CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202231Orig1s000

OTHER REVIEW(S)

REGULATORY PROJECT MANAGER
PLR FORMAT LABELING REVIEW

Application: NDA 202231

Name of Drug: Proprietary name - none
Established name - Levothyroxine Sodium for Injection

Applicant: APP Pharmaceuticals, LLC

Labeling Reviewed

Submission Date: August 30, 2010

Receipt Date: August 30, 2010

Summary Description

Indication: myxedema coma

Dosage form: Lyophilized Powder for Injection

Route of administration: Intravenous (IV)

Proposes new indication, dosage form, dosing regimen, and route of administration

Drug chemical classification: 7-Drug Already Marketed but Without an Approved NDA
Review priority: Standard

Review

The submitted labeling was reviewed in accordance with 21 CFR 201.56 and 201.57 and relevant labeling guidance. Labeling issues are identified on the following pages with an "X."

Recommendations

All labeling issues identified on the following pages with an "X" will be conveyed to the applicant. The applicant will be asked to resubmit labeling that addresses all the identified labeling issues. The resubmitted labeling will be used for further labeling discussions.

Linda Galgay	March 23, 2011
Regulatory Project Manager	Date

LABELING CHECKLIST	FILING REVIEW
SECTION I: Highlights Overview	**08.30.10**
For more information, see Draft Guidance for Industry: Labeling for Human Prescription Drug and Biological Products - Implementing the New Content and Format Requirements; also refer to http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm.	
Check that the following items appear (in the following order):	
• **Highlights Limitation Statement** (required statement) (required bolding)	X
• **Drug names, dosage form, route of administration, and controlled substance symbol** (required information) (required bolding)	**X**
• **Initial U.S. Approval** (required information) (required bolding)	**X – Date of moiety approval** 1969
• **Boxed Warning** (required bolding)	
• **Recent Major Changes** (for a supplement)	
• **Indications and Usage**	
• **Dosage and Administration**	
• **Dosage Forms and Strengths**	
• **Contraindications** (required heading – if no contraindications are known, it must state "None")	X -Must keep heading with "None"
• **Warnings and Precautions**	
• **Adverse Reactions** (required AR contact reporting statement) (required bolding for AR contact reporting statement)	**X**
• **Drug Interactions** (optional heading – can be omitted)	
• **Use in Specific Populations** (optional heading – can be omitted)	
• **Patient Counseling Information Statement** (required statement) (required bolding)	**X – Not applicable**
• **Revision Date** (required information) (required bolding)	
[format] Highlights, excluding the boxed warning, must be limited in length to one-half page (e.g., would fit on one-half page if printed on 8.5" x 11 paper, single spaced, minimum 8 point type with ½ inch margins on all sides, in a two-column format)	
[format] All headings and subheadings must be in bold type.	
[format] All headings must be presented in the center of a horizontal line in upper-case letters and bold type. The horizontal line can be a solid or dashed line.	
[format] If there are multiple subheadings, each subheading must be preceded by a bullet point.	
[format] The information should be concisely summarized without repetition and presented in an easily accessible format (e.g., bulleted, tabular). There should be no redundancy of information.	
[format] Use command language (e.g., use "Discontinue" instead of "You should discontinue.")	
[format] Each summarized statement should be located under the appropriate Highlights heading and must reference the section(s) or	

LABELING CHECKLIST	FILING REVIEW
subsection(s) of the Full Prescribing Information (FPI) that contains more detailed information.	
[format] The preferred presentation of referencing in Highlights is the numerical identifier in parentheses [e.g., (1.1)] following the summarized labeling information, corresponding to the location of information in the FPI.	
[format] There should be white space between each major heading in Highlights.	
[format] The type size for all labeling information, headings, and subheadings must be a minimum of 8 points, except for labeling information that is on or within the package from which the drug is to be dispensed (i.e., trade labeling), which must be a minimum of 6 points. See Appendix E of Implementation Guidance for type size requirements.	**X**
[format] There is no requirement for a specific typeface for labeling as long as it is clear and legible. However, Arial Narrow font is not recommended because it may render the labeling illegible.	
[format] Do not use the asterisk (*) to footnote information in tables in Highlights since this symbol is used in the Table of Contents (i.e., *Sections or subsections omitted from the full prescribing information are not listed.)	
[format] We are no longer going to review the labeling for the "TM" or "R" symbols. Companies can add these symbols at will in Word and Adobe versions. These symbols will not appear in the rendering of labeling in SPL format due to style sheet restrictions.	

LABELING CHECKLIST	FILING REVIEW
SECTION II: Highlights Details	
Highlights Limitation Statement	
Must appear at beginning of Highlights in bold type and be placed on the line immediately beneath the heading – **HIGHLIGHTS OF PRESCRIBING INFORMATION**	
The verbatim statement must read: "**These highlights do not include all the information needed to use (insert name of drug product in upper case letters) safely and effectively. See full prescribing information for (insert name of drug product in upper case letters).**"	**X**
Drug names, dosage form, route of administration, and controlled substance symbol (must appear in bold type)	
• With SPL R4, the product title in HL is no longer added automatically. Since this field is added as free text, check carefully.	
• Include proprietary name and either established name of drug, OR proper name of biological product.	
• **For the established name of a drug**, the active moiety is generally used if the product is a salt. The salt is sometimes included in the name when it is important to know what salt is present for therapeutic reasons (e.g., a lot of Na or K; affect on therapeutic performance is known - absorption, distribution, metabolism, excretion). Include the entire drug substance name for esters, chelates, and complexes. • Also, the established name and expression of strength should match. As a general rule, if the strength is in terms of the salt/ester, the name includes the salt/ester. If the strength is in terms of the active moiety, the name is in terms of the active moiety.	X
• The drug names must be followed by drug's dosage form and route of administration. • Note that for biologic products, the dosage form and route of administration must be on the next line (i.e., underneath the proper name) since the proper name does not include the drug's dosage form or route of administration. See 21 CFR 600.3 (k) and Section 351 of the PHS Act • If the route of administration is typical for the dosage form and is commonly understood (e.g., tablets or capsules), omit the route of administration (for oral use). If the route of administration is not typical, it must be included.	
• If applicable, must include the controlled substance symbol designating the schedule in which the controlled substance is listed. • However, do not include a controlled substance symbol after drug names, dosage forms, and route of administration unless DEA scheduling action is final.	**N/A**

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