

# CENTER FOR DRUG EVALUATION AND RESEARCH

**APPLICATION: NDA 20-954**

## CONTENTS

	Included	Pending Completion	Not Prepared	Not Required
Approval Letter	X			
Tentative Approval Letter				X
Approvable Letter			X	
Final Printed Labeling		X		
Medical Review(s)	X			
Chemistry Review(s)	X			
EA/FONSI			X	
Pharmacology Review(s)	X			
Statistical Review(s)	X			
Microbiology Review(s)	X			
Clinical Pharmacology				
Biopharmaceutics Review(s)	X			
Bioequivalence Review(s)			X	
Administrative Document(s)	X			
Correspondence				

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

**Application Number:NDA 20-954**

**Trade Name: BUSULFEX INJECTION**

**Generic Name:(busulfan)**

**Sponsor:Orphan Medical, Inc.**

**Approval Date: February 4, 1999**

**Indication: Provides for the use of BUSULFEX (busulfan) Injection in combination with cyclophosphamide as a conditioning regimen prior to allogenic hematopoietic progenitor cell transplanation for chronic myelogenous leukemia.**

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Application Number:NDA 20-954**

**APPROVAL LETTER**

NDA 20-954

Orphan Medical, Inc.  
13911 Ridgedale Drive, Suite 475  
Minnetonka, MN 55305

FEB - 4 1999

Attention: Dayton T. Reardon, Ph.D., RAC  
Vice President of Regulatory Affairs

Dear Dr. Reardon:

Please refer to your new drug application (NDA 20-954) dated August 3, 1998, received August 4, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for BUSULFEX (busulfan) Injection.

We acknowledge receipt of your submissions dated September 30; October 15 and 20; November 25; December 3, 8, 11 (2 submissions), 17, and 28, 1998; January 8, 11, 15, 21, 25 and 28, 1999.

This new drug application provides for the use of BUSULFEX (busulfan) Injection in combination with cyclophosphamide as a conditioning regimen prior to allogeneic hematopoietic progenitor cell transplantation for chronic myelogenous leukemia. We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-954." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission via facsimile transmission dated January 28, 1999. These commitments, along with any completion dates

agreed upon, are listed below.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

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Division of Drug Marketing, Advertising, and Communications, HFD-40  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Patrick Guinn, Project Manager, at (301) 594-5767.

Sincerely,

/S/

Robert L. Justice, M.D.  
Acting Director  
Division of Oncology Drug Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure

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cc:

Archival NDA 20-954  
HFD-150/Div. Files  
HFD-150/RJustice  
HFD-150/JJohnson  
HFD-150/DGriebel  
HFD-150/NChidambaram  
HFD-150/XChen  
HFD-150/LZhou  
HFD-150/WMcGuinn  
HFD-150/PAndrews  
HFD-150/BBooth  
HFD-150/ARahman  
HFD-150/GChen  
HFD-150/DPease  
HFD-150/LVaccari  
HFD-150/PGuinn  
HF-2/MedWatch (with labeling)  
HFD-002/ORM (with labeling)  
HFD-101/ADRA (with labeling)  
HFD-40/DDMAC (with labeling)  
HFD-613/OGD (with labeling)  
HFD-21/ACS (with labeling) - for drug discussed at advisory committee meeting.  
HFD-35/Orphan Drugs  
HFD-95/DDMS (with labeling)  
HFD-810/DNDC Division Director  
DISTRICT OFFICE

Drafted by: PGuinn/2-1-99/2-3-99

Initialed by: DPease/2-2-99

WMcGuinn/2-1-99

BBooth/2-2-99

GChen/2-2-99

NChidambaram/2-2-99

XChen/2-2-99

DGriebel/2-2-99

PAndrews/2-2-99

ARahman/2-2-99

LZhou/2-2-99

JJohnson/2-2-99

F/T init. by: DPease/

*D Pease 2-3-99*

APPROVAL (AP)