



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-D-1862]

Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions; 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 “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions.” This guidance is intended to inform manufacturers, members of the medical and scientific community, and other interested persons that at this time FDA does not intend to take action against the marketing of single- and combination-ingredient, acetaminophen-containing, nonprescription (commonly referred to as over-the-counter (OTC)) drug products bearing a warning as described in the guidance alerting consumers that the use of acetaminophen may cause severe skin reactions.

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-2014-D-1862 for "Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions; 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 “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions.” Acetaminophen, included in many prescription and OTC products, is a common active ingredient indicated to treat pain and reduce fever. On August 1, 2013, FDA issued a Drug Safety Communication (DSC) informing the public that use of acetaminophen has been associated with a risk of rare but serious skin reactions.¹ These skin reactions, including Stevens-Johnson Syndrome, toxic epidermal necrolysis, and acute generalized exanthematous pustulosis, can be fatal.

¹ FDA Drug Safety Communication: FDA warns of rare but serious skin reactions with the pain reliever/fever reducer acetaminophen. <http://www.fda.gov/Drugs/DrugSafety/ucm363041.htm>.

The DSC explained that reddening of the skin, rash, blisters, and detachment of the upper surface of the skin can occur with the use of drug products that contain acetaminophen. These skin reactions can occur with the first-time use of acetaminophen or even if acetaminophen has been used in the past without any problems. FDA advised health care professionals to be aware of this rare risk and consider acetaminophen, along with other drugs already known to have such an association, when assessing patients with potentially drug-induced skin reactions. FDA also advised that anyone who develops a skin rash or reaction while using acetaminophen or any other pain reliever/fever reducer should stop taking the drug and seek medical attention right away. Furthermore, the announcement advised that anyone who has experienced a serious skin reaction when taking acetaminophen in the past should not take the drug again and should contact their health care professional to discuss alternative pain relievers/fever reducers.

In response to FDA's letters to manufacturers holding new drug applications and abbreviated new drug applications, most manufacturers of acetaminophen-containing prescription and OTC drug products marketed under an approved application now include a warning statement on their product labels to address the risk of serious skin reactions. FDA recommends that manufacturers of all acetaminophen-containing OTC drug products (both single- and combination-ingredient acetaminophen products) marketed under the Tentative Final Monograph (TFM) for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products include in labeling the language recommended in this guidance to warn consumers that acetaminophen may cause severe skin reactions. At this time, FDA does not intend to take action against the marketing of single- and combination-ingredient, acetaminophen-containing, OTC drug products bearing the recommended allergy warning that are otherwise marketed in compliance with the TFM and applicable regulations.

In the Federal Register of November 28, 2014 (79 FR 70879), FDA published a draft guidance entitled “Recommended Warning for Over-the-Counter Acetaminophen-Containing Drug Products and Labeling Statements Regarding Serious Skin Reactions.” See: <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm424898.pdf>. The November 2014 draft guidance gave interested persons an opportunity to submit comments through January 27, 2015. We have made changes to the guidance in response to comments received and have added labeling information about products that contain both acetaminophen and aspirin.

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 the recommended warning for OTC acetaminophen-containing drug products and labeling statements regarding serious skin reactions. 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 1995

Under the guidance, manufacturers may add to their drug product labeling a warning statement supplied by FDA that pertains to acetaminophen to address the risk of serious skin reactions. Inclusion of the warning statement on the labels for these drug products would be exempt from review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520) because the public disclosure of information originally supplied by the Federal government to the recipient for the purpose of disclosure to the public is not included within the definition of “collection of information” (see 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: January 5, 2017.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2017-00375 Filed: 1/10/2017 8:45 am; Publication Date: 1/11/2017]