CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 18-101/S-009
16-023/S-037

ADMINISTRATIVE DOCUMENTS

Regulatory Project Manager Labeling Review

NDA: 16-023 (SLR-037) Syrup
18-101 (SLR-009) Tablets

Date submitted: October 15, 2003

Date received: October 20, 2003

Sponsor: Endo Pharmaceuticals
100 Painters Drive
Chadds, PA 19317

Drug Name: Symmetrel (Amantadine Hydrochloride)
Dosage Form: Syrup and Tablets

Materials Reviewed: 1. Final Printed Labeling dated October 15, 2003.
2. Approval letter and draft labeling issued by the Division of Neuropharmacological Drug Products on September 3, 2003.
3. Last approved label by DADVP (NDA 16-023/S-035 and 18-101/S-007) letter dated 9-11-2000 and approved on 12-06-2000.

Background:

This "Changes Being Effected" supplemental new drug application provides for revisions to the WARNING, PRECAUTIONS, OVERDOSAGE, and ADVERSE REACTIONS sections of labeling as requested in an Agency letter dated June 19, 2002. These label supplements were submitted as official notification to the Division of Anti-viral Drug Products that the Division of Neuropharmacological Drug Products had approved the Changes Being Effected Supplements dated February 11, 2003 (NDA 17-111/S-008/S-009/S-011/S-014/S-015). The tablets and syrup share the same Package insert labeling and as previously stated the lead Division for the proposed labeling changes were reviewed and approved by the Division of Neuropharmacological Drug Products on September 3, 2003.

Summary of Review

The following contains the sponsor's proposed "CBE" labeling changes:

1. 17-118/SLR-008: Dated 11-16-1988
   - The addition of the following sentence to the **OVERDOSAGE** section of labeling:

2. 17-118/SLR-009: Dated 11-16-1988
   - The addition of the following sentence to the **PRECAUTIONS** section of labeling:

3. 17-118/SLR-011: Dated 09-30-1997 and amended on 03-31-1998
    - This supplement provides for changes to the **DESCRIPTION, CLINICAL, PHARMACOLOGY, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, OVERDOSAGE, DOSAGE AND ADMINISTRATION,** and **HOW SUPPLIED** sections.

4. 17-118/SLR-014: Dated 06-29-2000
    - This supplement provides for the following revisions to product labeling:
        - Revise the **WARNINGS** section to change the lowest reported acute lethal dose to 1 gram.
        - Revisions of the **PRECAUTION-Other** section
        - Revise the **OVERDOSAGE** section to change the lowest reported acute lethal dose to 1gram
        - Revise the **PRECAUTION** section regarding abrupt discontinuation.
        - Revise the **ADVERSE REACTIONS** section regarding abrupt discontinuation.

5. 17-118/SLR-015: Dated 10-10-2000
    - This supplement provides for the following revisions to product labeling:
        - Revise the **PRECAUTION** section regarding abrupt discontinuation.
        - Revise the **ADVERSE REACTIONS** section regarding abrupt discontinuation.

Conclusions/Recommendations:

The Final printed package insert for the Symmetrel syrup and tablets submitted electronically on October 15, 2003 is identical to the labeling enclosed in the approval letter dated September 3, 2003.

It should be conveyed to the applicant that the Final Draft Labeling is acceptable, and an approval letter should be sent.

Donald W. Reese, PharmD,MBA
Regulatory Project Manager

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/s/

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11/13/03 03:13:39 PM
CSO

CSO review for Symmetrel

Marsha Holloman
11/13/03 03:17:20 PM
CSO