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ISMP

Community/Ambulatory Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

QuarterWatch™ (2017 Annual Report)

Four severe adverse events and the leading suspect drugs

In the latest issue of ISMP's QuarterWatch™, we examine a full year of adverse drug event reports received by the US Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) during 2017, to identify the most frequently named suspect drugs in four distinctive and severe adverse drug events:

- **Rhabdomyolysis**, the destruction of skeletal muscle cells accompanied by the release of cellular proteins into the blood, with a substantial risk of causing acute renal failure
- **Serotonin syndrome (SS)** and **neuroleptic malignant syndrome (NMS)**, neurologic disorders caused by drugs that trigger abnormal serotonin levels (with SS) or block dopamine (with NMS), which results in aberrant behavior and thought, muscle spasms, and compromises to the autonomic nervous system
- **Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)**, a disorder in which the body's immune system attacks and destroys the skin, producing a condition similar to severe burns
- **Progressive multifocal leukoencephalopathy (PML)**, an often fatal viral infection of the brain that occurs when immunosuppressive drugs or human immunodeficiency virus (HIV) compromise the body's ability to hold a prevalent virus in check

While these disorders are thought to be relatively uncommon, at least in severe forms, their true incidence is unknown. The 4,631 cases of these adverse drug events reported to FDA in 2017 (**Table 1**), some of which were fatal, do not provide reliable insights into how frequently they may occur in exposed patients. All four adverse events are distinctive medical emergencies, and most are less likely to be confounded by signs and symptoms of the underlying medical problem being treated. Thus, the proportion of cases occurring that are subsequently reported for these disorders could be higher than for more typical and potentially elusive adverse drug events. While common adverse drug events like nausea often have many causes, with these four disorders, drugs are by far the most prominent cause. Thus, the key components of treatment are to manage the symptoms and identify and discontinue the causal drug.

Table 1. Cases reported to FDA for four severe adverse drug events, 2017

Adverse Drug Events	Number of Cases	Mortality Rate (%)
Rhabdomyolysis	1,549	12%
Serotonin and neuroleptic malignant syndromes	1,485	11%
Stevens-Johnson syndrome/toxic epidermal necrolysis	1,178	18%
Progressive multifocal leukoencephalopathy	419	29%

Rhabdomyolysis

Causes and symptoms. Many drugs have the unwanted ability to damage and destroy skeletal muscle cells. When this happens, the cells disintegrate and release

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SAFETY briefs

HIGH-ALERT

Clear instructions and patient education key for Xarelto. XARELTO (rivaroxaban), a direct oral anticoagulant, is approved for a number of indications, including the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE). For these two indications, the patient initially takes 15 mg twice daily with food. After three weeks (21 days) on this dose, the patient switches to 20 mg once daily with food for the remainder of treatment. However, we have received reports in which patients have been dispensed and taken both doses concurrently.

We first wrote about this situation in our November 2014 newsletter. A patient with a diagnosis of DVT was discharged from a hospital and provided with two prescriptions for Xarelto—one for 15 mg and another for 20 mg. Neither the prescription directions nor the discharge instructions given to the patient made it clear that the 20 mg tablets were not to be started until the 15 mg tablets were finished. The prescriptions were dispensed together at the patient's community pharmacy as the prescription benefit manager (PBM), pharmacy computer system, nor the pharmacist flagged the potential for duplicate therapy. The patient took the two prescriptions concurrently and was fortunate to not have any serious bleeding.

Just recently, ISMP received another report of this type of error that resulted in patient harm. During a clinic visit, an elderly patient was given two Xarelto prescriptions—Xarelto 15 mg twice daily for 21 days and Xarelto 20 mg daily with a start date of 21 days later. Similar to the first case, both prescriptions were dispensed at the same time by a community pharmacy. The patient was admitted to a local hospital 3 weeks later with a sub-

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Table 2. Strong signals for rhabdomyolysis, 2017

Suspect Drugs	Cases
Statins	**264**
atorvastatin	114
simvastatin	97
rosuvastatin	53
Antipsychotics*	**184**
ARIPiprazole	83
QUEtiapine	23
risperi**DONE**	19
OLANZapine	19
paliperidone	18
clo**ZAP**ine	12
haloperidol	10
Analgesics	**86**
methadone	30
acetaminophen	24
pregabalin	17
gabapentin	15
Anticonvulsants	**77**
lev**ETIRA**cetam	64
lamo**TRI**gine	13
Antineoplastics	**40**
nivolumab	25
trabectedin	15
Antidepressants	**25**
sertraline	13
venlafaxine	12
Other	**68**
met**FORMIN**	20
DAPTOmycin	15
furosemide	12
am**LODIP**ine	11
sacubitril/valsartan	10

* Most of these cases were secondary to NMS

their contents, including creatine kinase and myoglobin, into the bloodstream. If cell destruction is extensive, renal failure is possible if the kidneys cannot filter out the large quantities of cellular proteins that have been released. Notably, this is the most extreme subset of the spectrum of muscle damage induced by therapeutic drugs. Signs and symptoms of rhabdomyolysis include elevated creatine kinase, muscle pain, dark urine (from myoglobin), fever, vomiting, and muscle cramping. The release of calcium, potassium, and sodium from disintegrating cells can also trigger potentially life-threatening arrhythmias.

Suspect drugs. Rhabdomyolysis was notable for a substantial number of drugs implicated and the large population of patients exposed to this adverse drug event. The 25 drugs identified as having the strongest signals for rhabdomyolysis in 2017 are listed in **Table 2**. Overall, 179 different drugs were linked to 2 or more reports of rhabdomyolysis. Statins accounted for the largest proportion of cases. All the major statins were implicated, although not all met our criteria as a strong signal (10 or more cases). Also prominent were 7 of the most widely prescribed antipsychotic drugs. Most of these cases were secondary to another life-threatening adverse drug reaction, NMS (see details in the next section).

While many of the drugs in **Table 2** were already known suspects, we also identified two novel and more recently approved suspect drugs, nivolumab (**OPDIVO**) and sacubitril/valsartan (**ENTRESTO**). Nivolumab is among a group of new immune checkpoint inhibitors that block a key signaling protein (PD-1), opening tumor cells up to attack by T-cells. Growing evidence shows treatment can also result in additional T-cell attack on muscles and organs. Sacubitril/valsartan, a new combination product for heart failure, showed evidence of possible muscle harm during clinical trials.

Serotonin Syndrome (SS) and Neuroleptic Malignant Syndrome (NMS)

Causes and symptoms. SS and NMS share many similarities. The onset of both syndromes can be rapid—within hours of drug consumption for SS, and within days for NMS. Both involve neurotransmitters that help mediate many bodily functions, and both may lead to life-threatening disruptions of the central nervous system (CNS), including erratic or irregular heartbeats, irregular breathing, altered mental status, and loss of control over body temperature, mostly fever. The most common

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dural hematoma. It was noted by the patient's partner that the patient had been taking both strengths of Xarelto each day since the prescriptions were filled. The health system identified a few factors that contributed to the event, including 1) insufficient patient education at the time of prescribing and dispensing; 2) the labeling of the 20 mg daily prescription did not clearly indicated that the medication should not be taken until the 15 mg twice daily prescription was completed; and 3) limited use of the manufacturer's starter pack that guides patients to proper dosing for the first 30 days of treatment.

While it may be convenient for both prescriptions to be issued and dispensed at the same time, the safety of this practice is in question. Ideally, as the situation and patient conditions allow, the prescription for the 20 mg daily dose should not be communicated to the pharmacy until a few days before it is to start. If prescribers must prescribe both dosing regimens at the same time, provide clear directions to the patient and ensure they are understood. Prescribers should include prescription instructions for the 20 mg tablets to begin after the 15 mg tablet prescription supply is exhausted (after 21 days). The statement, "Begin taking after [date]" should be included in the Xarelto 20 mg directions. Pharmacists should make sure the patient has received these explicit instructions verbally and in writing.

For certain high-alert drugs and drug classes, improved, effective computer warnings that are not easy to bypass are required. Payer systems should also have an automated method to decline payment for prescriptions that may cause an overdose, like in this case with Xarelto.

Unfortunately, in many pharmacies today, more emphasis is placed on increasing prescription dispensing and vaccine administration volumes rather than ensuring the provision of proper, pharmacist-led

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symptom is clonus, which can be so severe that muscle cells are damaged, resulting in rhabdomyolysis.

Suspect drugs. One way that the syndromes differ is that SS is caused by drugs that can affect serotonin reuptake, and NMS is caused by drugs that block dopamine. The 19 drugs identified as having the strongest signals for SS in 2017 are listed in **Table 3**. Antidepressants, mostly selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs), accounted for the largest proportion of cases. But other drugs, including certain opioids, antipsychotics, and antiemetics that block serotonin receptors were also suspects. SS was infrequently caused by a single serotonergic drug at therapeutic doses. The most commonly reported causes were interactions between multiple serotonergic drugs, or accidental or intentional drug overdoses. The syndrome varies widely in severity and can range from mild symptoms such as hypertension to severe symptoms such as agitation, hallucinations, fever, vomiting, and spastic muscle contractions. The psychiatric symptoms can sometimes be mistaken for a worsening of the mental disorder being treated.

Table 3. Strong signals for serotonin syndrome, 2017

Suspect Drugs	Cases
Antidepressants	**284**
sertraline	63
venlafaxine	50
FLUoxetine	35
escitalopram	29
DULoxetine	26
citalopram	22
vortioxetine	21
PARoxetine	20
bu**PROP**ion	18
Opioids	**47**
tra**MAD**ol	37
tapentadol	10
Antipsychotics	**82**
ARIPiprazole	37
QUEtiapine	31
OLANZapine	14
Other	**61**
linezolid	17
methylphenidate	12
ondansetron	11
lithium	11
sodium oxybate	10

Table 4. Strong signals for neuroleptic malignant syndrome, 2017

Suspect Drugs	Cases
Antipsychotics	**497**
ARIPiprazole	189
OLANZapine	95
QUEtiapine	77
risperi**DONE**	50
haloperidol	34
clo**ZAP**ine	31
paliperidone	21

The 7 antipsychotics that are strong suspects for NMS are shown in **Table 4**. **ARIP**iprazole accounted for the largest proportion of cases. We found a few dozen additional reported cases with strong signals for drugs whose primary mechanism of action does not directly block dopamine receptors, including valproic acid, lithium, sertraline, mirtazapine, and **PAR**oxetine. NMS occurs at normal therapeutic doses, usually within a few days of starting treatment with (or switching between) antipsychotics or other drugs that affect neurotransmission. The syndrome can also occur upon abrupt withdrawal of drugs that block dopamine receptors. The hallmark symptoms are disturbed mental functioning, lead pipe muscle rigidity, and fever.

Confusion between syndromes. The similarity in symptoms between the two syndromes often leads to confusion in diagnosis. The cases are also confounded by polypharmacy, such as consumers taking both an antidepressant and antipsychotic drug. Still another layer of complexity arises because some antipsychotic drugs have active effects on both dopamine and serotonin receptors, notably **ARIP**iprazole. Furthermore, FDA warnings for antidepressant drugs, such as **PAR**oxetine, express uncertainty as to which of the two syndromes are expected to occur.

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patient education when dispensing new prescriptions. It is time for this paradigm to change and for patient education by pharmacists for selected high-alert drugs, such as anticoagulants, to be mandated.

Wrong resident errors. Wrong patient errors do not only happen at the point-of-sale in pharmacies or only impact retail customers. ISMP regularly receives reports of wrong long-term care (LTC) resident errors that occur when pharmacy staff enter a medication order into the wrong resident's profile. This erroneous order entry subsequently appears on the wrong resident's pharmacy-prepared medication administration record (MAR) increasing the risk that the error will reach the resident. Similar or the same last names of residents are at the root of many of these errors. The risk can be compounded if the resident's name is not clearly printed on the order.

In one event, the pharmacy received an order for warfarin 4 mg for a resident, but the order was entered into the profile of another resident with the same last name. Although the drug appeared on the wrong resident's MAR, the error was caught by a nurse before warfarin was given.

ISMP has also received reports in which medications for a resident in one LTC facility were accidentally entered into the pharmacy computer for a resident in another LTC facility. For example, a buprenorphine (**BUTRANS**) patch (7.5 mcg/hr) intended for an opioid-tolerant resident with chronic pain was dispensed to an opioid-naïve resident with the same last name in a different facility. Fortunately, a nurse noticed the error before the patch was applied.

Unlike traditional community pharmacy practice, those who provide medications to LTC residents cannot engage the residents to help in the identification process. Pharmacies must rely on the information they receive from the facility. Use at least two resident identifiers (i.e., full name and

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Stevens-Johnson Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN)

Causes and symptoms. SJS/TEN is a rare autoimmune disorder that causes T-cells and natural killer cells to attack and kill dermal cells, destroying the skin and causing a disfiguring and painful condition similar to severe burns. The outer skin layers slough off even when gently rubbed. The difference between SJS and TEN is the extent of body surface area (BSA) affected, with SJS limited to less severe cases in which less than 10% of the BSA is compromised. Recent studies suggest mortality rates range from 12% for the least severe cases to 49% for TEN cases with a larger BSA affected.

Table 5. Strong signals for Stevens-Johnson syndrome/toxic epidermal necrolysis, 2017

Suspect Drugs	Cases	Suspect Drugs	Cases
Anticonvulsants	**210**	**Analgesics**	**91**
lamo**TRI**gine	128	ibuprofen	39
car**BAM**azepine	34	acetaminophen	39
phenytoin	22	diclofenac	13
valproic acid	13	**Antineoplastics**	**72**
lev**ETIRA**cetam	13	nivolumab	23
Antibiotics/Antifungals	**105**	pembrolizumab	20
sulfamethoxazole/ trimethoprim	50	lenalidomide	17
vancomycin	18	cobimetinib	12
		Antipsychotics	**16**
ciprofloxacin	15	**ARIP**iprazole	16
		Other	**59**
fluconazole	12	allopurinol	43
clindamycin	10	omeprazole	16

Suspect drugs. Drugs are the primary but not exclusive cause of SJS/TEN, with more than 100 drugs implicated in published studies. In the 2017 adverse drug event data we identified 20 drugs with strong signals for SJS/TEN (**Table 5**). Lamo**TRI**gine was the most frequent suspect drug. Cases were also reported for some of the most widely used over-the-counter therapeutic drugs (ibuprofen, acetaminophen, and omeprazole), several antibiotics/antifungals, and 3 recently approved oncology drugs (nivolumab, pembrolizumab, and cobimetinib) with smaller patient populations. While our strongest signals were linked to 20 drugs, we identified 134 additional drugs with 2 to 9 reported cases of SJS/TEN, including 4 of the most widely used antibiotics (amoxicillin, levo**FLOX**acin, clarithromycin, and azithromycin).

Progressive Multifocal Leukoencephalopathy (PML)

Causes and symptoms. PML is an often fatal viral infection of the brain that occurs when immunosuppressive drugs or HIV compromise the body's ability to hold in check the widely prevalent John Cunningham virus (JCV), which lurks harmlessly in 50-70% of the population after initial infection, which usually occurs during childhood. Initial infection and later latency are without symptoms until the body is immunocompromised. This is caused mostly by monoclonal antibodies, which disable the body's defense to JCV in some people and allows the virus to attack the brain's white matter. Changes in behavior, confusion, aphasia, impaired gait, and visual disturbances follow. Published studies of small patient populations report incidence from about 1 per 1,000 patients taking natalizumab, to 1 per 32,000 patients taking ri**TUX**imab.

Suspect drugs. In 2017 we identified 419 reported cases of PML with a fatality rate of 29%, the highest for any of the four disorders. Four drugs had strong signals (**Table 6** on page 5). Natalizumab was initially withdrawn from the market in 2005 after 3 patients died of PML during clinical trials but was reintroduced in 2006 with prominent

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date of birth) to verify resident identity. If these identifiers are not available or illegible, pharmacy staff should contact the LTC facility to collect and verify the information. Pharmacies may also consider employing alerts to warn staff about possible name confusion when residents have the same or similar last names, particularly if residing in the same LTC facility.

Look-alike benzodiazepine bottles.

We were recently alerted to a photo of look-alike manufacturer medication bottles (**Figure 1**) posted on a listserv. Bottles of **LOR**azepam 2 mg tablets and **ALPRAZ**olam 2 mg tablets, both made by Actavis (**Figure 2**), look nearly identical. Both products have similar looking names and overlapping dosage strengths. In fact, both **LOR**azepam and **ALPRAZ**olam appear on the *ISMP List of Confused Drug Names* and *FDA and ISMP Lists of Look-Alike Drug Names with Recommended Tall Man Letters* because of multiple reports of mix-ups between the two names. The containers also use the same colors. The inclusion of the tablet images on the labels is good labeling practice but it's effectiveness is

Figure 1. Look-alike bottles of **LOR**azepam 2 mg tablets and **ALPRAZ**olam 2mg tablets from Actavis.

likely diminished by the shared look-alike characteristics of the labels. It is unlikely these products are routinely stored near one another, so the best way to prevent mix-ups between these products is to order one of them from a different manufacturer. Implementing barcode scanning during the production stage of the dispensing process also can identify when the wrong product is selected from the shelf.

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and dire warnings and a restricted distribution program. Thus, it is likely that a greater proportion of PML cases for natalizumab are reported to FDA. Ri**TUX**imab has a boxed warning for PML (and SJS/TEN, for which 9 reports were received in 2017). Fingolimod is available without the same prominent warnings or restrictions. PML is included as 1 of 11 warnings about severe adverse effects. Mycophenolate is associated with reactivation of numerous viral infections, including JCV, cytomegalovirus, and hepatitis B and C. Overall, 35 additional drugs were possible suspects, accounting for 2 to 9 case reports.

Table 6. Strong signals for progressive multifocal leukoencephalopathy, 2017

Suspect Drugs	Cases
natalizumab	154
ri**TUX**imab	59
fingolimod	20
mycophenolate	10

Conclusion

This issue of QuarterWatch™ examined four of the most distinctive and severe adverse drug events. We found the strongest signals for more than 75 drugs associated with these disorders from a wide array of therapeutic classes, including some of the most widely used medications. More research is needed to identify why certain patients are vulnerable to these life-threatening disorders. However, the risks associated with a few drugs appear so disproportionate that safer alternative treatments, considering their risk versus benefit for the particular patient, should be considered. These drugs include:

- **Natalizumab**, which led all other drugs in reported cases linked to PML
- **LamoTRIgine**, which led all other drugs in reported cases linked to SJS/TEN and has also been linked to several other forms of hypersensitivity, sudden unexplained deaths, suicidal behavior and ideation, and blood disorders
- **ARIPiprazole**, which ranked first as a suspect drug for NMS and was also a leading suspect for SS, rhabdomyolysis, and SJS/TEN, in addition to the toxicity it shares with other antipsychotic drugs

Several other findings stood out during the analysis. Atorvastatin, simvastatin, and rosuvastatin were most frequently associated with rhabdomyolysis; however, drug harm to skeletal muscle cells could be an underestimated risk, especially if the disorder does not lead to renal failure. Both consumers and physicians should be alert to less severe signs and symptoms of harm to skeletal muscle, including milder cases of muscle pain and elevation of creatine kinase. Tra**MAD**ol, an SNRI, was a suspect drug associated with SS, although physicians are often unaware that this opioid also inhibits serotonin reuptake, sharing that mechanism of action with many antidepressants. Physicians should be alert to the possibility that concomitant use with most antidepressants could result in life-threatening episodes of SS.

FDA has devoted substantial scrutiny to these potentially lethal risks and insists that most suspect drugs include clear warnings in the prescribing information and consumer *Medication Guides*. However, the agency has no published method for assessing how frequently these adverse events occur, and which drugs are most often the suspect. Because these events are distinctive, severe, and mostly drug-related, they are excellent candidates for study in the agency's Sentinel System (www.ismp.org/ext/83) or other electronic health record data system.

The full QuarterWatch™ report with references can be found on the ISMP website at: www.ismp.org/node/482.

Special Announcements

21st ISMP Cheers Awards: Medication Safety is Right Up Our Alley

Please join us on Tuesday evening, **December 4, 2018**, for the annual **ISMP Cheers Awards** dinner at Bowlmor Anaheim in Anaheim, CA. The awards celebrate a group of healthcare leaders who are in their own league when it comes to best practices and programs that prevent medication errors and protect patients. Highlights of the gala will include a keynote address by Ana McKee, MD, Executive Vice President and Chief Medical Officer of The Joint Commission. To register for the dinner or make a donation to support ISMP's lifesaving work, please visit: www.ismp.org/node/938.

Free ISMP webinar on Top Safety Issues

Join us on **November 15** for a **FREE** webinar, ***ISMP Update on Top Medication Safety Issues from 2018***. This webinar will provide an update on the top medication safety issues from 2018 based on reports to the ISMP National Medication Errors Reporting Program. Information will also be provided on certain safety standards and product changes that have occurred since the events were first reported. For details and to register, visit: www.ismp.org/node/1168.

ISMP INSTITUTE FOR SAFE MEDICATION PRACTICES

ISMP Medication *Safety Alert!* Community/Ambulatory Care (ISSN 1550-6290)

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

ISMP Medication Safety Alert! ActionAgenda

ISMP One of the most important ways to prevent medication errors is to learn about problems that have occurred in other organizations and to use that information to prevent similar problems at your practice site. To promote such a process, the following selected agenda items have been prepared for you and your staff to stimulate discussion and collaborative action to reduce the risk of medication errors. These agenda topics appeared in the ISMP Medication *Safety Alert!* Community/Ambulatory Care between May 2018 and August 2018. Each item includes a brief description of the medication safety problem, recommendations to reduce the risk of errors, and the issue to locate additional information. The Action Agenda is also available for download in a Word format at: www.ismp.org/node/1175.

Key: ⚠ — ISMP high-alert medication

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Prevent accidental daily methotrexate dosing					
08/18 ⚠	ISMP has designated oral methotrexate for nononcologic use as a high-alert medication since 2003. Although the risk of errors with oral methotrexate for nononcologic use has been known for a long time, harmful and fatal errors are still occurring. Ongoing errors suggest that more needs to be done to reduce the risk of patient harm.	Default to a weekly dosing schedule and require verification and entry of an oncologic indication for daily orders in order entry systems. Limit the prescription quantity to a 30-day supply and verify the dose and frequency on all medication lists and patient instructions. Educate patients and provide them with verbal and written instructions that specify the weekly dosing schedule. Provide clear instructions on pharmacy labels for weekly dosing and specify the day of the week (written in full, not abbreviated) the medication should be taken. More strategies are available in full newsletter article.			
Reduce the risk of medication errors at school					
08/18	Just like any other location where medications are administered, errors can and do happen at schools. Children may receive their medication at school from staff who have no medical training. Prescribers and pharmacists can take steps to help parents, school staff, and school nurses safely navigate the use of medications at school.	Prescribers: Provide complete instructions that parents, school staff, and nurses can use for prescription and over-the-counter medications. The instructions should include, for example, name of the child; date of the order; name, purpose, and dose of the medication; instructions on how often to administer the medication; by which route it should be administered; and any special instructions or precautions. Pharmacists: Ensure the pharmacy label's instructions include guidance on the time of administration and how long the medication should be given. Offer, as appropriate, to divide the child's medication into two bottles, each with its own label, so one can be kept at home and the other at school.			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Analysis of vaccine errors reported in 2017 shows errors continue with little change					
06/18	The vaccines involved most often in errors have not changed since 2012: HepA, DTaP-IPV, influenza virus, Tdap, HepB, MMRV, 9vHPV, DTaP, and DTaP-IPV/Hib. These errors have many of the same contributing factors previously identified, including: age-dependent formulations of the same vaccine; unfamiliarity with the indicated ages, dosing, and schedules; similar brand and generic names, abbreviations, and labeling; and failing to verify the patient's age or check the patient's record or vaccine registry prior to vaccination.	Examine protocols and how vaccine names are presented on computer screens and medication administration records. Set up the treatment area to reduce the risk of wrong patient errors. Take precautions during vaccine dispensing and verify the patient's immunization status. Be sure to provide education to the patient and staff. A table of staff educational topics associated with frequently reported vaccine errors can be found in the June 2018 issue of the ISMP Medication *Safety Alert!* Community/Ambulatory Care.			
Error reports with SHINGRIX and ZOSTAVAX herpes zoster vaccines					
06/18	Different storage requirements of components/diluents and routes of administration for Shingrix and Zostavax have led to errors. Shingrix lyophilized antigen and adjuvant suspension must both be refrigerated. The Zostavax lyophilized vaccine component must be frozen, and its sterile water diluent must be refrigerated or kept at room temperature. Shingrix is administered intramuscularly (IM) while Zostavax is given subcutaneously.	Educate staff about the differences between Shingrix and Zostavax. Label the storage bins/shelves using the updated Centers for Disease Control and Prevention (CDC) vaccine labels, which draw attention to the differences in storage, component/diluent, and routes of administration (www.ismp.org/sc?id=3101). Store the Shingrix lyophilized component and adjuvant suspension together to reduce the risk of using the wrong diluent.			
Implement a post-fill audit program					
08/18	While we try to prevent and intercept errors when entering and preparing prescriptions, some errors make it all the way through the dispensing process. For example, during order entry of a prescription for amitriptyline 10 mg, the pharmacist selected amitriptyline 100 mg by mistake. The wrong strength of medication was dispensed to the patient. However, the error was intercepted later when a second pharmacist was reviewing prescriptions that had been processed over the previous 24 hours.	Organizations need layers of strategies in place to intercept the error before it reaches the patient or causes harm. One strategy to implement is a post-fill audit program to compare the actual prescription received from the prescriber to the computer-generated label within 24 hours of dispensing the medication. If you already have a post-fill audit program in place, consider expanding this program to include random checks of the will call bins to compare the label to the actual product/contents dispensed.			

Issue	Problem	Recommendation	Organization Assessment	Action Required/Assignment	Date Completed
Managing the drug shortage crisis					
07/18	Many practitioners feel frustrated with the current state of drug shortages. Drug shortages are causing the use of less desirable, more expensive, or unfamiliar alternative drugs; errors and poor patient outcomes due to absent or delayed treatment; and preventable adverse drug events due to use of alternative drugs or dosage forms. Additionally, lack of advance notice reduces ability to properly prepare for an impending shortage.	Assess, communicate, and monitor each drug shortage situation. Other strategies include: identify drug shortages early; assess inventory on hand; determine an organizational position on alternative suppliers; collaborate with other local healthcare providers; determine therapeutic alternatives; conduct a proactive failure mode and effects analysis (FMEA) for therapeutic alternatives; prioritize and limit drugs based on patient categories; closely monitor adverse events; and do not hoard the drug or its alternatives.			
Safeguards needed when linking or copying old prescriptions to new prescriptions					
07/18	When copying a prescription for **ADDERRALL XR** (dextroamphetamine sulfate, dextroamphetamine saccharate, amphetamine sulfate and amphetamine aspartate), the pharmacist did not notice that the dose was changed from 20 mg to 10 mg. The prescription was filled with 20 mg capsules and dispensed to the patient. One factor contributing to this error was the computer system's functionality that allows the person conducting order entry to copy or link to a previous prescription for the same drug.	Evaluate if the efficiency gains of this functionality outweigh the safety risks. If used, review the workflow and prompts when copying or linking to old prescriptions. Design computer systems to guide the person to verify that each piece of information on the new prescription matches the one already on the patient's profile. Conduct a double check of the order entry by comparing the prescription information entered into the computer system to that contained on the original prescription. If the original prescription is placed on hold, this same verification should occur again when the prescription is eventually dispensed.			
Educate fluorouracil home infusion patients about accidental overinfusion					
07/18 ⚠	A physician prescribed a 7-day continuous infusion of fluorouracil for a patient at home via an elastomeric infusion pump. The patient received the entire infusion in just 4 days but waited until his scheduled doctor's appointment 4 days later to report the mishap. The patient experienced serious sequelae and was admitted to the hospital for 7 days.	Educate patients with ambulatory infusion pumps about how the pump works, what to expect during treatment, the infusion rate, how long the infusion should last, how much should be left in the container each day, and to immediately report any incident to their care team should the container empty sooner than anticipated so an antidote can be administered.			