CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-945/S-005

Administrative Documents

REGULATORY PROJECT MANAGER REVIEW

Application Number: 20-954/S-005

Name of Drug: Busulfex (busulfan) Injection

Sponsor: Orphan Medical

Material Reviewed

Supplement Number	Letter Date	Approval Date
003 (SLR)	June 19, 2002	April 24, 2002
005 (SCP)	May 10, 2002	November 13, 2002

Background and Summary Description:

S-005 provides an updated package insert with revisions to the **DESCRIPTIONS** section and the **Preparations for Intravenous Administration** subsection of the **DOSAGE and ADMINISTRATIONS** section. The revised labeling is the result of Orphan's request for the use of an alternate 5-micron syringe filter.

REVIEW

The package insert from S-005 was compared to the labeling included in the Busulfex supplement 003, which was approved by the Agency April 24, 2002.

CONCLUSION:

All of the suggested labeling revisions highlighted in this submission (S-005) should be approved with the exception of the forth sentence in the following paragraph found in the Preparations for Intravenous Administration subsection of the **DOSAGE and ADMINISTRATIONS** section:

[redacted]

The Agency feels that since there is no scientific evidence to support this statement; therefore, this statement should remain the same as previously approved and should read:

USE OF SYRINGE FILTERS OTHER THAN THE SPECIFIC TYPE INCLUDED IN THIS PACKAGE WITH EACH AMPOULE IS NOT RECOMMENDED.

/S/

Sean Bradley, R.Ph./13NOV02
Regulatory Project Manager

This review was reviewed and signed off by:

Concurrence: Dotti Pease (13NOV02)
Chief, Project Management Staff

Concurrence: Nallaperam Chidambaram (13NOV02)
Chemistry Reviewer

Concurrence: Ramzi Dagher, M.D. (13NOV02)
Medical Reviewer

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/s/

Sean Bradley
11/14/02 08:37:08 AM
CSO

Dotti Pease
11/14/02 09:54:58 AM
CSO

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO HFD-805/OPS, MICROBIOLOGY/ **PETER COONEY**			FROM: HFD-150/DIVISION OF ONCOLOGY DRUG PRODUCT R.LOSTRITTO/S. BRADLEY	
DATE MAY 21, 2002	IND NO.	NDA NO. 20-954/S-005	TYPE OF DOCUMENT CMC: CBE-30	DATE OF DOCUMENT MAY 13, 2002
NAME OF DRUG BUSULFEX® (busulfan) INJECTION		PRIORITY CONSIDERATION STANDARD	CLASSIFICATION OF DRUG CYTOTOXIC, ALKYLATING AGENT	DESIRED COMPLETION DATE OCTOBER 2002

NAME OF FIRM ORPHAN MEDICAL, INC

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ **MANUFACTURINGCHANGE/ADDITION**
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER (fax)
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- OTHER *(SPECIFY BELOW)*

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS OTHER

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS*(List below)*
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS: THIS SUBMISSION WAS SUBMITTED IN AN ELECTRONIC FORMAT. THE WEB ADDRESS IS

\\CDSESUB1\N20954\S_005\2002-05-10

SIGNATURE OF REQUESTER SEAN BRADLEY	METHOD OF DELIVERY *(Check one)* ✗ MAIL ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER SEAN BRADLEY

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/s/

Sean Bradley
5/23/02 09:50:42 AM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-954/S-005

CBE-30 SUPPLEMENT

Orphan Medical, Inc.
13911 Ridgedale Drive
Suite 250
Minnetonka, MN 55305

Attention: Carol S. Curme, J.D.
RAC, Senior Management of RA

Dear Dr. Curme:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Busulfex® (busulfan) Injection

NDA Number: 20-954

Supplement Number: S-005

Date of Supplement: May 10, 2002

Date of Receipt: May 13, 2002

This supplemental application, submitted as a "Supplement - Changes Being Effected in 30 days" supplement, proposes the following change: to use an alternate syringe filter (packaged with the DP) composed of [redacted]

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on July 12, 2002 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be November 13, 2002.

Please cite the application number listed above at the top of the first page of any communications concerning this application. All communications concerning this supplemental application should be addressed as follows:

U.S. Postal Service:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attention: Division Document Room 3067
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Oncology Drug Products, HFD-150
Attention: Division Document Room 3067
1451 Rockville Pike
Rockville, Maryland 20852-1420

If you have any questions, call Sean Bradley, R.Ph., Regulatory Health Project Manager, at 301-594-5750.

Sincerely,

/S/

{See appended electronic signature page}

Dotti Pease
Chief, Project Management Staff
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Sean Bradley
5/22/02 09:26:10 AM
Signing off for D. Pease