

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

NDA 22-156

APPROVAL LETTER



NDA 22-156

NDA APPROVAL

The Medicines Company
Attention: Gregory C. Williams, Ph.D.
8 Campus Drive
Parsippany, NJ 07054

Dear Dr. Williams:

Please refer to your new drug application (NDA) dated July 2, 2007, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Cleviprex (clevidipine butyrate) injectable emulsion 0.5 mg/mL .

We acknowledge receipt of your submissions dated July 25, August 8, September 6, 28, October 22, December 20, 2007 and January 8, February 6, 19, March 3, 11, 14, 21, 28, April 3, 7, 10, 14, 17, 18, 25, May 30, June 3, and July 2, 2008.

This new drug application provides for the use of Cleviprex (clevidipine butyrate) 0.5 mg/mL injectable emulsion for the reduction of blood pressure when the use of oral therapy is not feasible or not desirable.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CMC Comment:

Based on your drug product stability data, an expiration date of 24 months is granted for the 50 mL fill size when stored refrigerated (2 – 8°C). A 36 month shelf-life is granted for the 100 mL fill size when stored refrigerated. Both configurations can be stored for up to 2 months at controlled room temperature as “in-use” storage.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.htm> that is identical to the enclosed labeling. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, “SPL for approved NDA 22-156.”

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed inner carton, vial label, inner carton wafer seal and outer carton label as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission “**Final Printed Carton and Container Labels for approved NDA 22-156.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with labeling that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies until August 2011 because pediatric studies should be delayed until additional safety or effectiveness data have been collected as described below. However, we believe that Cleviprex should be available for use in adults while data are being collected in children.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required post-marketing studies. The status of these post-marketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

Deferred pediatric studies under PREA for the reduction of blood pressure in pediatric patients ages 1 to 16 years old.

Final Report Submission: **August 1, 2011**

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric post-marketing studies must be clearly designated “**Required Pediatric Assessments**”.

ADVISORY COMMITTEE

Your application was not referred to an advisory committee because this drug is not the first in its class, the clinical study design was acceptable, the application did not raise significant safety or efficacy issues, the application did not raise significant public health questions on the role of the drug in the diagnosis, cure, mitigation, treatment or prevention of a disease, and outside expertise was not necessary.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, please call:

Alisea Crowley, Pharm.D.
Regulatory Project Manager
(301) 796-1144

Sincerely,

{See appended electronic signature page}

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Agreed-upon labeling text

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Robert Temple
8/1/2008 05:23:37 PM