CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-496

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-496

Amphastar Pharmaceuticals, Inc.
Attention: Stephen A. Campbell, Esq.
Vice President, Corporate Regulatory Affairs
11570 Sixth Street
Rancho Cucamonga, CA 91730

Dear Mr. Campbell:

Please refer to your new drug application (NDA) dated February 28, 2002, received March 6, 2002, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Duocaine (lidocaine HCl-bupivacaine HCl injection) 1%/0.375%.

We acknowledge receipt of your submissions dated January 7 and 10, February 20, March 26, April 21, and 30, and May 19, 2003.

The March 26, 2003, submission constituted a complete response to our January 3, 2003, action letter.

This new drug application provides for the use of Duocaine (lidocaine HCl-bupivacaine HCl injection) 1%/0.375% for the production of local or regional anesthesia for ophthalmologic surgery by peripheral nerve block techniques such as parabulbar, retrobulbar, and facial nerve blocks.

We have completed our review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text submitted April 30, 2003. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical with the enclosed agreed upon labeling text for the package insert, dated April 30, 2003. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-496.**" Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Rlease submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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

If you have any questions, call Raphael R. Rodriguez, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic
and Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

APPEARS THIS WAY
ON ORIGINAL

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APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

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Rockville, MD 20857

NDA 21-496

Amphastar Pharmaceuticals, Inc.
Attention: Stephen A. Campbell, Esq.
Vice President, Corporate Regulatory Affairs
11570 Sixth Street
Rancho Cucamonga, CA 91730

Dear Mr. Campbell:

Please refer to your new drug application (NDA) dated February 28, 2002, received March 6, 2002, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Duocaine

We acknowledge receipt of your submissions dated April 1, 5, and 8, July 22, August 1, 19, and 28(two), November 1, and 25, 2002.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to address the following:

> During a recent inspection of the drug product manufacturing facility for this application, our field investigator conveyed deficiencies to the facility representative. All manufacturing facilities are required to conform to current good manufacturing procedures. Satisfactory resolution to these deficiencies is required before this application may be approved.

The submitted labeling is not consistent with 21 CFR 201.57. We will continue to work with you on the proposed labeling for this product.

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65.

Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you update your NDA by submitting all safety information you now have regarding your new drug.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications, HFD-42
5600 Fishers Lane
Rockville, MD 20857

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Raphael R. Rodriguez, Regulatory Project Manager, at (301) 827-2090

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic
and Ophthalmic Drug Product, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

**APPEARS THIS WAY
ON ORIGINAL**

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

/s/

Wiley Chambers
1/3/03 03:10:57 PM

APPEARS THIS WAY
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