on: **April 22 & 23, June 24 & 25,** and **August 5 & 6**. For details, visit: www.ismp.org/node/127.