## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. FDA–2012–D–0529]**

### Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen; Guidance for Industry; Availability

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice of availability.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen.'' The guidance is intended to inform manufacturers of certain nonprescription (also referred to as over-the-counter or OTC) internal analgesic, antipyretic, and antirheumatic (IAAA) drug products that contain acetaminophen of the circumstances for which FDA does not intend to object to the inclusion of a liver warning that differs from that required under FDA regulations, provided the warning appears as described in the guidance.

**DATES:** Submit either electronic or written comments on Agency guidances at any time.

**ADDRESSES:** You may submit comments as follows:

*Electronic Submissions*

Submit electronic comments in the following way:

- Federal eRulemaking Portal: *http://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *http://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *http://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

*Written/Paper Submissions*

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Division of Dockets Management, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

*Instructions:* All submissions received must include the Docket No. FDA–2012–D–0529 for ''Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen Guidance for Industry.'' Received comments will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *http://www.regulations.gov* or at the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *http://www.regulations.gov.* Submit both copies to the Division of Dockets Management. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *http://www.fda.gov/regulatoryinformation/dockets/default.htm.*

*Docket:* For access to the docket to read background documents or the electronic and written/paper comments received, go to *http://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

Submit written requests for single copies of this guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993–0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the guidance document.

**FOR FURTHER INFORMATION CONTACT:** Emily Baker, Office of Unapproved Drugs and Labeling Compliance, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Silver Spring, MD 20993–0002, 301–796–7524, *Emily.Baker@fda.hhs.gov.*

**SUPPLEMENTARY INFORMATION:**

## I. Background

FDA is announcing the availability of a guidance for industry entitled ''Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen.'' In the **Federal Register** of December 26, 2006 (71 FR 77314), FDA published a proposed rule on organ-specific warnings and related labeling for OTC IAAA drug products. In the **Federal Register** of April 29, 2009 (74 FR 19385), FDA published the final rule (2009 final rule). In the **Federal Register** of November 25, 2009 (74 FR 61512), FDA published a technical amendment to clarify several provisions in response to industry feedback. The 2009 final rule, as amended, changed some of the labeling requirements for OTC IAAA drug products to inform consumers about the risk of liver injury when using acetaminophen and the risk of stomach bleeding when using nonsteroidal anti-

inflammatory drugs. It went into effect April 29, 2010.

Under that rule, the labeling for OTC IAAA products that contain acetaminophen and are labeled for adults only must include the liver warning described below. Similarly, the labeling for OTC IAAA products that contain acetaminophen and are labeled for adults and children under 12 year of age must include a similar liver warning described below.

Adults Only (§ 201.326(a)(1)(iii)(A) (21 CFR 201.326(a)(1)(iii)(A))):

Liver warning: This product contains acetaminophen. Severe liver damage may occur if you take • more than [insert maximum number of daily dosage units] in 24 hours, which is the maximum daily amount [optional: ''for this product''] • with other drugs containing acetaminophen • 3 or more alcoholic drinks every day while using this product.

Adults and children under 12 years of age (§ 201.326(a)(1)(v)(A) (21 CFR 201.326(a)(1)(v)(A))):

Liver warning: This product contains acetaminophen. Severe liver damage may occur if • adult takes more than [insert maximum number of daily dosage units] in 24 hours, which is the maximum daily amount [optional: ''for this product''] • child takes more than 5 doses in 24 hours • taken with other drugs containing acetaminophen • adult has 3 or more alcoholic drinks every day while using this product.

Although the currently proposed maximum daily dose of acetaminophen is 4,000 milligrams (mg), some OTC IAAA products that contain acetaminophen have directions for use that provide a maximum daily dose of acetaminophen for that product that is less than 4,000 mg. For example, for some OTC IAAA drug products that contain both acetaminophen and one or more other active ingredients, the maximum number of daily dosage units might be limited by an active ingredient other than acetaminophen, which could result in a maximum daily dose of acetaminophen that is less than 4,000 mg for that product. The optional statement, ''for this product,'' in the first bullet of the liver warning is intended to address these situations by clarifying that the maximum number of daily dosage units for a product might not reflect the maximum daily dose of acetaminophen.

However, the Agency understands that in certain circumstances, despite this optional statement, the wording of the first bullet in the warnings shown above might be interpreted as indicating that severe liver damage is associated with a total daily dose of acetaminophen that is less than 4,000 mg. This suggestion is not the intent of the regulation. To address this potential confusion, the Agency does not intend to object to the inclusion of a liver warning that differs from that required under § 201.326(a)(1)(iii)(A) and § 201.326(a)(1)(v)(A), provided the warning appears as described in the guidance.

In the **Federal Register** of July 5, 2012 (77 FR 39710), FDA published a draft guidance entitled ''Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen.'' The July 2012 draft guidance gave interested persons an opportunity to submit comments through September 4, 2012. We have made changes to the guidance in response to comments received and have clarified the information in section III of the draft guidance.

This guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The guidance represents the current thinking of FDA on Organ-Specific Warnings: Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use—Labeling for Products That Contain Acetaminophen. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

## II. Paperwork Reduction Act of 1965

The recommendations in this guidance are not subject to review by the Office of Management and Budget because they do not constitute a ''collection of information'' under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the labeling statements are a ''public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public'' (5 CFR 1320.3(c)(2)).

## III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm* or *http://www.regulations.gov.*

Dated: November 12, 2015.

**Leslie Kux,**

*Associate Commissioner for Policy.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

**[Docket No. FDA–2014–N–0229]**

### Issuance of Priority Review Voucher; Rare Pediatric Disease Product

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is announcing the issuance of a priority review voucher to the sponsor of a rare pediatric disease product application. The Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Food and Drug Administration Safety and Innovation Act (FDASIA), authorizes FDA to award priority review vouchers to sponsors of rare pediatric disease product applications that meet certain criteria. FDA has determined that STRENSIQ (asfotase alfa), manufactured by Alexion Pharmaceuticals, Inc., meets the criteria for a priority review voucher.

**FOR FURTHER INFORMATION CONTACT:** Larry Bauer, Rare Diseases Program, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 6408, Silver Spring, MD 20993–0002, 301–796–4842, FAX: 301–796–9858, email: *larry.bauer@fda.hhs.gov.*

**SUPPLEMENTARY INFORMATION:** FDA is announcing the issuance of a priority review voucher to the sponsor of a rare pediatric disease product application. Under section 529 of the FD&C Act (21 U.S.C. 360ff), which was added by FDASIA, FDA will award priority review vouchers to sponsors of rare pediatric disease product applications that meet certain criteria. FDA has determined that STRENSIQ (asfotase alfa), manufactured by Alexion Pharmaceuticals, Inc., meets the criteria for a priority review voucher. Asfotase alfa is a long-term enzyme replacement therapy for patients with infantile- and juvenile-onset hypophosphatasia (HPP). HPP is a rare genetic disorder that affects the development of bones and teeth.

For further information about the Rare Pediatric Disease Priority Review Voucher Program and for a link to the full text of section 529 of the FD&C Act, go to *http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm.*

For further information about STRENSIQ (asfotase alfa), go to the