U.S. FOOD & DRUG ADMINISTRATION

DDI Webinar Series: May 2, 2017

Labeling on Drugs@FDA vs. DailyMed

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Office of New Drugs, Center for Drug Evaluation and Research, FDA

Learning Objectives

At the conclusion of this webinar, participants should be able to:

- Discuss the types of prescription drug labeling
- Discuss the types of labeling on Drugs@FDA and DailyMed
- Identify the differences between labeling on Drugs@FDA and DailyMed

Labels vs. Labeling[1]

- Labels: a display of written, printed, or graphic matter upon the immediate container of any article. For example:
  - e.g., 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:
  - FDA-approved patient labeling
  - Carton and container labeling
  - Prescribing information

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

Prescription Drug Labeling

Prescription Drug Labeling

Type of Prescription Drug Labeling	Audience
1. FDA-approved patient labeling: ➢ Medication Guides ➢ Patient Package Inserts ➢ Instructions for Use	Patients and/or caregivers
2. Prescribing Information	Healthcare providers
3. Carton and container labeling	➢ Healthcare providers (physician, pharmacist, nurse, pharmacy technician) ➢ Sometimes for patients or caregivers

Patient Labeling: Medication Guide

MEDICATION GUIDE

HUMIRA® (Hu-MARE-ah)

(adalimumab)

injection

Read the Medication Guide that comes with HUMIRA before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment.

What is the most important information I should know about HUMIRA?

HUMIRA is a medicine that affects your immune system. HUMIRA can lower the ability of your immune system to fight infections. **Serious infections have happened in people taking HUMIRA. These serious infections include tuberculosis (TB) and infections caused by viruses, fungi or bacteria that have spread throughout the body. Some people have died from these infections.**

- Your doctor should test you for TB before starting HUMIRA.

Patient Labeling: Patient Package Insert

Patient Information

Patient Information
femhrt (fĕ'mĕrt)
(norethindrone acetate/ethinyl estradiol)
Tablets

Read this Patient Information before you start taking femhrt and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your menopausal symptoms or your treatment.

What is the most important information I should know about femhrt (a combination of estrogen and progestin)?

- Do not use estrogens with progestins to prevent heart disease, heart attacks, strokes or dementia (decline of brain function).
- Using estrogens with progestins may increase your chances of getting a heart attack, strokes, breast cancer, or blood clots.
- Using estrogens with progestins may increase your chance of getting dementia, based on a study of women 65 years of age or older.
- Do not use estrogen-alone to prevent heart disease, heart attacks, strokes or dementia.
- Using estrogen-alone may increase your chance of getting cancer of the uterus (womb).
- Using estrogen-alone may increase your chances of getting strokes or blood clots.
- Using estrogen-alone may increase your chance of getting dementia, based on a study of women 65 years of age or older.
- You and your healthcare provider should talk regularly about whether you still need treatment with femhrt.

Patient Labeling: Instructions for Use

INSTRUCTIONS FOR USE

HUMIRA® (Hu-MARE-ah)

(adalimumab)

40 MG/0.8 ML

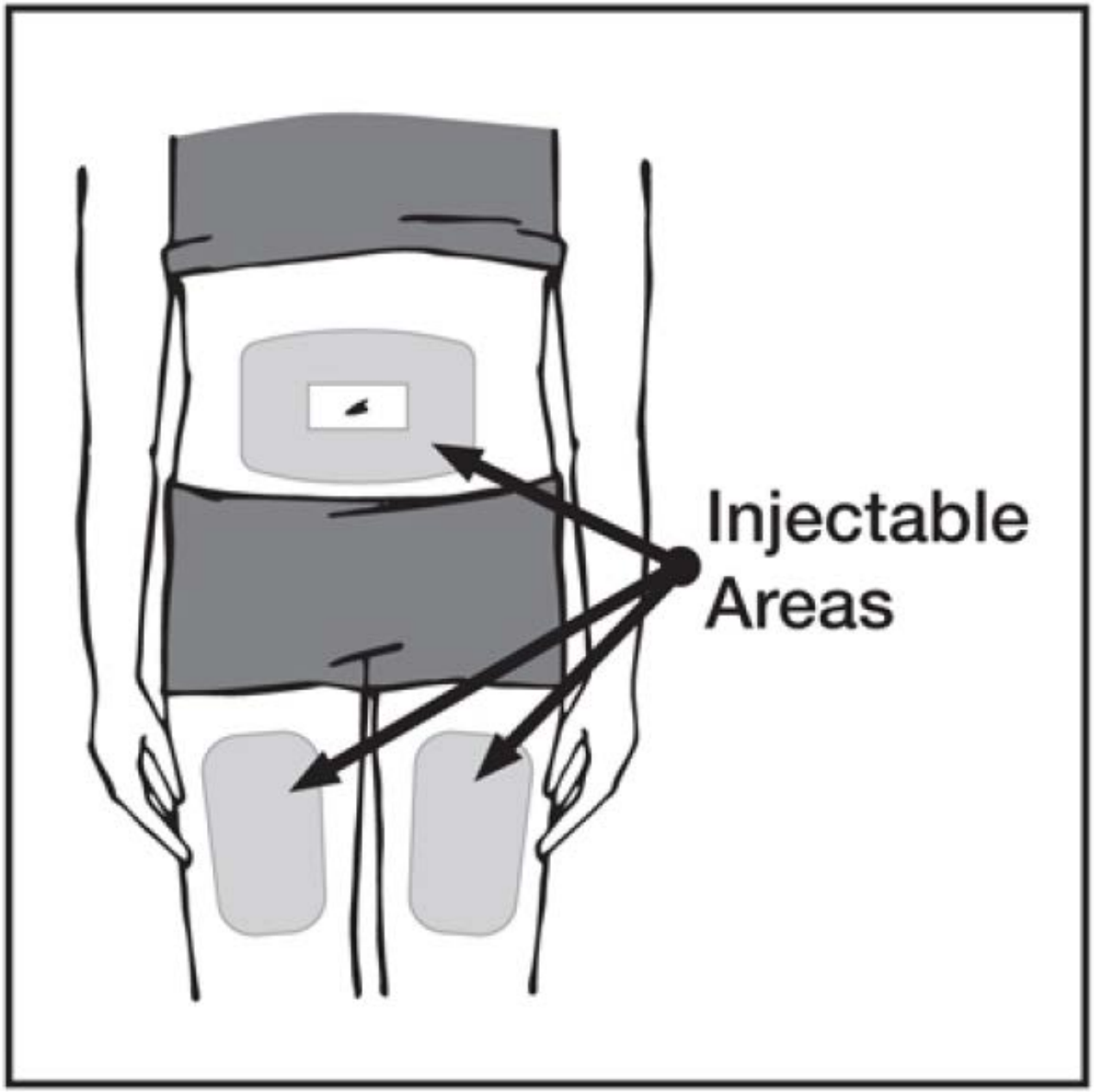
SINGLE-USE PEN

Do not try to inject HUMIRA yourself until you have been shown the right way to give the injections and have read and understand this Instructions for Use. If your doctor decides that you or a caregiver may be able to give your injections of HUMIRA at home, you should receive training on the right way to prepare and inject HUMIRA. It is important that you read, understand, and follow these instructions so that you inject HUMIRA the right way. It is also important to talk to your doctor to be sure you understand your HUMIRA dosing instructions. To help you remember when to inject HUMIRA, you can mark your calendar ahead of time. Call your healthcare provider if you or your caregiver have any questions about the right way to inject HUMIRA.

IMPORTANT:

- Do not use HUMIRA if frozen, even if it has been thawed.
- The HUMIRA Pen contains glass. Do not drop or crush the Pen because the glass inside may break.
- Do not remove the gray cap or the plum-colored cap until right before your injection.
- When the plum-colored button on the HUMIRA Pen is pressed to give your dose of HUMIRA, you will hear a loud "click" sound.
  - You must practice injecting HUMIRA with your doctor or nurse so that you are not startled by this click when you start giving yourself the injections at home.
  - The loud click sound means the start of the injection.
  - You will know that the injection has finished when the yellow marker appears fully in the window view and stops moving.

Patient Labeling: Instructions for Use



Carton and Container Labeling

Prescribing Information (PI) (1 of 2)

Written for healthcare providers and must:[1]

- Contain a summary of essential scientific information needed for safe and effective use of the **human prescription drug or biological product**
- Be informative and accurate and neither promotional in tone nor false or misleading
- Be updated when new information becomes available that causes labeling to become inaccurate, false, or misleading

[1] 21 CFR 201.56(a)(1) and (2)

Prescribing Information (PI) (2 of 2)

- Also known as “package insert”; however, FDA recommends using term “prescribing information”
- PI has two formats:
  - Physician Labeling Rule (PLR) format
  - Non-PLR “old” format
- Brand drugs PI:
  - ~ 61% of PI for brand drugs are in PLR format
- Generic drug PI
  - ~ 35% of PI for generic drugs are in PLR format

Question #1

Which labeling is **never** intended for the healthcare provider?

a. Prescribing information
b. Carton labeling
c. Container labeling
d. Medication Guide
e. (c) and (d)
f. (a), (b), and (c)

Boxed Warning
Description
Clinical Pharmacology
Indications and Usage
Contraindications
Warnings
Precautions
- 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

Adverse Reactions
Drug Abuse and Dependence
Overdosage
Dosage and Administration
How Supplied

Non-PLR Labeling Format[1]

- Limited format requirements
- **Not** included:
  - Concise summary of important information
  - Table of Contents
  - Numbered sections or subsections
- Information **not** ordered according to clinical relevance

[1] See 44 FR 37434 (June 26, 1979); 21 CFR 201.80

Physician Labeling Rule (PLR)[1]

January 2006 PLR amended regulations about format and content of PI

Rationale:

- Ensure PI contains necessary information for safe and effective use of product
- Make information easier for healthcare providers to access, read, and use
- Reduce medication errors

[1] Final Rule (PLR) "Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products" 71 FR 3922 (January 24, 2006)

PLR Highlights

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 (non-proprietary 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/201Y
Section Title, Subsection Title (x.x) M/201Y

----------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/201Y

PLR Highlights – Product Title

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Revised: M/201Y

PLR Highlights – Recent Major Changes

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Revised: M/201Y

PLR Highlights: Indication Statement

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Initial U.S. Approval: YYYY

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Revised: M/201Y

PLR Highlights: Adverse Reactions Reporting Contact Statement

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Revised: M/201Y

PLR Highlights: Revision Date

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Revised: M/201Y

PLR Table of Contents

FULL PRESCRIBING INFORMATION: CONTENTS*

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

PLR Full 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
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

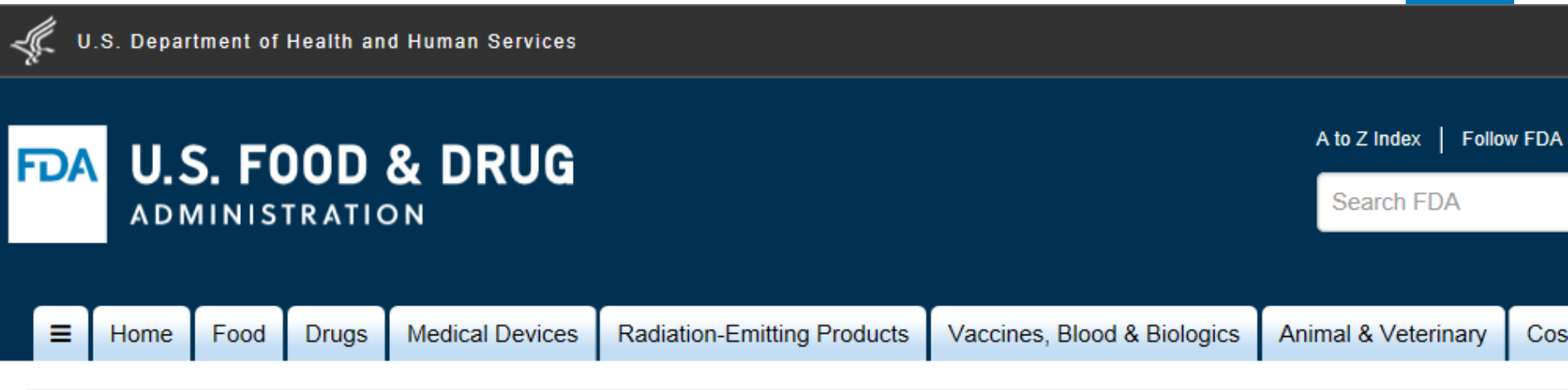
Question #2

Prescribing information in PLR and non-PLR format have the following in common:

a. Include the Highlights of Prescribing Information
b. Include numbered sections
c. Ordered according to clinical relevance
d. Include the DOSAGE AND ADMINISTRATION section
e. None of the above

Drugs@FDA

Drugs@FDA[1]



1 www.fda.gov/DrugsatFDA

Drugs@FDA: Types of Products

Includes information about FDA-approved products for human use:[1]

- Brand and generic prescription drugs (NDAs and ANDAs, respectively)
  - e.g., LIPITOR, atorvastatin calcium
- Brand prescription biological products[2] (BLAs)
  - e.g., ENBREL, BOTOX
- Brand and generic OTC drugs (NDAs and ANDAs)
  - e.g., ADVIL, ibuprofen

NDAs = New Drug Applications; ANDAs = Abbreviated New Drug Applications:; BLAs = Biologics License Applications; OTC = over-the-counter

[1] Products approved by Center for Drug Evaluation and Research (CDER) at FDA

[2] Biological products are made with or from live cells or organisms (includes biosimilar products)

Types of Products that Drugs@FDA Does NOT Include

- FDA-approved products **not** included:
  - Blood, vaccine, allergenic, or cellular/tissue products (e.g., albumin, GARDASIL, FLUMIST)[1]
  - FDA-approved drugs for animals
- FDA-regulated products **not** included:
  - OTC drugs approved under monograph system (e.g., TYLENOL, hydrocortisone, bacitracin zinc, diphenhydramine hydrochloride)
  - Dietary supplements (e.g., st. john's wort, vitamin E)

[1] Biological products approved by Center of Biologics Evaluation and Research (CBER) at FDA

Drugs@FDA: Includes

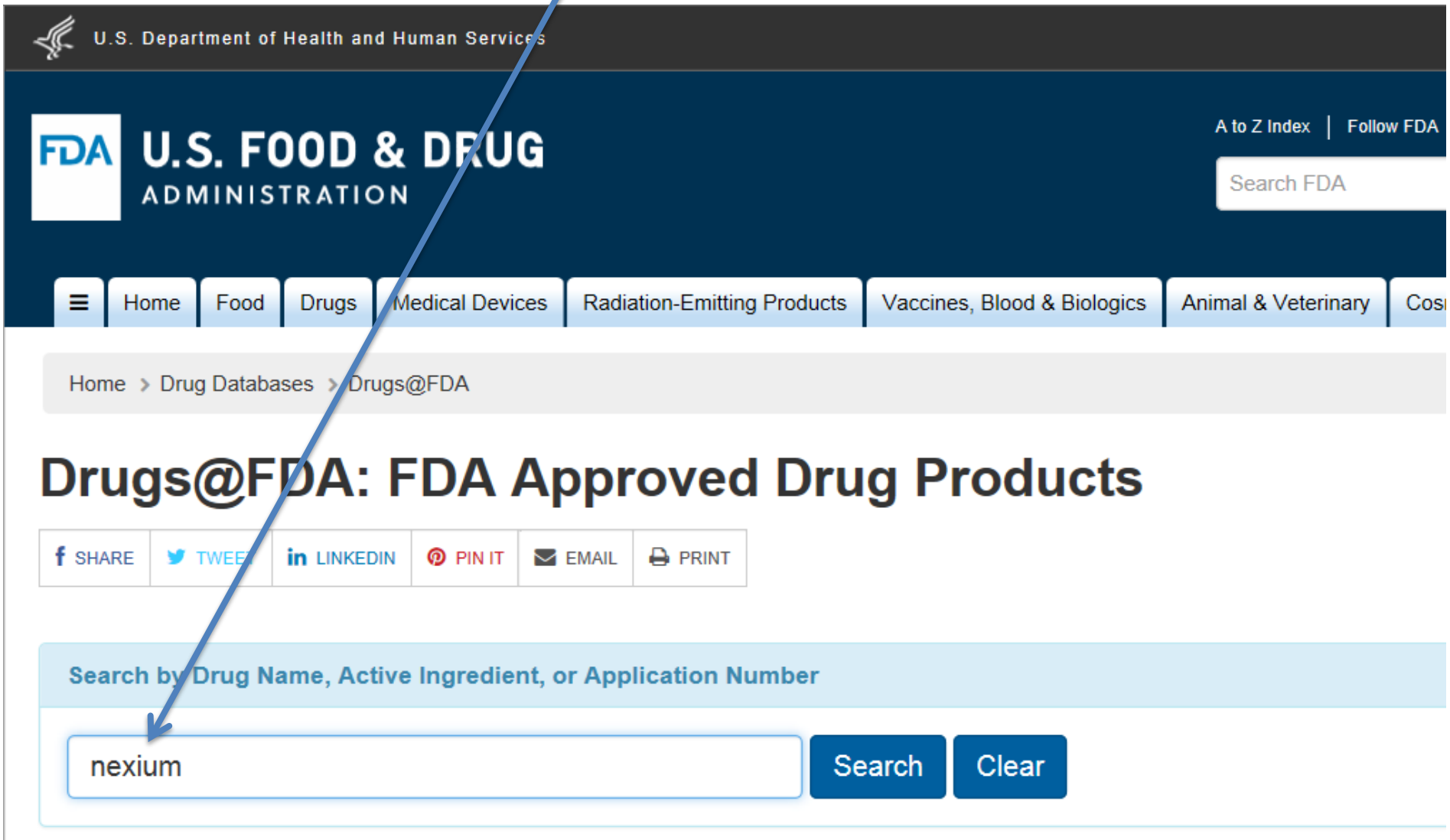
- Application type (e.g., NDA, ANDA, BLA) and number
- Information about product (drug name, active ingredient, dosage form, route of administration strength)
- Last approved labeling (e.g., prescribing information) and historical labeling
- Approval letters
- Scientific reviews
- Safety information
- Therapeutic equivalents for drug products

Drugs@FDA: What Gets Posted?

- Action packages include scientific reviews, approval letters, safety information, and prescription drug labeling
- Action packages:
  - New molecular entities (NMEs) and new biological products: must be posted within 30 days of approval
  - Other NDAs approved since 1998: are being posted
- Additional labeling (e.g., PI and Medication Guides) are posted for new NDAs/BLAs, efficacy supplements, labeling supplements

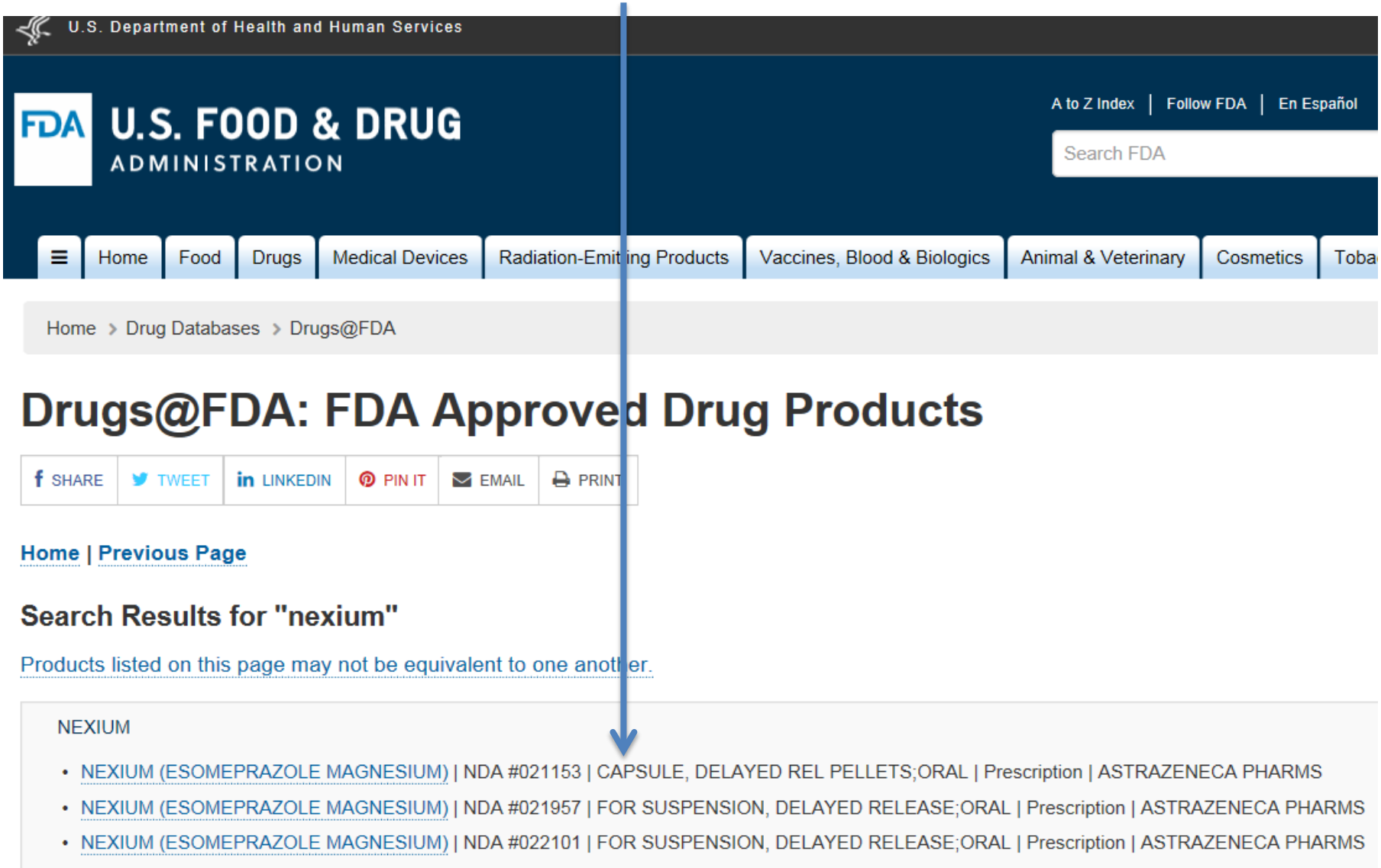
Drugs@FDA: How to Search Labeling

Step #1: Type in drug name



Drugs@FDA: How to Review Labeling

Step #2: After clicking on “NEXIUM”, choose dosage form



Drugs@FDA: How to Review Labeling

Step #3: After clicking on "Labels for NDA 021153", click on **most recent** labeling

Approval Date(s) and History, Letters, Labels, Reviews for NDA 021153

Labels for NDA 021153

CSV | Excel | Print

Action Date	Submission	Submission Classification or Approval Type	Letters, Reviews, Labels, Patient Package Insert
12/20/2016	SUPPL-51	Labeling	Label (PDF)
10/24/2016	SUPPL-52	Labeling	Label (PDF)
12/19/2014	SUPPL-50	Labeling-Package Insert	Label (PDF)

Historical labeling

Drugs@FDA: Review Labeling

Labeling is in PDF format

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NEXIUM safely and effectively. See full prescribing information for NEXIUM.
NEXIUM® (esomeprazole magnesium) delayed-release capsules, for oral use
NEXIUM® (esomeprazole magnesium) for delayed-release oral suspension
Initial U.S. Approval: 1989 (omeprazole)

RECENT MAJOR CHANGES

Warnings and Precautions, Atrophic Gastritis (5.2) removed	10/2016
Warnings and Precautions, Cutaneous and Systemic Lupus Erythematosus (5.5)	10/2016

INDICATIONS AND USAGE

NEXIUM is a proton pump inhibitor indicated for the following:

- Treatment of gastroesophageal reflux disease (GERD). (1.1)
- Risk reduction of NSAID-associated gastric ulcer. (1.2)
- *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence. (1.3)
- Pathological hypersecretory conditions, including Zollinger-Ellison syndrome. (1.4)

DOSAGE AND ADMINISTRATION

Indication	Dose	Frequency
Gastroesophageal Reflux Disease (GERD)		
Adults	20 mg or 40 mg	Once daily for 4 to 8 weeks
12 to 17 years	20 mg or 40 mg	Once daily for up to 8 weeks
1 to 11 years	10 mg or 20 mg	Once daily for up to 8 weeks

- *Clostridium difficile*-Associated Diarrhea: PPI therapy may be associated with increased risk. (5.3)
- Bone Fracture: Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. (5.4)
- Cutaneous and Systemic Lupus Erythematosus: Mostly cutaneous; new onset or exacerbation of existing disease; discontinue NEXIUM and refer to specialist for evaluation. (5.5)
- Interaction with Clopidogrel: Avoid concomitant use of NEXIUM. (5.6)
- Cyanocobalamin (Vitamin B-12) Deficiency: Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin. (5.7)
- Hypomagnesemia: Reported rarely with prolonged treatment with PPIs. (5.8)
- Interaction with St. John's Wort or Rifampin: Avoid concomitant use of NEXIUM. (5.9, 7.3)
- Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Increased chromogranin A (CgA) levels may interfere with diagnostic investigations for neuroendocrine tumors, temporarily stop NEXIUM at least 14 days before assessing CgA levels. (5.10, 12.2)
- Interaction with Methotrexate: Concomitant use with PPIs may elevate and/or prolong serum concentrations of methotrexate and/or its metabolite, possibly leading to toxicity. With high dose methotrexate administration, consider temporary withdrawal of NEXIUM. (5.11, 7.7)

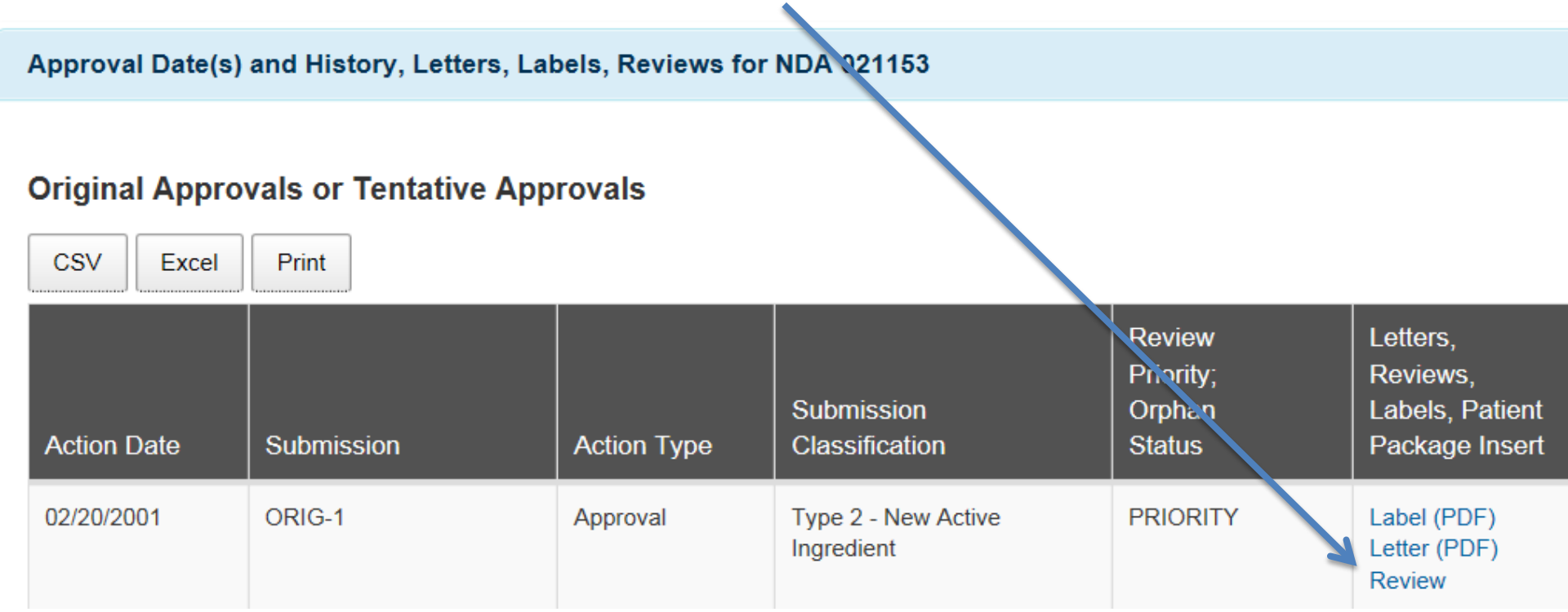
ADVERSE REACTIONS

Most common adverse reactions (6.1):

- Adults (≥ 18 years) (incidence ≥1%) are headache, diarrhea, nausea, flatulence, abdominal pain, constipation, and dry mouth.
- Pediatric (1 to 17 years) (incidence ≥2%) are headache, diarrhea, abdominal pain, nausea, and somnolence

Drugs@FDA: Scientific Reviews

- After following Steps #1 and #2, click on “Approval Date(s) and History, Letters, Labels, Reviews for NDA 021153”
- Then click on “Review”



Approval Date(s) and History, Letters, Labels, Reviews for NDA 021153

Original Approvals or Tentative Approvals

CSV | Excel | Print

Action Date	Submission	Action Type	Submission Classification	Review Priority; Orphan Status	Letters, Reviews, Labels, Patient Package Insert
02/20/2001	ORIG-1	Approval	Type 2 - New Active Ingredient	PRIORITY	Label (PDF) Letter (PDF) Review

Drugs@FDA: Scientific Reviews

Drug Approval Package

FDA Home › Drugs › Drug Approvals and Databases › Drugs@FDA

Nexium (Esomeprazole Magnesium) Delayed-Release Capsules
Company: AstraZeneca LP
Application No.: 21-153 & 21-154
Approval Date: 2/20/2001

- Approval Letter(s) (PDF)
- Printed Labeling (PDF)
- Medical Review(s)
  - Part 1 (PDF)
  - Part 2 (PDF)
  - Part 3 (PDF)
  - Part 4 (PDF)
  - Part 5 (PDF)
  - Part 6 (PDF)
  - Part 7 (PDF)
  - Part 8 (PDF)
  - Part 9 (PDF)
- Chemistry Review(s) (PDF)
- Pharmacology Review(s) (PDF)
- Statistical Review(s) (PDF)
- Microbiology Review(s) (PDF)
- Clinical Pharmacology Biopharmaceutics Review(s)
  - Part 1 (PDF)
  - Part 2 (PDF)

Medical officer review contains detailed review of efficacy and safety of product

Drugs@FDA: Therapeutic Equivalents

- How do you find generic drugs for a brand drug?
- After following Steps #1 and #2, click on “Therapeutic Equivalents for NDA 020702”

Approval Date(s) and History, Letters, Labels, Reviews for NDA 020702

Labels for NDA 020702

Therapeutic Equivalents for NDA 020702

LIPITOR

TABLET;ORAL; EQ 10MG BASE
TE Code = AB

CSV Excel Print

Drug Name	Active Ingredients	Strength	Dosage Form/Route	Marketing Status	RLD	TE Code	Application No.	Company
LIPITOR	**ATORVASTATIN CALCIUM**	**EQ 10MG BASE**	**TABLET;ORAL**	**Prescription**	**Yes**	**AB**	**020702**	**PFIZER**
ATORVASTATIN CALCIUM	ATORVASTATIN CALCIUM	EQ 10MG BASE	TABLET;ORAL	Prescription	No	AB	090548	APOTEX INC
ATORVASTATIN CALCIUM	ATORVASTATIN CALCIUM	EQ 10MG BASE	TABLET;ORAL	Prescription	No	AB	091650	DR REDDYS LABS LTD

Question #3

Drugs@FDA includes labeling from which products?

a. TYLENOL
b. LIPITOR
c. FLUMIST
d. Vitamin E
e. All of the above

DailyMed

DailyMed

https://dailymed.nlm.nih.gov/dailymed/index.cfm

ALL DRUGS | HUMAN DRUGS | ANIMAL DRUGS

Enter drug, NDC code, drug class, or Set ID

MORE WAYS TO SEARCH: ADVANCED SEARCH | BROWSE DRUG CLASSES | LABEL ARCHIVES | TABLET/CAPSULE ID TOOL

This website contains **89957** drug listings as submitted to the **Food and Drug Administration (FDA)**.
At the present time, this Web site does not contain a complete listing of labels for approved prescription drugs.

SHARE

NEWS

DailyMed Announcements

Posted: September 13, 2016

Update: 2016 DailyMed/RxNorm Jamboree Workshop scheduled for September 27

FDA GUIDANCES & INFORMATION

Drug Guidance, Compliance & Regulatory Information

View FDA Structured Product Labeling Resources
View FDA Drug Labeling Guidances
View All FDA Drug Guidances

DailyMed

- Contains > 90,000 product labeling
- Includes most-recently labeling submitted to FDA
- Labeling may be different than FDA-approved labeling:
  - Pending CBE-0 labeling supplements
    - Labeling supplements to add safety information under FDA review
    - Labeling changes have not been approved by FDA
  - Annual reportable changes
    - Changes have minimal potential to adversely affect product (e.g., change in inactive ingredient or how supplied information)

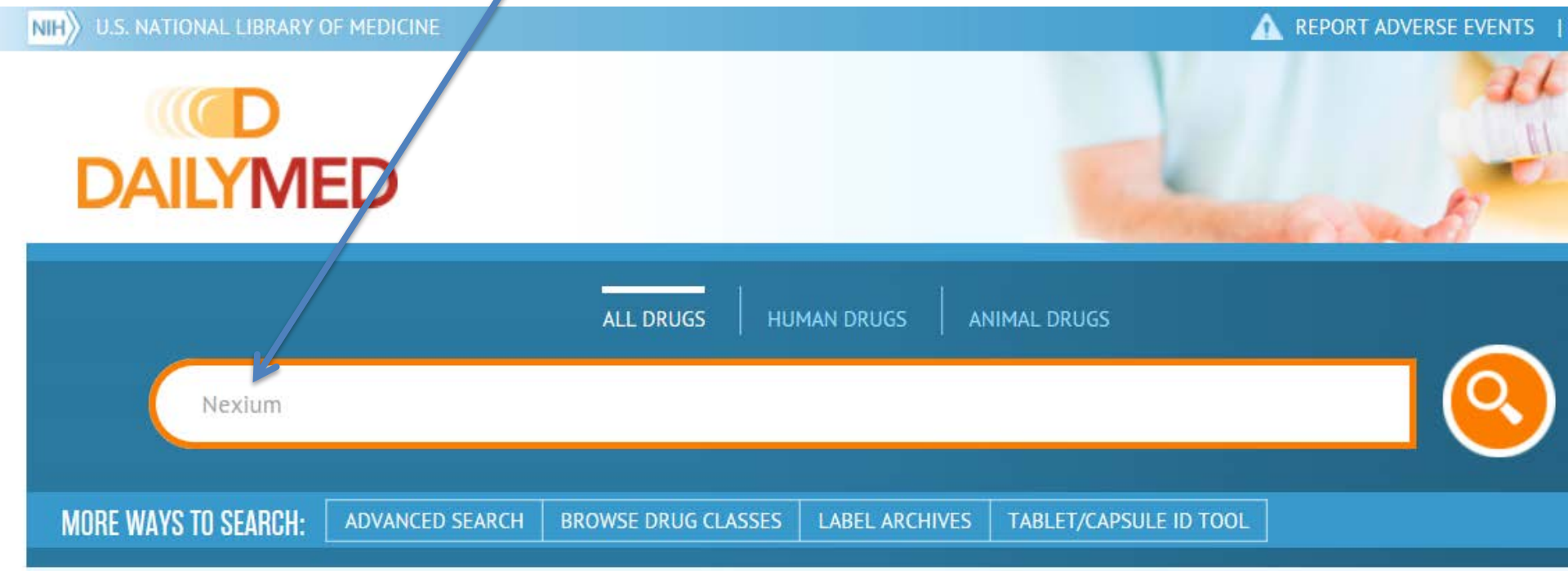
DailyMed: Types of Products

- Drugs for humans
  - Brand and generic prescription drugs (NDAs and ANDAs, respectively)
  - Biological products[1] (BLAs)
    - Therapeutic biologics and monoclonal antibodies
    - Blood, vaccine, allergenic, and cellular/tissue products
  - Brand and generic OTC drugs (NDAs and ANDAs; and monograph system)
- Other products for humans
  - Dietary supplements
  - Homeopathic products
- Animal prescription and OTC drugs

[1] Includes biosimilar products

DailyMed: How to Search Labeling

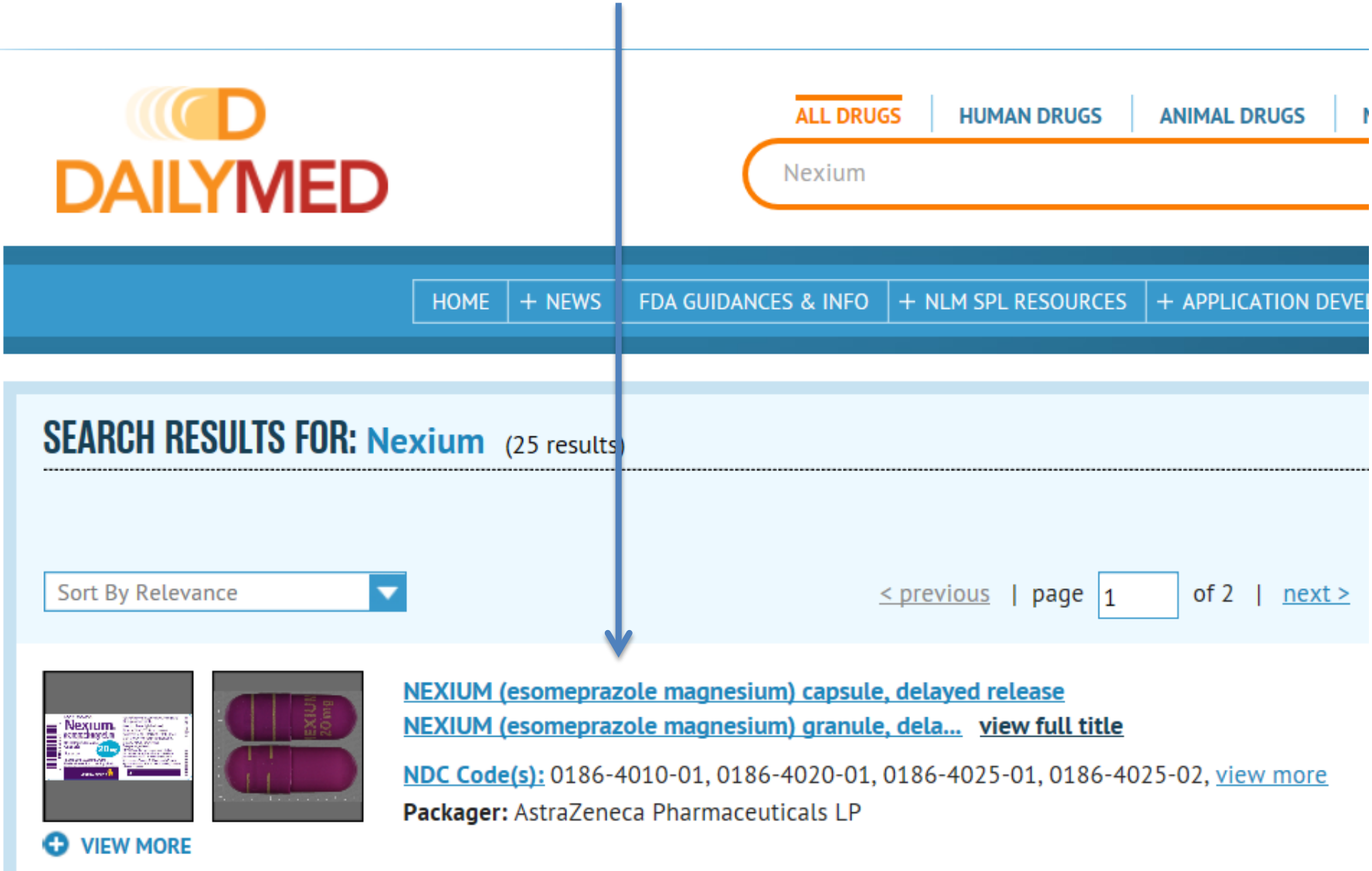
Step #1: Type in drug name



DailyMed: How to Review Labeling

FDA

Step #2: Choose dosage form



DailyMed: How to Review Labeling

Step #3: Choose method to view labeling (i.e., webpage, PDF, or SPL)

VIEW PACKAGE PHOTOS

VIEW MORE

VIEW DRUG PHOTOS

NDC Codes:
0186-5020-31

SAFETY

- Report Adverse Events
- FDA Safety Recalls
- Presence in Breast Milk

NDC Code(s): 0186-4010-01, 0186-4020-01, 0186-4025-01, 0186-4025-02, view more
Packager: AstraZeneca Pharmaceuticals LP

Category: HUMAN PRESCRIPTION DRUG LABEL
DEA Schedule: None
Marketing Status: New Drug Application

DRUG LABEL INFORMATION

Updated December 20, 2016

If you are a consumer or patient please visit this version.

DOWNLOAD DRUG LABEL INFO: PDF | XML MEDICATION GUIDE: HTML OFFICIAL LABEL (PRINTER FRIENDLY)

VIEW ALL SECTIONS

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NEXIUM safely and effectively. See full prescribing information for NEXIUM. NEXIUM - ® (esomeprazole magnesium ...

FULL PRESCRIBING INFORMATION: CONTENTS*

Table of Contents

1 INDICATIONS AND USAGE

1.1 Treatment of Gastroesophageal Reflux Disease (GERD) Healing of Erosive Esophagitis NEXIUM is

SPL (Structured Product Labeling) is based on extensible markup language (XML)

DailyMed: How to Review Labeling

SPL Labeling Format

NEXIUM- esomeprazole magnesium capsule, delayed release
NEXIUM- esomeprazole magnesium granule, delayed release
AstraZeneca Pharmaceuticals LP

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use NEXIUM safely and effectively. See full prescribing information for NEXIUM.
NEXIUM® (esomeprazole magnesium) delayed-release capsules, for oral use
NEXIUM® (esomeprazole magnesium) for delayed-release oral suspension
Initial U.S. Approval: 1989 (omeprazole)

RECENT MAJOR CHANGES

Warnings and Precautions, Atrophic Gastritis (5.2) removed 10/2016
Warnings and Precautions, Cutaneous and Systemic 10/2016

Lupus Erythematosus (5.5)

INDICATIONS AND USAGE

NEXIUM is a proton pump inhibitor indicated for the following:

- Treatment of gastroesophageal reflux disease (GERD). (1.1)
- Risk reduction of NSAID-associated gastric ulcer. (1.2)
- *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence. (1.3)
- Pathological hypersecretory conditions, including Zollinger-Ellison syndrome. (1.4)

DOSAGE AND ADMINISTRATION

Indication	Dose	Frequency
Gastroesophageal Reflux Disease (GERD)		
Adults	20 mg or 40 mg	Once daily for 4 to 8 weeks

Hyperlinks within document

- Acute Interstitial Nephritis: Observed in patients taking PPIs. (5.2)
- *Clostridium difficile*-Associated Diarrhea: PPI therapy may be associated with increased risk. (5.3)
- Bone Fracture: Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. (5.4)
- Cutaneous and Systemic Lupus Erythematosus: Mostly cutaneous; new onset or exacerbation of existing disease; discontinue NEXIUM and refer to specialist for evaluation. (5.5)
- Interaction with Clopidogrel: Avoid concomitant use of NEXIUM. (5.6)
- Cyanocobalamin (Vitamin B-12) Deficiency: Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin. (5.7)
- Hypomagnesemia: Reported rarely with prolonged treatment with PPIs. (5.8)
- Interaction with St. John's Wort or Rifampin: Avoid concomitant use of NEXIUM. (5.9,7.3)
- Interactions with Diagnostic Investigations for Neuroendocrine Tumors: Increased chromogranin A (CgA) levels may interfere with diagnostic investigations for neuroendocrine tumors, temporarily stop NEXIUM at least 14 days before assessing CgA levels. (5.10,12.2)
- Interaction with Methotrexate: Concomitant use with PPIs may elevate and/or prolong serum concentrations of methotrexate and/or its metabolite, possibly leading to toxicity. With high dose methotrexate administration, consider temporary withdrawal of NEXIUM. (5.11,7.7)

ADVERSE REACTIONS

Most common adverse reactions (6.1):

Question #4

DailyMed includes labeling from which products?

a. TYLENOL
b. LIPITOR
c. FLUMIST
d. Vitamin E
e. All of the above

Drugs@FDA vs. DailyMed Labeling (1 of 2)

	Drugs@FDA	DailyMed
Who posts/submits labeling?	FDA posts labeling	Firms submit labeling
FDA reviews labeling	Always	Generally no
Format	PDF	1. View on webpage 2. PDF 3. SPL • Hyperlinks • Allows for indexing
PI	Last approved PI and historical PI	Most recent PI submitted to FDA
Includes recent PI updates: • Annual reportable changes • Pending CBE-0 labeling supplements	No	Yes

PDF = Portable Document Format; SPL = Structured Product Labeling
CBE = Changes Being Effected

Drugs@FDA vs. DailyMed Labeling (2 of 2)

	Drugs@FDA	DailyMed
Patient labeling	Last approved patient labeling	Most recent patient labeling submitted to FDA
Carton/container labeling	Rarely present	Present
Generic product labeling	Rarely present	Present
Includes regulatory history and FDA reviews	Yes	No
Includes historical approved labeling	Yes	No

Question #5

Labeling on Drugs@FDA and DailyMed have the following in common:

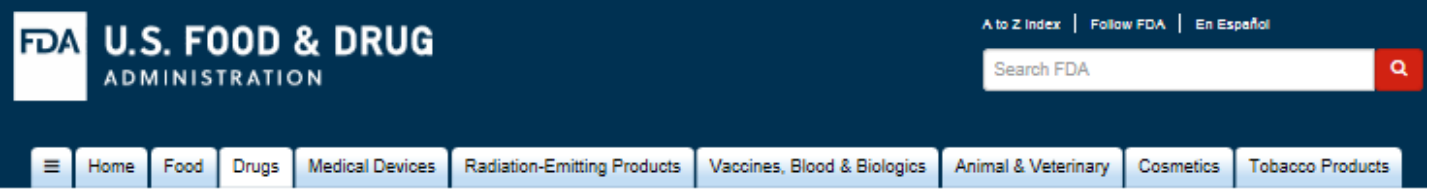
a. Contains most up-to-date labeling submitted to FDA
b. Almost always includes hyperlinks
c. Almost always includes carton and container labeling
d. Includes previously approved labeling
e. None of the above

Question #6

Labeling on Drugs@FDA and DailyMed may differ because:

a. Labeling on Drugs@FDA may include changes that have not been FDA-approved
b. Labeling on DailyMed may include minor changes such as new how supplied information
c. Labeling on Drugs@FDA may include minor changes such as changes to inactive ingredients
d. (a) and (c)
e. None of the above

Labeling Resources



Drugs

Home > Drugs > Guidance, Compliance & Regulatory Information > Laws, Acts, and Rules

Laws, Acts, and Rules

- Complete Response Letter Final Rule
- Metered-Dose Inhalers Clean Air Act Information
- **PLR Requirements for Prescribing Information**

Resources for You

- Drugs@FDA
- FDA Online Label Repository
- Labeling Development Team

PLR Requirements for Prescribing Information

http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm

link

On January 24, 2006, the U.S. Food and Drug Administration (FDA) issued final regulations governing the content and format of prescribing information (PI) for human drug and biological products. The rule is commonly referred to as the "**Physician Labeling Rule**" (PLR) because it addresses prescription drug labeling that is used by prescribers and other health care providers.

The goal of the PLR content and format requirements as described at 21 CFR 201.56 and 201.57 is to enhance the safe and effective use of prescription drug products by providing health care providers with clear and concise PI that is easier to access, read, and use. The PLR format also makes PI more accessible for use with electronic prescribing tools and other electronic information resources.

PI submitted with new drug applications (NDAs), biologic license applications (BLAs), and efficacy supplements must conform to the content and format regulations found at 21 CFR 201.56 and 201.57. The Labeling Development Team works with review divisions to ensure PI conforms with the PLR. This page includes links to the Final Rule, regulations, related guidance documents, and additional labeling resources.

On December 3, 2014, the FDA published the Pregnancy and Lactation Labeling Rule (PLLR). The goal of the PLLR is to enhance the safe and effective use of prescription drug products in pregnant women, lactating women, and females and males of reproductive potential.

PLR Final Rule and Labeling Requirements

- Physician Labeling Rule
  Requirements on content and format of labeling for human prescription drug and biological products, January 24, 2006 (Federal Register Notice)
- 21 CFR 201.56
  Requirements on content and format of labeling for human prescription drug and biological products
- 21 CFR 201.57
  PLR Labeling: Specific requirements on content and format of PLR labeling for human prescription drug and biological products described in § 201.56(b)(1)
- 21 CFR 201.80
  Older drugs: Specific requirements on content and format of labeling for human prescription drug and biological products; older drugs not described in § 201.56(b)(1)

Labeling databases

http://labels.fda.gov/

U.S. Department of Health & Human Services www.hhs.gov

U.S. Food and Drug Administration

A-Z Index Search go

Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products

FDA Online Label Repository

IMPORTANT DISCLAIMER

Please be aware of the following when using information from this Web site:

The drug labels and other drug-specific information on this Web site represent the most recent drug listing information companies have submitted to the Food and Drug Administration (FDA). (See 21 CFR part 207.) The drug labeling and other information has been reformatted to make it easier to read but its content has neither been altered nor verified by FDA. The drug labeling on this Web site may not be the labeling on currently distributed products or identical to the labeling that is approved. Most OTC drugs are not reviewed and approved by FDA, however they may be marketed if they comply with applicable regulations and policies described in monographs. Drugs marked "OTC monograph final" or "OTC monograph not final" are not checked for conformance to the monograph. Drugs marked "unapproved medical gas", "unapproved homeopathic" or "unapproved drug other" on this Web site have not been evaluated by FDA for safety and efficacy and their labeling has not been approved. In addition, FDA is not aware of scientific evidence to support homeopathy as effective.

The device labeling and other device-specific information on this website have been voluntarily submitted to the FDA by device manufacturers. FDA has not reviewed this information prior to posting on this website. The device labeling has been reformatted to make it easier to read but its content has not been altered nor verified by FDA. The device labeling on this website may not be the labeling on currently distributed products.

Proprietary Name Search **NDC Number Search**

Active Ingredient Search **Application Number or Regulatory Citation Search**

Company Search **Proprietary Name and Company Search**

Search for Labels on DailyMed

The labels are also available on the National Library of Medicine's DailyMed web site. You can search for labels by drug name and link to the Library's information resources about marketed drugs.

References

- Drugs@FDA: www.fda.gov/DrugsAtFDA
- DailyMed: https://dailymed.nlm.nih.gov/dailymed/index.cfm
- http://labels.fda.gov/
- PLR Requirements for Prescribing Information: https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm

Thank you!

Extra Slides

How FDA Reviews PI

- In response to application holder questions, FDA provides comments about draft PI before NDA/BLA submission
- Application holder submits an NDA/BLA that includes a draft PI that meets labeling regulatory requirements and is consistent with guidance recommendations
- FDA reviews PI upon submission and throughout review cycle
- FDA and application holder develop final PI
  - Iterative process of communications/discussions with both parties
- Final PI (PDF format) is approved by FDA and attached to approval letter (PI is posted on Drugs@FDA)