U.S. FOOD & DRUG ADMINISTRATION

FDA Drug Topics: The Ins and Outs of Prescription Drug 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.

Objectives

- Review the different types of FDA-approved prescription drug labeling
- Discuss the process for FDA approval of prescription drug labeling
- Describe the contents of selected parts of the Prescribing Information
- Explain the differences between generic drug labeling and reference listed drug labeling
- Discuss prescription drug labeling resources

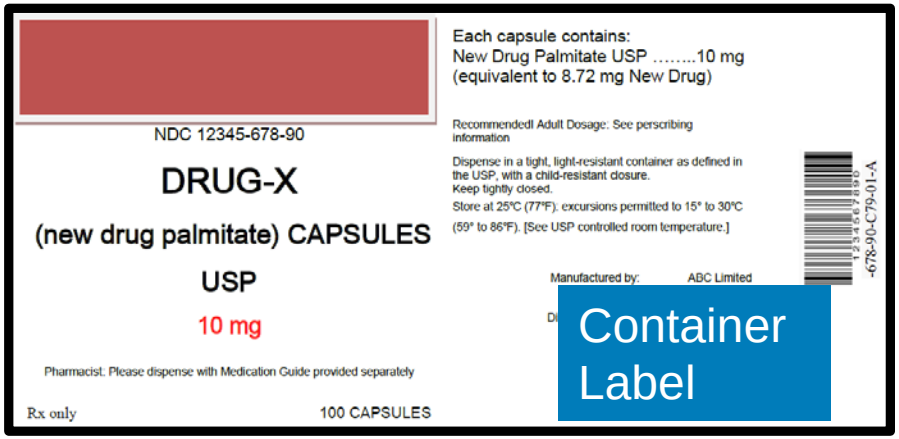
Different Types of FDA-Approved Prescription Drug Labeling

Labels vs. Labeling[1]

- Labels: a display of written, printed, or graphic matter upon the immediate container of any article. For example:
  - Container label
- Labeling: all labels and other written, printed, or graphic matters upon any article (or its containers or wrappers) or accompanying the article. Examples include:
  - Container label and carton labeling
  - FDA-approved patient labeling
  - Prescribing Information

[1] See Section 201, Chapter II, (k) and (m) of Food Drug and Cosmetic Act (FD&C Act)

Prescription Drug Labeling



Each capsule contains:
New Drug Palmitate USP ……..10 mg
(equivalent to 8.72 mg New Drug)

NDC 12345-678-90

DRUG-X

(new drug palmitate) CAPSULES

USP

10 mg

Recommended Adult Dosage: See prescribing information

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure.
Keep tightly closed.
Store at 25°C (77°F): excursions permitted to 15° to 30°C (59° to 86°F). [See USP controlled room temperature.]

Manufactured by: ABC Limited

-678-90-C79-01-A

Pharmacist: Please dispense with Medication Guide provided separately

Rx only

100 CAPSULES

Container Label

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

Patient Labeling

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

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

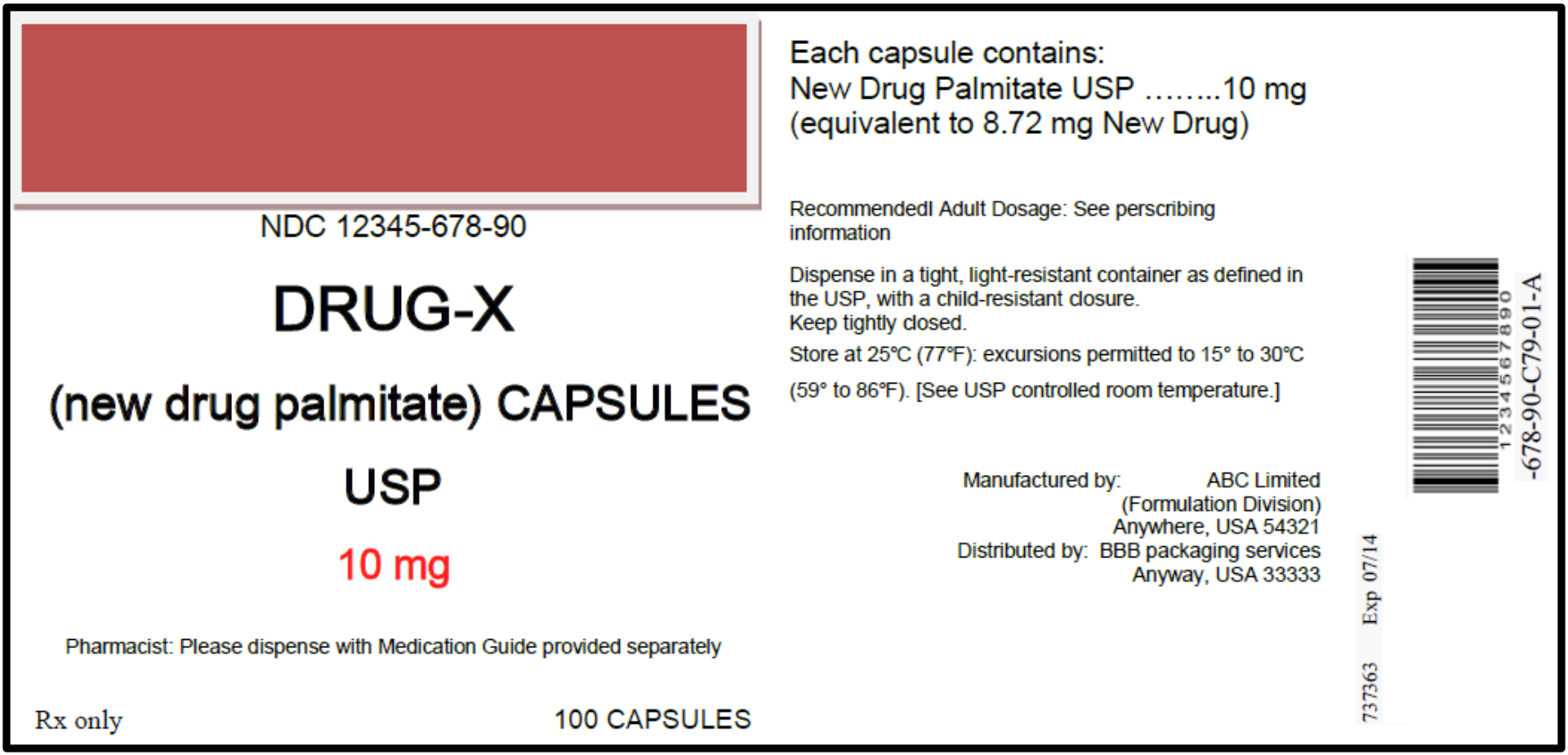
FULL PRESCRIBING INFORMATION: CONTENTS*

* 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
…

Container Label[1]



[1] 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 FDA's current thinking

Patient Labeling

FDA-Approved Patient Labeling

- Three most common types:
  - Medication Guides
  - Patient Package Inserts
  - Instructions for Use
- Proposed by applicant, and reviewed and approved by FDA
- Content is based on the Prescribing Information (PI)

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
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

[1] 21 CFR 208

PATIENT INFORMATION
MYDRUG [mye-drug]
(drugoxide injection)
for intramuscular use

WARNING TO WOMEN WHO SMOKE **Do not use MYDRUG if you smoke cigarettes and are over 35 years old. Smoking increases your risk of serious cardiovascular side effects (heart and blood vessel problems) from birth control pills, including death from heart attack, blood clots or stroke. This risk increases with age and the number of cigarettes you smoke.**
What is MYDRUG? …
How does MYDRUG Work? …
How well does MYDRUG work for contraception? …
Who should not take MYDRUG? …
Before you start taking MYDRUG: …
When to start MYDRUG: …
What should I do if I miss any pills? …
What are the most serious risks of taking MYDRUG? …
What are the common 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.
What else should I know about taking MYDRUG? …
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 Patient Information has been been approved by the U.S. Food and Drug Administration.

Revised: MM/YYYY

Patient Package Insert[1]

(FDA-Approved Patient Labeling)

[1] For oral contraceptives see 21 CFR 310.501) and for estrogen-containing products see 21 CFR 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 See the draft guidance for industry: *Instructions for Use — Patient Labeling for Human Prescription Drug and Biological Products and Drug-Device and Biologic-Device Combination Products— Content and Format* (July 2019). When final, this guidance will represent the FDA's current thinking on this topic.

Prescribing Information (PI)[1]

Written for healthcare providers and must:

- Contain a summary of essential scientific information needed for safe and effective use of drugs and biological products
- 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 PI[1]

- BOXED WARNING
- DESCRIPTION
- CLINICAL PHARMACOLOGY
- INDICATION AND USAGE
- CONTRAINDICATIONS
- WARNINGS
- PRECAUTIONS
  - General
  - Information for Patients
  - Laboratory Tests
  - Drug Interactions
  - Drug/Laboratory Test Interactions
  - Carcinogenes
  - Impairment of
  - Pregnancy
  - Labor and De
  - Nursing Mothers
  - Pediatric Use
  - Geriatric Use
- ADVERSE REACTIONS
- DRUG ABUSE AND DEPENDENCE
- OVERDOSAGE
- DOSAGE AND ADMINISTRATION
- HOW SUPPLIED

"Old" Format (1979 final rule)

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

PLR Format (2006 final rule)

FULL PRESCRIBING INFORMATION: CONTENTS*

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

- 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
- …

PI = Prescribing Information

[1] (1) "Old" format labeling and
(2) Physician Labeling Rule (PLR) labeling

"Old" Format[1] Labeling Sections

1979

- BOXED WARNING
- DESCRIPTION
- CLINICAL PHARMACOLOGY
- INDICATIONS AND USAGE
- CONTRAINDICATIONS
- WARNINGS
- **PRECAUTIONS**
- ADVERSE REACTIONS
- DRUG ABUSE AND DEPENDENCE
- OVERDOSAGE
- DOSAGE AND ADMINISTRATION
- HOW SUPPLIED

Subsections in PRECAUTIONS Section:
General, Information for Patients, Laboratory Tests, Drug Interactions, Drug/Laboratory Test Interactions, Carcinogenesis, Mutagenesis, Impairment of Fertility, Pregnancy, Labor and Delivery, Nursing Mothers, Pediatric Use, Geriatric Use

PLR Format[2]

(Full Prescribing Information Sections)

2006

- 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
- 8 USE IN SPECIFIC POPULATIONS
  - 8.1 Pregnancy
  - 8.2 Lactation
  - 8.3 Females and Males of Reproductive Potential
  - 8.4 Pediatric Use
  - 8.5 Geriatric Use
- 9 DRUG ABUSE AND DEPENDENCE
  - 9.1 Controlled Substance
  - 9.2 Abuse
  - 9.3 Dependence
- 10 OVERDOSAGE
- 11 DESCRIPTION
- 12 CLINICAL PHARMACOLOGY
  - 12.1 Mechanism of Action
  - 12.2 Pharmacodynamics
  - 12.3 Pharmacokinetics
- 13 NONCLINICAL TOXICOLOGY
  - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
  - 13.2 Animal Toxicology and/or Pharmacology
- 14 CLINICAL STUDIES
- 15 REFERENCES
- 16 HOW SUPPLIED/STORAGE AND HANDLING
- 17 PATIENT COUNSELING INFORMATION

[1] "Labeling and Prescription Drug Advertising; Content and Format for Labeling for Human Prescription Drugs"; 44 FR 37434 (June 26, 1979), 21 CFR 201.80

2 "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products,"; 71 FR 392221 (January 24, 2006),.CFR 201.56(d) and 21 CFR 201.57

CDER-Regulated NDA/BLA PI With PLR Format[1]

Month/Year	Proportion of CDER PI With PLR Format (NDAs/BLAs only)
January 2014	~ 45%
January 2016	~ 56%
January 2017	~ 61%
January 2018	~ 63%
March 2019	~ 66%
August 2020	**~ 70%**

[1] PI = Prescribing Information; CDER = Center for Drug Evaluation and Research; Analyses based on Structured Product Labeling (SPL) - generally only includes marketed products; excludes labeling from repackagers, relabelers, and authorized generics

Pregnancy, Lactation, and Females and Males of Reproductive Potential Information in Labeling[1]

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTION
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use

2006

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
CONTRAINDICATIONS
ARNINGS AND PRECAUTIONS
DVERSE REACTIONS
RUG INTERACTIONS
SE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use

2014

Under the Pregnancy and Lactation Labeling Rule (PLLR), the pregnancy letter categories are being removed.

[1] 21 CFR 201.57(c)(9). See also the final rule "Content and Format of Labeling for Human Prescription Drug and Biological Products; Requirements for Pregnancy and Lactation Labeling" (79 FR 72064, December 4, 2014).

Process for FDA Approval of Prescribing Information

How FDA Reviews PI (1 of 2)

- If requested, FDA provides comments about drug companies' draft PI *before application or supplement submission*
- Drug company submits an application to approve a drug or a supplement to an approved drug application that includes a draft PI
- FDA reviews PI upon submission and throughout review cycle
- FDA and drug company develop final PI
  - Iterative process of communications/discussions with both parties

PI = Prescribing Information; NDA = new drug application; BLA = biologics license application

How FDA Reviews PI (2 of 2)

- Final PI is approved by FDA and attached to approval letter
- PI uploaded to Drugs@FDA[1]
- After approval (within 14 days), drug company submits PI electronically[2] and PI posted on websites
- After approval, labeling is updated:
  - Drug company submits new supplement
  - FDA may contact drug company and request firm update PI or require firm update PI

PI = Prescribing Information

[1] Posted to Drugs@FDA as a PDF file: [2] Posted electronically as a Structured Product Labeling (SPL) file

Principles of Updating PI[1]
(in addition to ensuring scientific accuracy)

- Ensure PI meets statutory/regulatory requirements and is consistent with final guidance recommendations[2]
- Ensure consistent message
- Improve organization/formatting[3]
- Update terminology and remove/revise outdated, misleading, or clearly inapplicable information[3,4]
- When updating PI, review and develop *entire* PI

[1] PI = Prescribing Information; Guidance for industry: *Labeling for Human Prescription Drug and Biological Products - Implementing the PLR Content and Format Requirements* (February 2013); [2] Final guidances represents the Agency's current thinking (alternative approaches are acceptable if they satisfy statutes/regulations); [3] If applicable; [4] 21 CFR 201.56(a)(2) and 21 CFR 201.56(d)(4)

Selected Parts of the Prescribing Information

Highlights of Prescribing Information[1]

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

[1] Abbreviated as “Highlights” in this presentation

Table of Contents

FULL PRESCRIBING INFORMATION: CONTENTS*

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

Full Prescribing Information Sections

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
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

Highlights: Product Title[1]

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: T
See full prescribing informa

- **Text (4)**
- **Text (5.x)**

----------RECENT M
Section Title, Subsection Title (x
Section Title, Subsection Title (x

----------INDICATI
PROPRIETARY NAME is a (ins
class text phrase) indicated for .

Limitations of Use
Text (1)

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

- **Proprietary Name**
- **Nonproprietary name**
- **Dosage form and/or route of administration (if not included in the nonproprietary name)**
- **Controlled substance symbol**

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

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

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

EACTIONS----------
dence > x%) are text (6.x)

REACTIONS, contact name of
r FDA at 1-800-FDA-1088 or

ACTIONS----------

C POPULATIONS----------

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

Revised: M/YYYY

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[1] 21 CFR 201.57(a)(2); 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) (referred to as the Draft Product Titles Guidance). When final this guidance, will represent the FDA's current thinking on this topic.

Initial U.S. Approval

HIGHLIGHTS OF PRESCRIBING INFORMATION
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Initial U.S. Approval: YYYY

See full pr

- **Text (4)**
- **Text (5.x)**

Section Title, S
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- Text (2.x)
- Text (2.x)

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

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

----------WARNING

Four-digit year in which FDA initially approved a new molecular entity, new biological product, or new combination of active ingredients

----
re text (6.x)

ontact name of
-FDA-1088 or

- 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

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[1] 21 CFR 201.57(a)(3); 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 on this topic. See FDA's response to Comment #15 in the Preamble to the 2006 Physician Labeling Rule (71 FR 3922, January 24, 2006)

Initial U.S. Approval

Example #1

LIPITOR (atorvastatin calcium) tablets, for oral use

Application was approved in 1996 and the **Initial U.S. Approval is 1996**

Example #2

EPIPEN (epinephrine injection), for intramuscular or subcutaneous use

Application was approved in 1987, but the **Initial U.S. Approval is 1939** because the first epinephrine product approved by the FDA in 1939

Recent Major Changes (RMC) Heading[1]

RMCs pertains to substantive labeling changes to only five sections:

- **BOXED WARNING**
- **INDICATIONS AND USAGE**
- **DOSAGE AND ADMINISTRATION**
- **CONTRAINDICATIONS**
- **WARNINGS AND PRECAUTIONS**

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

manufacturer at toll-free phone # or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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

Must list RMCs for at least one year after the labeling change and remove at first printing after one year

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

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

Revised: M/YYYY

[1] 21 CFR 201.57(a)(5); Guidance for industry: *Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* (February 2013)

Established Pharmacologic Class in Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
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Section Title, Subsection Title (x.x) M/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)

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----------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

Established Pharmacologic Class (EPC)[1]

An EPC is a term that:

- Refers to a group of active moieties that share scientifically valid properties and are clinically meaningful
- Is associated with an approved indication

Active Moiety Name	FDA EPC Phrase
Tobramycin	aminoglycoside antibacterial
Testosterone	androgen
Lisinopril	angiotensin converting enzyme inhibitor
Losartan	angiotensin II receptor blocker
Sotalol	antiarrhythmic

[1] *Determining the Established Pharmacologic Class for Use in the Highlights of Prescribing Information MAPP* (MAPP 7400.13); guidance for industry: *Labeling for Human Prescription Drug and Biological Products — Determining Established Pharmacologic Class for Use in the Highlights of Prescribing Information* (October 2009)

[2] 21 CFR 201.57(a)(6)

FDA Posts EPCs[1]

FDA Listing of Established Pharmacologic Class Text Phrases January 2021	
Active Moiety Name	**FDA EPC Text Phrase** PLR regulations require that the following statement is included in the Highlights Indications and Usage heading if a drug is a member of an EPC [see 21 CFR 201.57(a)(6)]: "(Drug) is a (FDA EPC Text Phrase) indicated for [indication(s)]." For each listed active moiety, the associated FDA EPC text phrase is included in this document. For more information about how FDA determines the EPC Text Phrase, see the 2009 "Determining EPC for Use in the Highlights" guidance and 2013 "Determining EPC for Use in the Highlights" MAPP 7400.13.
DUTASTERIDE	5-alpha reductase inhibitor
FINASTERIDE	5-alpha reductase inhibitor
ZILEUTON	5-lipoxygenase inhibitor
BOTULINUM TOXIN TYPE A	acetylcholine release inhibitor
RIMABOTULINUMTOXINB	acetylcholine release inhibitor
GUANIDINE	acetylcholine releasing agent
DACTINOMYCIN	actinomycin
ADENOSINE	adenosine receptor agonist
REGADENOSON	adenosine receptor agonist
REGADENOSON ANHYDROUS	adenosine receptor agonist
METYRAPONE	adrenal steroid synthesis inhibitor

[1] See https://www.fda.gov/media/144963/download

Highlights: Adverse Reactions Reporting Contact Information[1]

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

[1] 21 CFR 201.57(a)(11)(ii) and guidance for industry: *Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* (February 2013)

Highlights: Revision Date[1]

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Revised: M/YYYY

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[1] 21 CFR 201.57(a)(15) and guidance for industry: *Labeling for Human Prescription Drug and Biological Products – Implementing the PLR Content and Format Requirements* (February 2013)

Full Prescribing Information Sections

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
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

Sections highlighted in blue will be discussed in this webinar

Indications and Usage (Section 1)[1]

Based on substantial evidence of effectiveness:

- Treatment, prevention, or diagnosis of a recognized disease or condition or manifestation of a recognized disease or condition
- Relief of symptoms associated with a recognized disease or condition

<u>Limitations of Use</u> include if, reasonable concern about risk-benefit profile

[1] 21 CFR 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 the FDA's current thinking on this topic.

Dosage and Administration (Section 2)[1]

Include the following dosage information if applicable:

- Recommended starting dosage (dose and frequency), 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) and guidance for industry: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (March 2010)

Dosage and Administration (Section 2)[1]

Include important preparation and administration instructions such as:

- Route(s) of administration
- Reconstitution and/or dilution instructions
- 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) and guidance for industry: *Dosage and Administration Section of Labeling for Human Prescription Drug and Biological Products — Content and Format* (March 2010)

Boxed Warning, Contraindications, and Warnings and Precautions[1]

BOXED WARNING

- Contraindications or warnings about serious adverse reactions that may lead to death or serious injury

CONTRAINDICATIONS (section 4)

- Situations for which risk from use clearly outweighs any possible benefit

WARNINGS AND PRECAUTIONS (section 5)

- Clinically significant adverse reactions or risks

[1] See 21 CFR 201.57(c)(1), (5), and (6) and guidance for industry: *Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format* (October 2011)

Adverse Reactions (Section 6)[1]

- Adverse reactions are undesirable effects, reasonably associated with the use of a drug, for which there is some basis to believe there is a causal relationship to drug and occurrence of the event
- Typically, includes two subsections:
  - Clinical Trials Experience (from premarketing and post-marketing studies)
  - Post-marketing Experience (from domestic and foreign spontaneous adverse reactions)

[1] 21 CFR 201.57(c)(7) and guidance for industry: *Adverse Reactions Section of Labeling for Human Prescription Drug and Biological Products – Content and Format* (January 2006)

Drug Interactions (Section 7)[1]

- Include description of clinically significant drug interactions (DI)
- Include mechanism of clinically significant DI
- Include practical instructions for preventing or managing clinically significant DI
- Do not include negative DI unless drug does not have same interaction as other drugs in class
- Do not include details of pharmacokinetic studies

If you want to learn more about drug interaction information in labeling, consider viewing an FDA webinar:
https://www.fda.gov/about-fda/fda-pharmacy-student-experiential-program/labeling-made-simple-how-what-and-where-drug-interactions-prescribing-information

[1] 21 CFR 201.57(c)(8)

How Supplied/Storage and Handling (Section 16)[1]

- Dosage form(s) and identifying characteristics
- Strength or potency in metric system (e.g., 10 mg)
- Units in which dosage form is ordinarily available for prescribing by practitioners (e.g., bottles of 100 tablets)
- National Drug Code (NDC) number(s)
- Special handling and storage conditions (e.g., protect from light, refrigerate, do not freeze)

[1] 21 CFR 201.57(c)(17)

Generic Drug Labeling

Generic Drug Labeling

- Generic drug company must identify a previously approved drug [reference listed drug (RLD)] and show, among other things, that the generic drug is bioequivalent to the RLD[1]
- Generic drug labeling must be the "**same as**" reference listed drug (RLD) labeling except for differences due to:[2]
  - Omission of information protected by patent or exclusivity
  - Inactive ingredients
  - Package size
  - Manufacturer, packer, distributor information

[1] The generic drug and the RLD are bioequivalent if the rate and extent of absorption of the generic drug does not show a significant difference from the rate and extent of absorption of the RLD under the same conditions. See Section 505(j)(8)(B)(i) of the FD&C Act.

[2] If the generic drug is not the same as the RLD (i.e., different active ingredient in a fixed combination drug product, route of administration, dosage form, or strength then the company must first obtain FDA permission via a suitability petition

Prescription Drug Labeling Resources

Prescription Drug Labeling Resources

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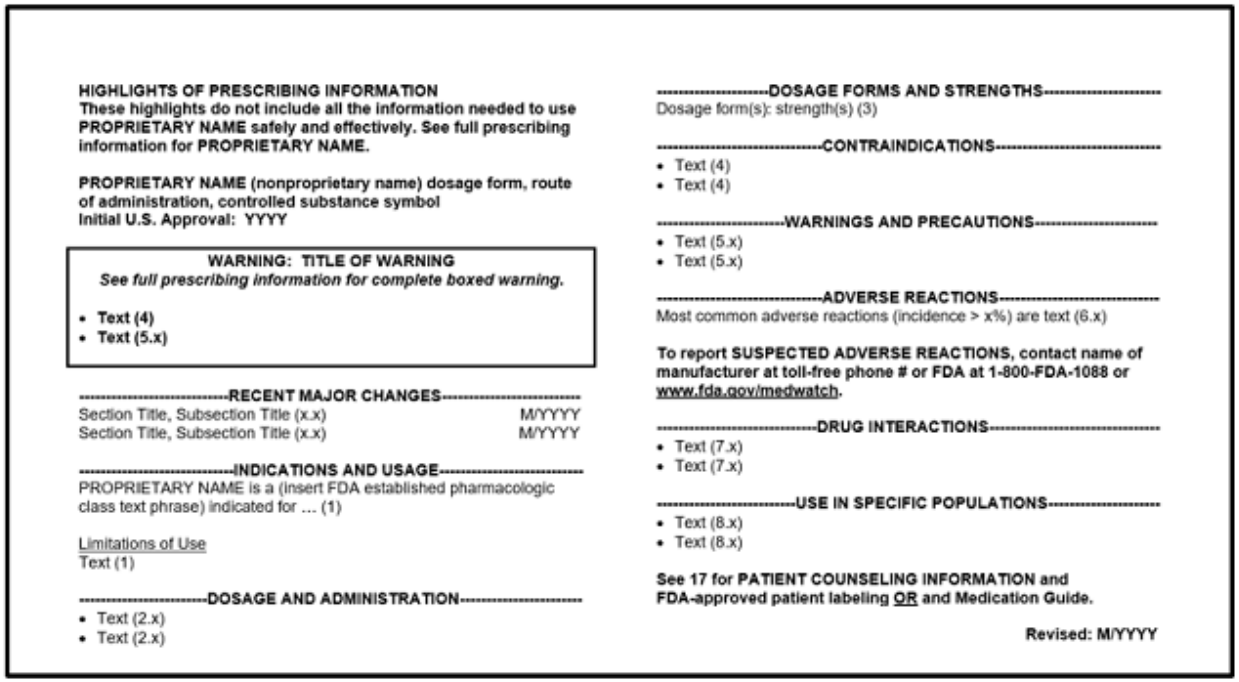
FDA's *Prescription Drug Labeling Resources* website provides over 150 labeling resources for the Prescribing Information, FDA-approved patient labeling, and/or carton and container labeling for human prescription drugs, including biological products (including over 50 guidances with labeling content) - see Overview of Website.

Highlights of Prescribing Information: Format Sample



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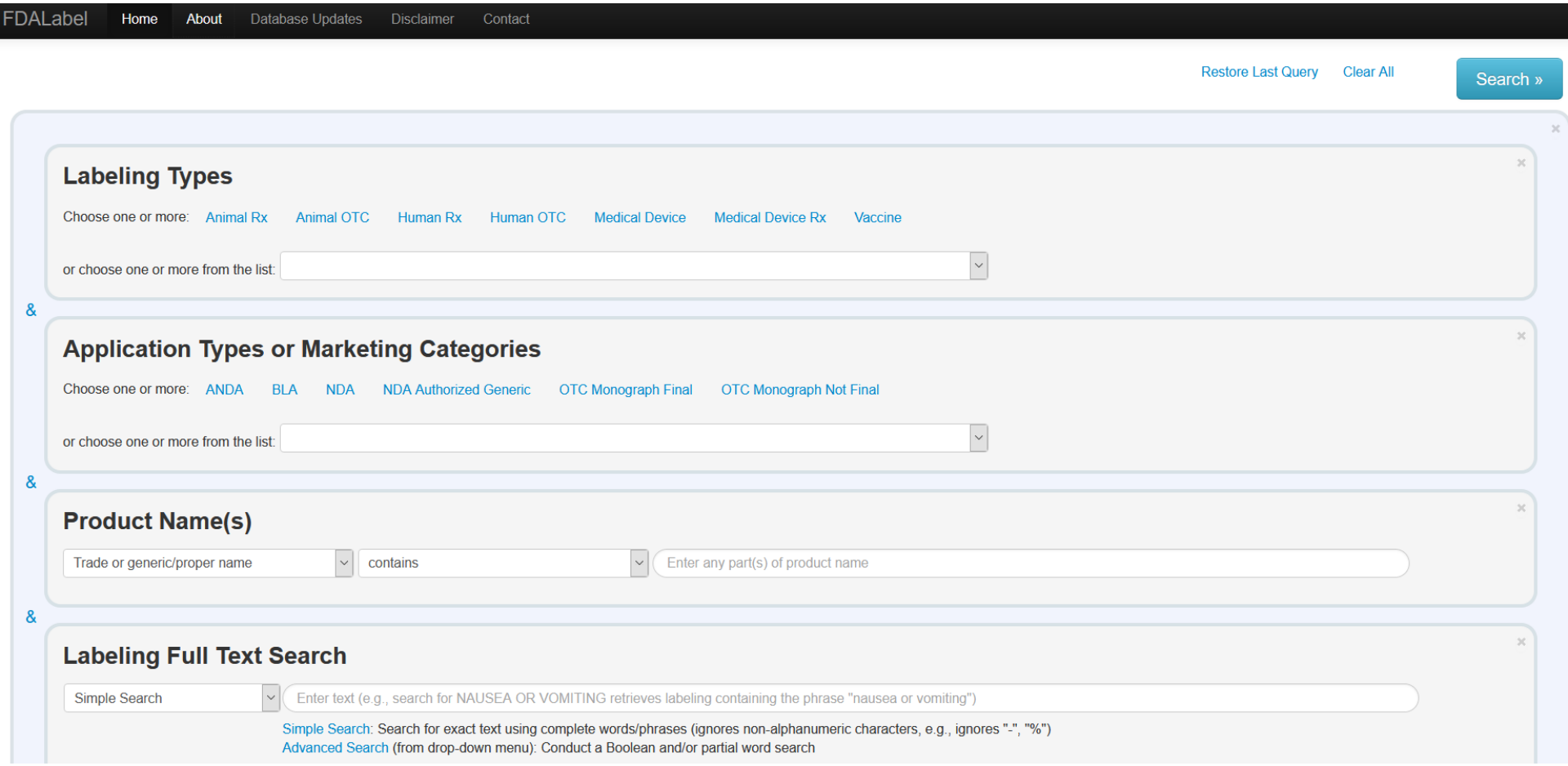
Revised: M/YYYY

https://www.fda.gov/drugs/laws-acts-and-rules/prescription-drug-labeling-resources

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



[1] FDALabel (https://nctr-crs.fda.gov/fdalabel/ui/search) contains > 130,000 SPL from human and animal drugs, unapproved homeopathic products, animal drugs, devices, dietary supplements, cosmetics, medical foods


FDA
U.S. FOOD & DRUG
ADMINISTRATION