Improving Consistency of Information Between Prescribing Information and Carton/Container Labeling

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Disclaimer

➢ The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.

➢ The labeling examples in this presentation are provided only to demonstrate current labeling development challenges and should not be considered FDA recommended templates.

➢ Reference to any marketed products is for illustrative purposes only and does not constitute endorsement by the FDA.
Learning Objectives

➢ Review examples of inappropriate inconsistencies between Prescribing Information (PI) and carton/container (c/c) labeling

➢ Discuss use of appropriate dosage terminology statement and dosage recommendations on c/c labeling

➢ Discuss considerations for using the term “Prescribing Information” rather than “package insert” on c/c labeling
<table>
<thead>
<tr>
<th>Intended Primary Audience</th>
<th>Prescribing Information(^1)</th>
<th>Carton/Container Labeling(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthcare practitioners</td>
<td>Healthcare practitioners, and/or patients or caregivers</td>
<td></td>
</tr>
<tr>
<td>Contains</td>
<td>Summary of essential scientific information needed for the safe and effective use of the drug(^1)</td>
<td>Critical information for the identification and safe use of the drug(^2)</td>
</tr>
<tr>
<td>Presentation</td>
<td>5-83 pages(^3)</td>
<td>Small containers to large cartons</td>
</tr>
</tbody>
</table>

\(^1\) 21 CFR 201.56(a)

\(^2\) c/c labeling communicate critical information for the identification and safe use of the drug from the initial prescription, to procurement, stocking, selection, dispensing, preparation, and administration. See draft guidance for industry: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (April 2013) (when final, this guidance will represent the FDA’s current thinking)

\(^3\) PI could be shorter or longer
Examples of Acceptable Differences in Content and Format Between PI and C/C Labeling

<table>
<thead>
<tr>
<th>PI</th>
<th>C/C Labeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed information about indication(s), recommended dosage(s), warnings, adverse reactions, drug interactions, etc.</td>
<td>Present</td>
</tr>
<tr>
<td>“Rx only”, lot number, bar code, expiration date</td>
<td>Typically absent</td>
</tr>
</tbody>
</table>

Also, there are acceptable differences between format/organization of PI and c/c labeling

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1 List is not comprehensive
Recommend Consistent Information Across PI and C/C Labeling (if applicable)

➢ Drug product information the PI and on the c/c labeling should be as consistent as possible

➢ Inappropriate inconsistencies in presentation of product information between c/c labeling and PI can lead to confusion and/or medication errors

Draft guidance for industry: Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format (January 2018) (when final, this guidance will represent the FDA’s current thinking); Guidance for industry: Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements (February 2013)
Recommend Reviewing Content in PI and C/C Labeling for Consistency

<table>
<thead>
<tr>
<th>Product Quality Focused Content¹</th>
<th>Clinically Focused Content¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nonproprietary name</td>
<td>• Dosage statement terminology</td>
</tr>
<tr>
<td>• Dosage form(s)</td>
<td>• Dosage recommendations</td>
</tr>
<tr>
<td>• Strength(s)</td>
<td>• Warnings or cautionary statements</td>
</tr>
<tr>
<td>• Package type terms</td>
<td>• Route(s) of administration</td>
</tr>
<tr>
<td>• Discard statements</td>
<td>• Indication(s)</td>
</tr>
<tr>
<td>• Identifying characteristics</td>
<td></td>
</tr>
<tr>
<td>• Storage</td>
<td></td>
</tr>
<tr>
<td>• Net quantity</td>
<td></td>
</tr>
<tr>
<td>• Active ingredient</td>
<td></td>
</tr>
<tr>
<td>• Reconstitution and/or dilution instructions</td>
<td></td>
</tr>
</tbody>
</table>

¹ Lists are not comprehensive (some items in the table have product quality and clinical content)
Ensure Consistent Product Quality-Related Items Between C/C Labeling and PI (when appropriate)

For the fictitious examples in the following slides, all of the required and recommended elements may not be displayed on the c/c labeling or the PI (for presentation purposes)
Dosage Form Inconsistent Between PI and C/C Labeling

Carton Labeling

NDC 12345-678-90  Rx

**DRUG-X®**  Correct!
(drugoxide)
**for injection**
100 mg per vial

Pharmacist: Dispense with accompanying Medication Guide to each patient

Must reconstitute prior to intravenous infusion.
Reconstitute lyophilized powder with 10 mL of Sterile Water for Injection, USP; shake until powder dissolves. After reconstitution, the concentration is 10 mg/mL. See Prescribing Information for detailed reconstitution instructions.

Contains 10 single-dose vials  ABC Corporation

Beginning of the Highlights of Prescribing Information

**HIGHLIGHTS OF PRESCRIBING INFORMATION**
These highlights do not include all the information needed to use DRUG-X safely and effectively. See full prescribing information for DRUG-X.

**DRUG-X (drugoxide) injection**, for intravenous use
Initial U.S. Approval: 2001

Word “for” before a dosage form describes a solid dosage form that requires reconstitution before use

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1 Draft guidance for industry: [Product Title and Initial U.S. Approval in the Highlights of Prescribing Information for Human Prescription Drug and Biological Products - Content and Format](https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM623733.pdf) (January 2018) (when final, this guidance will represent the FDA’s current thinking)
Strength Expression\(^1\) Inconsistent Between PI and C/C Labeling

Carton Labeling

NDC 12345-678-90

**DRUG-X**\(^\circledR\) **(drugoxide)**

**Injection**

**10 mg/2 mL**

For intravenous use only

5 x 2 mL single-dose vials

Discard unused portion

Sterile solution

Rx Only

Incorrect

Full Prescribing Information

3 DOSAGE FORMS AND STRENGTHS

Injection: 10 mg/2 mL (5 mg/mL) (clear, colorless solution) in a single-dose vial

Double expression of strength is correct!

\(^1\) See USP Chapter <7>
Package Type Term¹ Inconsistent Between PI and C/C Labeling

Carton Labeling

NDC 12345-678-90 Rx Only

DRUG-X® (drugoxide) Injection 10 mg/2 mL (5 mg/mL)

For intravenous use only
5 x 2 mL single-use vials ABC Corporation
Discard unused portion Sterile solution

Incorrect

Full Prescribing Information

3 DOSAGE FORMS AND STRENGTHS
Injection: 10 mg/2 mL (5 mg/mL) (clear, colorless solution) in a single-dose vial

Package term for injectable drug product for parenteral use is correct!

¹ See Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018) and USP Chapter <659>
Ensure Clinically Related Items Are Consistent Across C/C Labeling and PI (when appropriate)

For the fictitious examples in the following slides, all of the required and recommended elements may not be displayed on the c/c labeling or the PI (for presentation purposes)
Dosage Inconsistent Between PI and C/C Labeling

Carton Labeling

DRUG-X®
(drugoxide)
Tablets
10 mg

Usual Dosage: Take one tablet orally once daily. See Prescribing Information for complete dosage information.

Each tablet contains 10 mg of drugoxide.

Incorrect

Full Prescribing Information

2 DOSAGE AND ADMINISTRATION

The recommended daily dosage of DRUG-X is:

- 20 mg once daily for adult patients 70 kg or greater
- 10 mg once daily for adult patients less than 70 kg

Correct!

Inaccurate recommended dosage on c/c labeling can lead to medication errors

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Recommended Dosage in DOSAGE AND ADMINISTRATION Section of PI May be Complicated

➢ Recommended:
  ▪ Dosage
  ▪ Duration of use
  ▪ Dosage in specific populations
  ▪ Tapering

➢ Recommended premedication and concomitant medication

➢ Recommended dosage modifications due to:
  ▪ Adverse reactions or risks
  ▪ Drug interactions

If dosage is complex, consider cross-referencing to PI (without including any specific dosage on c/c labeling)

1 See 21 CFR 201.57(c)(3) and the Guidance for Industry: Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products - Content and Format (March 2010)
C/C Labeling Regulations: Must Include a Statement of “Recommended” or “Usual” Dosage

C/C labeling must include a statement of the “recommended or usual dosage” (with some exceptions):¹

➢ If the dosage is informative and realistic it should appear on the label
➢ If there are space limitations may refer to PI for the complete dosage information

¹ See 21 CFR 201.100(b)(2) and 21 CFR 201.55; Statement of dosage is not required for (1) small container drug product labels, (2) biological product container labels; or (3) single-dose biological product carton labeling

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Dosage Terminology Inconsistent Between PI and C/C Labeling

Carton Labeling

DRUG-X®
(drugoxide)
Tablets
10 mg

Full Prescribing Information

Prepared

2 DOSAGE AND ADMINISTRATION

The recommended daily dosage of DRUG-X is:

- 20 mg once daily for adult patients 70 kg or greater
- 10 mg once daily for adult patients less than 70 kg

Not Preferred

Preferred!
D&A Section Labeling Regulations: “Recommended Dosage”

➢ In 2006 under the Physician Labeling Rule (PLR), the terminology of the D&A section changed from “recommended usual dosage”\(^1\) to “recommended dosage”\(^2\)

➢ For PLR labeling, the D&A “section must state the recommended dosage”\(^2\)

➢ “Recommended dosage” may not equal “usual dosage”

D&A section = DOSAGE AND ADMINISTRATION section

\(^1\) See 21 CFR 201.80(j); \(^2\) See Final rule, “Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products,” 21 CFR 201.56(d) and 21 CFR 201.57; 71 FR 3922 published (January 24, 2006) and 21 CFR 201.57(c)(3)
For **PLR** Formatted PI, Consider Consistent Dosage Statement Terminology on C/C Labeling

PLR formatted PI must use terminology “recommended” dosage¹; thus, consider using following terms on c/c labeling:

- **Dosage**: See Prescribing Information OR
- **Recommended Dosage**: See Prescribing Information

¹ See 21 CFR 201.57(c)(3)
For “Old” (Non-PLR) Formatted PI, Consider Consistent Dosage Statement Terminology on C/C Labeling

“Old” formatted PI typically use “usual dosage” terminology; thus, consider using following terms on c/c labeling:

- **Dosage**: See Prescribing Information OR
- **Usual Dosage**: See Prescribing Information
Consider Using Terminology “Prescribing Information” Rather Than “Package Insert” on C/C Labeling

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Consider Using Term “Prescribing Information” Rather Than “Package Insert” on C/C Labeling\(^1\) (1 of 2)

C/C labeling regulations\(^2\) state if it is not possible to present an informative or useful dosage statement on limited space on c/c labeling, the statement of dosage “requirement would be met by a statement such as ‘See package insert for dosage information’”

This regulatory statement is an example; other statements may be acceptable

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\(^1\) See 21 CFR 201.55; Statement of dosage is not required for (1) small container drug product labels, (2) biological product container labels; or (3) single-dose biological product carton labeling

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Consider Using Term “Prescribing Information” Rather Than “Package Insert” on C/C Labeling (2 of 2)

- Many healthcare providers obtain labeling via electronic means.
- Many types of labeling are included in the package in addition to the PI (e.g., MG, IFU).
- Recent labeling statutes, rules, regulations, and guidances use the term “Prescribing Information” not “package insert”.
- Sections of the PI use the term “Prescribing Information”: Highlights of Prescribing Information, Full Prescribing Information: Contents, and Full Prescribing Information.

MG = Medication Guide; IFU = Instructions for Use
C/C Labeling Specific Guidances

Carton/Container Labeling Specific Resources

- Allowable Excess Volume and Labeled Vial Fill Size in Injectable Drug and Biological Products
- Product Identifiers Under the Drug Supply Chain Security Act Questions and Answers (draft)
- Product Identifier Requirements Under the Drug Supply Chain Security Act – Compliance Policy
- Bar Code Label Requirements Questions and Answers
- Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (draft)
Product Quality-Related Labeling Resources

- Considerations for Product Quality Information in Prescribing Information (2017 presentation)
- Product Title and Initial U.S. Approval in the Highlights of Prescribing Information (draft)
- Example Product Titles in Highlights of Prescribing Information
- Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use
- Tablet Scoring: Nomenclature, Labeling, and Data for Evaluation
- Naming of Drug Products Containing Salt Drug Substances Guidance
- Naming of Drug Products Containing Salt Drug Substances MAPP
- Quality Attribute Considerations for Chewable Tablets
- Recommendations for Labeling Medical Products to Inform Users that the Product or Product Container is not Made with Natural Rubber Latex
- Child-Resistant Packaging Statements in Drug Product Labeling
- Gluten in Drug Products and Associated Labeling Recommendations (Draft)
- Liposome Drug Products: Chemistry, Manufacturing, and Controls; Human Pharmacokinetics and Bioavailability; and Labeling Documentation
- Metered Dose Inhaler (MDI) and Dry Powder Inhaler (DPI) Drug Products—Quality Considerations (Draft)
- Use of Liquids and/or Soft Foods as Vehicles for Drug Administration: General Considerations for Selection and In Vitro Methods for Product Quality Assessments (Draft)
- Best Practices in Developing Proprietary Names for Drugs (draft)
- Incorporation of Physical-Chemical Identifiers into Solid Oral Dosage Form Drug Products for Anticounterfeiting

1 Prescription Drug Labeling Resources webpage
Question #1: What Content Can Differ Between the PI and C/C Labeling?

a) Dosage recommendations
b) Expression(s) of strength
c) Package type terms for parental injectable products
d) Dosage form
e) None of the above
Summary

➢ When developing PI and c/c labeling ensure consistent information across labeling types (if applicable)

➢ Use appropriate dosage statement terminology and dosage recommendations on c/c labeling

➢ Consider using the term “Prescribing Information” rather than “package insert” on c/c labeling

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