4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2014-N-0374]

Postmarketing Requirements for the Class-Wide Extended-Release/Long-Acting Opioid Analgesics; Public Meeting; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public meeting; request for comments.

SUMMARY: The Food and Drug Administration (FDA) is announcing a public meeting to obtain stakeholder input on the design and conduct of the postmarketing requirements (PMRs) for the class-wide extended-release/long-acting (ER/LA) opioid analgesic drug products to further assess the serious risks of misuse, abuse, hyperalgesia, addiction, overdose, and death associated with their long-term use.

FDA is seeking input on these issues from stakeholders, including patients, academia, researchers, State and other Federal regulators, health care organizations, health care providers, the pharmaceutical industry, and others from the general public.

DATES: The public meeting will be held on May 19 and 20, 2014, from 8 a.m. to 5 p.m. Individuals who wish to present at the meeting must register by May 9, 2014. See section III under the SUPPLEMENTARY INFORMATION section for information on how to register to speak at the meeting.

ADDRESSES: The public meeting will be held at FDA's White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (rm. 1503), Silver Spring, MD 20993-0002. Participants must enter through Building 1 and undergo security screening. For

parking and security information, please refer to http://www.fda.gov/AboutFDA/WorkingatFDA/BuildingsandFacilities/WhiteOakCampusInformation/ucm241740.htm.

Submit either electronic or written comments by June 19, 2014. Submit electronic comments 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. Identify all comments with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Janelle Derbis, Center for Drug Evaluation and Research, Food and Drug Administration, 20 North Michigan Ave., suite 510, Chicago, IL 60602, 312-596-6516, FAX: 312-886-1682, email: ERLAOpioidPMRMeeting@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is committed to improving the safe and appropriate use of ER/LA opioid analgesics and preserving appropriate access for those patients who rely on these medications to manage their pain. In May 2012, FDA hosted a scientific workshop to discuss the assessment of analgesic treatment of chronic pain, during which presenters raised concerns about the safe and appropriate use of opioid analgesics.[1] Over the past 2 years, FDA has reviewed numerous submissions to Agency dockets, including citizen petitions and comments to petitions, and relevant literature about the benefits and risks associated with opioid drug products, including the serious risks of misuse, abuse, hyperalgesia, addiction, overdose, and death associated with the

[1] Assessment of Analgesic Treatment of Chronic Pain: A Scientific Workshop (see http://www.fda.gov/Drugs/NewsEvents/ucm283979.htm). Information and comments from that workshop are available at www.regulations.gov, Docket No. FDA-2012-N-0067.

long-term use of ER/LA opioid analgesics. FDA has concluded that more data are needed regarding these serious risks.

FDA described these data requirements in its September 10, 2013, letter to all new drug application (NDA) applicants for ER/LA opioid analgesics. Data are needed to address the following issues:

- The incidence of and risk factors for misuse, abuse, addiction, overdose, and death associated with long-term use of opioids for chronic pain.
- Validated measures of misuse, abuse, addiction, overdose, and death.
- Validated coded medical terminologies used to identify misuse, abuse, addiction, overdose, and death.
- Validated definitions of "doctor/pharmacy shopping" as outcomes suggestive of misuse, abuse, and addiction.
- The serious risk of developing hyperalgesia following use of ER/LA opioid analgesics for at least 1 year to treat chronic pain.

In the September 10, 2013, letter, FDA informed the ER/LA opioid analgesic NDA application holders of the requirement to conduct postapproval studies (also referred to as postmarketing requirements or PMRs) and established milestone dates for completion of those studies, which include observational studies and a clinical trial (see section II for more details). The deadline for the applicants' final protocol submissions is August 2014.

II. Purpose and Scope of Meeting

The purpose of this public meeting is to obtain stakeholder input on the design and conduct of the PMRs (described in the following paragraph) for the ER/LA opioid analgesic drug products to assess the serious risks of misuse, abuse, hyperalgesia, addiction, overdose, and death

associated with their long-term use. FDA and NDA applicants will consider stakeholder input when preparing final protocols to be submitted by August 2014.

The PMRs described in FDA's September 10, 2013, letter to NDA applicants of ER/LA opioid analgesics are as follows:

(1) PMR # 2065-1: Conduct one or more studies to provide quantitative estimates of the serious risks of misuse, abuse, addiction, overdose, and death associated with long-term use of opioid analgesics for management of chronic pain among patients prescribed ER/LA opioid products. Include an assessment of risk relative to efficacy.

These studies should address at a minimum the following specific aims:

a. Estimate the incidence of misuse, abuse, addiction, overdose, and death associated with long-term use of opioids for chronic pain. Stratify misuse and overdose by intentionality wherever possible. Examine the effect of product/formulation, dose and duration of opioid use, prescriber specialty, indication, and other clinical factors (e.g., concomitant psychotropic medications, personal or family history of substance abuse, and history of psychiatric illness) on the risk of misuse, abuse, addiction, overdose, and death.

b. Evaluate and quantify other risk factors for misuse, abuse, addiction, overdose, and death associated with long-term use of opioids for chronic pain, including, but not limited to, the following: Demographic factors, psychosocial/behavioral factors, medical factors, and genetic factors. Identify confounders and effect modifiers of individual risk factor/outcome relationships. Stratify misuse and overdose by intentionality wherever possible.

(2) PMR # 2065-2: Develop and validate measures of the following opioid-related adverse events: Misuse, abuse, addiction, overdose, and death (based on the Department of

Health and Human Services' definition, or any agreed upon definition), which will be used to inform the design and analysis for PMR # 2065-1 and any future postmarketing safety studies and clinical trials to assess these risks. This can be achieved by conducting an instrument development study or a validation study of an algorithm based on secondary data sources.

(3) PMR # 2065-3: Conduct a study to validate coded medical terminologies (e.g., ICD9, ICD10, and SNOMED) used to identify the following opioid-related adverse events: Misuse, abuse, addiction, overdose, and death in any existing postmarketing databases to be employed in the studies. Stratify misuse and overdose by intentionality wherever possible. These validated codes will be used to inform the design and analysis for PMR # 2065-1.

(4) PMR # 2065-4: Conduct a study to define and validate "doctor/pharmacy shopping" as outcomes suggestive of misuse, abuse, and addiction. These validated codes will be used to inform the design and analysis for PMR # 2065-1.

(5) PMR # 2065-5: Conduct a clinical trial to estimate the serious risk for the development of hyperalgesia following use of ER/LA opioid analgesics for at least 1 year to treat chronic pain. We strongly encourage you to use the same trial to assess the development of tolerance following use of ER/LA opioid analgesics. Include an assessment of risk relative to efficacy.

III. Attendance and Registration

Attendance is free and will be on a first-come, first-served basis. Individuals who wish to present at the public meeting must register on or before May 9, 2014, at https://erlaopioidpmrmeeting.eventbrite.com. In section II, FDA has listed the PMRs. You should identify which PMR(s) you wish to address in your presentation, or whether your comments apply to all PMRs, so FDA can consider that in organizing the presentations. FDA

will do its best to accommodate requests to speak and will determine the amount of time allotted to each presenter and the approximate time that each oral presentation is scheduled to begin. An agenda and additional meeting background material will be available approximately 2 weeks before the meeting at http://www.fda.gov/Drugs/NewsEvents/ucm384489.htm.

Individuals who wish to attend the meeting but do not wish to make a presentation should register by May 12, 2014. Onsite registration on the day of the meeting will be based on space availability.

If you need special accommodations due to a disability, please contact Janelle Derbis (see FOR FURTHER INFORMATION CONTACT) at least 7 days in advance.

A live Web cast of this meeting will be viewable at https://collaboration.fda.gov/opmr/ on the day of the meeting. A video record of the meeting will be available at the same Web address for 1 year.

IV. Comments

Interested persons may submit either electronic comments regarding this document to http://www.regulations.gov or written comments to the Division of Dockets Management (see ADDRESSES). 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. To ensure consideration, submit comments by June 19, 2014. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at http://www.regulations.gov.

V. Transcripts

As soon as possible after a transcript of the public meeting is available, it will be accessible at http://www.regulations.gov. It may be viewed at the Division of Dockets

Management (see ADDRESSES). A transcript will also be available in either hardcopy or on CD-ROM, after submission of a Freedom of Information request. Written requests are to be sent to the Division of Freedom of Information (ELEM-1029), Food and Drug Administration, 12420 Parklawn Dr., Element Bldg., Rockville, MD 20857.

Dated: April 17, 2014.

Leslie Kux,

Assistant Commissioner for Policy.

[FR Doc. 2014-09123 Filed 04/21/2014 at 8:45 am; Publication Date: 04/22/2014]