CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-716

PHARMACOLOGY REVIEW

PHARMACOLOGY/TOXICOLOGY COVER SHEET

NDA number: **NDA 21-716**
Review number: 000
Sequence number/date/type of submission: 000/October 23, 2003/Commercial
Information to sponsor: Yes ( ) No (X)
Sponsor and/or agent: Prima Pharm, Inc., 3443 Tripp Court, San Diego, CA 92121 (Tel: 859-259-0717; Fax: 859-259-8268)
Manufacturer for drug substance: [redacted]

Reviewer name: Zhou Chen, Ph.D.
Division name: Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products
HFD #: HFD-550
Review completion date: January 21, 2004

Drug:

Trade name: **Hydase**
Generic name (list alphabetically): Hyaluronidase injection USP
Code name: Not provided.
CAS number: 37326-33-3
Chemical name: Hyaluronoglucosaminidase
Chemical structure: Unknown.
Molecular formula: Unknown.
Molecular weight: Not provided.

Relevant INDs/NDAs/DMFs: NDA 6-343

Drug class: Protein enzyme

Indication: Hydase is indicated as an adjuvant to increase the absorption and dispersion of other injected drugs; for hypodermoclysis; and as an adjunct in subcutaneous urography for improving resorption of radiopaque agents.

Clinical formulation: 150 USP unit/ml

Ingredients	Amphadase
Hyaluronidase	150 USP unit/ml
Sodium chloride USP	8.5 mg/ml
Edetate disodium dihydrate USP	1 mg/ml
Calcium chloride dihydrate NF	0.4 mg/ml
Monobasic sodium phosphate	
NaOH	pH
Water for injection USP	qs

Route of administration: Parenteral injection

Executive Summary

I. Recommendations

A. Recommendation on Approvability

Approval is recommended for this NDA application from a nonclinical perspective.

B. Recommendation for Nonclinical Studies

No nonclinical studies were submitted. Wydase, a DESI drug product [Federal Register Vol 35, No 185, p14800-14801 for hyaluronidase (Wydase, NDA 6-343)] that was withdrawn for reasons unrelated to safety and efficacy, was referenced by this NDA submission. The sponsor indicated that Hydase is equivalent to Wydase with the same active ingredient, inactive ingredients, dosage form, strength, route of administration, and indication. Due to many years of marketing experience of Wydase in the US, the safety profile for hyaluronidase has already been established. No nonclinical studies were necessary in support of this application.

C. Recommendations on Labeling

The labeling for the Carcinogenesis, Mutagenesis, Impairment of Fertility section and the Pregnancy section are similar to the labeling for Wydase. No modification is recommended.

II. Summary of Nonclinical Findings

A. Brief Overview of Nonclinical Findings

No nonclinical studies were submitted.

B. Pharmacologic Activity

No nonclinical studies were submitted.

C. Nonclinical Safety Issues Relevant to Clinical Use

There are no nonclinical safety issues relevant to clinical use.

III. Administrative

A. Reviewer signature: _____

B. Supervisor signature: Concurrence - _____

Non-Concurrence - _____
(see memo attached)

C. cc: list:

NDA 21-716/Division File
NDA 21-716/Original NDA
HFD-550/CSO/Gorski
HFD-550/MO/Lim
HFD-550/TL Pharm/Yang
HFD-550/Pharm/ChenZh

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/s/

Zhou Chen
3/8/04 04:21:23 PM
PHARMACOLOGIST

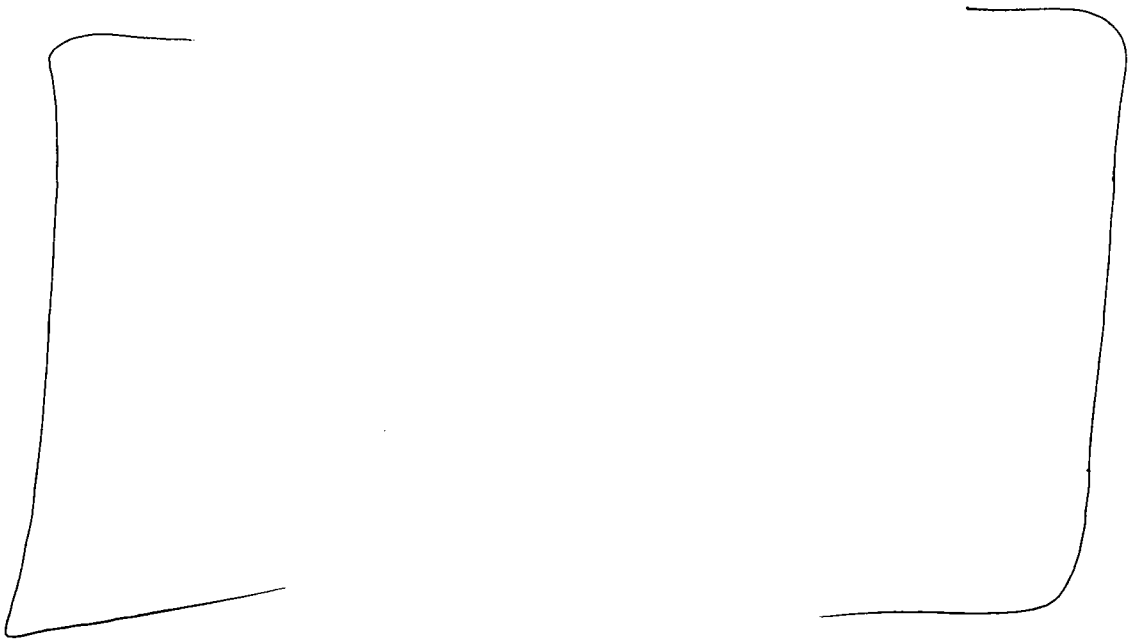
Josie Yang
3/8/04 04:29:06 PM
PHARMACOLOGIST

Memorandum

From:	**Zhou Chen**
Through:	**Josie Yang**
Date:	**September 15, 2004**
Re:	**Labeling Review for Hydase NDA21-716**
Sponsor:	**Prima Pharm, Inc.**

In this NDA submission, the nonclinical study-related sections of the proposed labeling are based on the labeling for Wydase, a DESI drug product [Federal Register Vol 35, No 185, p14800-14801 for hyaluronidase (Wydase, NDA 6-343)]. After several discussions within the review team, the following changes in the labeling are recommended.

1. In the "CLINICAL PHARMACOLOGY" section, two paragraphs referring findings from animal studies (see below) should be removed.



2. The "Teratogenic Effects—Pregnancy Category" under the "Pregnancy" section will remain to be a "C". However, this section is revised as followings: "No adequate and well controlled animal studies have been conducted with hyaluronidase to determine reproductive effects. No adequate and well-controlled studies have been conducted with hyaluronidase in pregnant women. Hyaluronidase should be used during pregnancy only if clearly needed."

cc: list:

HFD-550/CSO/Gorski
HFD-550/TL Pharm/YangJ
HFD-550/Pharm/ChenZh

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/s/

Zhou Chen
9/16/04 04:12:55 PM
PHARMACOLOGIST

Josie Yang
9/16/04 04:16:58 PM
PHARMACOLOGIST