CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

204200Orig1s000
204200Orig2s000

Trade Name: Adrenalin, 1 mg/mL.

Generic Name: epinephrine injection

Sponsor: JHP Pharmaceuticals, LLC

Approval Date: December 7, 2012

Indications: Original 1 – Emergency treatment of allergic reactions (Type 1), including Anaphylaxis

Original 2 – Induction and maintenance of mydriasis during ocular surgery

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204200Orig1s000
204200Orig2s000

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APPLICATION NUMBER:

204200Orig1s000
204200Orig2s000

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204200/Original 1
NDA 204200/Original 2

NDA APPROVAL

JHP Pharmaceuticals, LLC
Attention: Carla English
Manager, Regulatory Affairs
One Upper Pond Road
Building D, 3rd Floor
Parsippany, NJ 07054

Dear Ms. English:

Please refer to your New Drug Application (NDA) dated and received March 7, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Adrenalin (epinephrine injection), 1 mg/mL.

We acknowledge receipt of your amendments dated:

April 9, 2012(2)	April 18, 2012	May 15, 2012
May 16, 2012 (2)	May 17, 2012 (2)	June 4, 2012
June 19, 2012 (2)	July 3, 2012 (2)	July 20, 2012 (2)
August 2, 2012 (2)	August 21, 2012 (2)	August 22, 2012
September 5, 2012 (3)	October 15, 2012 (2)	October 22, 2012
November 9, 2012 (4)	November 28, 2012	November 29, 2012 (2)
November 30, 2012 (2)	December 4, 2012 (2)	December 5, 2012 (2)
December 6, 2012 (2)	December 7, 2012 (2)	

NDA 204200 provides for the use of Adrenalin (epinephrine injection, USP), 1 mg/mL for the following indications which, for administrative purposes, we have designated as follows:

- NDA 204200/Original 1 – Emergency treatment of allergic reactions (Type 1), including anaphylaxis
- NDA 204200/Original 2 – Induction and maintenance of mydriasis during ocular surgery

The subject of this action letter is NDA 204200/Original 1 and NDA 204200/Original 2.

We have completed our review of this application as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text, which is identical to the labeling text submitted on December 6, 2012. The shelf life period granted for Adrenalin (epinephrine injection, USP), 1 mg/mL is fifteen months when stored between 20°C to 25°C (68°F to 77°F).

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As,* available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels which are identical to the carton and immediate container labels submitted on December 6, 2012, 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 (June 2008)." 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 204200**." Approval of this submission by FDA is not required before the labeling is used.

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

ADVISORY COMMITTEE

Your application for Adrenalin was not referred to an FDA advisory committee because the application did not raise significant public health questions on the role of Adrenalin in the diagnosis, cure, mitigation, treatment, or prevention of a disease.

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.

This product is appropriately labeled for use in all relevant pediatric populations. Therefore, no additional pediatric studies are needed at this time.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

1977-1 Evaluate formulation and process improvements to reduce the levels of impurities with Adrenalin (epinephrine injection). In your evaluation, conduct at least one study to determine the possible cause(s) of (b) (4) formation and take appropriate measures to minimize the level of this impurity. Using the results from these investigations, re-evaluate the acceptance limits for (b) (4) and (b) (4) and lower the limits for these impurities. As part of an interim report, include your evaluation of the formulation/process improvements undertaken to mitigate the level of impurities, in particular (b) (4) and (b) (4) as well as a summary of all technical work performed using the results of the conducted study(ies). The interim report should also include a proposed development plan for future batches which will ensure consistency and reliability of product quality.

The timetable you submitted on December 7, 2012, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	January 2013
Interim Report Submission:	April 2013
Study/Trial Completion:	March 2014
Final Report Submission:	May 2014

Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment**

Protocol," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

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 to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
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, 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 Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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 Carol Hill, Regulatory Project Manager, at (301) 796-1266.

Sincerely,

{See appended electronic signature page}

Lydia I. Gilbert-McClain, MD, FCCP
Deputy Director
Division of Pulmonary, Allergy, and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures: Content of Labeling
Carton and Container Labeling

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

/s/

LYDIA I GILBERT MCCLAIN
12/07/2012

RENATA ALBRECHT
12/07/2012