Regulatory Education for Industry (REdI): PRESCRIPTION DRUG LABELING - CHALLENGES AND ISSUES

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Highlights of Prescribing Information

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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 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 MAPPs:

- 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

Format: What can be Improved? (1 of 2)

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)
  - 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

Format: What can be Improved? (2 of 2)

Product Title: Continuous wrapping text to preserve space

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

Add space

INDICATIONS AND USAGE

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  - 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)
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Shift to left

DOSAGE FORMS AND STRENGTHS

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- 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)

Shift to left

Add space

ADVERSE REACTIONS

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USE IN SPECIFIC POPULATIONS

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

Remove bullet

Revised: May 2013

Improved Format*

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)
  - 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**
  - 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**
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- 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

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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: 5/2013

* 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

HARVONI

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 (1)

----------DOSAGE AND ADMINISTRATION----------
- Recommended dosage: One tablet (90 mg of ledipasvir and 400 mg of sofosbuvir) taken orally once daily with or without food (2.1)
- Recommended treatment duration (2.1):
  - 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 (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 90 mg ledipasvir and 400 mg sofosbuvir. (3)

----------CONTRAINDICATIONS----------
None

----------WARNINGS AND PRECAUTIONS----------
Use with other drugs containing sofosbuvir, including SOVALDI, is not recommended (5.2)

----------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 (6.1)

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 (5.1, 7, 12.3)
- Consult the full prescribing information prior to use for potential drug interactions (5.1, 7, 12.3)

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

Revised: 10/2014

LONSURF

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)

DOSAGE AND ADMINISTRATION

- Recommended dose: 35 mg/m^2/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)

DOSAGE FORMS AND STRENGTHS

Tablets:

- 15 mg trifluridine/6.14 mg tipiracil (3)
- 20 mg trifluridine/8.19 mg tipiracil (3)

CONTRAINDICATIONS

None. (4)

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

HL: Product Title*

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.

To report SUSPECTED ADVERSE REACTIONS, contact na manufacturer at toll-free phone # or FDA at 1-800-FDA-108 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:

* 21 CFR 201.57(a)(2)

HL: Product Title

- "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

HL: Initial U.S. Approval*

- 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

HL: Initial U.S. Approval

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

HL: EPC Text Phrase

HIGHLIGHTS OF PRESCRIBING INFORMATION
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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

How to Find FDA EPC Text Phrase (1 of 2)

How to Find FDA EPC Text Phrase (2 of 2)

Active Moiety Name	FDA Established Pharmacologic Class (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.
2,2'-dithiobisbenzothiazole	standardized chemical allergen
2-mercaptobenzothiazole	standardized chemical allergen
2-mercaptoethanesulfonic acid	cytoprotective agent
4-hydroxybutanoic acid	central nervous system depressant
abacavir	HIV nucleoside analog reverse transcriptase inhibitors (HIV NRTI)
abatacept	selective T cell costimulation modulator
abies balsamea pollen	non-standardized pollen allergenic extract
abies concolor pollen	non-standardized pollen allergenic extract
abies grandis pollen	non-standardized pollen allergenic extract
abies procera pollen	non-standardized pollen allergenic extract
abiraterone	CYP17 inhibitor
acacia	non-standardized plant allergenic extract
acacia baileyana pollen	non-standardized pollen allergenic extract
acacia dealbata pollen	non-standardized pollen allergenic extract
acacia longifolia pollen	non-standardized pollen allergenic extract
acacia pollen	non-standardized pollen allergenic extract
acarbose	alpha glucosidase inhibitor
acebutolol	beta adrenergic blocker
acer macrophyllum pollen	non-standardized pollen allergenic extract
acer negundo pollen	non-standardized pollen allergenic extract
acer pseudoplatanus pollen	non-standardized pollen allergenic extract
acer rubrum pollen	non-standardized pollen allergenic extract
acer saccharinum pollen	non-standardized pollen allergenic extract
acer saccharum pollen	non-standardized pollen allergenic extract
acetazolamide	carbonic anhydrase inhibitor
acetohydroxamic acid	urease inhibitor
acetylcholine	cholinergic agonist
acetylcysteine	mucolytic antidote for acetaminophen overdose

EPC Text Phrase in HL Indications Statement: Combination Products*

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)

* Section IV - Determining EPC for Use in Highlights Guidance

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

HL: D&A - SOMAVERT

----------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 SOMAVERT 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)

HL: W&P - STRENSIQ*

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

Thank you!