FDA Drug Topics:
ROLE OF FDA AND ISMP IN PREVENTING MEDICATION ERRORS

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Learning Objectives

• Describe FDA’s role in pre-marketing and post-marketing activities to prevent and address medication errors.

• Outline strategies aimed to increase the safe use of drug products by minimizing use error that is related to the design, naming, labeling, and/or packaging of drug products.

• Review examples of recent medication error reports.

• Summarize how healthcare providers can help identify, prevent, and mitigate medication errors.
DMEPA’s Premarket and Postmarket Activities in Preventing Medication Errors

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Associate Director, FDA, CDER, OSE, OMEPRM, Division of Medication Error Prevention and Analysis (DMEPA)
Overview of DMEPA

Division of Medication Error Prevention and Analysis

• CDER lead for medication error prevention and analysis for drug and therapeutic biological products
• Scientists and healthcare professionals with varied backgrounds

Mission:
To increase the safe use of drug products by minimizing use error that is related to the *naming, labeling, packaging, or design* of drug products
Definition: Medication Error

• “A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer”
  – National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP)

• Intentional or deliberate uses (e.g., abuse, misuse, off label use) are generally not considered medication errors

Medication Errors are a Global Public Health Burden

Estimated annual cost of U.S. outpatient and inpatient preventable medication errors

$21 BILLION

Among adult outpatients... 52% (95% CI: 42–62%) of adverse drug reactions were preventable

52%

Among inpatients... 45% (95% CI: 33–58%) of adverse drug reactions were preventable [errors]


Medication Errors and Product Life Cycle

Discovery & development
Preclinical research
Clinical research
FDA review
Market approval
Postmarket safety monitoring

Premarket (pre-approval)
Postmarket (post-approval)
WHAT DO WE DO?

DMEPA Review Activities

Reviews take into account current federal regulations, applicable Guidance for Industry, USP Standards, and relevant postmarket experience.

- PROPRIETARY NAMES
  Primary/signatory authority on review of proprietary names.

- NONPROPRIETARY NAME SUFFIX

- PRODUCT LABELING

- PRODUCT PACKAGING

- HUMAN FACTORS/PRODUCT DESIGN
  Primary/signatory authority on human factors protocols.

- POSTMARKET PHARMACOVIGILANCE
Safety assessment of proposed proprietary name for risk of drug name confusion that may lead to medication errors.

Considerations:
- **spelling** of the name
- **pronunciation** of the name when spoken
- **appearance** of the name when scripted throughout the medication use system
Look-Alike Sound-Alike Safety Assessment

Proprietary Name Review

- **OPDP***: Conducts **misbranding** assessment of the proposed proprietary name
  
  *For OTC products, the misbranding review is conducted by the Office of Nonprescription Drugs (ONPD)

- **OND**: Provides **misbranding** and **safety** concerns with the proposed proprietary name based on clinical, chemistry, and/or pharmacology data that may impact acceptability

- **DMEPA**: Conducts **safety** assessment of the proposed proprietary name for risk of drug name confusion that may lead to medication errors.
Proprietary Name Review
Misbranding Assessment

DMEPA will object to a proposed name if it may misbrand the product for the following reasons:

• The proprietary name suggests that the drug is safer or more effective than has been demonstrated by scientific evidence.
• The proprietary name is “fanciful” and suggests that it has some unique effectiveness or composition when it does not. (21 CFR 201.10(c)(3)).
Proprietary Name Review
Safety Assessment

Focus: Prevent medication errors due to drug name confusion

21 CFR 201.10 (c.) The labeling of a drug may be misleading by reason (among other reasons) of:
(5) Designation of a drug or ingredient by a proprietary name that, because of similarity in spelling or pronunciation, may be confused with the proprietary name or the established name of a different drug or ingredient.

Draft Guidance: Best Practices in Developing Proprietary Names for Drugs
Proprietary Name Review
Safety Assessment

• Preliminary safety assessment:
  — United States Adopted Names (USAN) stems
  — other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors

• Similarity in printing, writing, and speech

• FDA Prescription Simulation Studies
  — handwritten prescriptions
  — verbal pronunciation of the drug name
  — computerized provider order entry

• Similarity of names by using FDA’s Phonetic and Orthographic Computer Analysis (POCA) program and assessment of POCA scores

Proprietary Name Review
Safety Assessment

Role of product characteristics in proprietary name review

Coumadin 4 mg or Avandia 4 mg?

- Indications
- Strength
- Dose
- Dosage form
- Unit of measure, typical quantity or volume
- Route of administration
- Frequency of administration

- Instructions for Use
- Patient population
- Prescriber population
- Product Packaging
- Physical attributes
- Storage conditions
- Setting of use
Proprietary Name Review
Safety Assessment

Considerations for Computerized Provider Order Entry

“Starts with”
Provides choices after typing only a few letters

“Contains”
Provides all options that contain what was typed

Brintellix
Brilinta
Ranexa
Tranexamic acid

Brintellix name changed to Trintellix in May 2016 http://www.fda.gov/Drugs/DrugSafety/ucm497942.htm
SAFETY

CONSIDERATIONS FOR
CONTAINER LABELS
and
CARTON LABELING
TO MINIMIZE
MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Guidance for Industry

Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

Draft Guidance

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5650 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the Federal Register.

For questions regarding this draft document contact (CDER), Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis, Carol Holquist at 301-796-0171.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2013

Drug Safety

Product container labels and carton labeling should communicate information that is critical to the safe use of a medication throughout the medication use system.
SAFETY CONSIDERATIONS FOR CONTAINER LABELS AND CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Critical product information should appear the most prominent on the Principal Display Panel (PDP).

<table>
<thead>
<tr>
<th>Established name or proper name</th>
<th>Proprietary name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mydrug (drugozide) Injection</td>
<td></td>
</tr>
<tr>
<td>Rx only</td>
<td></td>
</tr>
<tr>
<td>NDC 12345-6789-30</td>
<td></td>
</tr>
<tr>
<td>Product strength</td>
<td>Dosage form</td>
</tr>
<tr>
<td>50 mg/10 mL (5 mg/mL)</td>
<td></td>
</tr>
<tr>
<td>Route of administration</td>
<td>Warnings or cautionary statements</td>
</tr>
<tr>
<td>For continuous infusion after dilution</td>
<td>Single-dose vial – Discard unused portion.</td>
</tr>
<tr>
<td>10 mL single dose vial</td>
<td></td>
</tr>
</tbody>
</table>

The Principal Display Panel is the portion of the container label or carton labeling that is most likely to be displayed, presented, shown, or examined by the user when the product is on a shelf.
SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Product information on side and back panels

Side Panel
- Usual Dosage
- Product strength equivalency statement
- Reconstitution instructions
- Storage

Principal Display Panel
Rx only
NDC 12345-6789-30

Mydrug (drugozide) Injection
50 mg/10 mL
(5 mg/mL)

For continuous infusion after dilution

Manufacturer name and logo

10 mL single dose vial

Special storage requirements
Special preparation instructions

SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Text Size, Font Style, and Color on the Principal Display Panel

• Use at least a 12-point sans-serif font (e.g., Arial)

• Choose text and background color to afford adequate legibility of text

• Avoid color combinations that do not afford maximum legibility of text
SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Product Name

- The proprietary and established or proper name should be the most prominent information on the label
- The established name should be at least ½ the size of the proprietary name
- The established name should include the dosage form

Mydrug (drugozide) Injection

10 mg/2 mL
(5 mg/mL)

Rx only NDC 12345-6789-30

For continuous infusion after dilution
Single-dose vial – Discard unused portion
SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Product Strength Expression

- **Use metric units of measure (e.g., mg, mcg, mL)**

- **Nitroglycerin**
  - Nitroglycerin in 5% Dextrose Injection
  - 25 mg/250 mL (100 mcg/mL)

- **Small volume parenteral products**: Express strength as the quantity per total volume followed in close proximity by quantity per milliliter enclosed by parentheses

- **Dry powder parenteral products**: Express strength as the amount per container

- **Blister packs**: Express strength per unit; may also display the dose in certain instances
SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Product Strength and Net Quantity Statements

Note the placement of strength and net quantity

Note prominence of strength
SAFETY CONSIDERATIONS FOR CONTAINER LABELS AND CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY
APRIL 2013

Product Strength Differentiation

Ensure the product strength stands out on the container label and carton labeling

Techniques include:
- Boxing
- Prominent typeface or type weight
- Color differentiation

Rx only  NDC 12345-6789-30
Mydrug (drugozide) Injection
10 mg/2 mL
(5 mg/mL)
For continuous infusion after dilution.
Single-use vial = Discard unused portion.
1 single use vial

Rx only  NDC 12345-6789-30
Mydrug (drugozide) Injection
50 mg/10 mL
(5 mg/mL)
For continuous infusion after dilution.
Single-use vial = Discard unused portion.
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Mydrug (drugozide) Injection
50 mg/10 mL
(5 mg/mL)
For continuous infusion after dilution.
Single-use vial = Discard unused portion.
1 single use vial

10 mg  20 mg  30 mg  40 mg  50 mg  60 mg  70 mg  80 mg
Route of Administration

- Must be present on the PDP for non-oral products per 21 CFR 201.100 (b)(3)
- Avoid abbreviations
- Use affirmative statements (e.g., use “for irrigation” instead of “not for injection”) because “not” can be obscured or overlooked
SAFETY CONSIDERATIONS FOR CONTAINER LABELS and CARTON LABELING TO MINIMIZE MEDICATION ERRORS

DRAFT GUIDANCE FOR INDUSTRY APRIL 2013

Warnings for Critical Information

• Use affirmative statements
  — For intravenous infusion
  — Fatal if given by any other route
  — Must dilute before use

• Consider whether the statement is helpful to ensure safe use

Patient: Took 1 mg orally once daily.
Patient stated she was following directions on the bottle

Avoid Crowding, Visual Clutter, Dangerous Abbreviations, and Acronyms

- Crowded labels/labeling may make important information difficult to read and/or easily overlooked
- Safety considerations:
  - Separate lines or blocks of text with sufficient blank space
  - Place non-critical information on side/back panels
  - Refer to ISMP’s “List of Error Prone Abbreviations, Symbols, and Dose Designations”
  - Don’t superimpose text over images or logos
SAFETY CONSIDERATIONS FOR PRODUCT DESIGN TO MINIMIZE MEDICATION ERRORS

GUIDANCE FOR INDUSTRY
APRIL 2016

Safety Considerations for Product Design to Minimize Medication Errors
Guidance for Industry

FDA EXPECTS MANUFACTURERS TO:

1. Investigate, understand and correct identified risks
   Use analytical methods to develop drug products

2. Build safety into the product design
   Apply these methods early in drug development and throughout the drug product’s life cycle

3. Enable safe and correct use
   Eliminate or reduce design elements that can cause use-related hazards
Drug product user interface refers to all parts of a product a user interacts (e.g., sees and touches)

SAFETY CONSIDERATIONS FOR PRODUCT DESIGN TO MINIMIZE MEDICATION ERRORS

GUIDANCE FOR INDUSTRY APRIL 2016
Most effective strategies focus on improvements to design of drug product user interface.

• Consider effect of each design choice on end user

• Evaluate using proactive risk assessments before finalizing design

• Evaluate how and why problems have occurred with similar products
  • Identify error prone features and eliminate them from design
  • Prevent same errors from occurring

• Sponsors should consider lessons learned to minimize risks associated with their designs
Container Closure Design

• Is the container closure design:
  – safe for the route of administration?
  – appropriate for the intended users?

• Avoid use of a container closure that implies a route of administration other than the route intended, unless there are no other options available.
Product Strength

• Review for inconsistency between drug product strength and dosing
  – Multiple units (e.g. tablets, capsules, vials, syringes) required to achieve a usual single dose?

• Dosing errors due to:
  – miscalculations
  – forgetting how much has already been administered
SAFETY
CONSIDERATIONS FOR
PRODUCT DESIGN
TO MINIMIZE
MEDICATION ERRORS

GUIDANCE FOR INDUSTRY
APRIL 2016

Product Strength

- Co-packaged dosage delivery device should be consistent with recommended dosing regimen/directions for use
- Printed matter appearing on dosage delivery device is considered labeling
  - Dose markings must be easy to read
- Dosing devices for oral solutions should use *metric unit markings*
Human Factors?
“...the application of knowledge about human capabilities (physical, sensory, emotional, and intellectual) and limitations to the design and development of tools, devices, systems, environments, and organizations....”

Human Factors Considerations

SAFETY CONSIDERATIONS FOR PRODUCT DESIGN TO MINIMIZE MEDICATION ERRORS

GUIDANCE FOR INDUSTRY APRIL 2016
Human Factors Validation Studies

- Systematic collection of data from representative participants in realistic situations
- Help determine whether users can safely and correctly perform critical tasks involved in using the product
- Results can be used to update the Failure Mode and Effects Analysis (FMEA)
- Should be conducted before product is submitted for approval, before any product modifications or additions to a product line
- Recommend that sponsors conduct human factors studies to characterize risks as well as develop mitigation strategies
  - Studies are generally small in size and short in duration (as compared to clinical studies that support drug approval)
  - Relatively small investment of resources early in product development can avoid the need to resolve issues post-approval
Postmarket Surveillance of Medication Errors
Why is postmarket surveillance necessary?

• Limitations of premarket clinical trials
  – Trials are conducted under controlled conditions, and may not use the final approved name, labels, labeling, and packaging
  – Numbers of patients tested is too small to detect serious but rare problems, and some errors may fall into this category
  – Trials are often of short duration

• FDA has a robust program to identify potential errors and address them prior to approval. However, medications errors remain a significant burden on public health*

• Allows us to monitor error reports and address those causes of errors that may be related to a drug’s name, label and labeling, or packaging (before a product is widely distributed).

Medication error case reports

- FDA has Memorandum of Understanding (MOU) agreements with ISMP and other organizations to share publicly available medication error information.

- The FDA Adverse Event Reporting System (FAERS) is FDA’s primary source for monitoring medication errors, but we surveil other sources, including ISMP newsletters.

Medication errors are underreported

- Extent of underreporting is unknown
  - Elliott, et.al., “estimated that 237 million medication errors occur at some point in the medication process in England per year”

- No U.S. requirement to report medication errors to FDA
- Likelihood of reporting medication errors versus adverse events
Barriers for reporting medication errors

Fear of punishment or litigation

Embarrassment of having been involved a medication error

Different definitions for medication error

Not knowing where, why, or what to report

No allowance for anonymous reporting

Organizational culture

Workload/amount of time required for reporting
Example of Progression from Nonserious Event to **SERIOUS**

Report warning of potential look-alike container and cartons

DMEPA performs risk assessment, notifies FDA review division and company

Multiple reports of "near miss"

Company issues safety alert, distributes stickers, prepares to revise labeling

First serious report received (patient received wrong drug)

Labels and labeling urgently revised
Summary

• We encourage healthcare providers to report all medication errors to MedWatch.

• If we are aware of potential problems, we can work to provide effective interventions that may help minimize further errors.

• Post marketing experience also helps us anticipate potential errors.

• We aim to identify and address the risk prior to marketing to help prevent medication errors.
Resources

Guidances for Industry:
• Best Practices in Developing Proprietary Names for Drugs (Draft) – May 2014
• Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (Draft) – April 2013
• Safety Considerations for Product Design to Minimize Medication Errors – April 2016
• Applying Human Factors and Usability Engineering to Medical Devices – February 2016

We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database

Regulations*:
• 21 CFR 200s, 300s and 600s

*http://www.ecfr.gov/cgi-bin/text-idx?SID=c8497935ae0f040dfcfe06c6251ba507&mc=true&tpl=/ecfrbrowse/Title21/21tab_02.tpl
A Lot Happens When You Report A Medication Error or Hazard to FDA and ISMP

Michael R. Cohen RPh, MS, ScD (hon), DPS (hon)
President, Institute of Safe Medication Practices (ISMP)
(www.ismp.org)
ISMP National Medication Error Reporting System

— Early warning system
  • Issue nationwide hazard alerts and press releases

— Learning
  • Dissemination of information and tools

— Change
  • Product nomenclature, labeling, and packaging changes, device design, practice issues

— Standards and Guidelines
  • Advocates for national standards and guidelines
ISMP and ECRI Institute Join Forces

By joining together, ECRI Institute and ISMP create one of the largest healthcare quality and safety institutions in the world, driving greater value to the healthcare organizations they serve with unrivaled expertise, resources, and solutions.

LEARN MORE
ISMP National Medication Errors Reporting Program

Thank you for submitting a report to the ISMP National Medication Errors Reporting Program (MERP).

- Please provide as much detail as possible when telling us the story of what went wrong or could go wrong, the causes or contributing factors, how the event or condition was discovered or intercepted, and the actual or potential outcome of the involved patient(s).
- Be sure to include the names, dosage forms, and dose/strength of all involved products. For product-specific concerns (e.g., labeling and packaging risks), please include the manufacturer.
- Share your recommendations for error prevention.
- If possible, submit associated materials (e.g., photographs of products, containers, labels, de-identified prescription orders) that help support the report being submitted.

Please complete the form below and click on the “Submit” button to report the error or hazard to the ISMP National Medication Errors Reporting Program.

Name: ___________________________ (optional)
Email: ___________________________
Confirm email: _____________________
Error Description: Please describe the incident as best you can. This information will be handled in confidence.
Upload Images (optional)
Up to three images can be uploaded. Input area will appear after each image is selected up to 3.

Submit
Reporting to ISMP as a PSO
Where does ISMP get its information? Where does it go?

ISMP MERP and VERP

Providers, Consumers

FDA MedWatch

News media, other sources

ISMP Canada
ISMP Spain
ISMP Brazil
IMSN

Healthcare providers

Healthcare organizations

Consumers

Regulatory

Industry
Process when you report a hazard or error to ISMP – Every report is indispensable!

- Report received and entered into ISMP database
- ISMP professional staff review every report and gather additional information if necessary
- Report identified as requiring further investigation for sharing the lessons learned
- Further investigation conducted, with additional resources accessed
- Realistic, measurable and attainable recommendations identified along with ambitious recommendations to drive further improvements
- Hazard/error story & recommendations shared via newsletters and direct conversations with FDA, manufacturers, vendors, other regulatory agencies & other key stakeholders
- Aggregate data from error databases analyzed and published periodically
Report received and entered into ISMP database

- Report entered into one of our databases and initially reviewed by ISMP nurse or pharmacy technician analyst.
- ISMP sends an email to reporter to confirm receipt of the report and thank him or her for reporting.
ISMP professional staff review every report and gather additional information if necessary

- Report redacted of identifying provider and/or facility information
- Nurse or analyst distributes reports and accompanying photographs, screen shots or attachments through secure portal to ISMP interdisciplinary professional staff
- Professional staff reviews every report, shares comments on topic with one another via the portal
ISMP professional staff review every report and gather additional information if necessary

- Similar hazards, errors identified
- Suggest questions to ask reporter to better understand the report, make recommendations for mitigating the risk
- Reports incite conversation among professional staff
- Gain understanding of the reported risks and underlying causes
Report identified as requiring further investigation for sharing the lessons learned

- Significant factor - is report actionable? Leads to further investigation and sharing of lessons learned
- Can patients, vendors, standards organizations and regulators take specific actions to prevent or reduce risk of similar error, or mitigate potential patient harm?
- Is hazard or error new? Has it caused or could it cause harm? Does it require action by FDA or manufacturer, state professional board, standards organizations such as USP or The Joint Commission?
Steps ISMP may take to investigate hazards or errors:

- Reach out to reporter to ask clarifying questions, seek out additional information, graphics or examples
- Conduct professional literature, drug information and error-reporting database searches
- Seek out expert advice from established advisory groups or organizations with extensive knowledge in key subject areas

Further investigation conducted, with additional resources accessed
Further investigation conducted, with additional resources accessed

• Interact with other federally listed patient safety organizations (PSOs), such as our ECRI affiliate

• Interact with FDA Division of Medication Error Prevention and Analysis and others within the agency.

• Memorandum of Understanding with CDER
Further investigation conducted, with additional resources accessed

- Formal monthly calls and two face to face meetings annually
- Contact the pharmaceutical product manufacturer, device and technology vendors, drug information vendors and other service providers
- Conduct surveys to learn more about specific types of errors
• Primary focus is on a few well-thought-out, high-leverage, long-term recommendations that are realistic, measurable, and attainable with reasonable resources

• Because ISMP is not a standards-setting organization, we sometimes make ambitious recommendations to drive practice, process, and technology improvements

• Many reports trigger FDA, manufacturer, device/technology vendors to further investigate and respond
Aggregate data from error databases analyzed and published periodically

2017-2018 BIENNIAL REPORT

The ISMP National Vaccine Errors Reporting Program (VERP)


https://www.ismp.org/node/14240
Hazard/error story & recommendations shared with FDA and via newsletters, interaction with manufacturers, vendors, other key stakeholders

- ISMP’s primary vehicles are publication in one or more of our 5 subscription-based newsletters
- Urgent medication advisories requiring immediate notification of healthcare providers published first in a National Alert Network (NAN) bulletin to both ISMP email lists, ASHP members, ISMP website and member organizations of National Coordinating Council Medication Error Reporting and Prevention (NCCMERP)
- Error information contextually deidentified as necessary. Stories make information memorable
A lot happens when you report a hazard or error to ISMP — there’s no “black hole” here!

BY SCOTT M. SEGERS, RPh, CSHA, ISMP Senior Advisor, Medication Safety

January 2028 — Volume 19, Issue 1

When ISMP receives a report of a potential medication error or hazardous practice, we cannot simply allow hazards to go unnoticed or uncorrected. When we receive such reports, our staff of professional experts, who are accomplished and experienced in medicine, medication management, and patient safety, conduct a thorough investigation to get at the root cause of the problem. Our goal is to use our investigations to prevent future harm, to learn from each other, and to share that knowledge with all of our members. That is why we created The Medication Error Reporting Program (MERP). It’s an invaluable tool for healthcare professionals and other preventable medication errors. As our previous articles have indicated, MERP is an essential part of any healthcare organization’s commitment to patient safety. And it’s a powerful tool that helps us learn from each other.

The process of conducting an investigation begins when a report of a potential error or hazardous practice is received. Our investigators then conduct a thorough analysis to determine what happened and why. This analysis includes identifying all of the factors that contributed to the error or hazardous practice, as well as determining the potential impact on patient safety. Once this analysis is complete, our investigators work with the organization to develop strategies for preventing similar events in the future. This process is ongoing and can take several weeks to complete. The results of each investigation are shared with the organization, as well as with other members of the ISMP community. This sharing of knowledge helps us all learn from each other and improve our practices.

The impact of our investigations is significant. In addition to preventing future harm, our investigations help to identify areas for improvement within healthcare organizations. This, in turn, leads to the implementation of new safety measures and the development of safer systems. For example, in one recent investigation, we identified a number of factors that contributed to a medication error. As a result of this investigation, the organization in question implemented new systems and procedures to prevent similar errors from occurring in the future.

In summary, the impact of our investigations is significant. Our investigations help to prevent future harm, identify areas for improvement, and lead to the implementation of new safety measures and procedures. By sharing our findings with other members of the ISMP community, we are able to learn from each other and improve our practices. This is why we continue to invest in our investigation process and why we are dedicated to using the knowledge we gain to protect patients and improve healthcare systems.

For more information on The Medication Error Reporting Program (MERP), please visit our website at www.ismp.org/merp. If you have any questions or would like to report a potential error or hazardous practice, please contact us at info@ismp.org.

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COVID-19-related medication errors

In our April 8, 2020 newsletter (www.ismp.org/node/16888), we shared an idea to add a question, “Is this event related to COVID-19 (corona- virus) or to existing medication-related sources, allow rapid analysis of quickly emerging risks, and reduce leadership’s reaction time in knowing about and addressing some of these issues. Since then, we have received several COVID-19-related medication errors each week and wanted to update you on a few important issues.

Remdesivir: investigational drug labeling confusion

ISMP received a report last week about a missing compounding issue due to past label confusion with the investigational drug remdesivir. Some facilities have received this drug, manufactured by Gilead Sciences, under a compassionate use program during a period of expanded access and through an emergency use authorization (EUA) issued by the US Food and Drug Administration (FDA). The label had implemented an investigational study using intravenous (IV) doses of remdesivir for patients with severe COVID-19. The adult protocol called for an initial loading dose of 200 mg administered by infusion over 1 hour, followed by subsequent 100 mg doses. Each vial of remdesivir contains a total of 100 mg, instead of using 1 vial to prepare each 100 mg subsequent dose, 2 vials were used, thus providing 200 mg for each subsequent dose instead of the intended 100 mg.

Remdesivir is available for use in clinical trials in at least two different dosage forms: a lyophilized powder for injection and a liquid solution for injection. Like many investigational drug container labels, the vials are not clearly labeled, and the information presented is presented in a small font (see our 2-part article about problems with investigational drug labeling: www.ismp.org/node/9980 www.ismp.org/node/16891). The vials have a label listing the total amount (100 mg) of drug in the vial (Figure 1). The vials of remdesivir injectable solution have a label that lists the per unit, strengths, “Remdesivir (GS-5734) Injection, 5 mg/mL” (Figure 2). Below the 5 mg/mL listing, the vial label notes the total volume in the vial, “Contents: 21.2 mL” which may be confusing.

Special Alert!

Persuasive views on intranasal corticosteroids without risk assessments can lead to the increase in demand for neuromuscular blocking agents for critically ill COVID-19 (non-COVID-19) patients on long-term treatments, including glucorticoids. This could impact on the availability of these important agents. To improve patient care, the ISMP recommends that healthcare professionals carefully consider the risks and benefits of using neuromuscular blocking agents for critically ill COVID-19 (non-COVID-19) patients on long-term treatments.
ISMP Publications

— Regular Journal and Newsletter Features:

• Pharmacy Practice News
• Nursing 2020
• Hospital Pharmacy
• Pharmacy Times
• Pharmacy Today
• US Pharmacist
• Journal of Emergency Nursing
• Home Healthcare Now
Reporter’s Event Description

— “81 y.o. male admitted to hospital with slurred speech and gait change to R/O stroke. Blood glucose 57 mg/dL (Hgb A1C was 13.9% upon admission).

— It was discovered that the patient had not been removing the inner cap of his pen needle for his insulin until the day prior to admission.

— For over a year, the patient’s physician was constantly increasing the patient’s insulin dose to 150 units in the morning and 156 units at bedtime (plus 80 units insulin lispro before each meal).

— The patient described that when he injected his insulin, he would use a napkin to soak up the excess insulin that spilled when he injected himself.

— He confirmed he would use an entire pen per day. On day PTA he realized he had not been removing the pen needle inner cap as instructed during diabetes self-management education.

— Patient took off the inner cap and injected the prescribed amount of insulin resulting in hypoglycemia.

— The patient was treated and recovered. During hospital stay he required significantly less insulin (glargine 15 units subcutaneously hs and insulin lispro 4-6 units before meals).”
Hazard/Error Story & Recommendations Shared

Unusual explanation for hyperglycemia in patients on insulin

From a regulatory standpoint, hospitals are required by the FDA CPT codes 2,009 for “preparation and with proper controls that eliminate occupational exposure or reduce it to the lowest feasible extent.” Whatever the reason, insulin must be stored in the hospital (preferably a separate and secure area) to prevent it from being lost.

One example of a safety needle for use with the NaNOID insulin, available from Medtronic, is the Flexi-Fine Autoclavable (Figure 1). The needle is covered while the needle is in use. The needle is then removed by the physician, who remains unharmed, can be used again.

The Autoclavable system is quite different from standard insulin pen needles, which patients purchase at their pharmacy, which may not employ a shield system. A hospital pharmacist and a nurse reported that some patients who became familiar with the NovoTide Autoclavable while in the hospital were later confirmed that they were using a standard insulin needle (ID Ultra Fine III) after discharge. The needle also has a clear, visible, red injection site. It is not reusable, but is disposable after use. The needle has a white stainless steel needle with the standard insulin needle for diagnostic purposes. The patient developed diabetic ketosis and other symptoms.

To protect staff from needlestick injuries and against the reuse of needles, many hospitals use insulin pen needles that automatically re-cover and lock the needle once injection has been completed and the needle has been removed from the unit. Such products include NOVODERM AUTOCLOSING (from Nordoril) and NOAUTOCLOSING DISPOSABLE. These safety needles are also recommended for some patients with manic depression or psychosis and for caregivers administering the injection to the patient.

With the NovoTide Autoclavable (Figure 1) needle safety is provided by a safety needle cover that is automatically re-covered and locked after injection, preventing reuse of the needle. The needle is then removed by the physician, who remains unharmed, can be used again.

The Autoclavable safety needle system is different from standard insulin pen needles widely used by patients in the home, which do not employ an automatic needle shield. These standard needles are available from brand and generic manufacturers. Because standard pen needles and those with an automatic needle shield may look similar, patients may not be aware of the differences in preparation for administration. Both the automatic safety needle and standard needle systems have a larger outer protection cover that, when removed, exposes either a retractable needle shield (Figure 1) or a plain inner needle cover (Figure 2). The automatic safety needle shield is contained at page 68.
Your Reports at Work

FDA tells pen injector needle manufacturers to improve patient instructions

Thanks to your reporting about patients who failed to remove the inner pen needle cover prior to administering insulin, the US Food and Drug Administration (FDA) has asked needle manufacturers to update labeling and improve patient instructions for use.

Standard pen needles have outer and inner needle covers, both of which must be removed prior to injection. However, hospitals often use safety needles for medication pens. These have an outer cover that must be removed, but there is no inner cover to remove. An inner shield over the needle automatically retracts during injection and covers the needle after injection to prevent needlestick injuries. After discharge, patients may receive standard pen needles from their pharmacy and not know that the inner needle cover must be removed, especially if they have not been taught this step while hospitalized. If the inner cover of a standard pen needle is not removed, patients may not receive the medication.


In response to these concerns, FDA has asked needle manufacturers to review their labeling and educational materials and to update and clarify the need to remove the inner needle cover/cap before injection. The agency also requested manufacturers to add a warning in the labeling, such as: “Remove both the outer cover and the inner needle cover before injection. If both the outer cover and the inner needle cover are not removed before use, the medication or dose may not be injected, which may result in serious injury or death.” The FDA labeling request can be accessed at: www.ismp.org/ext/155.

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Working with industry to improve products
October 2019

IMPORTANT DRUG WARNING

Subject: Potential of carton confusion between UDENYCA® and Prolia® packaging associated with the risk of administration or dispensing error and adverse events

Dear Health Care Provider,

The purpose of this letter is to make you aware of the potential of carton confusion between the UDENYCA® (pegfilgrastim-cchv) and Prolia® (denosumab) packaging which could lead to a risk of product administration or dispensing error and adverse events.

Potential of carton confusion between UDENYCA® and Prolia®

UDENYCA® and Prolia® have a similar carton appearance (Figure 1) which has led to product administration or dispensing errors and adverse events.

1. Carton Appearance: Both cartons look similar with a green/white color scheme and green horizontal bands across the top (Figure 1).
2. Presentation and Strength: Both cartons hold one single-dose prefilled syringe, and both medications are intended for subcutaneous administration. The UDENYCA® syringe contains 6 mg and the Prolia® syringe contains 60 mg.
   a. The needle guard of UDENYCA® syringe is colorless while the Prolia® syringe is translucent green (Figure 2).
3. Storage: Both are refrigerated upon receipt and have the potential to be stored next to each other.

Figure 1: UDENYCA® (left) and Prolia® (right) Cartons

Figure 2: UDENYCA® (left) and Prolia® (right) Syringes

Coherus BioSciences, Inc. 586 Twin Dolphin Drive, Suite 600 Redwood City, CA 94065
New recommendations to improve drug allergy capture and clinical decision support

The Partnership for Health IT Patient Safety, a national collaborative convened by IHI Partnerships, 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. The report, "Safe Practices for Drug Allergies—Using CDS and Health IT," presents the findings of a multi-stakeholder workgroup composed of members from the Partnership, including healthcare providers, members from professional and patient safety organizations, and quality advocates, health IT developers, and academic researchers. The workgroup was co-led by ISMP President Michael Cohen and ISMP Medication Safety Specialist Christine 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 safer tools to provide more actionable allergy information, monitoring alerts effectively, and engaging patients. A summary of key highlights from the report follows.³

Importance of Drug Allergy Information and CDS Tools

Timely access to accurate, up-to-date drug allergy information is critical to any potentially life-threatening adverse drug reactions that can delay the delivery of 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 appropriately, and captured in a standardized location. Outdated allergy information may also be removed from the patient's list of active allergies.

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 and groups that have demonstrated exemplary commitment to the continued success and safety of medication therapy through innovative and creative projects and educational efforts, standard setting, and research. The celebrated nominees will receive an ISMP Cheers Award, which will be presented during an evening ceremony early December of each year — more to follow on the goal!

Nominations for this year’s Cheers Awards will be accepted through September 4. ISMP accepts external nominations, including self-nominations. The prestigious Awards spotlight efforts from all levels of decision making, and nominees have included process improvements 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, engage in professional associations, present at peer-reviewed publications, share on the internet, willingness to share learning in ISMP newsletters. To submit a nomination, visit: www.ismp.org/cheers17.
Error reporting outcomes

- Improvements in patient safety as a result of hundreds of specific product-related changes
  - Drug naming, labeling, packaging, medication-related device design, measuring devices, infusion pump safety issues.
- Some products withdrawn from market due to medication error issues
- Thousands of product label and labelling changes as a result of new FDA requirements or changes in USP standards (USP <7>) due to reported medication errors.
  - Dangerous abbreviations and dose designations, ratio expression, expression of drug concentration, certain new drug packaging requirements, etc.
- Practice-related standards (CMS, Joint Commission, etc.)
(7) LABELING

INTRODUCTION

This general chapter provides definitions and standards for labeling of official articles. Labeling standards for an article recognized in USP-NF are expressed in the article’s monograph and applicable general chapters. It is intended that all articles in USP or NF will be subject to the labeling requirements specified in this chapter by means of a provision in General Notices, 19 Preservation, Packaging, Storage, and Labeling, unless different requirements are provided in a specific monograph. As with compendial standards for naming, identity, strength, quality, and purity, compendial requirements for labeling have a role in the elaboration and maintenance of federal law (see the Federal Food, Drug, and Cosmetic Act (FFDCA) sections 501(a), 502(c)(3)(B), 502(g), and 502(h)). Exceptions or additional requirements specific to animal drug products and compounded preparations are provided in separate sections. The labeling is not included in this general chapter.

DEFINITIONS

The term “labeling” includes all labels and other written, printed, or graphic matter on an article’s immediate container or on, in, or on any package or wrapper in which it is enclosed, except any outer shipping container. The term “label” is that part of the labeling on the immediate container. A shipping container that contains a single article, unless the container also is essentially the immediate container or the outside of the consumer package, must be labeled with a minimum of product identification (except for controlled substances), lot number, expiration date, and conditions for storage and identification. Beyond-use dates (BUDs) and expiration dates are not the same. An expiration date identifies the time during which a conventionally manufactured product, active ingredient, or excipient can be expected to meet the requirements of a compendial monograph. If one exists, it is kept under the prescribed storage conditions. The expiration date limits the time during which the conventionally manufactured product, active pharmaceutical ingredient (API), or excipient may be dispensed or used. Expiration dates are assigned by manufacturers of conventionally manufactured products based on statistical and performance testing of the stability, chemical and physical stability, and packaging integrity of the product. Expiration dates are specific for a particular formulation in its container and at stated exposure conditions of illumination and temperature. The beyond-use date (BUD) is the time or date by which a compounded preparation must be discarded. The date or time is determined from the date the preparation was compounded.

LABELS AND LABELING FOR DRUG PRODUCTS AND COMPOUNDED PREPARATIONS EXPRESSED AS ACTIVE MOIETY IN NAME AND STRENGTH

The names and strengths of drug products and compounded preparations formulated with a salt of an acid or base are to be expressed in terms of the active moiety on the label (see Monograph: T121: Monograph Naming Policy for Soft Drug Substances in Drug Products and Compounded Preparations).

Labeling

The labeling clearly states the specific salt form of the active moiety that is present in the product or preparation because this information may be useful to practitioners and patients. The names and strengths of both the active moiety and specific salt form (when applicable) are provided in the labeling.

Exceptions

In rare cases in which the use of the specific salt form of the active moiety in the title provides vital information from a clinical perspective, an exception to this policy may be considered. In such cases, when the monograph title contains the specific salt form of the active moiety, the strength of the product or preparation is also expressed in terms of the specific salt form.

LABELS AND LABELING FOR INJECTABLE PRODUCTS

The labels and the labeling state the following information:

- Name of the product
- In the case of a lyophilized product, the quantity or proportion of each active moiety or drug substance in a specified volume
- In the case of any product to which a diluent must be added before use, the quantity or proportion of each active moiety or drug substance, name and volume of diluent to be added, the concentration after the diluent is added, directions for proper storage of the constituted solution, and a BUD (see Expiration Date and Beyond Use Date)

- Route(s) of administration

*There are some limitations, see 21 CFR 201.101, 21 CFR 201.103(a), 21 CFR 201.5(a), 21 CFR 201.6(a).*
FDA Guidance Statements

Guidance for Industry
Best Practices in Developing Proprietary Names for Drugs

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to http://www.regulations.gov/. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5600 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes the Federal Register.

For questions regarding this draft document contact (CDER) Office of Surveillance and Epidemiology, Division of Medicines Error Prevention and Analysis, Kellie Taylor at 301-796-0157, or (CDER) Office of Communications, Outreach and Development at 888-852-4700 or 240-402-7800.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

May 2014
Drug Safety

Safety Considerations for Product Design to Minimize Medication Errors
Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2016
Drug Safety
Public Health Advisories
FDA Drug Safety Communications for Drug Products Associated with Medication Errors

- FDA Drug Safety Communication: FDA approves brand name change for antidepressant drug Brintellix (vortioxetine) to avoid confusion with antiplatelet drug Brilinta (ticagrelor)
- FDA Drug Safety Communication: FDA cautions about dosing errors when switching between different oral formulations of antifungal Noxafil (posaconazole); label changes approved
- FDA Drug Safety Communication: FDA cautions about dose confusion and medication error with antibacterial drug Avycaz (ceftazidime and avibactam)
- FDA Drug Safety Communication: FDA cautions about dose confusion and medication errors for antibacterial drug Zerbaxa (ceftolozane and tazobactam)
- FDA Drug Safety Communication: FDA Alerts Pharmacists and Health Care Professionals to Potential for Injury when Dispensing the Similar-Sounding Drugs Durezol and Durasal
- FDA Drug Safety Communication: FDA requires label warnings to prohibit sharing of multi-dose diabetes pen devices among patients
- FDA Drug Safety Communication: FDA requiring color changes to Duragesic (fentanyl) pain patches to aid safety-emphasizing that accidental exposure to used patches can cause death
- FDA Drug Safety Communication: FDA warns about potential medication errors resulting from confusion regarding nonproprietary name for breast cancer drug Kadcyla (ado-trastuzumab emtansine)
FDA Advise-ERR in ISMP Medication Safety Alert! publications and FDA website

ISMP FDA Advise-ERR Articles

- FDA Advise-ERR: Taking Crysvita with active vitamin D analogs is contraindicated
- FDA Advise-ERR: Covers still being applied without the cloNIDine patch
- FDA Advise-ERR: Lumoxiti has unique preparation instructions!
- FDA Advise-ERR: Vyxeos: Verify Drug Name and Dose to Avoid Errors!
- FDA Advise-ERR: Concomitant use of Entresto and ACE inhibitors can lead to serious outcomes
- FDA Advise-ERR: Veterinary Drug and Human Drug à A Drug Name Mix-up
- FDA Advise-ERR: Avoid using the error-prone abbreviation, TPA
- FDA Advise-ERR: MefloquineâNot the same as Malarone!
ISMP educational programs

Manage the Safety Risks Associated with IV Push Medication Use

Working Together to Address Global Drug Safety Issues with Packaging and Labeling

Michael R. Cohen, RPh, MS, ScD (hon), DPS (hon) FASHP
President, Institute for Safe Medication Practices
Chairperson, International Medication Safety Network

Just Culture
Training for Managers

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ISMP Practice Guidelines

Guidelines for Optimizing Safe Implementation and Use of Smart Infusion Pumps

Guidelines for the Safe Use of Automated Dispensing Cabinets

ISMP Targeted Medication Safety Best Practices for Hospitals

ISMP Guidelines for Optimizing Safe Subcutaneous Insulin Use in Adults

Recommendations for the Safe Management of Patients with an External Subcutaneous Insulin Pump During Hospitalization