CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-553

LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-552 and 76-553
Dates of Submission: November 27, 2002 (original)
Applicant's Name: Gensia Sicor Pharmaceuticals
Established Name: Medroxyprogesterone Acetate Injectable Suspension USP, 150 mg/mL vial and prefilled syringe, single dose.

Labeling Deficiencies:

1. **GENERAL COMMENT**:

   Please add the words "contraceptive injection" to the main panel on your labels and labeling as seen on the reference listed drug (RLD) labels and labeling.

2. **CONTAINER:** 150 mg / mL (vial and prefilled syringe)

   a. Revise the storage temperature to reflect our standard language as "Store at 20 - 25°C (68-77°F), [See USP Controlled Room Temperature]."

   b. You have a green color scheme for the syringe container (same as your vial). However, the cartons and shelf pack are gray. We encourage the gray color scheme for your prefilled syringe container so that it is consistent with the color scheme seen on your prefilled syringe carton and shelf pack. Please provide a side-by-side copy of your proposed prefilled syringe with that of the RLD.

   c. In an effort to decrease the potential for medication errors with methyltestosterone we recommend using "MedroxyPROGESTERone" on the container, carton and shelf pack.

   d. You may designate your total content for your single use products as 150 mg (150 mg/mL) rather than "150 mg/mL (150 mg/mL)". That is total content will be represented as "150 mg".

3. **CARTON:** vial (1s) and prefilled syringe kit (1s, 5s and 25s)

   a. See comments under Container.
   b. We encourage you to cite the quantity per carton "1 single dose vial".

4. **SHELF PACK:** 10s vials

   a. See comments under Carton.
   b. Please indicate the quantity per shelf pack.

5. **INSERT:**

   a. DESCRIPTION

      I. Revise the first sentence as follows - ...suspension, a contraceptive injection, contains medroxyprogesterone...

      II. If your product is "sterile" you must make a statement to that fact. Therefore, the third paragraph, revise to read ...1 mL of medroxyprogesterone acetate sterile aqueous suspension 150 mg/mL as seen in the reference listed drug labeling.

iii. You state that your application does not make reference to the prefilled syringe. However, 76-553 reference both the vial and prefilled syringe. The reference listed drug also cites both containers in a single insert. Your related ANDA 76-552 provides for the prefilled syringe. The ingredients in the vial and prefilled syringe applicants are the same. You may elect to keep reference to both containers (vial and syringe) in a combined insert. However, please modify the HOW SUPPLIED section to include both the syringe and vial information. Or otherwise, delete text regarding prefilled syringe from the DESCRIPTION and DOSAGE AND ADMINISTRATION sections.

b. HOW SUPPLIED

i. See standard storage temperature statement above under CONTAINER.
ii. See comment 4.a.iii under Insert. Cited both vial and syringe information here.
iii. We encourage you to identify which package sizes are "kit packages" and cite the content of the kit.
iv. Please clarify whether each prefilled syringe or vial is individual cartoned and then placed into an outer carton of 5s, 25s for the prefilled syringe or shelf packed of 10s for the vials.

5. **PATIENT INSTRUCTION SHEET** - Satisfactory in draft.

Please revise your labels and labeling, as instructed above, and submit final print labels and labeling or draft insert and patient labeling if you prefer.

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

ANDA Number	76-552 and 76-553
Date of Submission	
Applicant	GensiaSicor
Drug Name	Medroxyprogesterone Acetate Injectable Suspension USP,
Strength(s)	150 mg/mL vial and prefilled syringe

FPL Approval Summary		
Container Labels 150 mg/mL	XXXXXXXX	Submitted vol. XX
Carton		
Shelf Pack		
Package Insert Labeling Patient leaflet	#XXXXRev.	vol. XX

BASIS OF APPROVAL:

Patent Data for NDA 20-246

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None			PII	Same As

Exclusivity Data for NDA 20-246

Code/sup	Expiration	Description	*Labeling impact*
None			

Reference Listed Drug

RLD on the 356(h) form	Depo-Provera
NDA Number	20-246
RLD established name	Medroxprogesterone Acetate Suspension
Firm	Pharmacia Upjohn
Currently approved PI	S-012
AP Date	8/12/98

Note. Please Note an open supplement is pending.

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's 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 24**		X	
Is this name different than that used in the Orange Book?		X	
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 -See applicant's packaging configuration in FTR			
Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		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	
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs		X	

Concentrate, Warning Statements that might be in red for the NDA)			
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 (p. #) 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 p. # 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?[see FTR]		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		
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		

FOR THE RECORD:

1. MODEL LABELING

This review was based on the labeling for Depo-Provera (Pharmacia Upjohn; NDA 20-264/S-012; Approved 8/12/98).

2. PATENTS/EXCLUSIVITIES [Vol. A1.1 pg. 14]

3. MANUFACTURING FACILITY OF FINISHED DOSAGE FORM

GensiaSicor; 19 Hughes St, Irvine Ca [Vol. B1.1 pg. 238]

4. CONTAINER/CLOSURE

2 ml vial, with flint-glass tubing type 1, stopper is gray with flip off lacquered cap and aluminum seal. [Vol. B1.1 pg. 495]

5. INACTIVE INGREDIENTS

The description of the inactive ingredients in the insert labeling appears accurate according to the composition statement. [Vol. B1.1 pg. 147 and 178]

6. PACKAGING CONFIGURATIONS

RLD: Clear glass SDV, 2 mL capacity; packaged in shelf cartons of 1s, 5s and 25s; 6 and 24 prefilled syringe.
ANDA: Same as RLD.

7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

USP: None.
RLD: Store at CRT 20 - 25C (68-77F) See USP.
ANDA: Same as RLD.

8. DISPENSING STATEMENTS COMPARISON

USP: Store in Preserve in SDV or MDV containers, preferably of Type I glass.
RLD: Handle according to the handling of cytoxotic agents.
ANDA: Same as

9. BIOAVAILABILITY/BIOEQUIVALENCE:

Firm's request for a waiver of *in vivo* bioequivalence study requirements.

10. ANDA 76-553 is a 150 mg/mL vial while 76-552 is a 10 mg/mL prefilled syringe. RDA has both.

Date of Review: 1/27/03 Date of Submission: 11/27/02

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ANDA: 76-553 AND 76-552
DUP/DIVISION FILE
HFD-613/aPayne/JGrace (no cc)
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Review

Jane 2/4/03
John Grace 3/24/2003

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

ANDA Number	76-553
Date of Submission	April 25, 2003
Applicant	GensiaSicor
Drug Name	Medroxyprogesterone Acetate Injectable Suspension USP, (contraceptive injection)
Strength(s)	150 mg/mL vial and prefilled syringe

FPL Approval Summary		
Container Labels		**Submitted**
150 mg/mL	1 mL	Apr. 25, 2003 vol. 2.1A
Carton	1s X 1 mL	Apr. 25, 2003 vol. 2.1A
Shelf Pack	1 mL x 1s x 25s	Apr. 25, 2003 vol. 2.1A
Package Insert Labeling	#Y3600063A Rev. 3/2003	Apr. 25, 2003 vol. 2.1A
Patient leaflet	#Y3600064A Rev. 3/2003	Apr. 25, 2003 vol. 2.1A

BASIS OF APPROVAL:

Patent Data for NDA 20-246

Patent No	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None			PII	Same As

Exclusivity Data for NDA 20-246

Code/sup	Expiration	Description	*Labeling impact*
None			

Reference Listed Drug

RLD on the 356(h) form	Depo-Provera
NDA Number	20-246
RLD established name	Medroxprogesterone Acetate Suspension
Firm	Pharmacia Upjohn
Currently approved PI	S-012
AP Date	8/12/98

Note. Please note an open supplement is pending. ✓ amp 6/7/04 still pending

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Applicant's 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 24**	X		
Is this name different than that used in the Orange Book?		X	
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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
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Is this a new packaging configuration, never been approved by an ANDA or NDA for this drug product? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC. [see FTR]		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		
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Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
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Date of Review: 5/22/03 Date of Submission: Apr. 25, 2003

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cc:

ANDA: 76-553 ~~AND 76-552~~
DUP/DIVISION FILE
HFD-613/aPayne/JGrace (no cc)
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Review

5/27/03
5/28/2003