CDER Prescription Drug Labeling Conference
December 4th and 5th 2019

U.S. FOOD & DRUG ADMINISTRATION

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

Eric Brodsky, M.D.

Associate Director, Labeling Policy Team*, Office of New Drug Policy, Office of New Drugs, Center for Drug Evaluation and Research, FDA

* Labeling Policy Team (previously known as the Labeling Development Team)

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

Key Differences Between PI[1] and C/C Labeling[2]

	Prescribing Information[1]	Carton/Container Labeling[2]
Intended Primary Audience	Healthcare practitioners	Healthcare practitioners, and/or patients or caregivers
Contains	Summary of essential scientific information needed for the safe and effective use of the drug[1]	Critical information for the identification and safe use of the drug[2]
Presentation	5-83 pages[3]	Small containers to large cartons

[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 See draft guidance for industry: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (April 2013) (when final, this guidance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[1]

	PI	C/C Labeling
Detailed information about indication(s), recommended dosage(s), warnings, adverse reactions, drug interactions, etc.	Present	Absent
“Rx only”, lot number, bar code, expiration date	Typically absent	Present

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

[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[1]
- Inappropriate inconsistencies in presentation of product information between c/c labeling and PI can lead to confusion and/or medication errors

[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* (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

Product Quality Focused Content[1]	Clinically Focused Content[1]
• Nonproprietary name • Dosage form(s) • Strength(s) • Package type terms • Discard statements • Identifying characteristics • Storage • Net quantity • Active ingredient • Reconstitution and/or dilution instructions	• Dosage statement terminology • Dosage recommendations • Warnings or cautionary statements • Route(s) of administration • Indication(s)

[1] Lists are not comprehensive (some items in the table have product quality and clinical content)

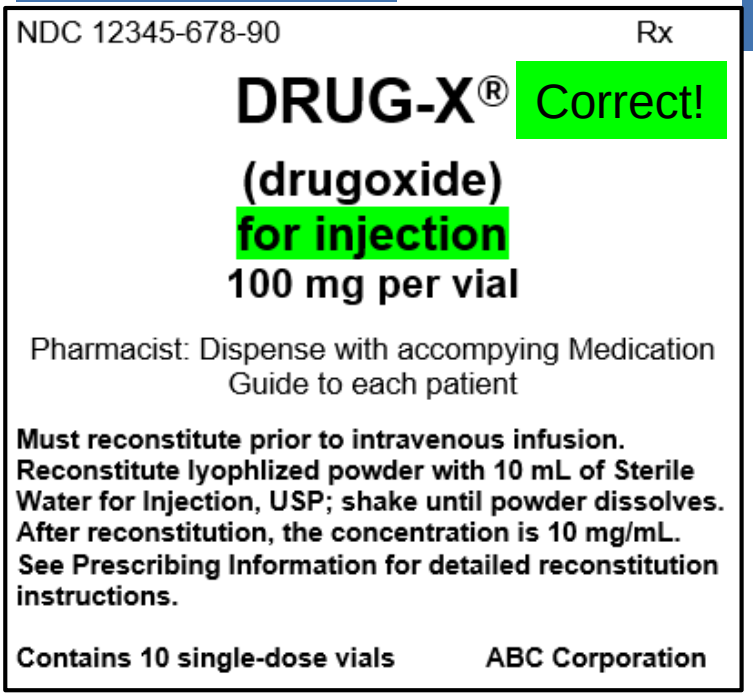
Ensure Consistent Product Quality-Related Items Between C/C Labeling and PI

(when appropriate)

[1] 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 accompying Medication Guide to each patient

Must reconstitute prior to intravenous infusion. Reconstitute lyophlized 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.

Incorrect

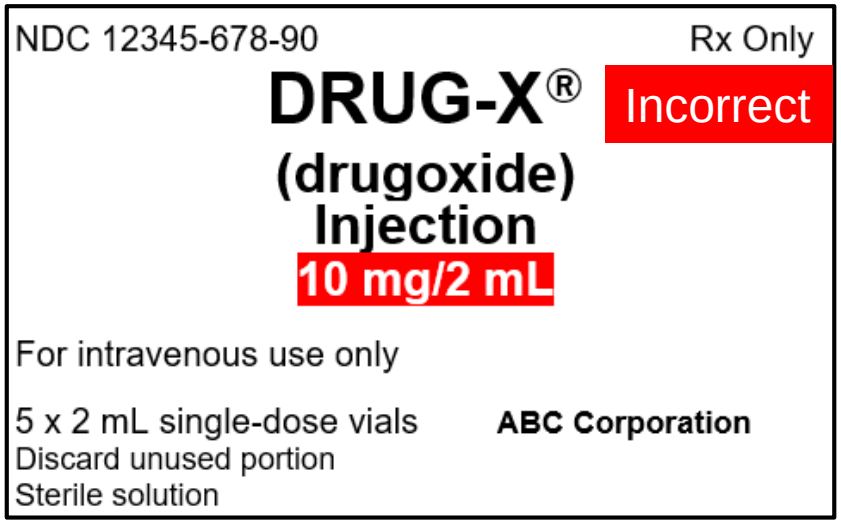
DRUG-X (drugoxide) injection, for intravenous use
Initial U.S. Approval: 2001

Word “for” before a dosage form describes a solid dosage form that requires reconstitution before use[1]

[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* (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



Full Prescribing Information

3 DOSAGE FORMS AND STRENGTHS

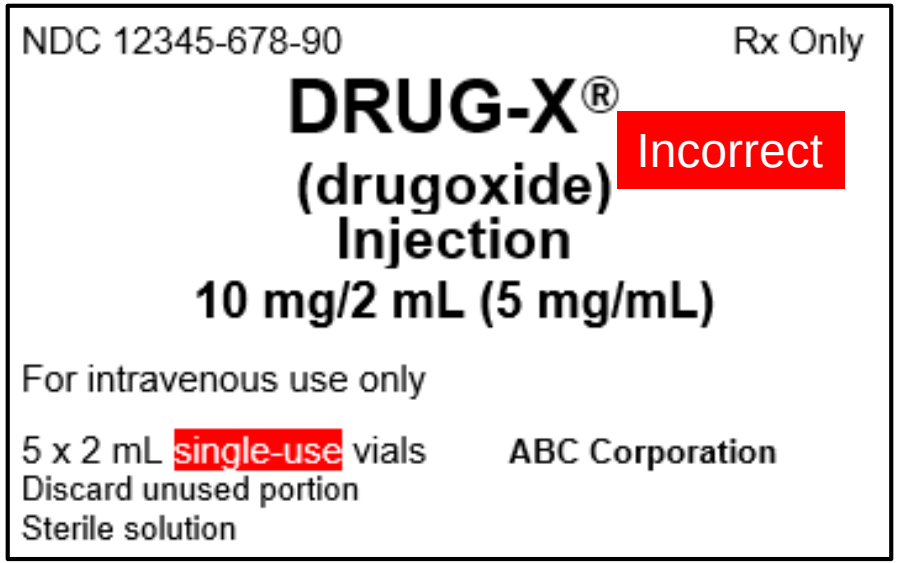
Injection: 10 mg/2 mL (5 mg/mL) (clear, colorless solution) in a single-dose vial

Double expression of strength is correct!

[1] See USP Chapter <7>

Package Type Term[1] Inconsistent Between PI and C/C Labeling

Carton Labeling



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)

[1] 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

Incorrect

Full Prescribing Information

Correct!

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

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

Recommended Dosage in DOSAGE AND ADMINISTRATION Section of PI May be Complicated[1]

- 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[1]

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

Dosage Terminology Inconsistent Between PI and C/C Labeling

Carton Labeling

DRUG-X®

(drugoxide)
Tablets
10 mg

737363 Exp 07/14

12345678901 -678-90-C79-01-A

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

Each tablet contains 10 mg of drugoxide

Store at 25°C (77°F): excursions permitted to 15° to 30°C (59° to 86°F). [See USP controlled room temperature.]

Not Preferred

Full Prescribing Information

Preferred!

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

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" dosage[1]; thus, consider using following terms on c/c labeling:

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

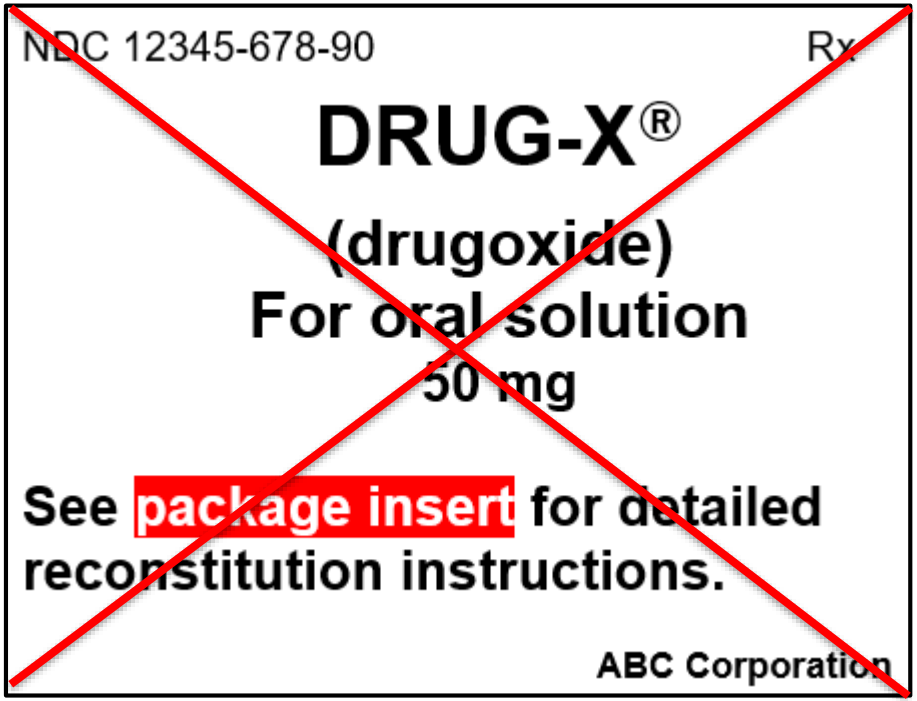
[1] See 21 CFR 201.57(c)(3)

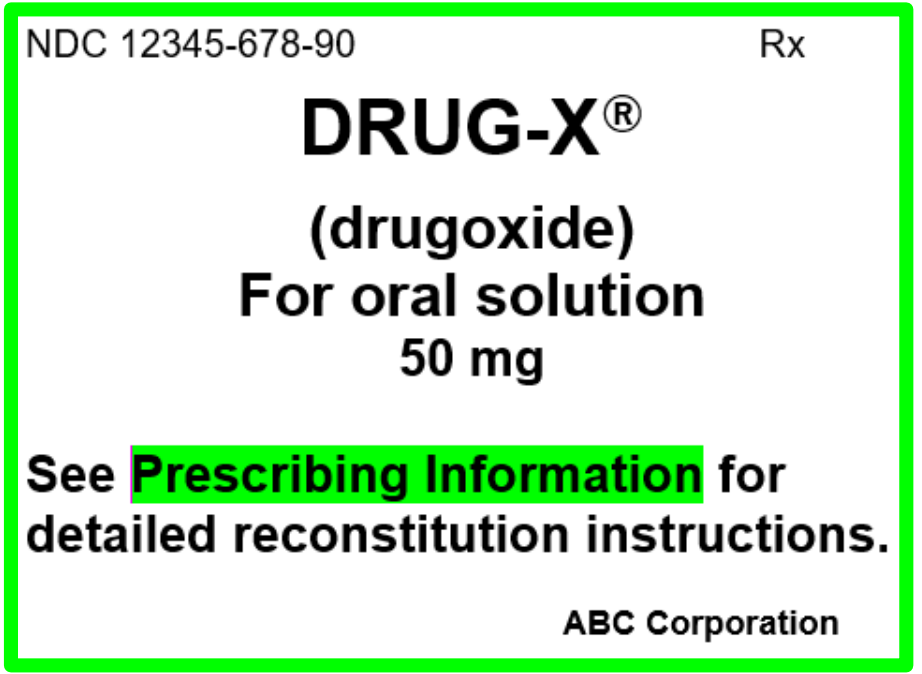
For "Old" (Non-PLR) Formatted PI, Consider Consistent Dosage Statement Terminology on C/C Labeling

"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





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

[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

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[1]

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)

[1] Prescription Drug Labeling Resources webpage

Product Quality-Related Labeling Specific Guidances[1]

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

Questions: cdersbia@fda.gov

Questions: cdersbia@fda.gov