



NDA 205003/S-002

**SUPPLEMENT APPROVAL  
FULFILLMENT OF POSTMARKETING  
REQUIREMENT**

Symplmed Pharmaceuticals, LLC  
Attention: Erik Emerson  
President and Chief Executive Officer  
5375 Medpace Way  
Cincinnati, OH 45227

Dear Mr. Emerson:

Please refer to your Supplemental New Drug Application (sNDA) dated May 26, 2016, received May 26, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prestalia (perindopril arginine/amlodipine) tablets, 3.5/2.5 mg, 7/5 mg, 14/10 mg.

This Prior Approval supplemental new drug application proposes to incorporate the results of the trial conducted under Post Marketing Requirement 2858-1 to conduct a bioequivalence trial of Prestalia (perindopril and amlodipine) and ACEON (perindopril erbumine) in healthy volunteers to provide an accurate estimate of the relative bioavailability of perindopril and the active metabolite perindoprilat to enable appropriate dosing instructions for elderly (age > 65) patients, or for patients with heart failure, renal impairment (creatinine clearance < 60 mL/min), or hepatic impairment.

This Prior Approval Supplement added, in Section 2 **DOSAGE AND ADMINISTRATION**, subsection 2.2 Dosage Adjustment in Renal Impairment, Subsection 2.3 Monitoring in Elderly Patients (Over 65 Years of Age) and, in Section 5 **WARNINGS AND PRECAUTIONS** edited Subsection 5.7 Impaired Renal Function and added Subsection 5.8 Hepatic Failure, and in Section 8 **USE IN SPECIFIC POPULATIONS**, edited Subsection 8.5 Geriatric Use, Subsection 8.6 Renal Impairment, and deletes Subsection 8.7 Hepatic Impairment and Subsection 8.8 Heart Failure, and edits Section 12 **CLINICAL PHARMACOLOGY** Subsection 12.3 Pharmacokinetics.

**APPROVAL & LABELING**

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

## **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, text for the patient package insert), with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## **FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)**

We also refer to your Supplemental New Drug Application (sNDA) dated May 26, 2016, received May 26, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Prestalia (perindopril arginine/amlodipine) tablets, 3.5/2.5 mg, 7/5 mg, 14/10 mg.

We have received your submission dated May 19, 2016 and May 26, 2016, containing the final report for the following postmarketing requirement listed in the January 21, 2015 approval letter.

- 2858-1      A bioequivalence trial of Prestalia (perindopril and amlodipine) and ACEON (perindopril erbumine) in healthy volunteers. The proposed trial will provide an accurate estimate of the relative bioavailability of perindopril and the active metabolite perindoprilat to enable appropriate dosing instructions for elderly (age > 65) patients, or for patients with heart failure, renal impairment (creatinine clearance < 60 mL/min), or hepatic impairment.

The timetable you submitted on January 12, 2015, via email states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	05/15
Trial Completion:	02/16
Final Report Submission:	06/16

We have reviewed your submission and conclude that the above requirement was fulfilled.

This completes all of your postmarketing requirements and postmarketing commitments acknowledged in our January 21, 2015, approval letter.

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. 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>.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the

revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

### **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 Wayne Amchin, RAC, Regulatory Project Manager, at (301) 796-0421.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, M.D., Ph.D.  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE:  
Content of Labeling

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

/s/  
-----

WAYNE S AMCHIN  
11/23/2016

NORMAN L STOCKBRIDGE  
11/23/2016