CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-665

PHARMACOLOGY REVIEW(S)

PHARMACOLOGY/TOXICOLOGY COVER SHEET

NDA number: **NDA 21-665**
Review number: 000
Sequence number/date/type of submission: 000/June 6, 2003/Commercial
Information to sponsor: Yes ( ) No (X)
Sponsor and/or agent: Amphastar Pharmaceuticals, Inc., 11570 Sixth Street, Rancho Cucamonga, CA 91730 (Tel: 909-980-9484 Ext. 2019; Fax: 626-459-5592)
Manufacturer for drug substance: —

Reviewer name: Zhou Chen, Ph.D.
Division name: Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products
HFD #: HFD-550
Review completion date: November 9, 2003

Drug:

Trade name: **Amphadase**
Generic name (list alphabetically): Hyaluronidase injection USP (Bovine hyaluronidase)
Code name: Not provided.
CAS number: 9001-54-1
Chemical name: Hyaluronidase
Chemical structure: Unknown.
Molecular formula: Unknown.
Molecular weight: —

Relevant INDs/NDAs/DMFs: DMFs — and — NDA 6-343

Drug class: Protein enzyme

Indication: Amphadase 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 — USP	1 mg/ml
Calcium chloride — NF	/
Monobasic sodium phosphate	
Thimerosal NMT	0.1 mg/ml
—	/
—	

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a DESI drug product [Federal Register Vol 35, No 185, p14800-14801 for hyaluronidase (Wydase, NDA 6-343)] that was withdrawn for reasons unrelated to safety and efficacy, was referenced by this NDA submission.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 Amphadase 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 identical with the labeling for Wydase, with the exception that the name Wydase is replaced with Amphadase. 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 21-665/Division File
NDA 21-665/Original NDA
HFD-550/CSO/Puglisi
HFD-550/MO/Boyd
HFD-550/TL Pharm/Yang
HFD-550/Pharm/ChenZh

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Zhou Chen
11/17/03 11:51:50 AM
PHARMACOLOGIST

Josie, Please sign this review. Thanks. Zhou

Josie Yang
11/17/03 11:56:56 AM
PHARMACOLOGIST