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ISMP 25 YEARS ADVANCING MEDICATION SAFETY

Acute Care ISMP Medication Safety Alert!®

Educating the Healthcare Community About Safe Medication Practices

New recommendations to improve drug allergy capture and clinical decision support

The *Partnership for Health IT Patient Safety*, a national collaborative convened by ECRI Institute, has released a new report on drug allergy interactions and how clinical decision support (CDS) and health information technology (IT) can be used to improve safety.[1] The report, ***Safe Practices for Drug Allergies—Using CDS and Health IT***, presents the findings of a multistakeholder workgroup composed of members from the *Partnership*, including healthcare providers, members from professional and patient safety organizations, safety and quality advocates, health IT developers, and academic researchers. The workgroup was co-chaired by ISMP President Michael Cohen and ISMP Medication Safety Specialist Christina Michalek and funded in part by the Gordon and Betty Moore Foundation. The report sets forth evidence-based safe practices and suggested implementation strategies for using technology to standardize allergy documentation, enabling CDS tools to provide more actionable allergy information, monitoring alerts for effectiveness, and engaging patients. A summary of key highlights from the report follows.[1]

Importance of Drug Allergy Information and CDS Tools

Timely access to accurate, up-to-date drug allergy information is critical to avoid potentially life-threatening adverse drug reactions that can delay the delivery of an appropriate treatment, necessitate additional treatments, increase care costs, and negatively impact patient outcomes. To facilitate the appropriate triggering of alerts, the information must be documented using the correct allergy terminology, coded properly, and captured in a standard location. Outdated allergy information must also be removed from the patient's list of active allergies.

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22nd Annual ISMP Cheers Awards Nominations

In our ongoing effort to improve patient safety, ISMP takes great joy in recognizing others who share this same vision for the future. Each year, ISMP celebrates individuals, institutions, and groups that have demonstrated exemplary commitment to the continued science and study of medication safety through innovative and creative projects, educational efforts, standard setting, and/or research. The celebrated winners will receive an ISMP Cheers Award, which will be presented during an evening ceremony in early December of each year—more to follow on the gala!

Nominations for this year's Cheers Awards will be accepted through **September 9**. ISMP accepts external nominations, including self-nominations. The prestigious Awards spotlight efforts from all healthcare disciplines, and winners have included representatives from hospitals, health systems, long-term care, ambulatory care, community pharmacies, professional associations, federal and state agencies, as well as individual advocates. Cheers Award winners demonstrate a willingness to share learning beyond the organization (e.g., professional presentations; articles in peer-reviewed publications; tools shared on the internet; willingness to share learning in ISMP newsletters). To submit a nomination, visit: www.ismp.org/node/1036.

SAFETY briefs

Prolia-Udenyca look-alike update. We continue to receive reports about potential look-alike mix-ups between cartons of **PROLIA** (denosumab; Amgen), an osteoporosis drug, and **UDENYCA** (pegfilgrastim-cbqv; Coherus BioSciences), a biosimilar leukocyte growth factor associated with the reference pegfilgrastim product, **NEULASTA**. The US Food and Drug Administration (FDA) initially approved Prolia in 2010. Udenyca was approved in November 2018, and since its launch in January, we have received 12 reports of potential mix-ups. None of the reports have mentioned an actual error involving a patient. However, as reported in our May 23, 2019 issue, we have received reports of dispensing and drug storage errors. In several cases, a Prolia syringe carton was stocked in place of Udenyca, and vice versa, in automated dispensing cabinet refrigerators in outpatient infusion sites.

Figure 1. Package similarity has led to dispensing and storage errors.

The reports all indicate that the similar appearance of the outer cartons of these medications increases the risk of a medication error (**Figure 1**). Each carton holds a single syringe. Each outer carton has similar green and white coloring, and the packaging appears to be of similar size and dimension. Both medications are marked "for subcutaneous use." The concentration for each drug is listed in a green circle in the same location. Both concentrations include the numbers 6 and 0, which one

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How drug allergy information is gathered, documented, communicated, and used remains a challenge. The process is increasingly influenced by various CDS tools, including immediate electronic alerts and reminders in the electronic health record (EHR), as well as allergy information available in patient assessments, order sets, care plans, protocols, patient data summaries and flowsheets, medication administration records (MARs), and knowledge resources. Much of the focus with drug allergy interaction prevention has been on CDS alerts; however, alert override rates have risen from 50% in the mid-1990s to almost 90% in 2015 because many alerts are considered insignificant or unclear, or do not provide all the information needed for effective decision-making.

Excessive alerts and subsequent overrides are also caused by inaccurate or outdated allergy information; inappropriate detection of cross-reactivity or sensitivity; and unnecessary triggers for mild, non-immune-mediated adverse drug reactions. On the other hand, an appropriate alert may not be triggered at all if the drug allergy information has not been gathered and accurately documented in the EHR, or if the information is captured in a free-text field.

Despite the use of CDS, including alerts and informational content provided during electronic prescribing and transmission, adverse events due to drug allergies continue to occur. To reduce the frequency of these events, organizations must focus on optimizing CDS for drug allergy interactions and providing tools to facilitate and communicate the right drug allergy information at the right time within the workflow. Technologies, both those presently available and those still in development, offer potential solutions for decreasing the incidence of drug allergy events, enabling safer and less costly healthcare.

Methodology of Collaborative Workgroup

Expert recommendations. To explore the goal of optimizing CDS for drug allergy interactions, the *Partnership's* workgroup first considered the findings of a multidisciplinary group of experts who, in 2017, identified a set of conceptual and practical recommendations for improved drug allergy alerts:[2]

- **Improved allergy documentation**, including a more detailed specification and characterization of the patient's allergies to ensure that alerts are triggered when they matter most and avoided for mild intolerances or previously tolerated medications
- **Patient engagement** in the allergy reconciliation process to create and maintain a meaningful allergy list in the EHR
- **Improved alerting mechanisms** that consider reaction severity and other contextual information (e.g., match between the allergen and prescribed medication, probability of reaction occurrence, information on whether the alert was fired or overridden in the past) when presenting alerts to clinicians
- **Policies and guidelines** for clinicians to support a more patient-centered allergy alerting system
- **Continuous alert monitoring and improvement** by tracking the frequency of drug allergy alerts and override rates over time and making appropriate changes to impact allergy safety

These recommendations formed the foundation of the workgroup's investigation regarding how technology could be used to improve safety.

Literature review. The workgroup conducted a literature review that identified 62 studies published between 2003 and 2018 about drug allergy documentation and CDS. Seven studies met inclusion criteria for the analysis and were associated with one of the following outcomes: improved accuracy of drug allergy documentation;

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reporter thought could add to the confusion. The Prolia 1 mL syringe contains 60 mg, and the Udenyca 0.6 mL syringe contains 6 mg. Prolia and Udenyca are likely to be dispensed to the same outpatient centers. Both are refrigerated items and may be near one another if stored alphabetically by brand name. Once the carton is opened, the syringes look different, but this may not be helpful in differentiating the medications unless the person handling it already knows what it should look like.

If you use these medications anywhere in your health system, please be sure to directly observe how these products are stored, including in ambulatory care cancer centers or other clinical areas. Make sure staff are aware of the potential for confusion should both drugs be available. Be sure that staff are using available barcode scanning to verify the medication before it is dispensed or administered. Another suggestion made in May was for pharmacy staff to consider circling (with a permanent marker) the drug name on the carton to draw attention to it. Coherus BioSciences informed us that it is actively investigating the situation and will soon decide on necessary actions.

Fatal error due to Paxil-Trexall sound-alike error. Yet another fatal methotrexate error has occurred, prompting ISMP to, once again, call upon healthcare providers to implement critical risk-reduction strategies to prevent these errors. In the most recent event, **PAXIL** (**PAR**oxetine) was newly prescribed for an elderly woman with depression. A prescription for a 30-day supply of Paxil 10 mg (1 tablet) daily was called into the pharmacy. Unfortunately, pharmacy staff likely misheard Paxil as **TREXALL** (methotrexate), perhaps thinking Trexall was pronounced as "TREX-ILL." Trexall 10 mg tablets were dispensed with directions to take 1 tablet daily. The dosing error was not detected prior to dispensing, and the woman was not counselled when she picked up the medication. The pharmacy label prominently displayed the brand name, Trexall, but the woman thought this was the newly prescribed antidepressant and began taking it daily. Seven days later, she became extremely ill. Her family took her to the hospital, where she was admitted to an intensive care unit. Sadly, she died within a week.

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more appropriate triggering of drug allergy alerts; improved efficiency of clinical care; or change in the rate of prescriptions for drugs to which the patient is allergic. Review of these studies suggested that, while drug allergy alerts have the potential to improve safety, alerts are frequently overridden and may fire inappropriately. While health IT interventions such as patient portals and risk stratification algorithms have shown potential, little evidence of their effectiveness was available.

Event analysis. The workgroup also examined 320 events gathered from the *Partnership's* members, ECRI Institute Patient Safety Organization (PSO), other collaborating PSOs, and ISMP. Most events were associated with drug allergy interaction alerts and reminders in the EHR, and CDS related to ordering, administration, or documentation. Events were most frequently linked to drug allergy alerts that did not function as intended or were overridden. Examples include alerts that were not triggered at various stages in the workflow or for various clinicians; alerts that were not triggered because allergy information was not recorded or in a computable format; serious alerts that were overridden due to alert fatigue; and unavailable alerts caused by workarounds. The most common allergens involved in the events were anti-infectives, opioids, cardiovascular drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), and anticoagulants.

Recommended Safe Practices

Building upon information from the literature, event analysis, and other discussions around allergy interactions, the workgroup identified four evidence-based safe practices and implementation strategies for healthcare providers and IT vendors/developers for using technology to ensure the "five rights" of allergy information and CDS:

- the *right* drug allergy information
- presented to the *right* person
- in the *right* format using CDS tools
- through the *right* channel within the EHR
- at the *right* time in the workflow.

① Use technology to standardize the documentation of drug allergy status.

To help achieve CDS interoperability, documentation of drug allergy information must be standardized to facilitate mapping and aid in triggering drug allergy alerts based on criticality and necessity. To do this:

- Characterize and distinguish adverse drug reactions as a side effect, toxicity, intolerance, idiosyncrasy, or allergy.
- Use CDS to provide standard definitions of these characterizations and require practitioners to document these fields for optimization.
- Collect detailed information about patient allergies at the time of entry or reconciliation to ensure alerts are triggered when they matter most and to avoid unnecessary alerts for mild intolerances or previously tolerated medications.
- Consider including standardized fields for reaction type, reaction description, and patient preference.
- Eliminate free-text allergy or intolerance documentation.
- Ensure drug allergy information is reconciled with the patient and that inaccurate information is updated or corrected.

② Provide actionable drug allergy alerts to improve the safety and effectiveness of drug allergy communications.

To reduce unnecessary alerts, minimize clinician burden, and facilitate greater attention to alerts with the highest severity, develop an oversight team, including appropriate subject matter experts, to evaluate the following:

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This is the first report we have received of a fatal daily methotrexate order linked to a Paxil-Trexall mix-up. However, this sound-alike name pair is particularly concerning. Unlike generic brands of methotrexate, which are available only as 2.5 mg tablets, Trexall is available in 5 mg, 7.5 mg, 10 mg, and 15 mg tablet strengths, some of which can overlap with low doses of Paxil. We will be adding this name pair to the **ISMP List of Confused Drug Names** (www.ismp.org/node/102).

Please keep in mind, methotrexate errors can originate in any care setting and can occur in many different ways. One pharmacist recently informed us that his hospital has encountered errors during both admissions and discharges, and that staff detect and correct at least 8 to 10 methotrexate errors per year. Some of these errors are associated with potentially fatal daily rather than weekly dosing of oral methotrexate.

How many more patients must be harmed before systems are strengthened to prevent these errors? Daily doses of methotrexate are reserved for specific cancer diagnoses. Both electronic health records (EHRs) and pharmacy computer systems should be programmed to default to a weekly oral methotrexate dose and should be designed to alert practitioners to potentially inadvertent daily doses. In the most recent fatal methotrexate error, we do not know if the pharmacy computer system defaulted to a weekly dose, was configured to intercept this type of error, or what type of alerts, if any, may have been displayed to the pharmacist. However, important risk-reduction strategies—such as, default to a weekly dose and an alert with a hard stop for daily doses—have been recommended for years, including in our **Targeted Medication Safety Best Practices for Hospitals** (# 2; www.ismp.org/ext/237). Yet, there are still many healthcare providers, including hospitals, that have not fully implemented these critical recommendations.

In addition to these critical recommendations, patients filling prescriptions for oral methotrexate should always be counselled when picking up prescriptions to verify the instructions and indication for taking methotrexate. A consumer learning guide for oral methotrexate from ISMP is freely

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- Criteria for triggering an alert (should be founded on appropriate alert tiering based on allergy severity, clinical relevance, and history of clinician response to the same alert [e.g., different clinicians receiving the same alert or notice])
- Display and format of alert text (should promote understanding and appropriate action)
- Alert intrusiveness (a combination of interruptive and informative alerts should be used as necessary)
- Alert frequency
- The timing of when the alert fires (should be close to the point of decision)
- Clinician time to decision (from when alert fires until next keystroke)
- Alert overrides (and reasons)

③ Use technology to monitor the effectiveness of allergy alerts.

To improve the appropriateness and effectiveness of allergy alerts and decrease clinician burden, employ technology to collect the following metrics:

- Alert frequency
- Alert adherence rates (e.g., discontinued or retracted orders)
- Override rates
- Override reasons
- Appropriateness of overrides (e.g., overriding an alert does not mean it was not useful)
- Feedback from clinicians regarding commonly encountered issues and usefulness of specific alerts

It is important to not only gather and monitor this information regularly but also to communicate it to those who can then analyze it and take action (e.g., oversight team). This information may be displayed in clinician dashboards, provided in summary reports, and discussed by those working to improve allergy alerting. The full report includes a sample CDS drug allergy dashboard that can be used to display the gathered metrics, and an algorithm to assist with the review process for CDS and drug allergies.

④ Engage patients through the use of technology to provide accurate drug allergy communications.

To ensure readily available, accurate, and up-to-date drug allergy information:

- Develop and use patient-facing technologies (e.g., web-based patient portals that are easy to understand and interpret) in order for patients themselves to communicate and update allergy information (and changes) with caregivers and the healthcare team.
- Encourage patient input of allergy information into the web-based patient-facing technologies.
- Review and validate patient-supplied allergy information, including information provided through web-based patient-facing technologies, using appropriately trained clinicians.
- Reconcile drug allergy information with the patient at every encounter (similar to medication reconciliation) and make any necessary updates and corrections.

Conclusion

ISMP encourages every healthcare provider to read the report[1] and to fully consider the expert workgroup's evidence-based safe practices to guide organizational improvements in drug allergy interaction prevention. The full report provides several tools to assist with implementation of these recommendations, including a checklist

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available to provide to patients who take oral methotrexate to treat conditions other than cancer (www.ismp.org/ext/221). Among other important safety tips, the learning guide clearly warns patients not to take oral methotrexate every day.

If Paxil and/or Trexall are available at your location, we highly recommend a computer alert to warn of possible confusion. The above case also demonstrates the danger with telephone orders. Please review our May 18, 2017, article about safe practices when giving or receiving verbal/telephone orders (www.ismp.org/node/204). Whenever possible, outpatient or discharge prescriptions should include the indication and should be electronically transmitted to pharmacies.

HIGH-ALERT

European actions to prevent methotrexate dosing errors. Medication errors with methotrexate are a global issue. In fact, the European Medicines Agency's (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) recently published recommendations to reduce the risk of dosing errors with medications containing methotrexate. ISMP and other international safety organizations involved with the International Medication Safety Network (IMSN) (www.intmedsafe.net) participated in an EMA-solicited consultation on this topic last year. For patients taking the drug weekly for non-oncologic conditions, EMA recommendations include:

- Restricting who can prescribe methotrexate-containing medications to doctors with expertise in using them
- Ensuring that patients or caregivers can follow the once-weekly dosing schedule
- Making warnings on the packaging more prominent to serve as a reminder of how the medication should be used
- Providing patients who take the oral tablets with a card (leaflet) emphasizing the weekly dosing for inflammatory diseases
- Providing educational materials for healthcare professionals, who should then counsel patients accordingly
- Using blister packages of the med-

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of safe practices for improving drug allergy CDS and an educational PowerPoint file describing the workgroup's findings and recommendations, which can be used to garner support for the organization's effort. Developing technologies that will incorporate fields to capture accurate information will allow external CDS tools to function more effectively and accurately. Development of allergy alert tiering, attention to alert appropriateness, and encouragement of patient involvement are also important, but these efforts require vigilant attention. It is essential to monitor these activities to ensure that the right information is available and that it gets to the right person, in the right intervention format, through the right channel, at the right time in the workflow.

References

1) Partnership for Health IT Patient Safety. Safe practices for drug allergies—using CDS and health IT. ECRI Institute. 2019;1-42. www.ismp.org/ext/282
2) Topaz M, Goss F, Blumenthal K, et al. Towards improved drug allergy alerts: multidisciplinary expert recommendations. *Int J Med Inform.* 2017;97:353-5.

Special Announcements

Attend ISMP program at FSHP meeting

Will you be at the Florida Society of Health-System Pharmacists (FSHP) Annual Meeting in **Orlando** this August? If so, register now for a **FREE** ISMP breakfast seminar, supported by Fresnius Kabi, on ***Improving Intravenous Drug Delivery Safety***, which will be held Saturday, **August 3**. Program speakers will discuss the primary safety issues, at-risk behaviors, and ISMP guidelines and best practices associated with intravenous (IV) drug therapy. They also will discuss findings from the *Consensus Development Conference on the Safety of IV Drug Delivery Systems*. Seats go fast! For more information or to register, visit: www.ismp.org/node/1472.

FREE FDA "Home Study" CE webinars

The US Food and Drug Administration's (FDA) Division of Drug Information is offering a number of educational webinars for healthcare professionals that can be accessed at home. If you are a physician, physician assistant, nurse, pharmacist, or pharmacy technician, you can obtain continuing education (CE) credit upon completion. Refer to the individual webinar listing for details. For more information about the Home Study webinars, visit: www.ismp.org/ext/283.

Get intensive about medication safety

The **Medication Safety Intensive (MSI)** workshops sold out quickly last year! Act now to avoid being put on the waiting list in 2019; you won't want to miss this unique opportunity to maximize your error prevention efforts and learn to look at your organization through the eyes of leading safety experts. For information and to register, visit: www.ismp.org/node/127.

2019 MSI dates

- **September 12-13**—Orlando, FL
- **December 6-7**—Las Vegas, NV

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ication that guide proper weekly dosing instead of loose tablets in bottles
- Deleting a recommendation in the oral tablet product information to split the weekly dose into divided doses (thus avoiding confusion by recommending a single weekly dose instead of two or three doses 12 hours apart)

The EMA PRAC recommendations will now be sent to the Committee for Medicinal Products for Human Use (CHMP) that recommends changes to marketing authorization. Healthcare professionals in Europe will be informed in writing of any changes.

HIGH-ALERT

Cybersecurity issues with subcutaneous insulin pump. The US Food and Drug Administration (FDA) recently announced that Medtronic has recalled certain MiniMed insulin pumps due to cybersecurity risks. The company agreed to provide alternative pumps to about 4,000 US patients. FDA became aware that unauthorized individuals could potentially connect wirelessly to a nearby MiniMed insulin pump with cybersecurity vulnerabilities. They could then change pump settings that could result in over- or under-delivery of insulin to a patient. Although FDA said the agency is not aware of any actual reports of patient harm, it did warn patients waiting for replacement pumps to get help right away if they think their settings or insulin delivery has changed, or if they have symptoms of severe hypoglycemia or diabetic ketoacidosis as described in the FDA alert (www.ismp.org/ext/281). FDA urged device manufacturers to assess and monitor cybersecurity concerns with their pumps and to be proactive about disclosing vulnerabilities and mitigations to address them. Sad to say, but healthcare providers need to keep cybersecurity issues in mind if unexpected changes occur while a patient is receiving subcutaneous insulin via an insulin pump.

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Report medication and vaccine errors to ISMP: Please call 1-800-FAIL-SAF(E), 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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