



NDA 16-126/S-025

Whitehall-Robins
Attention: Ms. Sharon Heddish
Five Giralda Farms
Madison, NJ 07940-0871

Dear Ms. Heddish:

Please refer to your supplemental new drug application, (NDA) dated March 6, 2000, received on March 7, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Primatene Mist Inhalation Aerosol (epinephrine 5.5 mg/mL).

We acknowledge receipt of your amendments dated June 14, June 21, and November 10, 2000, and July 6, 2001, received March 15, June 23, and November 14, 2000, and July 9, 2001.

The supplemental new drug application provides for:

- (1) revised storage condition specifications statement per approvable letter for S-015 dated February 27, 1998
- (2) addition of a warning statement under the subheading, "When using this product" to alert consumer not to tamper with the container
- (3) conformance with "Drug Facts" labeling in content and format in accordance with 21 CFR 201.66 (c) and (d)

We have completed the review of this supplemental 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 draft labeling dated March 6, 2000, with the minor editorial revisions listed below. Accordingly, the application is approved effective on the date of this letter provided that the following changes are made to the labeling:

I. Outer Carton Label for ½ oz. with Mouthpiece, ½ oz. Refill and ¾ oz. Refill:

- A. "Drug Facts" labeling - revise according to the attached prototype.
- B. On all panels, where it reads "Epinephrine Inhalation Aerosol Bronchodilator," relocate the word "Bronchodilator" to a separate line.

C. For the 3/4 fl. oz. Refill:

1. add "Drug Facts (continued)" to the bottom panel.
2. left panel, above "Questions or comments,?" add "Drug Facts (continued)" and a hairline underneath that heading.

II. Consumer information insert:

A. The title "Drug Facts" can remain as submitted or be removed. If the words "Drug Facts" are used, move the Directions for Use of the Mouthpiece outside the Drug Facts box, move the heavy black line from the right to the middle, extend the hair lines to within 2 spaces of either side of the box, and relocate the "Questions or comments" to an area immediately preceding the Directions for Use of the Mouthpiece. Add "Drug Facts (continued)" if it is necessary to use the second column. The Directions for Use of the Mouthpiece could then remain at the right of the middle line. If the sponsor elects to remove the title "Drug Facts," the Directions for Use of the Mouthpiece can remain anywhere on the Consumer Information Insert.

B. Same changes be made as on the carton labeling.

III. Container labels for ½ fl. oz. and ¾ fl. oz. sizes - same changes be made as on the carton labeling.

If final printed labeling (FPL) has not been printed, please revise the labeling as indicated above and submit FPL as an amendment to this supplement. If FPL has been printed, please revise the labeling as indicated above at the time of the next printing or within 180 days, whichever comes first, and submit as a new supplement to this application.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted draft labeling (carton and container labels, and Consumer Information Insert submitted March 6, 2000). 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 copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. For administrative purposes, this submission should be designated "FPL for approved NDA 16-126." Approval of this submission by FDA is not required before the labeling is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

NDA 20-463

Page 3

If you have any questions, call Babette Merritt, Project Manager, at (301) 827-2222.

Sincerely,

Charles Ganley, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Attachment: Prototype "Drug Facts" Label

Prototype "Drug Facts" Label

<i>Drug facts</i>	
<i>Active ingredient (in each inhalation)</i>	<i>Purpose</i>
Epinephrine 0.22 mg.....	Bronchodilator
<i>Uses</i>	
<ul style="list-style-type: none"> ■ temporarily relieves shortness of breath, tightness of chest, and wheezing due to bronchial asthma ■ eases breathing for asthma patients by reducing spasms of bronchial muscles 	
<i>Warning</i>	
For inhalation only	
Do not use	
<ul style="list-style-type: none"> ■ unless a doctor has said you have asthma ■ if you are now taking a prescription monoamine oxidase inhibitor (MAOI) (certain drugs for depression, psychiatric, or emotional conditions, or Parkinson's disease), or for 2 weeks after stopping the MAOI drug. If you do not know if your prescription drug contains an MAOI, ask a doctor or pharmacist before taking this product. 	
Ask a doctor before use if you have	
<ul style="list-style-type: none"> ■ heart disease ■ thyroid disease ■ diabetes ■ high blood pressure ■ ever been hospitalized for asthma ■ trouble urinating due to an enlarged prostate gland 	
When using this product	
<ul style="list-style-type: none"> ■ overuse may cause nervousness, rapid heart beat, and heart problems ■ do not continue to use, but seek medical assistance immediately if symptoms are not relieved within 20 minutes or become worse ■ do not puncture or throw into incinerator. Contents under pressure. ■ do not use or store near open flame or heat above 120°F (49°C). May cause bursting. 	
Contains CFC 12, 114, substances which harm public health and environment by destroying ozone in the upper atmosphere	
If pregnant or breast-feeding, ask a health professional before use.	
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.	
<i>Directions</i>	
<ul style="list-style-type: none"> ■ do not use more often or at higher doses unless directed by a doctor ■ supervise children using this product ■ adults and children 4 years and over: start with one inhalation, then wait at least 1 minute. If not relieved, use once more. Do not use again for at least 3 hours. ■ Children under 4 years: ask a doctor 	
<i>Other information</i>	
<ul style="list-style-type: none"> ■ store at room temperature, between 20-25°C (68-77°F) ■ see insert for mouthpiece use and care instructions 	
<i>Inactive ingredients</i> alcohol 34%, ascorbic acid, fluorocarbons (propellant), water	
<i>Questions or comments?</i> Call 1- 8 PRIMATENE or 1-877-462-8363 weekdays 9 AM-5 PM EST	
www.Primatene.com	

The prototype label shown above should be followed in content only. The font sizes for title, headings, subheadings, condensed text and other graphic features are required to be in accordance with provisions of 21 CFR 201.66.

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

/s/

Charles Ganley
8/30/01 12:14:57 PM