CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-699

LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-699 Date of Submission: March 28, 2003

Applicant's Name: Schwarz Pharma

Est. Name: Carbidopa and Levodopa Orally Disintegrating Tablets , 10 mg/100 mg, 25 mg/100 mg, & 25 mg/ 250 mg

Labeling Deficiencies:

1. GENERAL

   Your proposed proprietary name, PARCOPA™, has been submitted to the Division of Medication Errors and Technical Support (DEMTS), Office of Drug Safety. We defer final comment on your proposed name until it has been evaluated by DMETS.

2. CONTAINER (100's)

   a. Ensure the strengths are differentiated.

   b. Revise the storage temperature statement to read "Store at 20° to 25°C (68° to 77°F)[See USP Controlled Room Temperature]. Protect from moisture and light." You may retain the "excursion" statement however all the storage temperature statements should be consistent (e.g., the "excursion" statement should be on the sample carton labeling if it's present on the insert labeling and container label).

   c. Add "Do not remove PARCOPA Tablets from the bottle until immediately before use."

3. CARTON (Professional Sample - 6's)

   See CONTAINER comments (a) and (b).

4. INSERT

   a. DESCRIPTION

      i. Revise the molecular weight of carbidopa to 244.24 per USP 26.

      ii. Revise the molecular weight of anhydrous carbidopa to 226.23 per USP 26.

      iii. Replace the last two sentences of the first paragraph with "PARCOPA is an orally administered formulation of carbidopa-levodopa which rapidly disintegrates on the tongue and does not require water to aid dissolution or swallowing.

      iv. "FD&C blue #2 HT aluminum lake" instead of "FD&C blue #2".

      v. "yellow 10 iron oxide" instead of "yellow iron oxide".

   b. WARNINGS

      Add "(carbidopa-levodopa)" after your proposed proprietary name in the first sentence of the first paragraph.

   c. PRECAUTIONS (Drug Interactions)

      i. See WARNINGS comment.

ii. Information for Patients

a.) Relocate the "Phenylketonurics" subsection to this subsection as the first paragraph.

b.) Add the following as the second paragraph:

"Patients should be instructed not to remove PARCOPA Tablets from the bottle until just prior to dosing. With dry hands, the tablet should be gently removed and immediately placed on the tongue to dissolve and be swallowed with the saliva."

d. DOSAGE AND ADMINISTRATION (How to Transfer Patients from Levodopa)

i. See WARNINGS comment.

ii. Replace the "Administration" subsection with the following and relocate it to the beginning of the section:

"Instructions for Use/Handling PARCOPA Tablets. Just prior to administration, GENTLY remove the tablet from the bottle with dry hands. IMMEDIATELY place the PARCOPA Tablet on top of the tongue where it will dissolve in seconds, then swallow with saliva. Administration with liquid is not necessary."

e. HOW SUPPLIED

i. Add "flat faced" in describing the tablets.

ii. See CONTAINER comment (b).

Please revise your labeling as instructed above and submit 12 final printed copies of labels and labeling for a full approval of this application.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

- Do you have 12 Final Printed Labels and Labeling?
- Container Labels:
- Professional Package Insert Labeling:
- Revisions needed post-approval:

BASIS OF APPROVAL:

- Was this approval based upon a petition?
- What is the RLD on the 356(h) form:
- NDA Number:
- NDA Drug Name:
- NDA Firm:
- Date of Approval of NDA Insert and supplement #:
- Has this been verified by the MIS system for the NDA?
- Was this approval based upon an OGD labeling guidance?
- Basis of Approval for the Container Labels:
- Basis of Approval for the Carton Labeling:

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 26		X	
Is this name different than that used in the Orange Book?	X (See FTR 9)		
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		X	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
		X	

Are there any other safety concerns?			
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		X	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X (see FTR 7)		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST:
FOR THE RECORD:

1. MODEL LABELING: NDA 17-555/S-055, approved April 11, 2001, for Sinemet (carbidopa-levodopa) 10/100 mg, 25/100 mg, 25/250 mg Tablets. Also used the labeling for Zofran ODT to identify language suitable for this dosage form (i.e. Description and D&A sections).
2. INACTIVE INGREDIENTS: This list of inactive ingredients are consistent with the application in section VII, Vol. 1.2, page 001.

3. **PATENTS/EXCLUSIVITIES**

Patent Data –

No	Expiration	Use Code	Use	File
None	None	None	None	

Exclusivity Data -

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		

4. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON**

USP: Not USP

NDA: NONE

ANDA: Insert and container - "Store at controlled room temperature 20° to 25°C (68° to 77°F) excursions permitted between 15° - 30°C (59° - 86°F). Protect from moisture." Sample Carton - " Store at controlled room temperature 20° to 25°C (68° to 77°F). Protect from moisture." Firm is asked to revise to "Store at 20° to 25°C (68° to 77°F)[See USP Controlled Room Temperature]. Protect from moisture and light." **Firm's stability study will be performed at 25°C ±2° C at 60% ± 5% RH and at 30°C ±2° C at 60% ± 5% RH.**

5. **DISPENSING STATEMENT COMPARISON**

- **NDA: Dispense in a well-closed, light-resistant container.**
- **ANDA: Dispense in a tight container as defined in the USP/NF. Firm is asked to revise to "Dispense in a tight, light-resistant container as defined in the USP."**

6. **PACKAGE CONFIGURATION**

- **NDA: bottles of 100 and unit dose packages of 100 for all strengths.**
- **ANDA: bottles of 100 for all strengths and professional samples (6 blisters of unit-dose tablets for all strengths).**

7. **CONTAINER/CLOSURE**

- **Container: HDPE. [redacted] (see pages 076 & 080, Sect. XIII, Vol. 1.4)**
- **Closure: Non-CRC for the bottles.**
- **Blister: Foil/Paper**

8. **FINISHED DOSAGE FORM**

- **NDA: Scored tablets**
- **ANDA: Scored tablets.**

9. **Suitability petition approved on September 25, 2002 (Docket #02P-0033/CP1) for orally disintegrating tablets.**

10. **PHENYLKETONURIC statement is included in the insert and carton labeling and container labels.**

11. **The manufacturer is CIMA LABS INC.**

12. **Disintegration:** "Finished Product Certificates of Analysis" subsection of Controls for Finished Dosage Form section (XIV). The mean disintegration times are 30 seconds for the 10 mg/100 mg tablet, 31 seconds for the 25 mg/100mg tablet and 52 seconds for the 25 mg/250 mg tablet.

Date of Review: July 21, 2003 **Date of Submission: March 28, 2003**

Primary Reviewer: Koung Lee **Date:**

Team Leader: Lillie Golson **Date:**

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ANDA: 76-643
DUP/DIVISION FILE

HFD-613/KLee/LGolson(no cc)
V:\FIRMSNZ\RANBAXY\LTRS&REV\76643NA.Labeling
Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-699 Date of Submission: April 12, 2004

Applicant's Name: Schwarz Pharma

Est. Name: Carbidopa and Levodopa Orally Disintegrating Tablets , 10 mg/100 mg, 25 mg/100 mg, & 25 mg/ 250 mg

Labeling Deficiencies:

1. GENERAL

   We have resubmitted your proposed proprietary name, PARCOPA™, to the Division of Mediation Errors and Technical Support (DMETS), Office of Drug Safety for final review. We defer final comment on your proposed name until it has been finalized by DMETS.

2. CARTON (6)

   a. Revise "[redacted]" to read "For the treatment of the symptoms of idiopathic Parkinson's disease (paralysis agitans), postencephalitic parkinsonism, and symptomatic parkinsonism which may follow injury to the nervous system by carbon monoxide intoxication and/or manganese intoxication."

   b. The package insert labeling does not include statements to support "[redacted]" therefore this statement should be deleted.

   c. Replace "[redacted]" and "[redacted]" with "• Disintegrates on the tongue-without water" and "Disintegrates on the tongue", respectively.

Please revise your labeling as instructed above and submit 12 final printed copies of labels and labeling for a full approval of this application.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address -

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

- Do you have 12 Final Printed Labels and Labeling?
- Container Labels:
- Professional Package Insert Labeling:
- Revisions needed post-approval:

BASIS OF APPROVAL:

- Was this approval based upon a petition?
- What is the RLD on the 356(h) form:
- NDA Number:
- NDA Drug Name:
- NDA Firm:
- Date of Approval of NDA Insert and supplement #:
- Has this been verified by the MIS system for the NDA?
- Was this approval based upon an OGD labeling guidance?
- Basis of Approval for the Container Labels:
- Basis of Approval for the Carton Labeling:

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 26		X	
Is this name different than that used in the Orange Book?	X (See FTR 9)		
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		X	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
		X	

Are there any other safety concerns?			
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		X	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X (see FTR 7)		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. MODEL LABELING: NDA 17-555/S-055, approved April 11, 2001, for Sinemet (carbidopa-levodopa) 10/100 mg, 25/100 mg, 25/250 mg Tablets.

2. INACTIVE INGREDIENTS: This list of inactive ingredients are consistent with the application in section VII, Vol. 1.2, page 001.

3. PATENTS/EXCLUSIVITIES

Patent Data –

No	Expiration	Use Code	Use	File
				III

Exclusivity Data -

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Not USP

NDA: NONE

ANDA: "Store at 20° to 25°C (68° to 77°F), excursions permitted between 15° - 30°C (59° - 86°F) (See USP Controlled Room Temperature). Protect from moisture and light." **Firm's stability study will be performed at 25°C ±2° C at 60% ± 5% RH and at 30°C ±2° C at 60% ± 5% RH.**

5. DISPENSING STATEMENT COMPARISON
   - NDA: Dispense in a well-closed, light-resistant container.
   - ANDA: Dispense in a tight container as defined in the USP/NF. Firm is asked to revise to "Dispense in a tight, light-resistant container as defined in the USP/NF."

6. PACKAGE CONFIGURATION
   - NDA: bottles of 100 and unit dose packages of 100 for all strengths.
   - ANDA: bottles of 100 for all strengths and professional samples (6 blisters of unit-dose tablets for all strengths).

7. CONTAINER/CLOSURE
   - Container: HDPE. [redacted] (see pages 076 & 080, Sect. XIII, Vol. 1.4)
   - Closure: Non-CRC for the bottles.
   - Blister: Foil/Paper

8. FINISHED DOSAGE FORM
   - NDA: Scored tablets
   - ANDA: Scored tablets.

9. Suitability petition approved on September 25, 2002 (Docket #02P-0033/CP1) for orally disintegrating tablets.

10. PHENYLKETONURIC statement is included in the insert and carton labeling and container labels.

11. Statements on the Professional Sample Carton were modeled after Schwarz's other orally disintegrating tablet statements for KEMSTRO (baclofen orally disintegrating tablets). According to Dr. Chan Park, Schwarz Pharma provided evidence that the new drug division approved similar statements on professional sample labeling.

Date of Review: May 10, 2004 Date of Submission: April 12, 2004

Primary Reviewer: Koung Lee Date: 5/14/04

Team Leader: Lillie Golson Date: 5/17/04

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cc:

ANDA: 76-699
DUP/DIVISION FILE
HFD-613/KLee/LGolson(no cc)
V:\FIRMSNZ\RANBAXY\LTRS&REV\76699NA2.Labeling Review

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-699 Date of Submission: June 18, 2004

Applicant's Name: Schwarz Pharma

Name: PARCOPA™ (Carbidopa and Levodopa Orally Disintegrating Tablets) 10 mg/100 mg, 25 mg/100 mg, & 25 mg/ 250 mg

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):

- Do you have 12 Final Printed Labels and Labeling?

	Submission Date	Revised	Code	Location	Recommendation
25/100 Bottle of 100	6/18/04	01/03	L4572	\\Cdsesubogd1\n76699\N_000\2004\container25_100mg.pdf	Acceptable for Approval
25/100 Blister Card (2x3)	6/18/04	01/03	BU334206	\\Cdsesubogd1\n76699\N_000\2004\blister25_100mg.pdf	Acceptable for Approval
25/100 Carton (6)	6/18/04	01/03	CR4573	\\Cdsesubogd1\n76699\N_000\2004\carton25_100mg.pdf	Acceptable for Approval
25/100/Display (5 cartons of 6)	6/18/04	01/03	CR4574	\\Cdsesubogd1\n76699\N_000\2004\diplay25_100mg.pdf	Acceptable for Approval
10/100 Bottle of 100	6/18/04	01/03	L4569	\\Cdsesubogd1\n76699\N_000\2004\container10_100mg.pdf	Acceptable for Approval
10/100 Blister Card (2x3)	6/18/04	01/03	BU334106	\\Cdsesubogd1\n76699\N_000\2004\blister10_100gm.pdf	Acceptable for Approval
10/100 Carton (6)	6/18/04	01/03	CR4570	\\Cdsesubogd1\n76699\N_000\2004\carton10_100mg.pdf	Acceptable for Approval
100/100 Display (5 cartons of 6)	6/18/04	01/03	CR4571	\\Cdsesubogd1\n76699\N_000\2004\display10_100mg.pdf	Acceptable for Approval
25/250 Bottle 100	6/18/04	01/03	L4575	\\Cdsesubogd1\n76699\N_000\2004\container25_25mg.pdf	Acceptable for Approval
25/250 Blister Card (2x3)	6/18/04	01/03	BU334306	\\Cdsesubogd1\n76699\N_000\2004\blister25_250mg.pdf	Acceptable for Approval
25/250 Carton (6)	6/18/04	01/03	CR4576	\\Cdsesubogd1\n76699\N_000\2004\carton25_250mg.pdf	Acceptable for Approval
25/250 Display (5 cartons of 6)	6/18/04	01/03	CR4577	\\Cdsesubogd1\n76699\N_000\2004\display25_250mg.pdf	Acceptable for Approval
INSERT	6/18/04	01/03	PC4578	\\Cdsesubogd1\n76699\N_000\2004\pi.pdf	Acceptable for Approval

- Revisions needed post-approval: Yes

  CARTON (6)

  In the first sentence on the "Dear Patient" paragraph, revise to read "...tongue to relieve resting tremor, rigidity and bradykinesia."

BASIS OF APPROVAL:

- Was this approval based upon a petition? Yes, approved **on September 25, 2002 (Docket #02P-0033/CP1) for orally disintegrating tablets.**
- What is the RLD on the 356(h) form: Sinemet
- NDA Number: 17-555
- NDA Drug Name: Sinemet
- NDA Firm: DuPont Pharmaceuticals Company
- Date of Approval of NDA Insert and supplement #: April 11, 2001; S-055
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side by side.

- Basis of Approval for the Carton Labeling: Side by side.

Other Comments:

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 26		X	
Is this name different than that used in the Orange Book?	X (See FTR 9)		
If not USP, has the product name been proposed in the PF?		X	
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?		X	
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	x		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Because of proposed packaging configuration or for any other reason, does this applicant meet fail to meet all of the unprotected conditions of use of referenced by the RLD?		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?		X	
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.		X	
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			

Is the scoring configuration different than the RLD?		X	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?		X	
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		X	
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?	X (see FTR 7)		
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		X	
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.		X	

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. MODEL LABELING: NDA 17-555/S-055, approved April 11, 2001, for Sinemet (carbidopa-levodopa) 10/100 mg, 25/100 mg, 25/250 mg Tablets.
2. INACTIVE INGREDIENTS: This list of inactive ingredients is consistent with the application in section VII, Vol. 1.2, page 001.
3. PATENTS/EXCLUSIVITIES

Patent Data –

No	Expiration	Use Code	Use	File
				III

Exclusivity Data -

Code/sup	Expiration	Use Code	Description		Labeling Impact
			There is no unexpired exclusivity for this product		

4. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: Not USP

NDA: NONE

ANDA: "Store at 20° to 25°C (68° to 77°F), excursions permitted between 15° - 30°C (59° - 86°F) (See USP Controlled Room Temperature). Protect from moisture and light." **Firm's stability study will be performed at 25°C ±2° C at 60% ± 5% RH and at 30°C ±2° C at 60% ± 5% RH.**

5. DISPENSING STATEMENT COMPARISON
   - NDA: Dispense in a well-closed, light-resistant container.

- ANDA: Dispense in a tight, light-resistant container as defined in the USP/NF.

6. PACKAGE CONFIGURATION
   - NDA: bottles of 100 and unit dose packages of 100 for all strengths.
   - ANDA: bottles of 100 for all strengths and professional samples (6 blisters of unit-dose tablets for all strengths).
7. CONTAINER/CLOSURE
   - Container: HDPE. [redacted] (see pages 076 & 080, Sect. XIII, Vol. 1.4)
   - Closure: Non-CRC for the bottles.
   - Blister: Foil/Foil

Size	10mg/100 mg Strength	25mg/100 mg strength	25 mg/250 mg Strength
100's	100 cc white round HDPE bottle and 38 mm screw cap	100 cc white round HDPE bottle and 38 mm screw cap	250 cc white round HDPE bottle and 53 mm screw cap
Blister	[redacted]		

8. FINISHED DOSAGE FORM
   - NDA: Scored tablets
   - ANDA: Scored tablets.
9. Suitability petition approved on September 25, 2002 (Docket #02P-0033/CP1) for orally disintegrating tablets.
10. PHENYLKETONURIC statement is included in the insert and carton labeling and container labels.
11. Statements on the Professional Sample Carton were modeled after Schwarz's other orally disintegrating tablet statements for KEMSTRO (baclofen orally disintegrating tablets). Accroding to Dr. Chan Park, Schwarz Pharma provided evidence that the new drug division approved similar statements on professional sample labeling.
12. The proprietary name, PARCOPA™, was found acceptable on May 18, 2004 by DMETS.

Date of Review: June 29, 2004 Date of Submission: June 18, 2004

Primary Reviewer: Koung Lee Date: 7/9/04

Team Leader: Lillie Golson Date: 7/9/04

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cc:

ANDA: 76-699
DUP/DIVISION FILE
HFD-613/KLee/LGolson(no cc)
V:\FIRMSNZ\RANBAXY\LTRS&REV\76699AP.Labeling Review