



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2013-D-1170]

Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment;
Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled “Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment.” The purpose of this draft guidance is to assist sponsors in all phases of development of direct-acting antiviral (DAA) drugs for the treatment of chronic hepatitis C. This draft guidance revises the draft guidance of the same name that was issued on October 23, 2013.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

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-2013-D-1170 for “Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment; Draft Guidance for Industry; Availability.” 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 the draft 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 draft guidance document.

FOR FURTHER INFORMATION CONTACT: Jeffrey Murray, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6360, Silver Spring, MD 20993-0002, 301-796-1500.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled “Chronic Hepatitis C Virus Infection: Developing Direct-Acting Antiviral Drugs for Treatment.” This draft guidance addresses nonclinical development, early phases of clinical development, and phase 3 protocol designs. Important issues addressed in this draft guidance include: Trial design options, noninferiority margin for active-controlled phase 3 trials in the evaluation of interferon (IFN)-free regimens, and trial design options and safety evaluation for specific populations, including patients with decompensated cirrhosis, patients either pre- or post-liver transplant, patients with chronic kidney disease, and clinical virology considerations.

This draft guidance revises the draft guidance of the same name that issued October 23, 2013 (78 FR 63218). Significant changes in this draft guidance compared to the previous version are:

- Modification of several sections to focus on IFN-free DAA regimens.
- Additional details on phase 2 and phase 3 trial design options for the evaluation of IFN-free regimens in treatment-naïve and treatment-experienced populations, including DAA-experienced populations. Specifically, the guidance now recommends that each marketing application contain at least one active-controlled comparative trial.
- Additional clarification on DAA drug development in specific populations, including trial design options for human immunodeficiency virus/hepatitis C virus co-infected patients, pediatric patients, patients with advanced chronic kidney disease, patients with decompensated cirrhosis, patients either pre- or post-liver transplantation, and patients who failed to respond to a prior DAA-based regimen.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on developing DAA drugs for treatment of chronic hepatitis C virus infection. 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. The Paperwork Reduction Act of 1995

This draft guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 312 have been approved under 0910-0014, the collections of information in 21 CFR part 314 have been approved under 0910-0001, and the collections of information referred to in the guidance for industry "Establishment and Operation of Clinical Trial Data Monitoring Committees" have been approved under 0910-0581.

III. Electronic Access

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

Dated: April 28, 2016.

Leslie Kux,

Associate Commissioner for Policy.

[FR Doc. 2016-10390 Filed: 5/3/2016 8:45 am; Publication Date: 5/4/2016]