4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2012-D-0432]

Draft Guidance for Industry on Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval." FDA's accelerated approval regulations permit approval of a new drug to treat a serious disease on the basis of an effect on a surrogate endpoint reasonably likely to predict the clinical benefit of the drug. This draft guidance is intended to assist applicants in designing trials to support marketing approval of drugs to treat breast cancer in the neoadjuvant (preoperative) setting using pathologic complete response (pCR) as a surrogate endpoint that could support approval under the accelerated approval regulations. Despite advances in systemic therapy of early-stage breast cancer over the past few decades, there remains a significant unmet medical need for certain high-risk or poor prognosis populations of early-stage breast cancer patients. This guidance is intended to encourage industry innovation and expedite the development of breakthrough therapies to treat high-risk early-stage breast cancer.

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on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance, submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, 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 See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

Submit electronic comments on the draft guidance to http://www.regulations.gov. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Pathologic Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval." Under the accelerated approval regulations (21 CFR part 314, subpart H, and 21 CFR part 601, subpart E), FDA may grant marketing approval for a new drug on the basis of adequate and well-controlled trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit (e.g., an effect on survival or irreversible morbidity), provided that the applicant conducts additional trials after approval to verify and describe the predicted clinical benefit. This draft guidance is intended to assist applicants in designing trials to support marketing approval of drugs to treat breast cancer in the neoadjuvant (preoperative) setting using pCR as a surrogate endpoint that could support approval under the accelerated approval regulations. The guidance proposes a uniform definition of pCR for regulatory purposes. The guidance also advises on appropriate patient populations for inclusion and on the trial designs intended to verify the predicted clinical benefit associated with pCR to support conversion to full approval.

FDA recognizes that despite advances in adjuvant systemic therapy of breast cancer over the past few decades, there remains a significant unmet medical need for certain high-risk or poor prognosis populations of early-stage breast cancer patients. Developing highly effective new drugs for these populations is an FDA priority. In providing guidance on the use of pCR as a surrogate endpoint that could support accelerated approval in the neoadjuvant setting, FDA hopes to encourage industry innovation and expedite the development of breakthrough therapies to treat high-risk early-stage breast cancer.

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 Agency's current thinking on the use of pCR in neoadjuvant treatment of high-risk early-stage breast cancer as an endpoint to support accelerated approval. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. The Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR parts 312 and 314 have been approved under OMB control numbers 0910-0014 and 0910-0001, respectively. The collections of information for special protocol assessments have been approved under OMB control number 0910-0470.

III. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. 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: May 15, 2012.

Leslie Kux,

Assistant Commissioner for Policy.

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