

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-019

CSO LABELING REVIEW(S)

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

ANDA Number: 76-019

Date of Submission: October 31, 2000

Applicant's Name: Abbott Laboratories, Inc.

Established Name: Deferoxamine Mesylate for Injection USP, 500 mg/vial

Labeling Deficiencies:

1. CONTAINER - 500 mg/vial
 - a. Does your proposed container label reflect the true size? To be acceptable as final print, labels must be of actual size, color and clarity. Please assure that these criteria are met prior to submission of final print.
 - b. Replace with "Reconstituted Exp."
 - c. Include the phrase "For single use only".
 - d. Include the text "Discard unused portion."

2. CARTON
 - a. See comments under CONTAINER except (b).
 - b. Revise to read "Usual Dosage".
 - c. Include a comma after the term "subcutaneous".

3. INSERT
 - a. GENERAL

Please note that the labeling for the reference listed drug, Desferal® Injection was last approved on May 25, 2000. The following comments are based on this labeling.
 - b. TITLE

We encourage the inclusion of "Rx Only" beneath the title.
 - c. DESCRIPTION
 - i. ...is N-[5-3-[(5-Aminopentyl)... [note upper case "A"]
 - ii. Include the molecular formula.
 - d. INDICATIONS AND USAGE

Deferoxamine mesylate for injection is ... [add "for injection"]

e. WARNINGS

i. First paragraph, second sentence:

...acuity including visual loss; impaired peripheral, color, and night vision; and retinal pigmentary abnormalities. The auditory...

ii. First paragraph, last sentence – Revise to read as follows:

... cessation of treatment. Slit-lamp examinations performed in patients treated with deferoxamine mesylate for acute iron intoxication have not revealed cataracts.

iii. Penultimate paragraph:

... pretreatment rates. [delete the parenthetical statement]

f. PRECAUTIONS

i. General

A) Second paragraph, first sentence:

...*enterocolitica* infections. In some...

B) Third paragraph – Revise to read as follows:

[

]

C) Delete all remaining text in this subsection from the fourth paragraph on.

ii. Drug Interactions

Delete this subsection in its entirety.

iii. Information for Patients

Delete the first paragraph.

iv. Pediatric Use

A) Delete the first paragraph.

B) Second paragraph:

...established (see INDICATIONS AND USAGE).

g. ADVERSE REACTIONS

i. First item (At the injection site) – Replace with the following text.

Skin: Localized irritation and pain, swelling and induration, pruritus,

erythema, wheal formation.

- ii. Hypersensitivity Reactions and Systemic Allergic Reactions – Revise to read.

Hypersensitive Reactions: Generalized erythema (rash), urticaria, anaphylactic reaction.

- iii. Body as a Whole

Delete this item in its entirety.

- iv. Hematologic, Musculoskeletal, Nervous system

Delete these three subsections.

- v. Special Senses - Revise to read as follows:

Special Senses: Ocular and auditory disturbances (see WARNINGS)

- vi. Respiratory, Skin, Urogenital

Delete these three subsections.

- vii. Include the following as the last item.

h. OVERDOSAGE

- i. Signs and Symptoms – Revise to read as follows.

Since deferoxamine mesylate is available only for parenteral administration, acute poisoning is unlikely to occur. However, tachycardia, hypotension, and gastrointestinal symptoms have occasionally developed in patients who received overdoses of deferoxamine mesylate.

- ii. Treatment

A) Delete the second sentence of the first paragraph.

B) Add the following as the new second paragraph.

i. DOSAGE AND ADMINISTRATION

- i. Acute Iron Intoxication

A) Intravenous Administration

B) Dosage – Combine the first two paragraphs and revise to read as

[]

ii. Chronic Iron Overload - Intramuscular Administration:

A) First sentence:

... Solution above. [delete a comma]

B) Delete the last sentence.

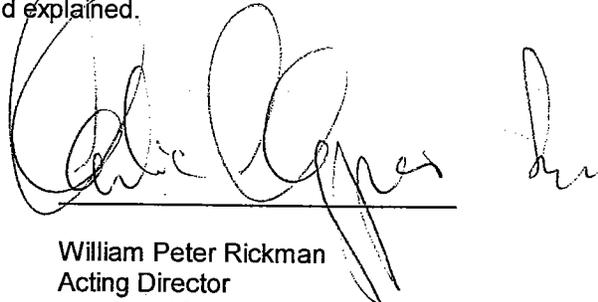
j. HOW SUPPLIED

Include the text "For single use only" and "Discard unused portion."

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

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-
http://www.fda.gov/cder/ogd/rld/labeling_review_branch.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.



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

FOR THE RECORD:

1. MODEL LABELING – Desferal® Injection, 16-267/S-033 (approved May 25, 2000). This is the last approved labeling for a new strength of 2 gm/vial. The innovator's insert labeling submitted for the side-by-side comparison is different from the model labeling.
2. I sent the following e-mail to the PM for this product in the new drug division on 8/14/00 at the time of review of ANDA 75-879.

Alice,

I have a question about the insert labeling of this drug product. We note that insert labeling of Desferal submitted in one generic application for the side-by-side comparison contains the following language as a last sentence under DOSAGE AND ADMINISTRATION, Chronic Iron Overload, Intramuscular administration. This important safety-related information **does not appear in the approved Desferal labeling**. Has the revised insert labeling containing this information been submitted as a supplement? If yes, would it be reviewed soon? Please let me know when you have a chance. Thanks again for your help,

"The total daily dose should not exceed 1,000 mg in the absence of a transfusion, or 6,000 mg even if transfused three or more units of blood or packed red blood cells."

Chan

Answer: That sentence was proposed in SLR-034, which has not been approved yet. S-034 was submitted on March 15, 1999 & was made AE on March 10, 2000.

SLR-034 proposed many revisions to the Warnings, Precautions, Adverse Reactions, Overdosage, Dosage and Administration sections. We did not have a problem with that sentence, however, we requested revisions to their revisions. An AE letter was sent March 10, 2000.

According to my phone log, the regulatory contact called on June 22 & said that they would be responding in about a month. I just called & left a VM message asking when they would be responding.

Feel free to give me a call if you need additional information regarding this.

Alice

3. As of 12/27/00 16-267/S-034 has still NOT been approved. An amendment to this supplement was submitted on December 13, 2000. We have to update the generic labeling once this supplement has been approved by HFD-180.
4. This drug product is the subject of a USP monograph.
5. There is **no inactive ingredient** used for the formulation of this product.
6. PATENTS/EXCLUSIVITIES – Paragraph II
7. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: Do not store above 25°C (77°F). Both RLD and ANDA has identical storage condition for the reconstituted solution.

8. Abbott is the manufacturer for this product. (p.81, B.1.1)

Date of Review: 12/27/00

Date of Submission: 10/31/00

Primary Reviewer: Chan Park

Date:

1/3/01

Team Leader: Charlie Hoppes

Date:

Chan
CH 1/3/01

cc:

ANDA: 76-019
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Review

APPEARS THIS WAY
ON ORIGINAL

**(APPROVAL SUMMARY)
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH**

ANDA Number: 76-019

Date of Submission: November 7, 2001

Applicant's Name: Abbott Laboratories, Inc.

Established Name: Deferoxamine Mesylate for Injection USP, 500 mg/vial & 2 g/vial

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

Do you have 12 Final Printed Labels and Labeling? Yes (Checked with the blue jackets)

CONTAINER LABELS - 500 mg/vial & 2 g/vial

Satisfactory in FPL as of 11/7/01 submission

CARTON LABELING - 4s

Satisfactory in FPL as of 11/7/01 submission

PROFESSIONAL PACKAGE INSERT LABELING:

Satisfactory in FPL as of 11/7/01 submission

REVISIONS NEEDED POST-APPROVAL:

1. CARTON

Encourage the use of different color for the expression of the two different strengths.

2. INSERT

Use the term "to" rather than a hyphen to express a numerical range.

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Desferal® Injection

NDA Number: 16-267/S-034

NDA Drug Name: Desferal® Injection

NDA Firm: Novartis Pharmaceuticals Corporation

Date of Approval of NDA Insert and supplement #:
S-034/approved April 9, 2001

Has this been verified by the MIS system for the NDA?

Yes

2-1

Bi U
Haley

Was this approval based upon an OGD labeling guidance? No

Basis of Approval for the Container Labels: Desferal labels approved on May 25, 2000 (S-033)

Basis of Approval for the Carton Labeling: Desferal carton labeling approved April 9, 2001 (S-034)

FOR THE RECORD:

1. MODEL LABELING – Desferal® Injection, 16-267/S-034 (approved April 9, 2001). The sponsor's amendment was based on this most recently approved labeling as directed by the Agency, overriding the labeling comments forwarded to the sponsor because the last labeling review was not based on this last approved labeling.
 2. In the amendment dated November 7, 2001, the sponsor has added a new strength, 2 g/vial to this application.
 3. This drug product is the subject of a USP monograph.
 4. There is **no inactive ingredient** used for the formulation of this product.
 5. PATENTS/EXCLUSIVITIES – Paragraph II
 6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: Do not store above 25°C (77°F). Both RLD and ANDA has identical storage condition for the reconstituted solution.
 7. Abbott is the manufacturer for this product. (p.81, B.1.1)
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-

Date of Review: 1/4/01

Date of Submission: 11/7/01

Primary Reviewer: Chan Park

Date:

Chan Park
1/9/02

Team Leader: Charlie Hoppes

Date:

Charlie Hoppes
1/9/02

cc:

ANDA: 76-019
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Review

* Current as of
2/12/04
C. J. Am

(This AP Summary supersedes one prepared on 1/9/02)
(APPROVAL SUMMARY)
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-019 Date of Submission: April 12, 2002

Applicant's Name: Abbott Laboratories, Inc.

Established Name: Deferoxamine Mesylate for Injection USP, 500 mg/vial & 2 g/vial

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

Do you have 12 Final Printed Labels and Labeling? Yes

CONTAINER LABELS - 500 mg/vial & 2 g/vial

Satisfactory in FPL as of 11/7/01 submission (vol.2.1)

CARTON LABELING - 4s

Satisfactory in FPL as of 11/7/01 submission (vol.2.1)

PROFESSIONAL PACKAGE INSERT LABELING:

Satisfactory in FPL as of 4/12/02 submission (Code #58-6776-R2, Rev. March, 2002, vol.2.1)

REVISIONS NEEDED POST-APPROVAL:

1. **CARTON**

 Encourage the use of different color for the expression of the two different strengths.

2. **INSERT**
 - a. **GENERAL**

 Use the term "to" rather than a hyphen to express a numerical range.

 - b. **HOW SUPPLIED**

 Increase the prominence of the text "For single use only. Discard unused portion."

BASIS OF APPROVAL:

Was this approval based upon a petition? No

What is the RLD on the 356(h) form: Desferal® Injection

NDA Number: 16-267/S-039

NDA Drug Name: Desferal® Injection

NDA Firm: Novartis Pharmaceuticals Corporation

Date of Approval of NDA Insert and supplement #:
S-039/approved February 14, 2002

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: Desferal labels approved on May 25, 2000 (S-033)

Basis of Approval for the Carton Labeling: Desferal carton labeling approved April 9, 2001 (S-034)

FOR THE RECORD:

1. MODEL LABELING – Desferal® Injection insert labeling, 16-267/S-039 (approved February 14, 2002). Desferal container labels approved on May 25, 2000 (S-033) and Desferal carton labeling approved April 9, 2001 (S-034)
2. In the amendment dated November 7, 2001, the sponsor has added a new strength, 2 g/vial to this application.
3. This drug product is the subject of a USP monograph.
4. There is **no inactive ingredient** used for the formulation of this product.
5. PATENTS/EXCLUSIVITIES – Paragraph II
6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

Both RLD and the ANDA: Do not store above 25°C (77°F). Both RLD and ANDA has identical storage condition for the reconstituted solution.
7. Abbott is the manufacturer for this product. (p.81, B.1.1)

Date of Review: 4/25/02

Date of Submission: 4/12/02

Primary Reviewer: Chan Park

Date: 5/15/02

Acting Team Leader: Lillie Golson

Date: 5/16/02

cc:

ANDA: 76-019
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Review