Highlights of Prescribing Information

Eric Brodsky, M.D.
Associate Director, Labeling Development Team
Office of New Drugs, Center for Drug Evaluation and Research
Food and Drug Administration (FDA)
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 fictitious and are provided only to demonstrate current labeling development challenges.
Overview of Presentation: Highlights

- Resources
- Basic Principles
- Format
- Product Title
- Initial U.S. Approval
- Boxed Warning
- Established Pharmacologic Class
- Dosage and Administration
- Warnings and Precautions
HL: Resources

Code of Federal Regulations:
- 21 CFR 201.57(a)

Labeling Guidances and MAPPPs:
- Implementing PLR Content and Format Requirements Guidance (2013)
- Determining EPC for Use in HL Guidance (2009)
- Determining EPC for Use in HL MAPP (7400.13) (2013)

Future Labeling Guidance:
- Draft Product Title and Initial U.S. Approval in HL Guidance (under development)
HL: Basic Principles

- A concise summary of crucial prescribing information
  - “These highlights do not include all the information needed to use DRUG-X safely and effectively. See full prescribing information for DRUG-X”*

- Length not to exceed one-half page (excluding length of Boxed Warning) when printed single-spaced in 2 columns on 8.5 x 11 inch paper in 8-point type with 1/2-inch margins on all sides and between columns**

- Should not have new content in HL that is not in FPI***
  - Exceptions include: Initial U.S. Approval, Adverse Reactions Reporting Statement, Revision Date

* 21 CFR 201.57(a)(1); ** 21 CFR 201.57(d)(8)
*** Section V(A) - Implementing PLR Content and Format Requirements Guidance
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DRUG-X safely and effectively. See full prescribing information for DRUG-X.

DRUG-X (Drugoxide Injection), for intravenous use
Initial U.S. Approval: 1939

INDICATIONS AND USAGE
DRUG-X, a cholinesterase inhibitor, is indicated for the reversal of the effects of non-depolarizing neuromuscular blocking agents (NMBAs) after surgery (1).

DOSEAGE AND ADMINISTRATION
• Should be administered by trained healthcare providers (2.1)
• Peripheral nerve stimulator and monitoring for twitch responses should be used to determine when DRUG-X should be initiated and if additional doses are needed (2.2)
  - For reversal of NMBAs with shorter half-lives, when first twitch response is substantially greater than 10% of baseline, or when a second twitch is present: 0.03 mg/kg by intravenous route (2.2)
  - For reversal of NMBAs with longer half-lives or when first twitch response is close to 10% of baseline: 0.07 mg/kg by intravenous route (2.2)
• Maximum total dosage is 0.07 mg/kg or up to a total of 5 mg (whichever is less) (2.2)
• An anticholinergic agent, e.g., atropine sulfate or glycopyrrolate, should be administered prior to or concomitantly with DRUG-X (2.4)

DOSAGE FORMS AND STRENGTHS
Injection: 0.5 mg/mL and 1 mg/mL in 10 mL multiple-dose vials (3)

CONTRAINDICATIONS
• Hypersensitivity to neostigmine (4)
• Peritonitis or mechanical obstruction of the intestinal or urinary tract (4)

WARNINGS AND PRECAUTIONS
• Bradycardia: Atropine or glycopyrrolate should be administered prior to DRUG-X to lessen risk of bradycardia. (5.1)
• Serious Reactions with Coexisting Conditions: Use with caution in patients with, coronary artery disease, cardiac arrhythmias, recent acute coronary syndrome or myasthenia gravis. (5.2)
• Neuromuscular Dysfunction: Can occur if large doses of DRUG-X are administered when neuromuscular blockade is minimal; reduce dose if recovery from neuromuscular blockade is nearly complete. (5.4)

ADVERSE REACTIONS
Most common adverse reactions during treatment: bradycardia, nausea and vomiting. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Sponsor Y at 1-877-622-2320 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS
• Pregnancy: No human or animal data. Use only if clearly needed.

Revised: May 2013
HIGHLIGHTS OF PRESCRIBING INFORMATION

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

DRUG-X (Drugoxide Injection)
for intravenous use
Initial U.S. Approval: 1939

INDICATIONS AND USAGE

DRUG-X, a cholinesterase inhibitor, is indicated for the reversal of the effects of non-depolarizing neuromuscular blocking agents (NMBAs) after surgery (1).

DOSAGE AND ADMINISTRATION

- Should be administered by trained healthcare providers (2.1)
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- For reversal of NMBAs with shorter half-lives, when first twitch response is substantially greater than 10% of baseline, or when a second twitch is present: 0.03 mg/kg by intravenous route (2.2)
- For reversal of NMBAs with longer half-lives or when first twitch response is close to 10% of baseline: 0.07 mg/kg by intravenous route (2.2)
- Maximum total dosage is 0.07 mg/kg or up to a total of 5 mg (whichever is less) (2.2)
- An anticholinergic agent, e.g., atropine sulfate or glycopyrrolate, should be administered prior to or concomitantly with DRUG-X

DOSED FORMS AND STRENGTHS

Injection: 0.5 mg/mL and 1 mg/mL in 10 mL multiple-dose vials (3)

CONTRAINdications

- Hypersensitivity to neostigmine (4)
- Peritonitis or mechanical obstruction of the intestinal or urinary tract (4)

WARNINGS AND PRECAUTIONS

- Bradycardia: Atropine or glycopyrrolate should be administered prior to DRUG-X to lessen risk of bradycardia. (5.1)
- Serious Reactions with Coexisting Conditions: Use with caution in patients with, coronary artery disease, cardiac arrhythmias, recent acute coronary syndrome or myasthenia gravis. (5.2)
- Neuromuscular Dysfunction: Can occur if large doses of DRUG-X are administered when neuromuscular blockade is minimal; reduce dose if recovery from neuromuscular blockade is nearly complete. (5.4)

ADVERSE REACTIONS

Most common adverse reactions during treatment: bradycardia, nausea and vomiting. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sponsor Y at 877-622-2320 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Pregnancy: No human or animal data. Use only if clearly needed.

Revised: May 2013
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use DRUG-X safely and effectively. See full prescribing information for DRUG-X.

DRUG-X (drugoxide injection), for intravenous use
Initial U.S. Approval: 1939

____________________ INDICATIONS AND USAGE __________________
DRUG-X, a cholinesterase inhibitor, is indicated for the reversal of the effects of non-depolarizing neuromuscular blocking agents (NMBAs) after surgery (1)

____________________ DOSAGE AND ADMINISTRATION __________________
• Should be administered by trained healthcare providers (2.1)
• Peripheral nerve stimulator and monitoring for twitch responses should be used to determine when DRUG-X should be initiated and if additional doses are needed (2.2)
  o For reversal of NMBAs with shorter half-lives, when first twitch response is substantially greater than 10% of baseline, or when a second twitch is present: 0.03 mg/kg by intravenous route
  o For reversal of NMBAs with longer half-lives or when first twitch response is close to 10% of baseline: 0.07 mg/kg by intravenous route
• Maximum total dosage is 0.07 mg/kg or up to a total of 5 mg (whichever is less) (2.2)
• An anticholinergic agent, e.g., atropine sulfate or glycopyrrolate, should be administered prior to or concomitantly with DRUG-X (2.4)

____________________ DOSAGE FORMS AND STRENGTHS __________________
Injection: 0.5 mg/mL and 1 mg/mL in 10 mL multiple-dose vials (3)

____________________ CONTRAINDICATIONS __________________
• Hypersensitivity to neostigmine (4)
• Peritonitis or mechanical obstruction of the intestinal or urinary tract (4)

____________________ WARNINGS AND PRECAUTIONS __________________
• Bradycardia: Atropine or glycopyrrolate should be administered prior to DRUG-X to lessen risk of bradycardia (5.1)
• Serious Reactions with Coexisting Conditions: Use with caution in patients with, coronary artery disease, cardiac arrhythmias, recent acute coronary syndrome or myasthenia gravis (5.2)
• Neuromuscular Dysfunction: Can occur if large doses of DRUG-X are administered when neuromuscular blockade is minimal; reduce dose if recovery from neuromuscular blockade is nearly complete (5.4)

____________________ ADVERSE REACTIONS __________________
Most common adverse reactions during treatment: bradycardia, nausea and vomiting (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sponsor Y at 1-877-622-2320 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

____________________ USE IN SPECIFIC POPULATIONS __________________
Pregnancy: No human or animal data. Use only if clearly needed.

* According to 21 CFR 201.57(a)(11), criteria used for adverse reaction (AR) inclusion must be stated (in this example, no incidence could be determined, e.g., older product)
Principles to Reduce HL Length*

- Summarize information in phrases
- Use command language. Instead of “You should discontinue”, state “Discontinue”
- Use bulleted lists and tables
- Avoid redundancy
- Reduce margins to ½ inch
- Omit following:
  - Less important information
  - Clinically irrelevant statements (e.g., absence of information)

* Section V - Implementing PLR Content and Format Requirements Guidance
HL: Good Examples
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use HARVONI™ safely and effectively. See full prescribing information for HARVONI.

HARVONI™ (ledipasvir and sofosbuvir) tablets, for oral use
Initial U.S. Approval: 2014

INDICATIONS AND USAGE
HARVONI is a fixed-dose combination of ledipasvir, a hepatitis C virus (HCV) NS5A inhibitor, and sofosbuvir, an HCV nucleotide analog NS5B polymerase inhibitor, and is indicated for the treatment of chronic hepatitis C (CHC) genotype 1 infection in adults.

DOSAGE AND ADMINISTRATION
- Recommended dosage: One tablet (90 mg of ledipasvir and 400 mg of sofosbuvir) taken orally once daily with or without food.
- Recommended treatment duration:
  - Treatment-naïve with or without cirrhosis: 12 weeks
  - Treatment-experienced without cirrhosis: 12 weeks
  - Treatment-experienced with cirrhosis: 24 weeks
- A dose recommendation cannot be made for patients with severe renal impairment or end stage renal disease.

DOSAGE FORMS AND STRENGTHS
Tablets: 90 mg ledipasvir and 400 mg sofosbuvir.

CONTRAINDICATIONS
None

WARNINGS AND PRECAUTIONS
Use with other drugs containing sofosbuvir, including SOVALDI, is not recommended.

ADVERSE REACTIONS
The most common adverse reactions (incidence greater than or equal to 10%, all grades) observed with treatment with HARVONI for 8, 12, or 24 weeks are fatigue and headache.

To report SUSPECTED ADVERSE REACTIONS, contact Gilead Sciences, Inc. at 1-800-GILEAD-5 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS
- P-gp Inducers (e.g., rifampin, St. John’s wort): May alter concentrations of ledipasvir and sofosbuvir. Use of HARVONI with P-gp inducers is not recommended.
- Consult the full prescribing information prior to use for potential drug interactions.

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

Revised: 10/2014
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LONSURF safely and effectively. See full prescribing information for LONSURF.

LONSURF (trifluridine and tipiracil) tablets, for oral use
Initial U.S. Approval: 2015

---------------INDICATIONS AND USAGE---------------
LONSURF is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor, indicated for the treatment of patients with metastatic colorectal cancer who have been previously treated with fluoropyrimidine-, oxaliplatin- and irinotecan-based chemotherapy, an anti-VEGF biological therapy, and if RAS wild-type, an anti-EGFR therapy. (1)

---------------DOSEAGE AND ADMINISTRATION---------------
- Recommended dose: 35 mg/m²/dose orally twice daily on Days 1 through 5 and Days 8 through 12 of each 28-day cycle. (2.1)
- Take LONSURF within 1 hour after completion of morning and evening meals. (2.1)

---------------DOSEAGE FORMS AND STRENGTHS---------------
Tablets:
- 15 mg trifluridine/6.14 mg tipiracil (3)
- 20 mg trifluridine/8.19 mg tipiracil (3)

---------------WARNINGS AND PRECAUTIONS---------------
- Severe Myelosuppression: Obtain complete blood counts prior to and on Day 15 of each cycle. Reduce dose and/or hold LONSURF as clinically indicated. (5.1)
- Embryo-Fetal Toxicity: Fetal harm can occur. Advise women of potential risk to a fetus. (5.2)

---------------ADVERSE REACTIONS---------------
The most common adverse reaction (≥10%) are anemia, neutropenia, asthenia/fatigue, nausea, thrombocytopenia, decreased appetite, diarrhea, vomiting, abdominal pain, and pyrexia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Taiho Oncology, Inc. at 1-844-878-2446 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------------USE IN SPECIFIC POPULATIONS---------------
- Lactation: Do not breastfeed. (8.2)
- Geriatric Use: Grade 3 or 4 neutropenia and thrombocytopenia and Grade 3 anemia occurred more commonly in patients 65 years old or older who received LONSURF. (8.5)
- Renal Impairment: Patients with moderate renal impairment may require dose modifications for increased toxicity. (8.7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 09/2015
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)

------------------------DOSEAGE 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).

To report SUSPECTED ADVERSE REACTIONS, contact the
manufacturer at toll-free phone # or FDA at 1-800-FDA-1088
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.

* 21 CFR 201.57(a)(2)
“Injection”: drugs available as solutions that will be injected

“For injection”: drugs supplied as a solid (e.g., lyophilized powder) and must be reconstituted before administration

Route of administration (ROA) is not repeated in Product Title if it precedes dosage form:*

MYDRUG (drugozide) topical solution

When ROA does not precede dosage form, ROA is presented as “for [insert ROA] use”*

MYDRUG (drugozide injection), for intravenous use

Proprietary name is in UPPER-CASE and rest of product title in lower case*

* Best labeling practice
Product Title Examples: Products With a Proprietary Name*

LEVITRA (vardenafil hydrochloride) tablets, for oral use
ZOMIG-ZMT (zolmitriptan) orally disintegrating tablets
FENTORA (fentanyl buccal tablets), CII
REVATIO (sildenafil) for oral suspension
OXYTROL (oxybutynin transdermal system)
ADASUVE (loxapine) inhalation powder, for oral inhalation use
SIMPONI (golimumab) injection, for subcutaneous use
BOTOX (onabotulinumtoxinA) for injection, for intramuscular, intradetrusor, or intradermal use

* Product title format is best labeling practice
Product Title Examples: Products Without Proprietary Name*

CYCLOPHOSPHAMIDE tablets, for oral use

PHENYLEPHRINE HYDROCHLORIDE injection, for intravenous use

GLUCAGON for injection, for intravenous or intramuscular use

DOXORUBICIN HYDROCHLORIDE for injection, for intravenous use

DOXORUBICIN HYDROCHLORIDE injection, for intravenous use

* Product title format is best labeling practice
On line immediately beneath Product Title, “Initial U.S. Approval:” must be displayed

- Four-digit year in which FDA initially approved NME, new biological product, or new combination of active ingredients
- Irrespective of salt, dosage form, ROA, indication, or dosage

Fixed Dose Combination (FDC) Products:

- First time a new combination is approved, Initial U.S. Approval is 4-digit year of FDC approval

First time active moiety is approved alone (previously FDC that contains active moiety approved), Initial U.S. Approval is 4-digit year of FDC

* 21 CFR 201.57(a)(3); Section V(B)(3) - Implementing PLR Content and Format Requirements Guidance; NME = new molecular entity
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
HL: Boxed Warning (BW)*

- Concise summary of clinically significant adverse reactions or risks in FPI BW
- Must not exceed 20 lines
- Should use bullets
- No information should be in HL BW that does not appear in FPI BW
- Title “WARNING” and heading must be bolded and in upper case; should be centered

* 21 CFR 201.57(a)(4); Section V(B)(4) - Implementing PLR Content and Format Requirements Guidance
HL: Established Pharmacologic Class (EPC)*

- EPC are term(s) that:
  - Refer to a group of active moieties that share scientifically valid properties
  - Are clinically meaningful
  - Are associated with an approved indication
  - Must be included in indications statement in HL (if established)

- Format:

  “DRUG-X is a (insert FDA text phrase for EPC) indicated for Indication Y”

* 21 CFR 201.57(a)(6); Determining EPC for Use in Highlights Guidance and MAPP
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
- FDA EPC Text Phrases for Highlights Indications and Usage heading (updated June 1, 2015) New!! (PDF - 2.2MB)

Search for EPC of approved drugs (EPCs are terms or phrases associated with an approved indication of an active moiety, which FDA has determined to be scientifically valid and clinically meaningful).
### How to Find FDA EPC Text Phrase (2 of 2)

<table>
<thead>
<tr>
<th>Active Moiety Name</th>
<th>Text Phrase</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,2'-dithiobisbenzothiazole</td>
<td>standardized chemical allergen</td>
</tr>
<tr>
<td>2-mercaptobenzothiazole</td>
<td>standardized chemical allergen</td>
</tr>
<tr>
<td>2-mercaptoethanesulfonic acid</td>
<td>cytoprotective agent</td>
</tr>
<tr>
<td>4-hydroxybutanoic acid</td>
<td>central nervous system depressant</td>
</tr>
<tr>
<td>abacavir</td>
<td>HIV nucleoside analog reverse transcriptase inhibitors (HIV NRTI)</td>
</tr>
<tr>
<td>abatacept</td>
<td>selective T cell costimulation modulator</td>
</tr>
<tr>
<td>abies balsamea pollen</td>
<td>non-standardized pollen allergenic extract</td>
</tr>
<tr>
<td>abies concolor pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<tr>
<td>abies grandis pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<tr>
<td>abies procer a pollen</td>
<td>non-standardized pollen allergenic extract</td>
</tr>
<tr>
<td>abiraterone</td>
<td>CYP17 inhibitor</td>
</tr>
<tr>
<td>acacia</td>
<td>non-standardized plant allergenic extract</td>
</tr>
<tr>
<td>acacia baileyana pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<td>acacia dealbata pollen</td>
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</tr>
<tr>
<td>acacia longifolia pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<tr>
<td>acacia pollen</td>
<td>non-standardized pollen allergenic extract</td>
</tr>
<tr>
<td>acarbose</td>
<td>alpha glucosidase inhibitor</td>
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<tr>
<td>acebutolol</td>
<td>beta adrenergic blocker</td>
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<td>acer pseudoplatanus pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<td>acer rubrum pollen</td>
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<tr>
<td>acer saccharum pollen</td>
<td>non-standardized pollen allergenic extract</td>
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<td>acetazolamide</td>
<td>carbonic anhydrase inhibitor</td>
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<tr>
<td>acetohydroxamic acid</td>
<td>urease inhibitor</td>
</tr>
<tr>
<td>acetylcholine</td>
<td>cholinergic agonist</td>
</tr>
<tr>
<td>acetylcysteine</td>
<td>mucolytic antidote for acetaminophen overdose</td>
</tr>
</tbody>
</table>

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.
For combination products where products have different EPCs:

“DRUG-X is a combination of drugoxide, an EPC #1, and drugsulfide, an EPC#2, indicated for …”

---INDICATIONS AND USAGE---

STRIBILD is a four-drug combination of elvitegravir, an HIV integrase strand transfer inhibitor (HIV-1 INSTI), cobicistat, a CYP3A inhibitor, and emtricitabine and tenofovir DF, both HIV nucleoside analog reverse transcriptase inhibitors (HIV NRTI) and is indicated as a complete regimen for the treatment of HIV-1 infection in adults who are antiretroviral treatment-naïve. (1)
HL: Dosage and Administration (D&A)*

- Concise summary of critical D&A information, including:
  - Recommended starting dosage
  - Dosage range
  - Titration
  - ROA
  - Dosage adjustments:
    - Due to concomitant drugs or adverse reactions
    - In specific populations (instead of Use in Specific Populations heading)

- For products with complex dosage or administration, cross-reference to FPI for details

* 21 CFR 201.57(a)(7); Section V(B)(7) - Implementing PLR Content and Format Requirements Guidance
DOSAGE AND ADMINISTRATION

- Administer a 40 mg loading dose subcutaneously under physician supervision (2.1)
- After proper injection instruction, on day after loading dose, patients or caregivers begin daily subcutaneous injections of 10 mg (2.1)
- Adjust dosage in 5 mg increments or decrements until serum IGF-I concentrations are maintained within age-adjusted normal range. Do not adjust dosage based on growth hormone (GH) levels or signs or symptoms of acromegaly (2.1)
- Dosage range is 10 to 30 mg once daily (2.1)
- Perform liver tests prior to first dosage and if greater than 3 time upper limit of normal should work-up prior to SOMAVERE administration (2.2)
- Follow reconstitution and injection procedures (2.3, 2.4)
HL: Warnings and Precautions (W&P)*

- Concise summary of most important safety concerns; include how to prevent or mitigate them**

- Include most important W&P
  - Not all W&P in FPI need to be included
  - Avoid skipping a W&P unless this information is presented elsewhere in HL

- For each listed W&P
  - Identify clinically significant AR or risk
  - Recommendations to prevent, monitor, or manage clinically significant AR or risk

- Avoid redundancy with other HL headings

* 21 CFR 201.57(a)(10); Section V(B)(10) - Implementing PLR Content and Format Requirements Guidance; best labeling practice
** 21 CFR 201.57(a)(10)
WARNINGS AND PRECAUTIONS

- Hypersensitivity Reactions: Monitor and if a severe reaction occurs, discontinue treatment and initiate appropriate medical treatment. (5.1)
- Lipodystrophy: Localized reactions were reported after several months of treatment; follow proper injection technique and rotate injection sites. (5.2)
- Ectopic Calcifications (eye and kidneys): Monitor using ophthalmologic examinations and renal ultrasounds at baseline and periodically during treatment. (5.3)

* Approved October 23, 2015
References

➢ PLR Requirements for Prescribing Information website:

Thank you!