

Acute Care

ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

Start the New Year off right by preventing these Top 10 Medication Errors and Hazards



Reflecting on 2019 and the 20-year anniversary of the Institute of Medicine report, *To Err is Human*, ISMP has identified the **Top 10 Medication Errors and Hazards (Table 1)** that appeared in the 2019 *ISMP Medication Safety Alert!* The list is not based only on the most frequently reported problems or those that have caused the most serious consequences to patients, although these factors were considered. Instead, all the errors and hazards on our list have been persistent and can be avoided or minimized with system and practice changes. We believe these issues warrant attention and priority in the coming year if you have not already taken action to mitigate the risk. Links to additional content in our newsletters and guidelines is provided along with the descriptions below (some links require you to sign into your ISMP account for access). We hope that knowing about these errors and hazards informs your 2020 medication safety improvement plan!

1 Selecting the wrong medication after entering the first few letters of the drug name

Entering just the first few letter characters of a drug name, or a combination of the first few letters and product strength, potentially allows the presentation of similar looking drug names on technology screens. This increases the risk of selection errors or population of a field with an unintended drug. For example, our first newsletter of 2019 (www.ismp.org/node/1326) described a tragic error in which a nurse entered “VE” into an automated dispensing cabinet (ADC) search field via override and mistakenly selected and removed vecuronium instead of **VERSED** (midazolam). Other examples of drug selection errors in 2019 that resulted after entering the first few letters of the drug name include mix-ups between: dexmedetomidine and dexamethasone injection; **AMBIEN** (zolpidem) and ambrisentan; **BRIVIACT** (brivaracetam) and **BRILINTA** (ticagrelor); and **ROMAZICON** (flumazenil) and rocuronium. Practitioners seem to read the first few letters of the first drug name on the list before confirmation bias ensues.

This is a problem that has increased in frequency with the upswing in technology use. In fact, wrong selection errors may rival or exceed those made with handwritten orders. For
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Table 1. Top 10 Medication Errors and Hazards

1	Selecting the wrong medication after entering the first few letters of the drug name
2	Daily instead of weekly oral methotrexate for non-oncologic conditions
3	Errors and hazards due to look-alike labeling of manufacturers' products
4	Misheard drug orders/recommendations during verbal/telephone communication
5	Unsafe “overrides” with automated dispensing cabinets
6	Unsafe practices associated with adult IV push medications
7	Wrong route (intraspinal injection) errors with tranexamic acid
8	Unsafe labeling of prefilled syringes and infusions by 503b compounders
9	Unsafe use of syringes for vinca alkaloids
10	1,000-fold overdoses with zinc

SAFETY briefs



Barcodes on curved surfaces. We have recently received several reports of significant scanning issues involving fentaNYL ampules from Hospira, because the barcode is printed on a curved C surface (**Figure 1**). When a barcode is printed on a manufacturer’s label over a curved surface, it is likely to make a successful scan extremely difficult or impossible. The October 19, 2017, and November 2, 2017, issues of the *ISMP Medication Safety Alert!* included articles about unreadable barcodes with examples of other products with similar issues. ISMP has notified both the US Food and Drug Administration (FDA) and Hospira about the problem. The company is aware of the issue and is making changes to address the problem. Hospira told us that, during the first quarter of 2020, it will return the barcode on ampule products to its original location, running vertically on the side of each ampule. The new orientation will allow the barcode to be scanned more easily without problems.



Figure 1. Linear barcode on Hospira fentaNYL ampule runs over a curved surface, which causes barcode scanning problems.

Other pharmaceutical companies need to take notice. Problems like this might not be noticed during the approval process if only looking at or scanning a label printed on a flat, two-dimensional surface. The label should be tested to see how it displays and scans on the container (e.g., bottle, ampule, prefilled syringe), taking into account the shape and type of packaging.

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example, entering “met” has often led to confusion between methylphenidate, methadone, met**OL**azone, methotrexate, met**FORMIN**, and metro**NIDAZOLE**; and entering “meth10” has led to confusion between methadone 10 mg and methylphenidate 10 mg.

In January 2019, we released the *ISMP Guidelines for Safe Electronic Communication of Medication Information*, which recommends a minimum of the first 5 letters of a drug name during product searches (statement 19, www.ismp.org/ext/329) to limit similar names from appearing together on the same screen. Just recently, Omnicell announced that new search functionality for its XT ADC is being implemented in support of our guidelines calling for a 5-character search (www.ismp.org/node/13648). BD Pyxis has also informed us it will make enhancements during its next software release. We hope that, in 2020, all technology vendors, including electronic health record vendors, will consider similar enhancements in product search functionality to reduce the frequency of menu screen selection errors. Until then, practitioner awareness of this problem may help change personal practice habits and promote the use of at least 5 letter characters when searching. Indication-based prescribing will also help avoid confusion.

2 Daily instead of weekly oral methotrexate for non-oncologic conditions

Prescribing, dispensing, and/or administering/taking oral methotrexate daily instead of weekly for non-oncologic conditions continued to occur in 2019. A December 2019 **QuarterWatch™** analysis (www.ismp.org/ext/336) of inadvertent daily methotrexate administration over 18 months between 2018 and 2019 demonstrated that about half of the reported errors were made by older patients who were confused about the frequency of administration, and the other half were made by healthcare providers who inadvertently prescribed, labeled, and/or dispensed methotrexate daily when weekly was intended. An analysis sponsored by the US Food and Drug Administration (FDA) suggests that up to 4 per 1,000 patients may mistakenly take the drug daily instead of weekly.

While ISMP has warned practitioners about this risk on more than 60 occasions in the *ISMP Medication Safety Alert!* prior to 2019, we more recently introduced three additional causes of methotrexate wrong frequency errors:

- A mix-up between the look-alike, round, yellow tablets of methotrexate and folic acid, the latter of which is often prescribed with methotrexate to lessen its toxicity (www.ismp.org/node/11772)
- A fatal mix-up between met**OL**azone 2.5 mg, the intended drug, and methotrexate 2.5 mg, caused in part by entering just “met” into the order entry system and selecting the wrong drug from the search menu (www.ismp.org/node/11772)
- A fatal mix-up between **PAXIL (PAR**oxetine) 10 mg, the intended drug, and **TREXALL** (methotrexate) 10 mg, caused by mishearing a prescription called into a community pharmacy (www.ismp.org/node/9651)

We encourage every healthcare provider to: 1) default to a weekly dosage regimen when entering electronic orders or prescriptions for oral methotrexate, 2) require an appropriate oncologic indication for all daily methotrexate orders, and 3) provide patient and family education about the importance of *weekly* administration (www.ismp.org/node/160). To assist with education, provide patients and families with a free copy of ISMP’s consumer leaflet on oral methotrexate (www.ismp.org/ext/290). Whenever possible, prescribers should simplify the dosing schedule to take methotrexate just once a week rather than in several divided doses 12 hours apart. No more than a 30-day supply should be dispensed.

3 Errors and hazards due to look-alike labeling of manufacturers’ products

Errors caused by look-alike packages and labels continue to occur. Highly stylized graphics and prominent corporate names and logos may overshadow essential information, and

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Mix-ups between Aimovig strengths and packages.

Outpatient hospital pharmacies, ambulatory care pharmacies, and community pharmacies should be aware that the US Food and Drug Administration (FDA) has received several reports of dispensing errors and patient administration errors with **AIMOVIG** (erenumab-aooe) injection. Aimovig is a monoclonal antibody indicated for adult migraine prophylaxis. The recommended dose is 70 mg or 140 mg injected subcutaneously once monthly. Aimovig is supplied in single-dose prefilled autoinjectors intended for patient self-administration.

When Aimovig was approved in May 2018, it was available in cartons containing either one 70 mg/mL autoinjector (for the 70 mg monthly dose) or two 70 mg/mL autoinjectors (for the 140 mg monthly dose). To enable patients to administer just one injection for a 140 mg dose, the manufacturer developed a 140 mg/mL autoinjector, which was approved in March 2019 (**Figure 1**). However, until the supply of the carton containing two 70 mg/mL autoinjectors is depleted, there are three different packages on the market: a carton containing one 140 mg autoinjector, a carton containing one 70 mg autoinjector, and a carton containing two 70 mg autoinjectors.



Figure 1. Aimovig 70 mg/mL (top) and 140 mg/mL (bottom) autoinjectors.

The introduction of the new 140 mg/mL strength and the change in packaging have inadvertently contributed to dispensing and patient administration errors. In continued on page 3 — **SAFETY** briefs >

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similar cap and label colors may make different products look alike, especially if they have similar names and dosages, are used in the same setting, and/or are stored near one another. Complicating the situation, humans tend to see what they want to see, rather than what is actually there (confirmation bias). In 2019, ISMP published about a dozen unique examples of errors and hazards with products that have look-alike packages and labels. Examples included both products from the same manufacturer (e.g., Alvogen's vials of tranexamic acid, midazolam, labetalol, and vancomycin injection) and different manufacturers (e.g., **UDENYCA** [pegfilgrastim-cbqv] and **PROLIA** [denosumab]).

While prospective analysis of the package and label is a must prior to market launch, often this review is conducted with flat two-dimensional proofs that may be larger than the size of the actual label. Thus, vulnerabilities that may lead to a mix-up with another product may not be noticed prior to FDA approval. For this reason, ISMP recommends establishing a process to ensure that all new products are evaluated by practitioners who may use them, looking at the actual packages in their work environment, *before* drugs are added to inventory. If look-alike problems are discerned, the product should be purchased from a different manufacturer if possible, or steps to avoid a mix-up should be established (e.g., separate storage, warning labels) before the drug is dispensed.

4 Misheard drug orders/recommendations during verbal/telephone communication

In an era of electronic health records, one might think that verbal or telephone orders are not necessary. Yet, certain conditions, such as prescribing a drug during an emergency or sterile procedure, or providing a recommendation during a telephone consultation, may necessitate oral communication of drug therapy, which can be easily misheard. For example, a verbal order for antithrombin during surgery was mistaken as thrombin by the time it was communicated by phone to the pharmacy (www.ismp.org/node/13424), and a recommendation for pralidoxime was mistaken as pyridoxine during telephone consultation with a poison control expert (www.ismp.org/node/1510). There were also errors in 2019 due to unnecessary use of verbal or telephone drug orders, which could have been transmitted electronically to prevent confusion.

Reserve verbal or telephone orders for use only during an emergency or when the provider is working in a sterile environment. If recommendations for drug therapy are made during telephone consultation with an expert, or the use of verbal orders is necessary in the above stated conditions, the receiver should **READ BACK** (or repeat back during sterile procedures) the drug therapy (drug, dose, route, frequency), **SPELLING** the drug name, and stating the dose in single digits (e.g., one-five for 15).

5 Unsafe “overrides” with automated dispensing cabinets

Automated dispensing cabinets have the potential to support safety while allowing required drugs to be readily accessible. However, throughout 2019, ISMP continued to hear about unsafe practices and pitfalls associated with ADC use, which placed patients in jeopardy. The three unsafe conditions we focused on in 2019 all involved the removal of a medication from an ADC without a pharmacist's review of the order (www.ismp.org/node/13032):

- 1) Overuse of overrides.** One of the biggest challenges to the safe use of ADCs is the ease with which medications can be removed upon override, many times unnecessarily and without a perceived risk.
- 2) Removal of a drug from an ADC without an order.** While rare circumstances may require the removal of a lifesaving drug without an order, the errors reported to ISMP mostly involved medications for which an order was *anticipated* (e.g., fenta**NYL** and bupivacaine in labor and delivery, moderate sedation in endoscopy, antibiotics in the emergency department [ED]).

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one example, a pharmacy dispensed two of the 140 mg/mL devices instead of a single 140 mg/mL device for the intended 140 mg dose. In another report, a patient accustomed to injecting two 70 mg/mL devices for the 140 mg dose used two 140 mg/mL devices, resulting in a 2-fold overdose. As these reports suggest, pharmacists and patients may not notice the difference in product strength, which could result in wrong dose errors.

Consider applying auxiliary labels on the cartons to prominently warn against confusion. Staff may also circle product strengths on the cartons using a permanent marker to draw attention to them. Barcode scanning should always be used to ensure the appropriate product is dispensed to patients. As always, patient (or caregiver) education is needed. Pharmacists should verify with the patient the intended dose and review the products being dispensed, along with the carton label and product information. Patients should be encouraged to review the product, label, and accompanying product information prior to every administration and to ask questions if they notice differences in the products dispensed.



Fatal route of administration mistakenly recommended in journal article.

In a recent article (Oliveira PP, et al. Patient safety in the administration of antineoplastic chemotherapy and of immunotherapies for oncological treatment: scoping review. *Texto Contexto Enferm* [online]. 2019;28:e20180312; www.ismp.org/ext/335), the following statements mistakenly substitute the word intravenous with intrathecal: "... labeling the infusion bags with vincristine preparations with an alert (for intrathecal use only)" and "... not using an infusion pump to infuse intrathecal vincristine." Mistakes can be made even in respected peer-reviewed publications, so do not immediately accept everything you read, especially when a recommendation seems questionable. We appreciate receiving information about this publication error from our colleague Andrew Seger, PharmD, a pharmacist from Boston's Brigham and Women's Hospital who tracks vinCRIStine errors from around

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3) Removal of an ordered drug from a non-profiled ADC. When removing a medication from a non-profiled ADC (not recommended), a pharmacist may never be notified about the order or have a chance to review the order retrospectively.

Now that ADC use is so widespread, 2020 is a good time to again review the safe use of ADCs using ISMP's *Guidelines for the Safe Use of Automated Dispensing Cabinets* (www.ismp.org/ext/328). Optimize the use of ADCs in the profiled mode in inpatient and outpatient areas. Always require a medication order (or protocol) prior to removing any drug from an ADC, even via override. Limit overrides to emergent circumstances (e.g., lifesaving antidotes and reversal agents) where waiting for a pharmacist to review the order could cause harm. If overrides must be used, mitigate the risk by limiting available drug quantities. Also, review the drugs available via override by location and practitioner type for appropriateness and safety.

6 Unsafe practices associated with adult IV push medications

Between January and April 2019, 233 facilities participated in the *ISMP Gap Analysis Tool (GAT) for Safe IV Push Medication Practices* (www.ismp.org/node/1188). Three areas scored low and represent a need for substantial improvement (www.ismp.org/node/11487):

- Only 22% of participants dispensed all adult IV push medications in a ready-to-administer form
- Only 23% had established and validated competency assessments for IV push medication preparation and administration
- Only 31% were confident that IV push medications were NOT diluted or reconstituted by drawing up the contents into a commercially available, prefilled flush syringe of 0.9% sodium chloride

We encourage providers to use the GAT to identify facility-specific opportunities for improvement (www.ismp.org/node/1188), and to implement the *ISMP Safe Practice Guidelines for Adult IV Push Medications* (www.ismp.org/ext/130), particularly the following:

- Require the pharmacy to dispense all adult IV push medications in a ready-to-administer form
- Establish standard competency assessments for IV push medication preparation and administration, and validate staff competencies regularly
- Educate practitioners about the risks associated with unnecessary dilution of the medication, as well as dilution or reconstitution in a commercially available prefilled flush syringe of 0.9% sodium chloride (which often remains mislabeled as containing only 0.9% sodium chloride)

7 Wrong route (intraspinal injection) errors with tranexamic acid

Multiple cases of accidental intraspinal injection of tranexamic acid were reported (www.ismp.org/node/8705), and a 2019 review article identified 21 additional cases (www.ismp.org/ext/264). This error has a mortality rate of 50% or otherwise results in harm. Previously reported cases involved mix-ups between tranexamic acid and bupivacaine or ropivacaine. All three products were available in vials with blue caps, which were stored upright with only the vial caps visible. These products are also used in areas where barcode scanning may not be utilized (e.g., operating room, labor and delivery).

We urge practitioners to purchase these products from various manufacturers to help differentiate vial appearance. Avoid upright storage of the vials so the labels are always visible. Store tranexamic acid vials away from other look-alike vials, and add an auxiliary label to vials to note the route of administration. When possible, employ barcode scanning prior to dispensing or administering these products. Exela Pharma Sciences manufactures a premixed bag of 1 g/100 mL of tranexamic acid, which should be used when appropriate

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the world. A February 9, 2017, *Safety Brief* mentioned two other cases where journal publications mistakenly associated vinCRISTine with the intrathecal route.

Incidentally, on multiple occasions we have heard people accidentally say, “intrathecal vinCRISTine” when they mean intravenous. That should be of concern as we slowly move toward the use of neuraxial connectors (NRFit), soon to be the new standard for neuraxial syringes and catheters. If “intrathecal vinCRISTine” is inadvertently communicated, a less experienced pharmacist or technician might place vinCRISTine in an NRFit syringe, which would lead to intrathecal administration. Continually reinforce with staff to always use the word “intravenous” when saying vinCRISTine. Take steps to ensure vinCRISTine can ONLY be administered after dilution in a minibag.



Nizatidine confused with tiZANidine.

In response to the voluntary recall of the H₂-receptor antagonist ranitidine because of unacceptable levels of N-nitrosodimethylamine (NDMA), some hospitals are substituting with nizatidine, also an H₂-receptor antagonist. We heard from a hospital this week about a prescribing error involving this drug that was caught by a pharmacist. The pharmacist saw an order from the emergency department for nizatidine, but it had been transmitted along with orders for pain medications for back spasms. He became suspicious and made a call to follow-up with the physician who prescribed the nizatidine. It was determined that the physician had wanted to prescribe the muscle relaxant tiZANidine, not the H₂-receptor antagonist nizatidine.

Both drugs have several letter characters that are similar, and the last few letters of tiZANidine are similar to the United States Adopted Names (USAN) stem -tidine (which is the stem associated with H₂-receptor antagonists [cimetidine type], including ranitidine). Also, tiZANidine is supplied as a bottle of 150 capsules, which might add to the risk of mix-ups if misread as the strength of nizatidine (150 mg). You might want to prepare for possible confusion between these two drugs if you are now using nizatidine in place of ranitidine.

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(indicated for hemophilia patients to reduce the risk of hemorrhage during/following tooth extraction), or have pharmacy prepare minibags to reduce the risk of mix-ups.

8 Unsafe labeling of prefilled syringes and infusions by 503b compounders

ISMP has received repeated complaints and reports of errors, some serious, related to the lack of standardized, FDA-reviewed labeling of prefilled syringes and premixed IV infusions prepared by compounding pharmacies. FDA does not hold outsourcing facilities to the same labeling standards as commercial manufacturers. For example, some compounders deviate from USP <7> labeling standards, listing the *strength per mL* as the primary expression on labels, rather than the *strength per total volume* (as required on all FDA-approved labels). Errors have occurred when the more prominent per mL strength is mistaken as the total amount of drug in the container. Look-alike syringes of drugs within the same class (e.g., **HYDRO**morphone and fenta**NYL**) have also led to mix-ups outside of the operating room (OR) when using the standard ASTM International color codes (e.g., blue for opioids) on the label. Also, unnecessary volume statements (www.ismp.org/node/9000) have led to confusion about the strength of the product.

When prefilled syringes or premixed IV infusions by compounders are needed, we advise using compounders that follow USP <7> labeling practices. Syringes with color-coded labels based on the ASTM International standard should not be used outside the OR. Employ barcode scanning when possible to verify that the correct medication is being dispensed and administered. We call on FDA to publish a guidance that calls for compounders to follow the labeling standards required of commercial manufacturers. Meanwhile, we encourage compounders to voluntarily comply with USP <7>.

9 Unsafe use of syringes for vinca alkaloids

Because errors in which vinca alkaloids were erroneously administered by the intrathecal route of administration continue, in early 2019, ISMP called upon FDA to remove administration by a syringe from the prescribing information (www.ismp.org/node/1486). Strong support for this request followed from both the National Comprehensive Cancer Network and The Joint Commission (www.ismp.org/node/1510). Administration by syringe has been at the root of all reported errors associated with vinca alkaloids inadvertently given by the intrathecal route; thus, the most effective way to prevent patient harm is to supply all vinca alkaloids in minibags, avoiding the risk of confusion with syringes.

Unfortunately, approximately 15-20% of US hospitals still use syringes at times to administer vinca alkaloids, mainly with pediatric patients. As we wait for FDA-mandated changes to the prescribing information, we urge hospitals to make it a rule to *always* dilute vinca alkaloids in a minibag prior to administration, even for pediatric patients.

10 1,000-fold overdoses with zinc

Yes, 1,000-fold dosing errors can happen when prescribing parenteral nutrition (PN) additives, particularly for pediatric patients. Similar to a fatal error more than a decade ago, one case in 2019 involved a child for whom 700 mg instead of 700 mcg of zinc was prescribed when the pediatric PN template defaulted to mg dosing units, which could not be changed to mcg had the physician even noticed the error (www.ismp.org/node/9404). Furthermore, a dose warning was not issued during the prescribing process.

We advise all healthcare providers to build, test, and heed maximum dose warnings in PN order entry systems, with a hard stop for critical zinc overdoses (e.g., above 250 mcg/kg for pediatric PN). Pediatric PN templates should default to mcg dosing units for zinc, which should also correspond to the way orders are entered in automated compounders. ISMP also encourages drug information database vendors to create needed critical dose warnings for IV zinc and other trace elements, if they do not currently exist.

Special Announcements

Become an ISMP fellow

ISMP fellowships can help you grow in your career and make major contributions to medication safety worldwide. ISMP is now accepting applications for three unique programs that begin this summer/fall—the **ISMP Safe Medication Management Fellowship**, the **ISMP International Medication Safety Management Fellowship**, and the **FDA/ISMP Safe Medication Management Fellowship**. The deadline for applications is **March 31, 2020**. For more information, including program descriptions and the application, visit: www.ismp.org/node/871.

FREE FDA webinar series

The US Food and Drug Administration's (FDA) Division of Drug Information is presenting a **FREE** webinar, **FDA Drug Topics: Research Funding Opportunities to Reduce Preventable Harm**, on **January 28**. Continuing education credit is available. For details, visit: www.ismp.org/ext/30, and to register, visit: www.ismp.org/ext/31.

Practitioner in Residence mentorship

Spend a week, **March 30 to April 3**, being mentored by medication safety experts as a **Practitioner in Residence (PIR)** at ISMP's office in suburban Philadelphia. To learn more or to enroll, call 215-947-7797 or visit: www.ismp.org/node/13263.

To subscribe: www.ismp.org/node/10



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Please call 1-800-FAIL-SAFE, or visit our website at: www.ismp.org/MERP or www.ismp.org/VERP. ISMP guarantees the confidentiality of information received and respects the reporters' wishes regarding the level of detail included in publications.

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Special thanks to our 2019 MSOS Briefings presenters



The Medication Safety Officers Society (MSOS) holds Briefings every other month on various medication safety topics. The MSOS Briefings are webinars that feature three 10-minute presentations from volunteer MSOS members highlighting a project, initiative, or relevant medication safety topic. The goal is for participants to take the information presented and use it to implement similar medication safety initiatives within their own organization. At each Briefing, ISMP president, Michael Cohen, also gives an update on ISMP activities. Please let us know (ismpinfo@ismp.org) if there is a medication safety topic you would like to present (or see presented) during a 2020 MSOS Briefing. We hope others can join us as presenters in 2020! (To join the MSOS and attend the Briefings, visit: www.medsafetyofficer.org/user/register.)

Production of the MSOS Briefings would not be possible without the assistance of voluntary MSOS member presenters. ISMP sincerely thanks all the 2019 presenters who have helped make the Briefings a valuable medication safety resource for MSOS members:

Thank You!

- ◆ **L. Hayley Burgess**, PharmD, MBA, BCPP, CPPS AVP, Clinical Pharmacy Services and Medication Safety Clinical Services Group, HCA Healthcare, Nashville, TN
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