

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

20-624/S-008

Trade Name: Anzemet

Generic Name: dolasetron mesylates

Sponsor: Aventis Pharmaceuticals Inc.

Approval Date: March 22, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-624/S-008

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**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-624/S-008

APPROVAL LETTER



NDA 20624/S-008

Aventis Pharmaceuticals, Inc.
Attention: Sima Patel
Sr. Regulatory Analyst, U.S. Regulatory Affairs
Somerset Corporate Center
300 Somerset Corporate Boulevard
Bridgewater, NJ 08807-2854

Dear Ms. Patel:

Please refer to your supplemental new drug application dated September 21, 2001, received September 24, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Anzemet® (dolasetron) Injection.

This supplemental new drug application provides for revisions to the ampul and vial labels and cartons to incorporate the revisions recommended in our letter dated May 21, 2001.

We have completed the review of this application 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 agreed upon labeling text with the minor editorial revisions listed below. Accordingly the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted labeling (ampul and vial immediate container and carton labels submitted September 21, 2001). These revisions are terms of the approval of this application.

1. Add the designation "USP" following "mannitol" on the ampul and vial carton labels.
2. Add Aventis' address following the phrase, "Mfd for Aventis Pharmaceuticals, Inc." on the Anagni vial immediate container label.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please mount individually ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically accordingly to the guidance for industry titled, *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-624/S-008". Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a “Dear Health Care Practitioner” letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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, call Brian Strongin, R.Ph., M.B.A., Regulatory Project Manager, at (301) 827-7310.

Sincerely,

{See appended electronic signature page}

Victor F.C. Raczkowski, M.D., M.Sc.
Acting Director
Division of Gastrointestinal and
Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

Joyce Korvick
3/22/02 11:10:26 AM
for Dr. Victor Raczkowski

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-624/S-008

LABELING

DIE IS FPO

ITEM # 50063997	DATE: 8/20/01
PRODUCT: CARTON, ANZEMET INJECTION, 12.5MG 6 AMPULES	
PRINTER: ANAGNI	
Pellex Blue	PMS 221
	PMS 366

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

Indicates Varnish Area
DOES NOT PRINT

Parenthesis surrounding the
generic name removed, and
generic name italicized

"USP" inadvertently
removed after "mannitol",
but will be added
back in.

Replaces the text
"Caution - Federal law
prohibits... prescriptions"
previously on the
front panel

Text revised
for consistency
with comment
"2b" of the
5/12/01
agency letter

Injection
graphic with
previous company
name removed

"Injection"
moved

Revised per 5/12/01
agency letter,
comment "2a".

Deleted per
5/12/01 agency
letter, comment
"2c".

Revised from
"0.625 mL - 6
Sterile Ampuls"
in the pink band.
Pink band was
also been removed
(consistent with
comment "2d"
of the 5/12/01
agency letter).

NDC 0088-1208-65

Anzemet® Injection
dolasetron mesylate injection

12.5 mg / 0.625 mL (20 mg/mL)

~~SINGLE-USE CONTAINERS -
WARNING: DISCARD UNUSED PORTION~~

6 Sterile Ampuls
0.625 mL

Added
Aventis

Anzemet® Injection
dolasetron mesylate injection

0.625 mL

Anzemet® Injection
dolasetron mesylate injection

12.5 mg / 0.625 mL (20 mg/mL)

Anzemet® Injection
dolasetron mesylate injection

FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.
Each ANZEMET® Injection 0.625 mL Ampul contains 12.5mg dolasetron
[mesylate and mannitol] with an acetate buffer in water for injection.
Dosage and Administration: See package insert for dosage information.
WARNING: Discard unused portion.
Store at controlled room temperature 20-25°C (68-77°F). Protect from
light.

Mfd by: Gruppo Lepetit S.p.A.
20020 Lainate, Italy
Mfd for: Aventis Pharmaceuticals Inc.
Kansas City, MO 64137 ©2001
Made in Italy
www.aventispharma-us.com

3 0088-1208-65 7 50063997

Moved from
front panel
of carton

Revised
Revised to address
company name
change and site

MAR 22 2002

APPROVED

ITEM # 50063996	DATE: 8/20/01
PRODUCT: LABEL, ANZEMET INJECTION, 12.5 MG 1 Ampul	
PRINTER: ANAGNI	
PMS 221	

APPROVALS

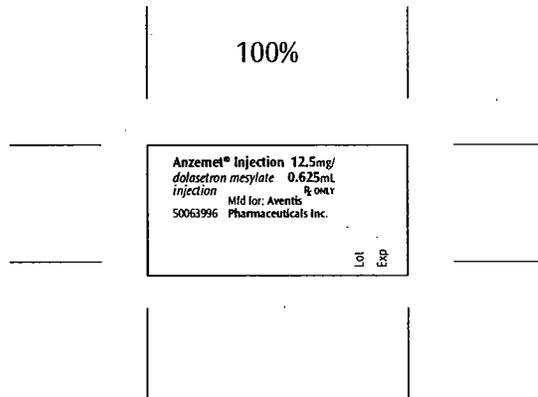
FUNCTIONAL

PROOFREADING

REGULATORY



MAR 22 2002

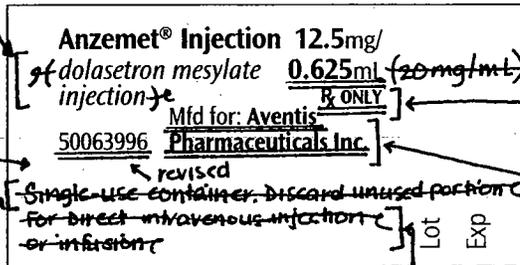


200%

Parenthesis surrounding generic name removed, and generic name italicized

The pink band with the text "sterile 0.625 mL Ampul" was removed (consistent with comment "1c" of the 5/21/01 agency letter).

The text here was deleted consistent with comment "1b" of the 5/21/01 agency letter.



Revised per 5/21/01 agency letter, comment "1a".

Added per 5/21/01 agency letter, comment "1d".

Revised to address company name change.

ITEM # 50063995	DATE: 8/15/01
PRODUCT: LABEL, ANZEMET INJECTION, 100 MG 1 CT.	
PRINTER: ANAGNI	
PMS 5415	

APPROVALS

FUNCTIONAL

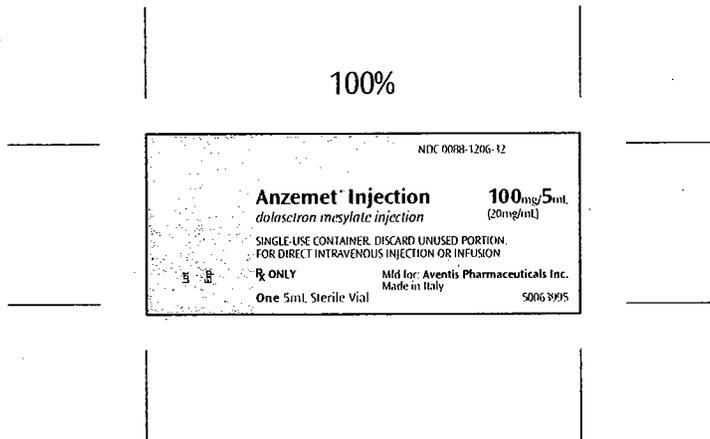
PROOFREADING

REGULATORY



MAR 22 2001

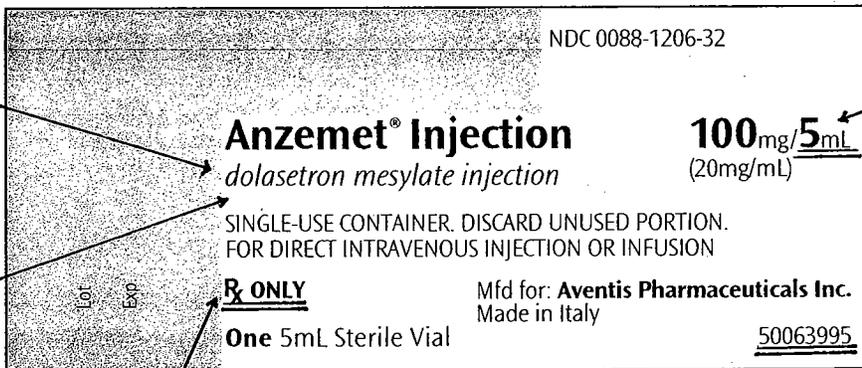
100%



200%

Parenthesis surrounding the generic name removed, and generic name italicized.

The pink band was removed (consistent with comment "3b" of the 5/21/01 agency letter)



Added per the 5/21/01 agency letter, comment "3a"

Revised per company name change
Revised

Added per the 5/21/01 agency letter, comment "3c"

APPROVED

MAR 22 2001

ITEM # 50063993	DATE: 8/20/01
PRODUCT: LABEL, ANZEMET INJECTION, 100MG, 5 ML, VIAL	
PRINTER: BEN VENUE	
Reflex Blue	PMS 5415

APPROVALS

FUNCTIONAL
PROOFREADING
REGULATORY

Parenthesis surrounding the generic name removed, and generic name italicized.
 Added per 5/21/01 agency letter, comment "3a."
 Added per 5/21/01 agency letter, comment "3c."
 Added
 Added
 Revised to address company name change
 Revised from "sterile 5mL vial." Pink band also removed (consistent with comment "3b" of 5/21/01 agency letter).

ITEM # 50063994	DATE: 8/16/01
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 1 CT.	
PRINTER: ANAGNI	
Reflex Blue	PMS 221
PMS 5415	

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY



MAR 22 2002

DIE IS FPO

Replaces text "Caution- Federal law prohibits... prescription."

Revised editorially "usp" after "mannitol" inadvertently removed, but will be added back in.

Replaces "prescribing"

Revised to address company name change

Revised

Injection graphic with previous company name removed

Added per the 5/21/01 agency letter, comment "4a".

Revised from "5 mL -1 sterile vial". Pink band also removed (consistent with comment "4b" of the 5/21/01 agency letter)

Annotation: Parenthesis surrounding generic name removed, and the generic name was italicized and moved down.

Product Information:
 Anzemet® Injection
 dolasetron mesylate injection
 Rx ONLY
 FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.
 Each ANZEMET® Injection 5mL Vial contains 100mg dolasetron mesylate (20mg/mL) and mannitol with an acetate buffer in water for injection.
 Dosage and Administration: See package insert for dosage information.
 WARNING: Discard unused portion. Store at controlled room temperature 20-25°C (68-77°F). Protect from light.
 Mfd by: Gruppo Lepetit S.p.A. 20020 Lainate, Italy
 Mfd for: Aventis Pharmaceuticals Inc. Kansas City, MO 64137 ©2001 www.aventispharma-us.com 50063994

Barcode: 3 0088-1206-32 5

Product Information (Front Panel):
 NDC 0088-1206-32
Anzemet® Injection
 dolasetron mesylate injection
100 mg/5 mL
 (20mg/mL)
 SINGLE-USE CONTAINER. WARNING: DISCARD UNUSED PORTION
One 5mL Sterile Vial
 ⚡Aventis

Product Information (Back Panel):
 NDC 0088-1206-32
Anzemet® Injection
 dolasetron mesylate injection
100 mg/5 mL
 (20mg/mL)
One 5mL Sterile Vial
 ⚡Aventis

APPROVED

ITEM # 50063992	DATE: 8/16/01
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 5 ML VIAL	
PRINTER: BEN VENUE	
Reflex Blue	PMS 221 PMS 5415

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

MAR 22 01

DIE IS FPO

Injection graphic with previous company name removed.

Added per the 5/21/01 agency letter, comment "4a".

Revised from "5 mL-1 sterile vial". Pink band has also been removed (consistent with comment "4b" of the 5/21/01 agency letter).

Parenthesis surrounding generic name removed, and generic name italicized, and moved down.

Front Panel: NDC 0088-1206-32, Anzemet Injection (dolasetron mesylate injection), 100 mg/5 mL (20mg/mL), SINGLE-USE CONTAINER. WARNING: DISCARD UNUSED PORTION. One 5mL Sterile Vial, Aventis.

Side Panel: NDC 0088-1206-32, Anzemet Injection (dolasetron mesylate injection), 100 mg/5 mL (20mg/mL), One 5mL Sterile Vial, Aventis.

Back Panel: Anzemet Injection (dolasetron mesylate injection), 100 mg/5 mL (20mg/mL), **Rx ONLY**, FOR DIRECT INTRAVENOUS INJECTION OR INFUSION, Each ANZEMET Injection 5mL Vial contains 100mg dolasetron mesylate (20mg/mL) and mannitol with an acetate buffer in water for injection. Dosage and Administration: See package insert for dosage information. WARNING: Discard unused portion. Store at controlled room temperature 20-25°C (68-77°F). Protect from light. Mfd by: Ben Venue Laboratories, Inc. Bedford, OH 44146. Mfd for: Aventis Pharmaceuticals Inc. Kansas City, MO 64137 USA ©2001 www.aventispharma-us.com 50063992

Added

Replaces text "Caution. Federal law prohibits... prescriptions."

Revised editorially. "use" after "mannitol" inadvertently removed but will be added back in

Replaces "prescribing" Moved from front panel of carton

revised

Added

Revised to address company name change

APPROVED

ITEM # 50056636	DATE: 8/1/00
PRODUCT: LABEL, ANZEMET INJECTION, 12.5 MG 1 Ampul	
PRINTER: ANAGNI	
PMS 368	

APPROVALS

_____ FUNCTIONAL

_____ PROOFREADING

_____ REGULATORY

MAR 22 2002

100%

Anzemet® Injection 12.5mg dolasetron mesylate (20mg/mL) injection Mfd for: Aventis 50056636 Pharmaceuticals Inc.	Lot Exp.
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200%

Anzemet® Injection 12.5mg dolasetron mesylate (20mg/mL) injection Mfd for: Aventis 50056636 Pharmaceuticals Inc.	Lot Exp.
---	-------------

ITEM # 50061716	DATE: 3/30/01
PRODUCT: LABEL, ANZEMET INJECTION, 12.5 MG 1 Ampul	
PRINTER: ANAGNI	
PMS 221	

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

APPROVED

MAR 22 2002

100%

Anzemet® Injection 12.5mg
dolasetron mesylate (20mg/mL)
 injection
 50061716 Mfd for: Aventis
 Pharmaceuticals Inc.

Lot
Exp

200%

Anzemet® Injection 12.5mg
dolasetron mesylate (20mg/mL)
 injection
 50061716 Mfd for: Aventis
 Pharmaceuticals Inc.

Lot
Exp

APPROVED

MAR 22 2002

APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

ITEM # 50006220		
DATE: 9/5/97 5:02 PM		
Pg. 1 of 1		CICERO JOB NO.: 28952
PRODUCT: LABEL, ANZEMET, INJECTION, 12.5 MG		
PRINTER: SONOCO—NEW JERSEY (LETTERPRESS)		
Black 	PMS 205 	Black#2 

NDC 0088-1208-65
ANZEMET® Injection
(dolasetron mesylate injection)
12.5 mg (20 mg/mL)
Sterile 0.425 mL Ampul
SINGLE-USE CONTAINER. DISCARD UNUSED
PORTION. FOR DIRECT INTRAVENOUS INJE-
CTION OR INFUSION.
Mfd for: Hoechst Marion Roussel, Inc.
50006220 Kansas City, MO 64137 USA

Lot:
Exp:

ITEM #	50006223
DATE:	9/30/01 2:49 PM
Pr. 1 of 1	CICERO JOB NO.: 28773
PRODUCT: CARTON UNIT, ANZEMET, INJECTION, 12.5 MG	
PRINTER: KELLER CRESCENT COMPANY	
Black	PRN5-2406

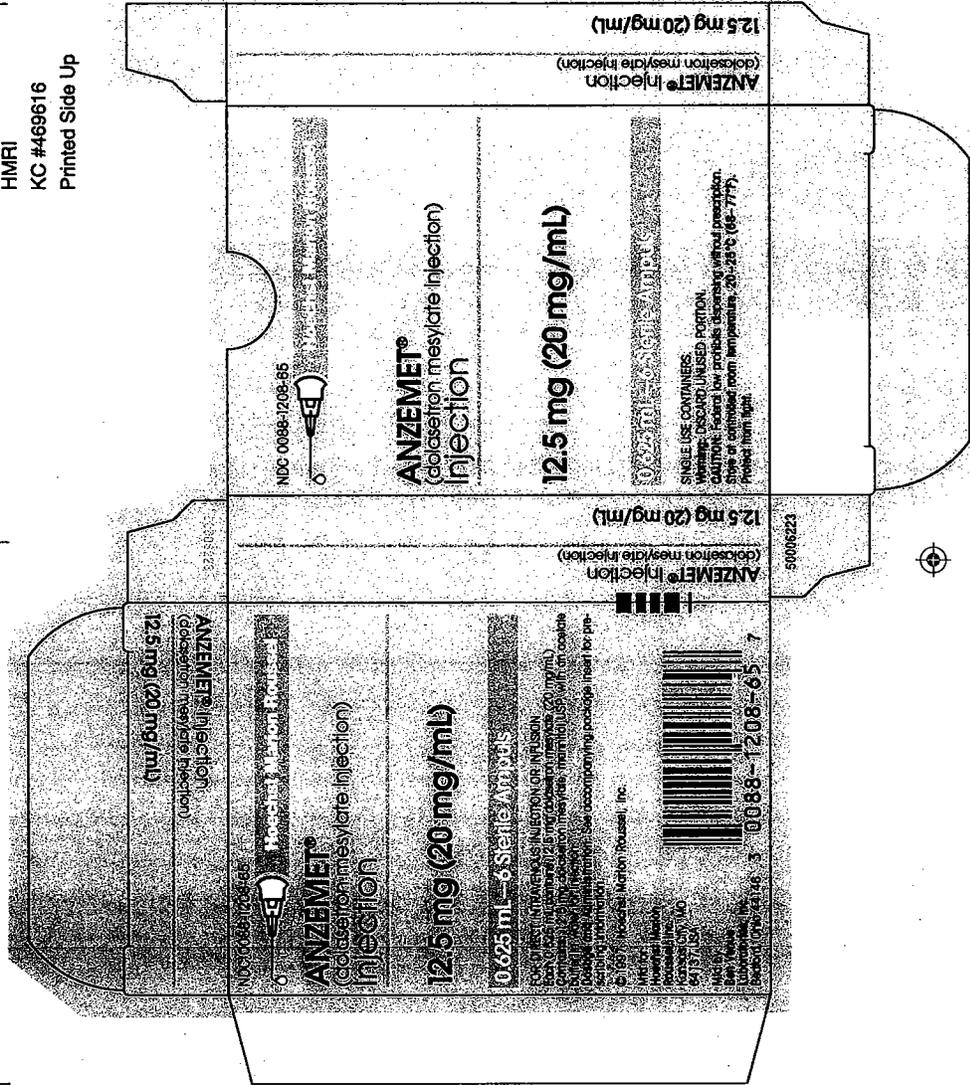
APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

HMRI
KC #469616
Printed Side Up



APPROVED

MAR 22 2002

APPROVALS

FUNCTIONAL
PROOFREADING
REGULATORY

Indicates No Varnish/Varnish Area
DOES NOT PRINT

ITEM # 50056634	DATE: 7/25/00
PRODUCT: CARTON, ANZEMET INJECTION, 12.5MG 6 AMPULES	
PRINTER: ANAGNI	
Reflex Blue	PMS 221
	PMS 368

DIE IS FPO

NDC 0088-1208-65

Anzemet®

12.5 mg
(20mg/mL)

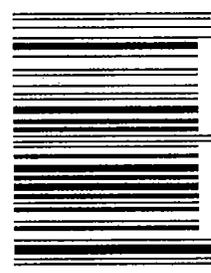
dolasetron mesylate injection

Injection

SINGLE-USE CONTAINERS.
WARNING: DISCARD UNUSED PORTION

6 Sterile Ampuls
0.625 mL

Aventis



3 0088-1208-65 7
50056634

12.5 mg
(20mg/mL)

Anzemet® Injection
dolasetron mesylate injection

Lot |
Exp |

Anzemet® Injection
dolasetron mesylate injection

FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.
Each ANZEMET® Injection 0.625 mL ampul contains 12.5 mg dolasetron mesylate (20mg/mL), mannitol USP, with an acetate buffer in water for injection.
Rx ONLY
Dosage and Administration: Read package insert for prescribing information.
WARNING: Discard unused portion.

Store at controlled room temperature 20-25°C (68-77°F). Protect from light.
Mfd by: Gruppo Lepetit S.p.A.
20020 Lainate, Italy
Mfd for: Aventis Pharmaceuticals Inc.
Kansas City, MO 64137 ©2000
Made in Italy
www.aventispharma-us.com
50056634

12.5 mg
(20mg/mL)

Anzemet® Injection
dolasetron mesylate injection

APPROVED

MAR 22 2002

APPROVED

MAR 22 2002

APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

ITEM # 50015690		
DATE: 10/1/97 2:48 PM		
Pg. 1 of 1	CICERO JOB NO.: 30139	
PRODUCT: LABEL, ANZEMET, INJECTION, 100 MG		
PRINTER: SONOCO—NEW JERSEY (LETTERPRESS)		
Black 	PMS 203 	Black #2 

NDC 0088-1206-32

ANZEMET[®] Injection
(dolasetron mesylate injection)

100 mg (20 mg/mL)

Sterile 5-mL Vial

SINGLE-USE CONTAINER.
DISCARD UNUSED PORTION.

FOR DIRECT INTRAVENOUS
INJECTION OR INFUSION

Mfd for:
Hoechst Marion Roussel, Inc.
Kansas City, MO 64137 USA

50015690

Lot:
Exp:

APPROVED

MAR 22 2002

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

ITEM # 50060620	DATE: 2/22/01
PRODUCT: LABEL, ANZEMET INJECTION, 100MG, 5 ML, VIAL	
PRINTER: BEN VENUE	
Reflex Blue	PMS 5415

NDC 0088-1206-32 **Rx ONLY**

Anzemet[®] Injection 100 mg (20mg/mL)

dolasetron mesylate injection

SINGLE-USE CONTAINER.
WARNING: DISCARD UNUSED PORTION.
FOR DIRECT INTRAVENOUS INJECTION OR INFUSION

Mfd for: **Aventis Pharmaceuticals Inc.** 50060620
Kansas City, MO 64137 USA ©2001

One 5mL Sterile Vial ***Aventis**

Lot
Exp

APPROVED

MAR 22 2002

ITEM # 50056635	DATE: 7/21/00
	CICERO JOB NO.: 32468
PRODUCT: LABEL, ANZEMET INJECTION, 100 MG 1 CT.	
PRINTER: ANAGNI	
PMS 5415	

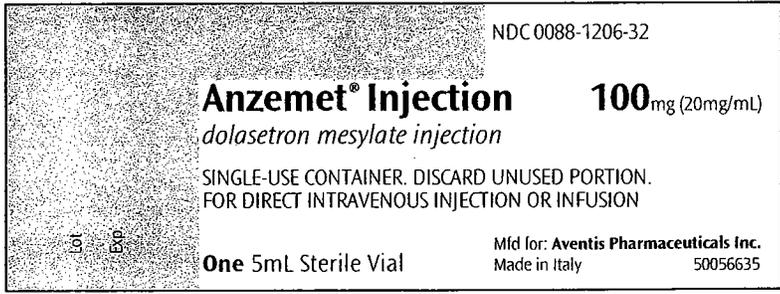
APPROVALS

- _____ FUNCTIONAL
- _____ PROOFREADING
- _____ REGULATORY

100%



200%



APPROVED

ITEM # 50060619	DATE: 3/01/01
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 5 ML VIAL	
PRINTER: BEN VENUE	
Reflex Blue	PMS 221
PMS 5415	

APPROVALS

_____ FUNCTIONAL

_____ PROOFREADING

_____ REGULATORY

MAR 22 2002



DIE IS FPO

APPROVED

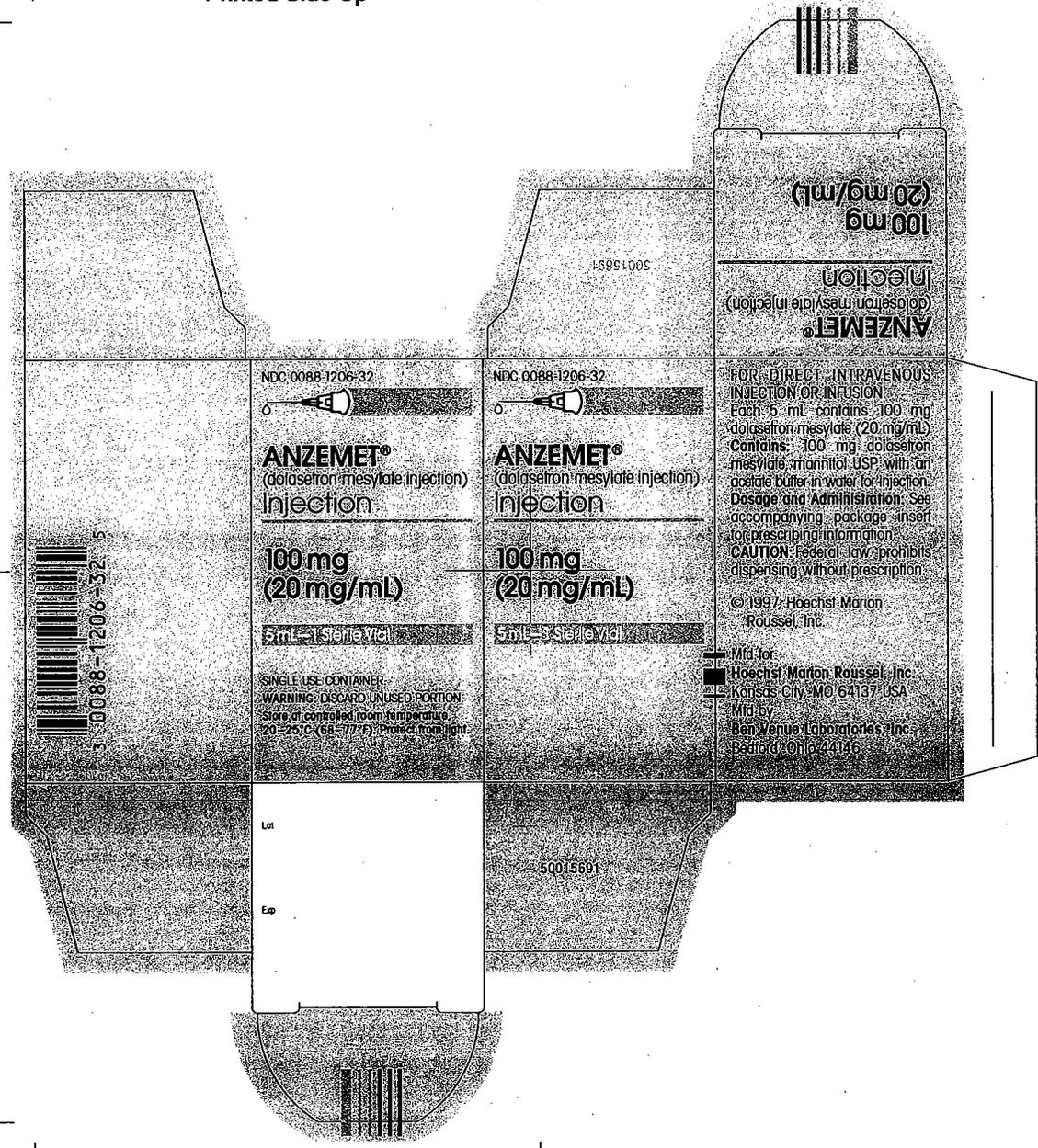
MAR 22 2007

ITEM # 50015691
DATE: 11/12/97 4:12 PM
Pg. 1 of 1 CICERO JOB NO.: 31172
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 1 VIAL
PRINTER: KELLER CRESCENT COMPANY
Black PMS 203

APPROVALS:

FUNCTIONAL
PROOFREADING
REGULATORY

KC #429721
Printed Side Up



ITEM # 50060615	DATE: 1/31/01
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 1 CT.	
PRINTER: ANAGNI	
Reflex Blue	PMS 221
PMS 5415	

APPROVALS

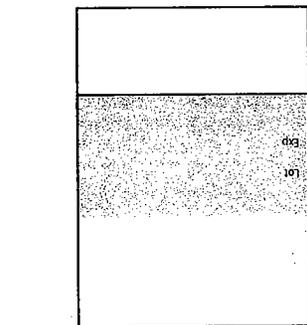
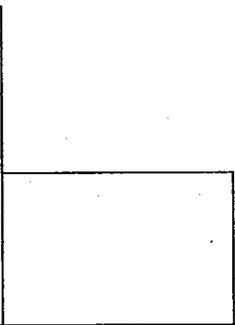
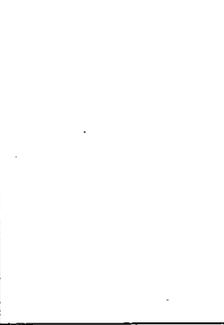
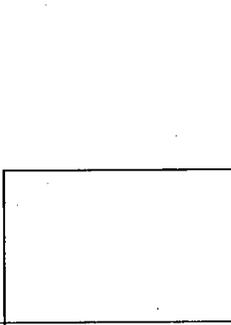
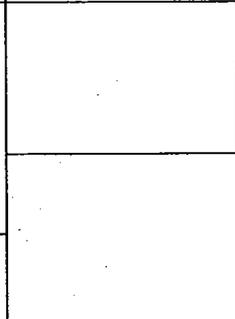
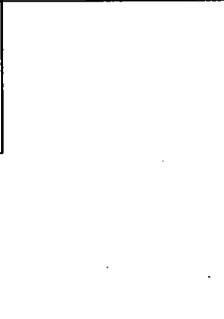
FUNCTIONAL
PROOFREADING
REGULATORY

DOES NOT PRINT
VARNISH/NO VARNISH
AREA

APPROVED

MAR 22 2002

DIE IS FPO

			
<p>Anzemet® Injection <i>dolasetron mesylate injection</i> Rx ONLY</p> <p>FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.</p> <p>Each ANZEMET® Injection 5mL Vial contains 100mg dolasetron mesylate (20mg/mL) and mannitol with an acetate buffer in water for injection.</p> <p>Dosage and Administration: See package insert for dosage information.</p> <p>WARNING: Discard unused portion. Store at controlled room temperature 20-25°C (68-77°F). Protect from light.</p> <p>Mfd by: Gruppo Lepetit S.p.A. 20020 Lainate, Italy Mfd for: Aventis Pharmaceuticals Inc. Kansas City, MO 64137 ©2001 Made in Italy www.aventispharma-us.com 50060615</p>	 <p>3 0088-1206-32 5</p>	<p>NDC 0088-1206-32</p> <p>Anzemet® Injection <i>dolasetron mesylate injection</i></p> <p>100 mg (20mg/mL)</p> <p>SINGLE-USE CONTAINER. WARNING: DISCARD UNUSED PORTION</p> <p>One 5mL Sterile Vial</p> <p>Aventis</p>	<p>NDC 0088-1206-32</p> <p>Anzemet® Injection <i>dolasetron mesylate injection</i></p> <p>100 mg (20mg/mL)</p> <p>One 5mL Sterile Vial</p> <p>Aventis</p>
<p>Anzemet® Injection <i>dolasetron mesylate injection</i></p> <p>100 mg (20mg/mL)</p>			<p>89011215</p>

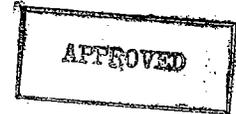
ITEM # 50056633	DATE: 7/20/00
PRODUCT: CARTON, ANZEMET, INJECTION, 100 MG, 1 CT.	
PRINTER: ANAGNI	
Reflex Blue	PMS 221 PMS 5415

APPROVALS

FUNCTIONAL
PROOFREADING
REGULATORY

DOES NOT PRINT
VARNISH/NO VARNISH
AREA

DIE IS FPO



MAR 22 2002

<p>Anzemet® <i>dolasetron mesylate injection</i> Injection 100 mg (20mg/mL)</p>			
<p>Anzemet® Injection <i>dolasetron mesylate injection</i></p> <p>FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.</p> <p>Each ANZEMET® Injection 5 mL vial contains 100 mg dolasetron mesylate (20mg/mL), mannitol USP, with an acetate buffer in water for injection.</p> <p>Rx ONLY</p> <p>Dosage and Administration: Read package insert for prescribing information.</p> <p>WARNING: Discard unused portion. Store at controlled room temperature 20–25°C (68–77°F). Protect from light.</p> <p>Mfd by: Gruppo Lepetit S.p.A. 20020 Lainate, Italy Mfd for: Aventis Pharmaceuticals Inc. Kansas City, MO 64137 ©2000 Made in Italy www.aventispharma-us.com 50056633</p>	 <p>3 0088-1206-32 5</p>	<p>NDC 0088-1206-32</p> <p>Anzemet® <i>dolasetron mesylate injection</i> Injection 100mg (20mg/mL)</p> <p>SINGLE-USE CONTAINER. WARNING: DISCARD UNUSED PORTION</p> <p>One 5mL Sterile Vial</p> <p>Aventis</p>	<p>NDC 0088-1206-32</p> <p>Anzemet® <i>dolasetron mesylate injection</i> Injection 100mg (20mg/mL)</p> <p>One 5mL Sterile Vial</p> <p>Aventis</p>
<p>Lot</p> <p>Exp</p>			

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20-624/S-008

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

Division of Gastrointestinal and Coagulation Drug Products

REGULATORY PROJECT MANAGER REVIEW

Application Number: NDA 20-624/SLR-008

Name of Drug: Anzemet® (dolasetron mesylate) Injection

Applicant: Aventis Pharmaceuticals, Inc.

Material Reviewed:

Submission Dates: October 11, 2002

Receipt Dates: October 15, 2002

Background and Summary

NDA 20-624 was approved September 11, 1997 for Anzemet® Injection for the following indications: 1) prevention of chemotherapy-induced nausea and vomiting; 2) prevention of post-operative nausea and vomiting; 3) treatment of post-operative nausea and vomiting. The Division sent Aventis a supplement request letter dated May 21, 2001 with recommendations to improve the clarity and legibility of the immediate container and carton labeling for Anzemet Injection. Supplement SLR-008, submitted September 21, 2001, provides for the incorporation of the revisions recommended in the May 21, 2001 letter. This supplement was approved on draft labeling March 22, 2002 with the following minor editorial revisions recommended in the letter:

The final printed labeling (FPL) must be identical, and include the minor editorial revisions indicated, to the submitted labeling (ampul and vial immediate container and carton labels submitted September 21, 2001). These revisions are terms of the approval of this application.

1. Add the designation "USP" following "mannitol" on the ampul and vial carton labels.
2. Add Aventis' address following the phrase, "Mfd for Aventis Pharmaceuticals, Inc." on the Anagni vial immediate container label.

(NOTE: Supplement S-005, approved April 26, 2000, provided for the addition of Gruppo Lepetit, Anagni, Italy as the manufacturing site for drug product. Prior to approval of this supplement, drug product was manufactured by Ben Venue Laboratories, Inc. in Marion, Ohio.)

Review

The following labeling (FPL) was submitted October 11, 2002 in response to the March 22, 2002 Approval letter for SLR-008 which contained labeling approved on draft:

Type of Labeling	Identification Number
12.5mg/0.625mL ampul immediate container	50063996
12.5mg/0.625mL ampul 6 x 0.625mL carton	50063997
100mg/5mL vial immediate container	50063995
100mg/5mL vial carton	50063994

The FPL submitted October 11, 2002 was compared to the draft labeling submitted with SLR-008 on September 21, 2001 which was approved on draft labeling March 22, 2002.. The following changes have been made.

I. 12.5mg/0.625mL Ampul

A. Immediate Container Label

The labeling submitted October 11, 2002 is identical to the labeling submitted September 21, 2001.

This labeling is acceptable.

B. Carton Labeling

i) Front Panel

- a) The phrase, "FOR DIRECT INTRAVENOUS INJECTION OR INFUSION" was moved from the back panel to the front panel.
- b) The phrase, "6 Sterile Ampuls 0.625mL" was changed to "6 Sterile 0.625mL Ampuls".

ii) Bottom and Side Panels

The Aventis corporate name and logo were added.

These are acceptable, minor editorial changes.

iii) Back Panel

- a) The quantity "23.875mg" and the designation "USP" were added before and after the ingredient "mannitol".
- b) The storage statement was changed from "Store at controlled room temperature 20 - 25°C (68 - 77°F). Protect from light" to, "Store at 20 - 25°C (68 - 77°F) with excursions permitted to 15 - 30°C (59 - 86°F). [See USP Controlled Room Temperature]. Protect from light."

The addition of the quantity of mannitol and the revised storage statement are acceptable per CMC reviewer, Art Shaw, Ph.D. The addition of the USP designation was requested in the March 22, 2002 Approvable letter.

II. 100mg/5mL Vial

A. Immediate Container

The address, "Kansas City, MO 64137© 2002" was added under the distributor, Aventis', name.

This change was requested in the March 22, 2002 Approvable letter and is therefore acceptable.

B. Carton Label

i) Front Panel

- a) The phrase, "FOR DIRECT INTRAVENOUS INJECTION OR INFUSION" was moved from the back panel in the September 21, 2001 labeling to the front panel in the October 11, 2002 labeling.
- b) The phrase, "Warning, Discard Unused Portion" was deleted from the front panel since it already appears on the back panel.
- c) The phrase, "One 5mL Sterile Vial" was changed to "1 Sterile 5mL Vial" on the front and side panels.

These changes are acceptable, editorial changes.

ii) Back Panel

- a) The quantity ' 1 / and the designation "USP" were added before and after the word "mannitol".
- b) The storage statement was changed as in the 12.5mg ampul carton label.

The quantity of mannitol and changed storage statement are acceptable per CMC Reviewer Art Shaw, Ph.D. The USP designation was added per our request in the March 22, 2002 Approvable letter. These changes are therefore acceptable.

Conclusions

The immediate container and carton labeling (FPL) for the 12.5mg ampul and the 100mg/5mL

NDA 20-624/SLR-008

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vial submitted October 11, 2002 are acceptable. The sponsor stated in the October 11, 2002 submission that they would submit 20 copies of the FPL when notified of its acceptability. They will be so notified. The 20 copies of FPL will be acknowledged and retained when they have been received.

{See electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Regulatory Project Manager

{See electronic signature page}

Arthur Shaw, Ph.D.
Review Chemist

Supervisory Comment/Concurrence:

{See electronic signature page}

Julieann DuBeau, RN, MSN
Chief, Project Management Staff

Drafted: BKS/January 29, 2003

Revised/Initialed: JD/February 4, 2003

Finalized: BKS/February 10, 2003

Filename: Anzemet S-008 Labeling Review

PM LABELING REVIEW

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

/s/

Brian Strongin
2/10/03 09:32:21 AM
CSO

Arthur B. Shaw
2/11/03 02:05:45 PM
CHEMIST
Storage statetment acceptable

Julieann DuBeau
2/11/03 03:38:27 PM
CSO

Division of Gastrointestinal & Coagulation Drug Products

PROJECT MANAGER'S REVIEW

Application Number: NDA 20-624/SLR-008

Name of Drug: Anzemet® (dolasetron) Injection

Sponsor: Aventis Pharmaceuticals Inc.

Material Reviewed:

Submission Date: September 21, 2001

Receipt Date: September 24, 2001

Background and Summary

NDA 20-624 was approved September 11, 1997 for the prevention of nausea and vomiting associated with emetogenic cancer chemotherapy. The Division of Gastrointestinal and Coagulation Drug Products consulted the Office of Post-Marketing Drug Risk Assessment (OPDRA) February 1, 2001 for an assessment of the immediate container and carton labeling regarding preventable medication errors. OPDRA's recommendations were sent to Aventis in a supplement request letter dated May 21, 2001. Supplement SLR-008, dated September 21, 2001, provides for revisions to the ampul and vial immediate container and carton labeling to incorporate the changes recommended in our May 21, 2001 letter.

As described in the following table, the currently approved ampul and vial immediate container and carton labeling will be compared to the proposed labeling and the differences noted below.

LABELING COMPONENT	CURRENTLY APPROVED (component number)	PROPOSED (component number)
Ampul Immediate Container	50006220	50063996
Ampul Carton	50006223	50063997
Vial Immediate Container	50015690	50063993 (Ben Venue) 50063995 (Anagni)
Vial Carton	50015691	50063992 (Ben Venue) 50063994 (Anagni)

(Note: Supplement S-005, approved April 26, 2000, provided for the addition of Gruppo Lepetit, Anagni, Italy as the manufacturing site for drug product. Prior to approval of this supplement, drug product was manufactured by Ben Venue Laboratories, Inc. in Marion, Ohio.)

Review

I. Ampul Label

- A. The NDC number was removed from the proposed labeling.
- B. The font was changed to red on a white background.
- C. Parenthesis surrounding the generic name, dolasetron mesylate injection, were removed. The font was changed to italics.
- D. The description of the strength was changed from, "12.5 mg (20 mg/mL)" to "12.5 mg/0.625 mL" as requested in our May 21, 2001 letter.
- E. The pink band with the text, "Sterile 0.625mL Ampul" was deleted as requested in our letter dated May 21, 2001.
- F. The text, "Single use container. Discard unused portion. For direct intravenous injection or infusion" was deleted as requested in our letter dated May 21, 2001.
- G. The phrase, "Mfd for: Hoechst Marion Roussel, Inc. Kansas City, MO 64137" was replaced by, "Mfd for: Aventis Pharmaceuticals, Inc." This reflects the change in NDA ownership.
- H. "Rx only" was added as requested in our May 21, 2001 letter.
- I. The labeling component number was changed from 50006220 to 50063996.

These changes are acceptable. Per, 21 CFR 201.2, the NDC number is requested but not required. It appears on the ampul carton label as well as in the package insert. The remaining changes are either editorial in nature or were requested in our May 21, 2001 letter.

II. Ampul Carton

- A. The Hoechst Marion Roussel corporate name and syringe graphic in the top portion of the label were replaced with the word "Aventis" (lower right corner front panel).

- B. Parenthesis surrounding the generic name, dolasetron mesylate injection, were removed. The font was changed to italics.
- C. The font was changed from black to red (proprietary name), green (strength) or blue (remainder of the label).
- D. The description of the strength was changed from, "12.5 mg (20 mg/mL)" to "12.5 mg/0.625 mL" as requested in our May 21, 2001 letter.
- E. The phrase, "0.625mL – 6 Sterile Ampuls" was changed to "6 Sterile Ampuls 0.625mL".
- F. The phrase, "Single use containers" was deleted as requested in our letter dated May 21, 2001.
- G. The phrase, "WARNING: Discard unused portion" was moved to the back panel.
- H. "Caution: Federal law prohibits dispensing without prescription" on the front panel was replaced with "Rx only" on the back panel.
- I. The storage statement was moved from the front panel to the back panel.
- J. The sentence, "Each 0.625mL contains 12.5 mg dolasetron mesylate (20 mg/mL). Contains: 12.5 mg dolasetron mesylate, mannitol USP with an acetate buffer in water for injection" was changed to, "Each Anzemet Injection 0.625mL Ampul contains 12.5 mg dolasetron mesylate and mannitol with an acetate buffer in water for injection" as recommended in our May 21, 2001 letter. The "USP" designation following "mannitol" was inadvertently omitted. Aventis should be directed to replace it when FPL is submitted (back panel).
- K. The sentence, "See accompanying package insert for prescribing information" was changed to, "See accompanying package insert for dosage information" (back panel).
- L. The phrase, "Mfd by: Ben Venue Laboratories, Inc. Bedford, Ohio 44146" was replaced by, "Mfd by: Gruppo Lepetit S.p.A. 20020 Lainate, Italy". The phrase, "Made in Italy" was added. (back panel) These changes reflect changes in the drug product manufacturing site approved in S-005.
- M. The sponsor's name was changed from, "Hoechst Marion Roussel, Inc." to "Aventis Pharmaceuticals, Inc." (back panel). This reflects change in the sponsor's corporate name.
- N. The labeling component number was changed from 50006223 to 50063997.

Aventis should be directed to replace the “USP” designation following “mannitol” when FPL is submitted. The remaining changes are either editorial in nature or were requested in our letter dated May 21, 2001 and are acceptable.

III. Vial Immediate Container (Ben Venue Vials)

- A. The strength designation, “100mg (20 mg/mL)” was replaced by, “100mg/5mL (20mg/mL)” as recommended in our letter dated May 21, 2001.
- B. The phrase, “Sterile 5-mL vial” was changed to, “One 5mL Sterile Vial”.
- C. The word “Warning” was added before the sentence, “Discard unused portion”.
- D. The name of the sponsor was changed from “Hoechst Marion Roussel” to “Aventis” to reflect a changed in corporate name.
- E. Parenthesis surrounding the generic name, dolasetron mesylate injection, were removed. The font was changed to italics.
- F. The designation “Rx Only” was added as recommended in our letter dated May 21, 2001.
- G. The labeling component number was changed from 50015690 to 50063993.

These changes are either made in response to our May 21, 2001 letter or are editorial in nature. They are acceptable.

IV. Vial Immediate Container (Anagni)

This label is identical to the Ben Venue vial immediate container with the following changes:

- A. The phrase, “Made in Italy” was added below the phrase, “Mfd for Aventis Pharmaceuticals, Inc.”.
- B. Aventis’ address was deleted.
- C. The labeling component number 50063995 was added.

Per 21 CFR 201.1, the name and address of the manufacturer, packer or distributor must appear on the label. Aventis’s address must be added when FPL is submitted. The remainder of the label is acceptable.

V. Vial Carton (Ben Venue)

- A. Parenthesis surrounding the generic name, dolasetron mesylate injection, were removed. The font was changed to italics. (front, side, top, and back panels)
- B. The text “5mL – 1 Sterile Vial” was changed to, “One 5mL Sterile Vial”. (front and side panels).
- C. The sponsor’s name “Aventis” was added. (lower right corner of the front and side panels).
- D. The syringe graphic was deleted (top of the front and side panels).
- E. The brand and generic names were added (back panel).
- F. The designation “Rx only” was added to replace, “Caution: Federal law prohibits dispensing without prescription” (back panel).
- G. The text, “Each 5mL contains 100mg dolasetron mesylate (20mg/mL). Contains: 100mg dolasetron mesylate, mannitol USP with an acetate buffer in water for injection” was revised to, “Each Anzemet Injection 5mL vial contains 100mg dolasetron mesylate (20mg/mL) and mannitol with an acetate buffer in water for injection” (back panel). The “USP” designation following “mannitol” was inadvertently omitted. Aventis should be directed to replace it when FPL is submitted.
- H. The strength designation, “100mg (20mg/mL)” was revised to, “100mg/5mL (20mg/mL)” as requested in our May 21, 2001 letter (front, side, and top panels).
- I. The sentence, “See accompanying package insert for prescribing information” was changed to, “See accompanying package insert for dosage information” (back panel).
- J. The storage statement was moved from the front panel to the back panel.
- K. The name of the sponsor was changed from “Hoechst Marion Roussel” to “Aventis” to reflect a changed in corporate name (back panel).
- L. The labeling component identifier was changed from 50015691 to 50063992.

Aventis should be directed to replace the “USP” designation following “mannitol” when FPL is submitted. The remaining changes are either editorial in nature or were requested in our letter dated May 21, 2001 and are acceptable.

VI. Vial Carton (Anagni)

This label is identical to the Ben Venue vial carton label with the following changes:

- A. The phrase, "Mfd by: Ben Venue Laboratories, Inc., Bedford, Ohio 44146" was replaced by, "Mfd by: Gruppo Lepetit S.p.A. 20020 Lainate, Italy".
- B. The labeling component number is 50063994.

These changes are acceptable.

Conclusions

Aventis should be directed to make the following changes to the draft labeling when FPL is submitted:

1. Replace the "USP" designation following "mannitol" on the ampul and vial carton labels when FPL is submitted.
2. Per 21 CFR 201.1, the name and address of the manufacturer, packer or distributor must appear on the Anagni vial immediate container label when FPL is submitted.

The submitted draft labeling is otherwise acceptable. An approval letter will be drafted.

{See appended electronic signature page}

Brian Strongin, R.Ph., M.B.A.
Regulatory Project Manager

Supervisory Comment/Concurrence:

{See appended electronic signature page}

Joyce Korvick, M.D.
Deputy Director

Drafted: BKS/March 12, 2002
Revised/Initialed: JK/March 14, 2002
Finalized: BKS/March 14, 2002
Filename: 20624302.0

PM LABELING REVIEW



NDA 20-624/S-008

PRIOR APPROVAL SUPPLEMENT

Aventis Pharmaceuticals Inc.
Attention: Sima Patel
Sr. Regulatory Analyst, U.S. Regulatory Affairs
Somerset Corporate Center
300 Somerset Corporate Boulevard
Bridgewater, NJ 08807-2854

Dear Ms. Patel:

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: Anzemet® (dolasetron) Injection

NDA Number: 20-624

Supplement Number: S-008

Date of Supplement: September 21, 2001

Date of Receipt: September 24, 2001

This supplement proposes the following change(s): revisions to the ampul and vial labels and cartons to incorporate the revisions recommended in our letter dated May 21, 2001.

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 November 23, 2001 in accordance with 21 CFR 314.101(a).

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/Courier/Overnight Mail:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Attention: Division Document Room
5600 Fishers Lane

NDA 20-624/S-008

Page 2

Rockville, Maryland 20857

If you have any questions, call me at (301) 827-7310.

Sincerely,

{See appended electronic signature page}

Brian Strongin
Project Manager
Division of Gastrointestinal and Coagulation Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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

/s/

Brian Strongin
9/25/01 02:56:40 PM

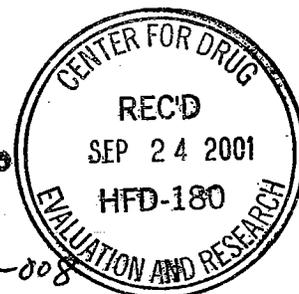
Aventis Pharmaceuticals

ORIGINAL



September 21, 2001

Lilia Talarico, M.D., Director
Division of Gastrointestinal & Coagulation Drug Products (HFD-180)
Office of Drug Evaluation III
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room #6B-45
5600 Fishers Lane
Rockville, MD 20857



NEW CORRESP

NDA 20-624
Anzemet® (dolasetron) Injection

NDA NO. 20-624 REF. NO. CSLR-008
NDA SUPPL FOR Labeling

Dear Dr. Talarico:

Reference is made to the approved NDA 20-624 for Anzemet® (dolasetron) Injection, and to the May 21, 2001, letter received from the agency. This supplement is submitted in accordance with 21 CFR314.70(b)(3)(i) in order to obtain approval for revisions made in the labeling of the Ampul and vial cartons and labels for Anzemet® (dolasetron) Injection. A copy of your letter is provided as attachment 1 for ease of review.

Labeling changes have been made to the Ampul and Vial, Labels and Cartons, for Anzemet® (dolasetron) Injection to incorporate the revisions recommended in the May 21, 2001 letter received from the agency. In addition to these changes, other editorial and formatting labeling revisions have been made and will be reported in the Annual Report for Anzemet® (dolasetron) Injection to be submitted this year.

The changes are described below:

Ampul Label

The label initially reviewed by the agency (component #50006220) was discontinued on 12/31/2000, and was replaced by component #50056636. This new version no longer included the text "Single-use container, discard unused portion", consistent with "1b" of the letter dated 5/21/01. The pink band was also eliminated as recommended in "1c" of the letter. This label was then superceded by component #50061716 (in use 5/2000) in which the text is identical to its predecessor, but in red. This label has now been revised (component #50063996) to incorporate the revisions requested in "1a" and "1d" of the letter. Attachment 2 contains a marked-up copy of the proposed label.

Ampul Carton

The label initially reviewed by the agency (component #50006223) was discontinued on 12/31/2000, and was replaced by component #50056634 in 11/2000. In this version (currently in use), the pink band was removed for increased legibility consistent with comment "2d" of the letter, and the text described in comment "2b" was revised to be consistent with the recommendation "2b" of the letter. Component #50063997 is the proposed label which incorporates revisions from comments "2a" (replacing "12.5 mg (20 mg/ml) with "12.5mg/0.625mL"), "2b" and "2c" (deleting the text "Single-use container, discard unused portion"). Attachment 3 contains a marked-up copy of the proposed label.

Vial Label

For product produced by Ben Venue, the label initially reviewed by the agency (component #50015690) was discontinued and was replaced by component #50060620 in August 2001. In this version (currently in use), the pink band was removed for increased legibility consistent with comment "3b" of the letter, and the text "Rx only" in comment "3c" was added. Component #50063993 is the proposed label that incorporates revisions from comments "3a" which replaces "100 mg (20 mg/mL)" with "100mg/5mL (20mg/mL)". Attachment 4 contains a marked-up copy of the proposed label.

For product produced by Anagni, the component #50056635 (currently in use) does not have a pink band, which is consistent with comment "3b" of the letter. Component #50063995 is the proposed label that incorporates revisions from comments "3a" which replaces "100 mg (20 mg/ml)" with "100mg/5mL (20mg/mL)" and from comment "3c" which adds the text "Rx only". Attachment 5 contains a marked-up copy of the proposed label.

Vial Carton

For product produced by Ben Venue, the label initially reviewed by the agency (component #50015691) was discontinued and was replaced by component #50060619 in August 2001. In this version (currently in use), the pink band was removed for increased legibility as requested in comment "4b" of the letter. Component #50063992 is the proposed label that incorporates revisions from comment "4a" which replaces "100 mg (20 mg/mL)" with "100mg/5mL (20mg/mL)". Attachment 6 contains a marked-up copy of the proposed label.

For product produced by Anagni, the component #50056633 (in use earlier this year) had the pink band removed, which is consistent with the request in comment "4b" of the letter. Component #50060615 (currently in use) superceded #50056633. Component #50063994 is the proposed label that incorporates revisions from comments "4a" which replaces "100 mg (20 mg/ml)" with "100mg/5mL (20mg/mL)". Attachment 7 contains a marked-up copy of the proposed label.

The revised labeling will be implemented upon approval.

In accordance with 21 CFR 314.71(b), this submission contains both an archival copy and a review copy.

If you have any questions concerning this amendment, please contact the undersigned by telephone at (908)243-7616 or fax at (908)243-6461.

Sincerely,



Ms. Sima Patel
Sr. Regulatory Analyst, U.S. Drug Regulatory Affairs

Attachment 1 – Copy of agency letter dated May 21, 2001

Attachment 2 – Ampul Label (12.5mg/0.625mL)- Component # 50006220
Component # 50056636
Component # 50061716
Component # 50063996

Attachment 3 - Ampul Carton (12.5mg/0.625mL)- Component # 50006223
Component # 50056634
Component # 50063997

Attachment 4 - Vial Label (100mg/5mL) Ben Venue: Component # 50015690
Component # 50060620
Component # 50063993

Attachment 5 - Vial Label (100mg/5mL) - Anagni: Component # 50056635
Component # 50063995

Attachment 6 -Vial Carton (100mg/5mL) Ben Venue:Component # 50015691
Component # 50060619
Component # 50063992

Attachment 7 - Vial Carton (100mg/5mL) - Anagni: Component # 50056633
Component # 50060615
Component # 50063994

cc: McNeil, Melodi