Rare Disease Day 2024

U.S. FOOD & DRUG ADMINISTRATION

Labeling for Prescription Medicines

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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.

Overview of Presentation

- Recognize the different types of labeling for prescription medicines
- Discuss how the labeling for prescription medicines are approved by the FDA
- Describe what happens to the labeling for prescription medicines after approval

Different Types of Labeling for Prescription Medicines

Different Types of Labeling for Prescription Medicines

MEDICATION GUIDE
MYDRUG [mye-drug]
(drugoxide injection)
for intramuscular use

What is the most important information I should know about MYDRUG?
…

What is MYDRUG?
…

Who should not take MYDRUG?
…

How should I take MYDRUG?
…

What should I avoid while taking MYDRUG?
…

What are the possible or reasonably likely side effects of MYDRUG?
…
Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General information about the safe and effective use of MYDRUG.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use MYDRUG for a condition for which it was not prescribed. Do not give MYDRUG to other people, even if they have the same symptoms that you have. It may harm them.

Drug Company X, City, State, zip code

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Revised: MM/YYYY

Patient Labeling

- Recommended Dosage
- Product strength equivalency statement
- Reconstitution instructions
- Storage

Rx only NDC 12345-6789-30

Mydrug

(drugozide) Injection

50 mg/10 mL

(5 mg/mL)

For continuous infusion after dilution
Single-dose vial – Discard unused portion.

10 mL single dose vial

XX/XX

0 123456 789012

Labeling on the Packaging

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PROPRIETARY NAME safely and effectively. See full prescribing information for PROPRIETARY NAME.

PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.
- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/YYYY
Section Title, Subsection Title (x.x) M/YYYY

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for … (1)

Limitations of Use
Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

Revised: M/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

Prescribing Information

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
…

Patient Labeling for Prescription Medicines

Patient Labeling for Prescription Medicines

FDA-Approved Patient Labeling

Medication Guides, Patient Package Inserts, and Instructions for Use

- Proposed by applicant
- Reviewed and approved by FDA
- Content is based on the Prescribing Information

Patient Labeling Not Approved by FDA

"Consumer medication information"

- Not submitted to FDA
- Not reviewed or approved by FDA

Medication Guide[1] (FDA-Approved Patient Labeling)

MEDICATION GUIDE
DRUG-X [drug X]
(drugimab-cznm)
injection, for intramuscular use

What is the most important information I should know about DRUG-X? …
What is DRUG-X? …
Who should not take DRUG-X? …
Before taking DRUG-X, tell your healthcare provider about all of your medical conditions, including if you: …
How should I take DRUG-X? …
What should I avoid while taking DRUG-X? …
What are the possible side effects of DRUG-X? … Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
How should I store DRUG-X? …
General information about the safe and effective use of DRUG-X. Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use DRUG-X for a condition for which it was not prescribed. Do not give DRUG-X to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about DRUG-X that is written for health professionals.
What are the ingredients in DRUG-X? Active ingredients: Inactive ingredients:
Manufactured for: Manufactured by:

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: MM/YYYY

[1] Medication Guide regulations [21 CFR 208] at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-C/part-208

Patient Package Insert[1] (FDA-Approved Patient Labeling)

PATIENT INFORMATION
DRUG-X [drug X]
(drugoxide-a and drugoxide-b tablets)
for oral use

What is DRUG-X? ...
Do not take DRUG-X if you: ...
Before taking DRUG-X, tell your healthcare provider about all of your medical conditions, including if you: ...
How should I take DRUG-X?
What should I avoid while taking DRUG-X? ...
What are the possible side effects of DRUG-X? ... Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
How should I store DRUG-X? ...
General information about the safe and effective use of DRUG-X. Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use DRUG-X for a condition for which it was not prescribed. Do not give DRUG-X to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about DRUG-X that is written for health professionals.
What are the ingredients in DRUG-X? Active ingredients: Inactive ingredients:
Manufactured for: Manufactured by:

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: MM/YYYY

[1] Oral contraceptives see regulations (21 CFR 310.501) at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-310/subpart-E/section-310.501; estrogen-containing products regulations (21 CFR 310.515) at https://www.ecfr.gov/current/title-21/chapter-I/subchapter-D/part-310/subpart-E/section-310.515

Instructions for Use[1]
(FDA-Approved Patient Labeling)

INSTRUCTIONS FOR USE
MYDRUG [mye-drug]
(drugoxide injection)
for intramuscular use

This Instructions for Use contains information on how to take MYDRUG.

Important Information You Need to Know Before Taking MYDRUG

…

Preparing to Take MYDRUG

…

Taking MYDRUG

…

Storing MYDRUG

…

Disposing of MYDRUG

…

Drug Company X, City, State, zip code

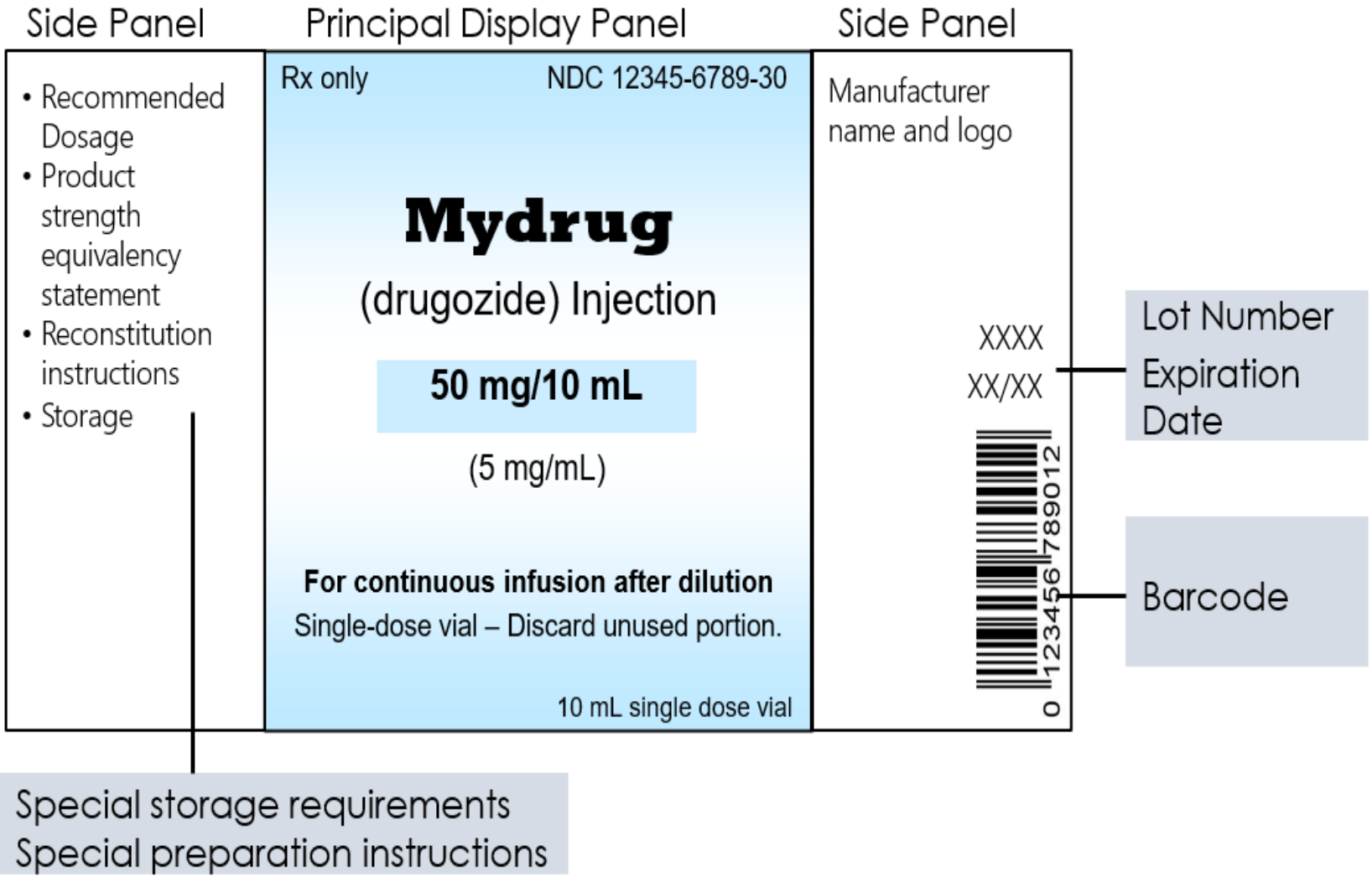
This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Approved: MM/YYYY

[1] Guidance for industry: *Instructions for Use — Patient Labeling for Human Prescription Drug and Biological Products — Content and Format* (July 2022) available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/instructions-use-patient-labeling-human-prescription-drug-and-biological-products-content-and-format

Labeling on the Packaging of Prescription Medicines

Labeling on the Packaging[1]



[1] Guidance for industry: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors* (May 2022) available at https://www.fda.gov/media/158522/download

Prescribing Information for Prescription Medicines

(labeling for healthcare providers)

Prescribing Information (PI)[1]

Written for healthcare practitioners and must:

- Contain a summary of essential scientific information needed for safe and effective use of drugs
- Be informative and accurate and neither promotional in tone nor false or misleading in any particular
- Be updated when new information becomes available that causes labeling to become inaccurate, false, or misleading

[1] Applies to Physician Labeling Rule (PLR) labeling and "old" (non-PLR) format labeling; 21 CFR 201.56(a)

Two Types of Prescribing Information (PI)

BOXED WARNING
DESCRIPTION
CLINICAL PHARMACOLOGY
INDICATION AND USAGE
CONTRAINDICATIONS
WARNINGS
PRECAUTIONS
- General
- Information for Patients
- Laboratory Tests
- Drug Interactions
- Drug/Laboratory T
- Carcinogenesis, M
- Impairment of Fertility
- Pregnancy
- Labor and Delivery
- Nursing Mothers
- Pediatric Use
- Geriatric Use

ADVERSE REACTIONS
DRUG ABUSE AND DEPENDENCE
OVERDOSAGE
DOSAGE AND ADMINISTRATION
HOW SUPPLIED

"Old" Format (1979 final rule)

PLR format = Physician Labeling Rule format

HIGHLIGHTS OF PRESCRIBING INFORMATION
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PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.
- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
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----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for … (1)

Limitations of Use
Text (1)

FULL PRESCRIBING INFORMATION: CONTENTS*
WARNING: TITLE OF WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Subsection Title
2.2 Subsection Title
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Subsection Title
5.2 Subsection Title
6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
6.2 Immunogenicity
6.2 or 6.3 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Subsection Title
7.2 Subsection Title
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation (if not required to be in PLLR format use Labor and Delivery)
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format use Nursing Mothers)
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Subpopulation X

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------

11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology
12.5 Pharmacogenomics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
14.1 Subsection Title
14.2 Subsection Title
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

* Sections or subsections omitted from the full prescribing information are not listed.

PLR Format (2006 final rule)

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
…

Highlights of Prescribing Information

HIGHLIGHTS OF PRESCRIBING INFORMATION
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PROPRIETARY NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

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----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a *([insert FDA established pharmacologic class text phrase]]* indicated for … (1)

Limitations of Use
Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
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To report SUSPECTED ADVERSE REACTIONS, contact name of manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling OR and Medication Guide.

Revised: M/YYYY

Table of Contents

FULL PRESCRIBING INFORMATION: CONTENTS*

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Full Prescribing Information Sections

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1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
9 DRUG ABUSE AND DEPENDENCE
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
13 NONCLINICAL TOXICOLOGY
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Indications and Usage (Section 1)[1]

Treatment, prevention, or diagnosis of a recognized disease or condition or manifestation of a recognized disease or condition (or a manifestation thereof)[2]

1 INDICATIONS AND USAGE

DRUG-X is indicated, in combination with methotrexate, for the treatment of juvenile idiopathic arthritis in pediatric patients 2 years of age and older who have had an inadequate response to TNF inhibitor therapy

[1] See regulations 21 CFR 201.57(c)(2) available at https://www.ecfr.gov/current/title-21/part-201/section-201.57#p-201.57(c)(2); draft guidance for industry: *Indications and Usage Section of Labeling for Human Prescription Drug and Biological Products – Content and Format*. (July 2018) (when final, this guidance will represent FDA's current thinking on this topic) available at https://www.fda.gov/media/114443/download

[2] Or relief of symptoms associated with a recognized disease or condition

Dosage and Administration (Section 2)[1]

Include the following dosage information, as appropriate:

- Recommended dosage (dose, frequency, and duration), method of titration, dosage range, maximum dosage
- Dosage in specific populations (e.g., pediatrics, renal impairment)
- Dosage modifications due to drug interactions or adverse reactions
- Recommended concomitant therapy
- Discontinuation instructions

[1] 21 CFR 201.57(c)(3) available at https://www.ecfr.gov/current/title-21/part-201/section-201.57#p-201.57(c)(3) and draft guidance for industry: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023). When final, this guidance will represent FDA's current thinking on this topic. Available at https://www.fda.gov/media/114443/download

Dosage and Administration (Section 2)[1]

Include important preparation and administration instructions such as:

- Reconstitution and/or dilution instructions
- Route(s) of administration
- Whether oral drug should be taken with or without food
- Specific injection site(s)
- Rate of administration of intravenous products

[1] 21 CFR 201.57(c)(3) available at https://www.ecfr.gov/current/title-21/part-201/section-201.57#p-201.57(c)(3) and draft guidance for industry: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (January 2023). When final, this guidance will represent FDA's current thinking on this topic. Available at https://www.fda.gov/media/114443/download

How Prescribing Information Are Approved

Step 1: Drug Company Submits Draft Prescribing Information

Drug company submits an application to approve a prescription medicine or a supplement for an approved prescription medicine[1]

- Application/supplement includes draft Prescribing Information

[1] If requested, FDA provides comments about drug companies' draft PI before the drug company submits the application or supplement to the FDA

Step 2: FDA Reviews Proposed Prescribing Information (PI) (1 of 2)

- FDA reviews PI from the time of submission to the time of FDA action
- FDA review team is multi-disciplined
  - For example, doctors with a specialty in the disease/condition being treated, clinical pharmacology staff, labeling specialists, product quality reviewers, pharmacology/toxicology staff, promotional content specialists, regulatory project managers, safety experts, statisticians)

Step 2: FDA Reviews Proposed Prescribing Information (PI): Principles of Review (2 of 2)

- Ensure scientific accuracy
- Ensure meets statutory/regulatory requirements and is consistent with final guidance recommendations
- Ensure consistent message
- Improve organization/formatting
- Update terminology and remove/revise misleading, or clearly inapplicable information

Step 3: FDA and Drug Company Discuss Proposed Prescribing Information (PI) and PI Approval

- FDA review team frequency asks the drug company for additional data to support or to clarify statements in the proposed PI
- PI development typically involving several rounds of editing and discussions between FDA and the drug company to arrive at a final agreed-upon PI
- Assuming everything else in the application is approvable, if the FDA and the drug company:
  - Agree on information in the PI, the PI is approved
  - Cannot agree on the information in the PI, the application will not be approved

What Happens After Prescribing Information Is Approved

Prescribing Information Distribution

- Upon approval of the application or supplement, PI are posted:
  - Drugs@FDA[1] (overwhelming majority)[2]
  - On Center for Biologics Evaluation and Research's webpage[3]
- Within 14 days of approval, the drug company submits Structured Product Labeling to FDA
- Subsequently, electronic labeling is posted to several webpages[4]

[1] Drugs@FDA is available at www.fda.gov/drugsatfda

[2] The overwhelming majority of PI for drugs regulated for "brand drugs" are posted on Drugs@FDA; however, the PI for generic drugs are not typically posted on Drugs@FDA

[3] CBER approves vaccines, allergenic products, blood products, cellular and gene therapy products. To find labeling for these products, see https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/biological-approvals-year

[4] Available on many websites including FDALabel (https://nctr-crs.fda.gov/fdalabel/ui/search)

How Is the Prescribing Information Updated After Approval?

- Drug company submits a supplement to their application:
  - Add safety information
  - To propose new indications, populations, dosages
- FDA may:
  - Ask the drug company to submit a supplement to their application to update the PI
  - Require the drug company to update their PI (new safety information)

Updating Labeling (1 of 2)

Drug Company's Responsibilities

- Should review labeling at least annually for outdated information[1]
- Labeling must be updated when new information becomes available that causes labeling to become inaccurate, false, or misleading[2]

Labeling Update Opportunities

FDA encourages labeling updates for multiple labeling type submissions

[1] Guidance for industry: *Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* (February 2013) available at https://www.fda.gov/media/71836/download

[2] 21 CFR 201.56(a)(2) available at https://www.ecfr.gov/current/title-21/part-201/section-201.56#p-201.56(a)

Updating Labeling (2 of 2)

Consistent with the updating labeling requirement, *"when revising existing information in the labeling, applicants should evaluate labeling content to ensure that it accurately reflects current knowledge about the use of the drug in [patients 65 years of age or older] for all approved indications ... [Drug companies] should review and update sections of labeling pertinent to ... information [about patients 65 years of age or older) as necessary when updating the labeling."*[1]

[1] Draft guidance for industry: *Geriatric Information in Human Prescription Drug and Biological Product Labeling* (September 2020). When final this guidance, will represent the FDA's current thinking on this topic. Available at https://www.fda.gov/media/142162/download.

Resources for Labeling for Prescription Medicines

Frequently Asked Questions about Labeling for Prescription Medicines

FDA webpage about labeling for prescription medicines

For Healthcare Professionals and Patients

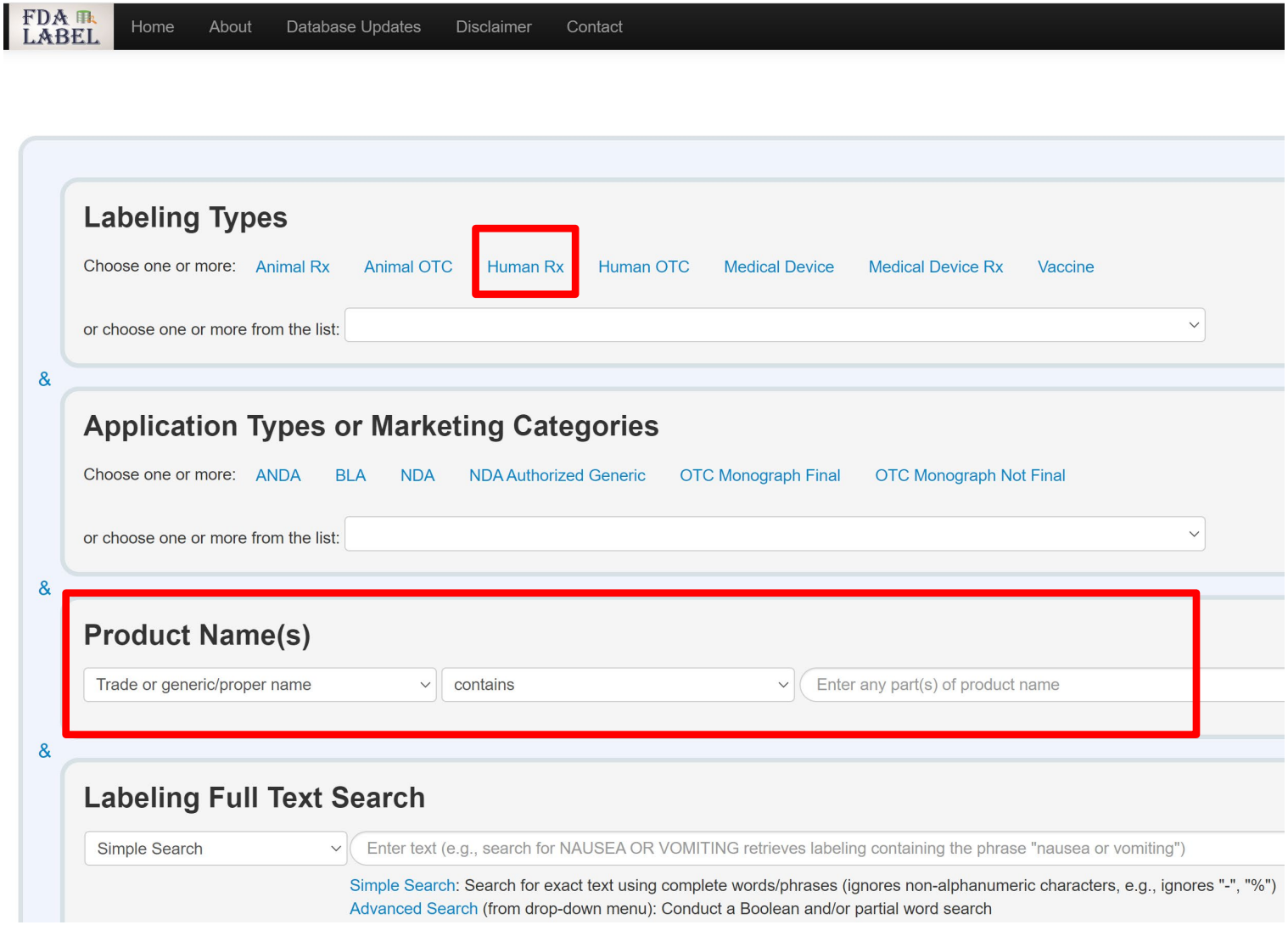
Frequently asked questions about labeling for prescription drugs (medicines) on this webpage are primarily directed to healthcare professionals (for example, doctors, nurse practitioners, physician assistants, pharmacists, nurses) and patients and their caregivers. For information about prescription drug labeling resources primarily directed to industry such as those for the Prescribing Information, FDA-approved patient labeling, carton and container labeling, biological product labeling, generic drug labeling, labeling databases, and product databases visit FDA's Labeling Resources for Prescription Drugs.

Labeling for prescription medicines is FDA's primary tool for communicating drug information to healthcare professionals, and patients and their caregivers. Labeling for prescription medicines includes:

- Prescribing Information (labeling for healthcare professionals),
- Carton and container labeling (cartons and containers are outside packaging that contain information about prescription medicines), and
- Labeling for patients or caregivers (e.g., Medication Guides, Patient Package Inserts, and Instructions for Use).

[1] See https://www.fda.gov/drugs/fdas-labeling-resources-human-prescription-drugs/frequently-asked-questions-about-labeling-prescription-medicines

FDALabel: Full-Text Search of Labeling for FDA-Regulated Products[1]



[1] FDALabel (https://nctr-crs.fda.gov/fdalabel/ui/search) contains > 140,000 Structured Product Labeling from human and animal drugs, animal drugs, devices, dietary supplements, cosmetics, medical foods


FDA
U.S. FOOD & DRUG
ADMINISTRATION