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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

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

ITEM # 50063997	DATE: 8/20/01
PRODUCT: CARTON, ANZEMET INJECTION, 12.5MG 6 AMPULES	
PRINTER: ANAGNI	
Reflex Blue · PMS 221 · PMS 368	

APPROVALS

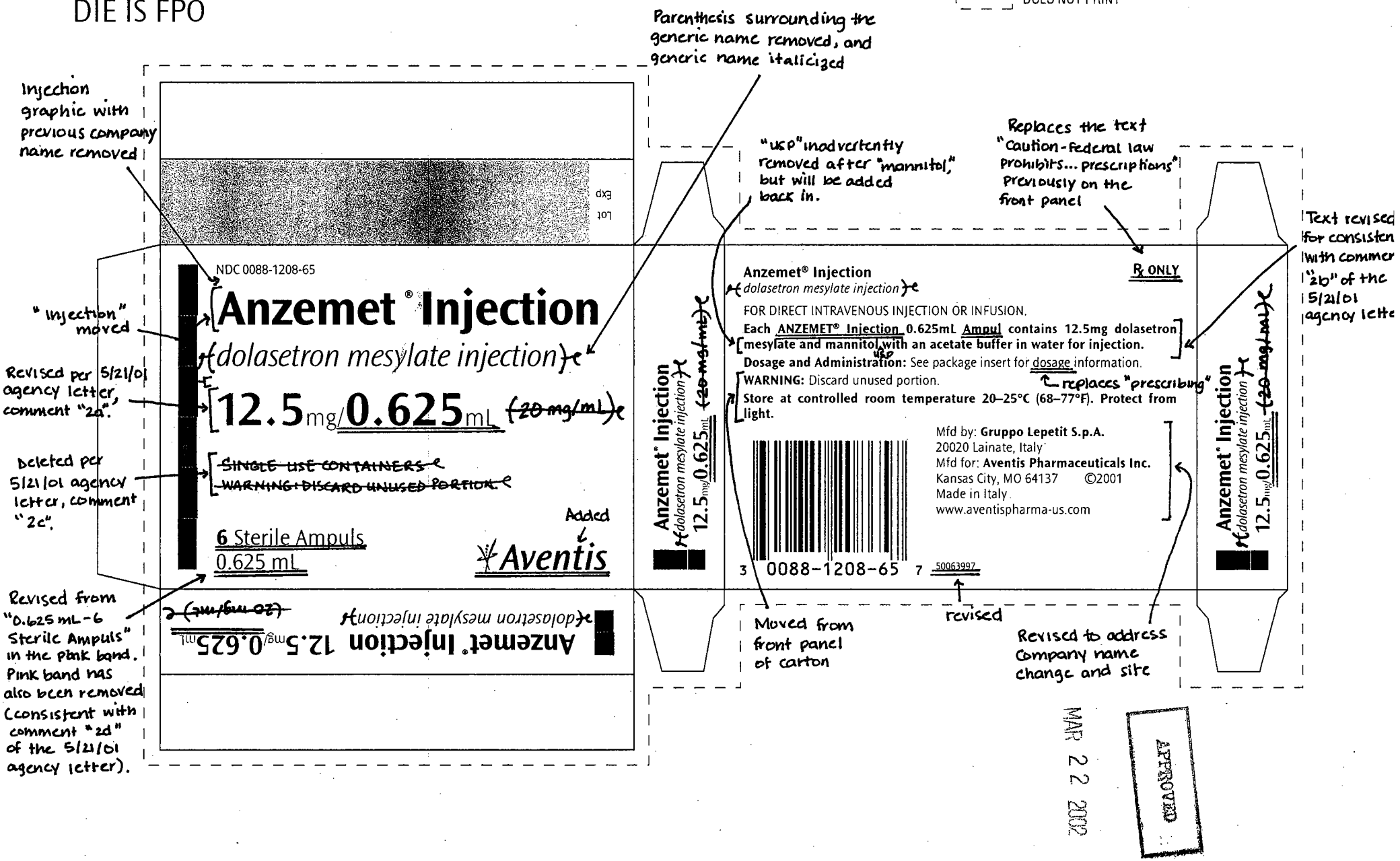
FUNCTIONAL

PROOFREADING

REGULATORY

Indicates Varnish Area
DOES NOT PRINT

DIE IS FPO



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

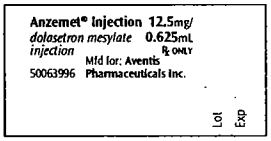
PROOFREADING

REGULATORY

APPROVED

MAR 22 2002

100%

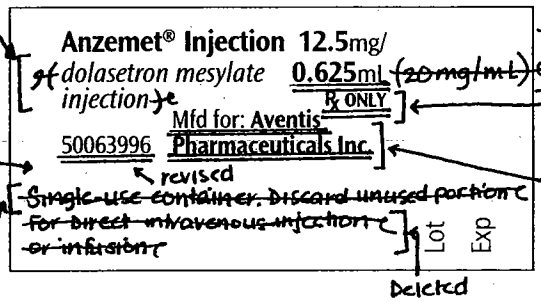


200%

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

APPROVED

MAR 22 2001

100%

NDC 0088-1206-32

Anzemet® Injection **100**mg/**5**mL (20mg/mL)

dolasetron mesylate injection

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

℞ ONLY

Mfd for: **Aventis Pharmaceuticals Inc.**
Made in Italy

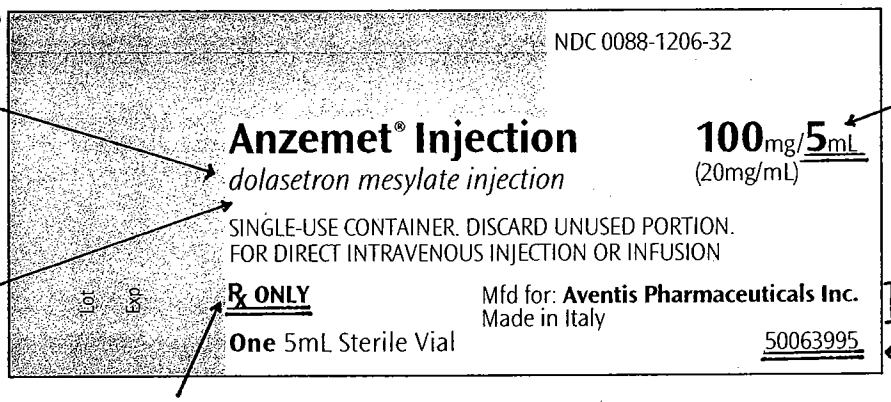
One 5mL Sterile Vial

50063995

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 2002

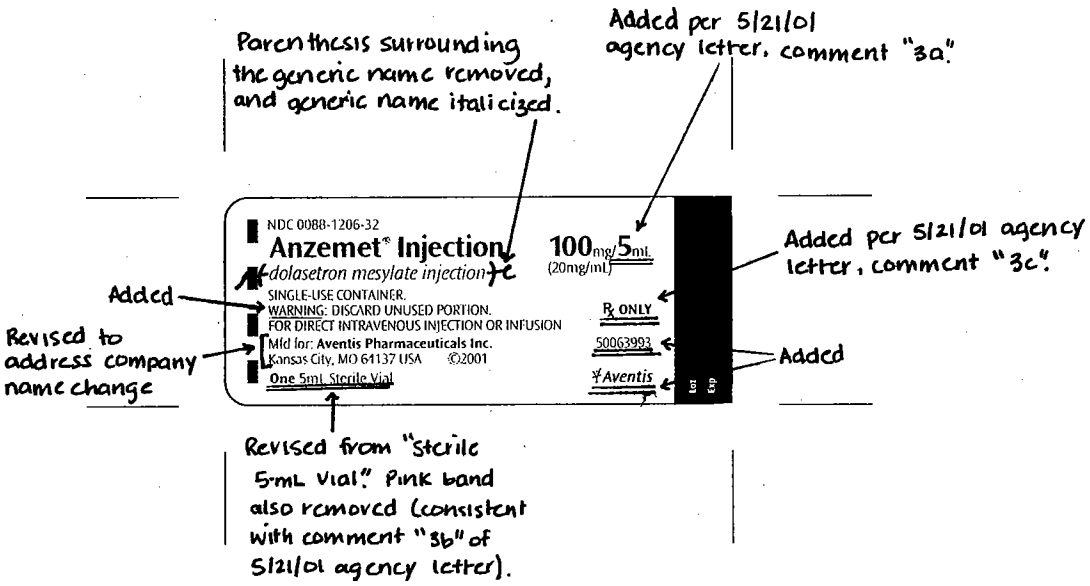
ITEM # 50063993	DATE: 8/20/01
PRODUCT: LABEL, ANZEMET INJECTION, 100MG, 5 ML, VIAL	
PRINTER: BEN VENUE	
Reflex Blue PMS 5415	

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY



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

APPROVALS

FUNCTIONAL

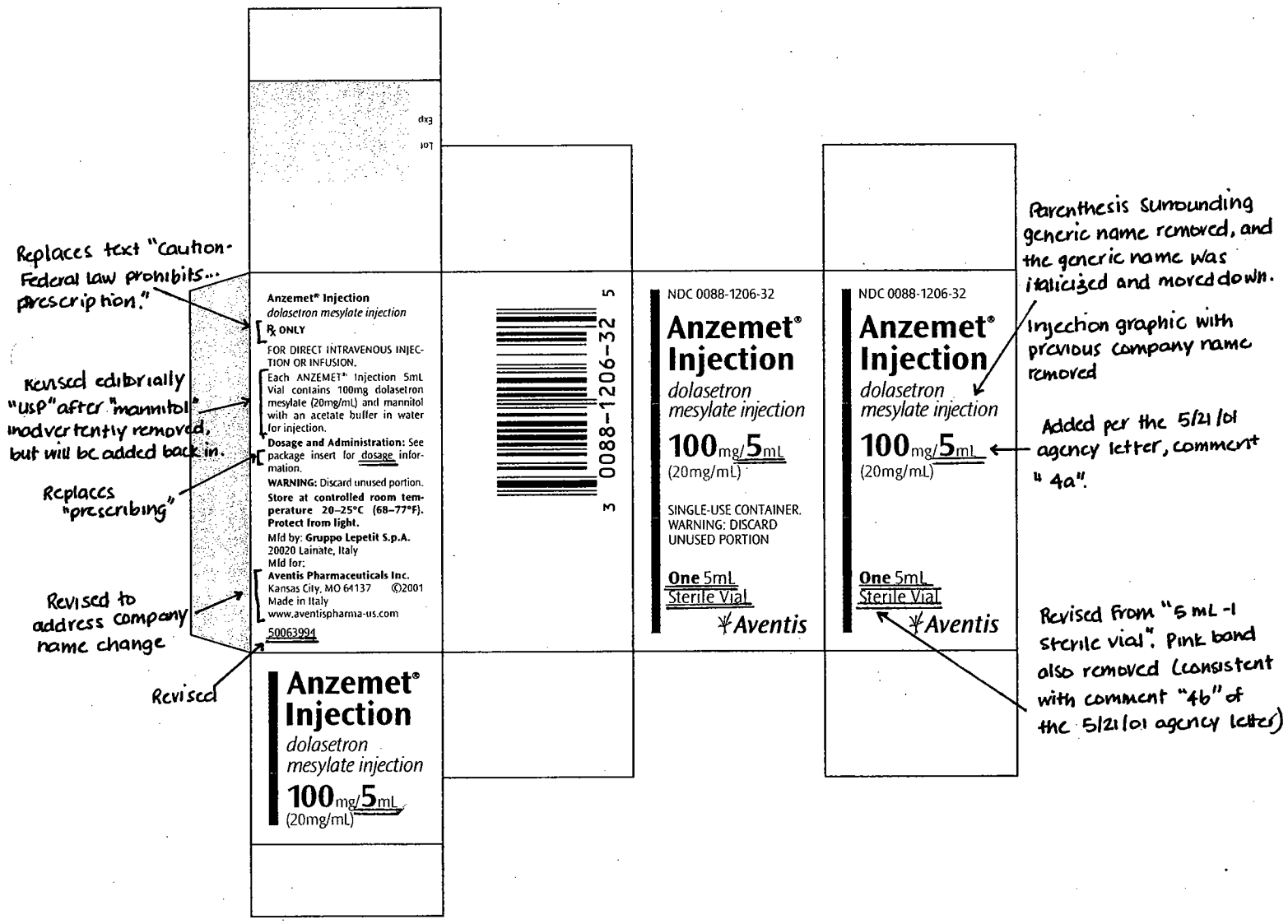
PROOFREADING

REGULATORY

APPROVED

MAR 22 2002

DIE IS FPO



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

APPROVED

APPROVALS

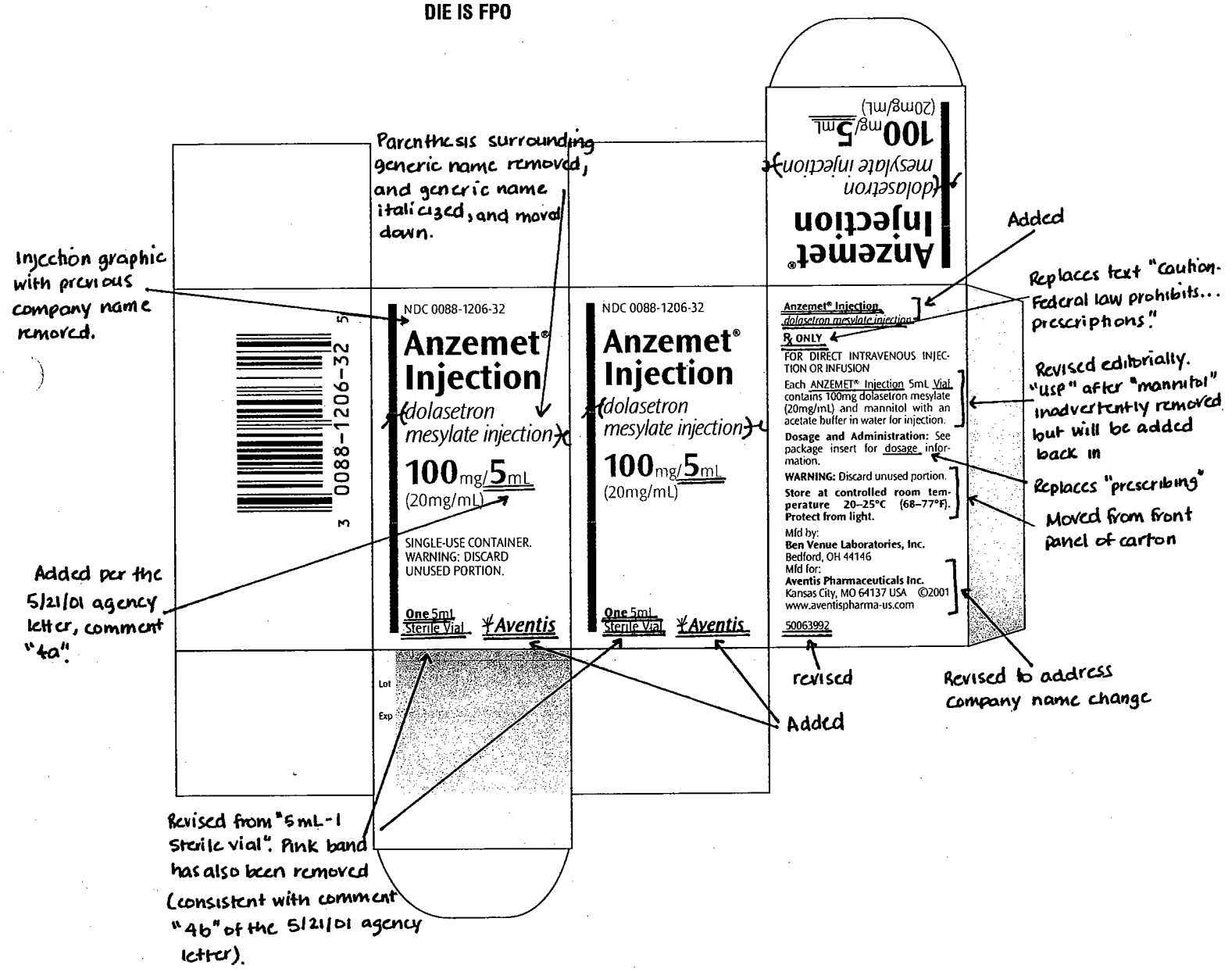
FUNCTIONAL

PROOFREADING

REGULATORY

MAR 22

DIE IS FPO



APPROVED

MAR 22 2002

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

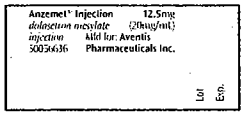
APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

100%



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

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 [redacted]	PMS 205 [redacted] Black#2 [redacted]

APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

NDC 0088-1208-65

ANZEMET® Injection

(dolasetron mesylate injection)

12.5 mg (20 mg/mL)

Sterile 0.625 mL Ampul

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

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

50006220

[redacted]
Lot:
Exp:

ITEM # 50006223	
DATE: 8/30/01 2:49 PM	
Pg. 1 of 1	CICERO JOB NO.: 28773
PRODUCT: CARTON UNIT, ANZEMET, INJECTION, 12.5 MG	
PRINTER: KELLER CRESCENT COMPANY	
Black	

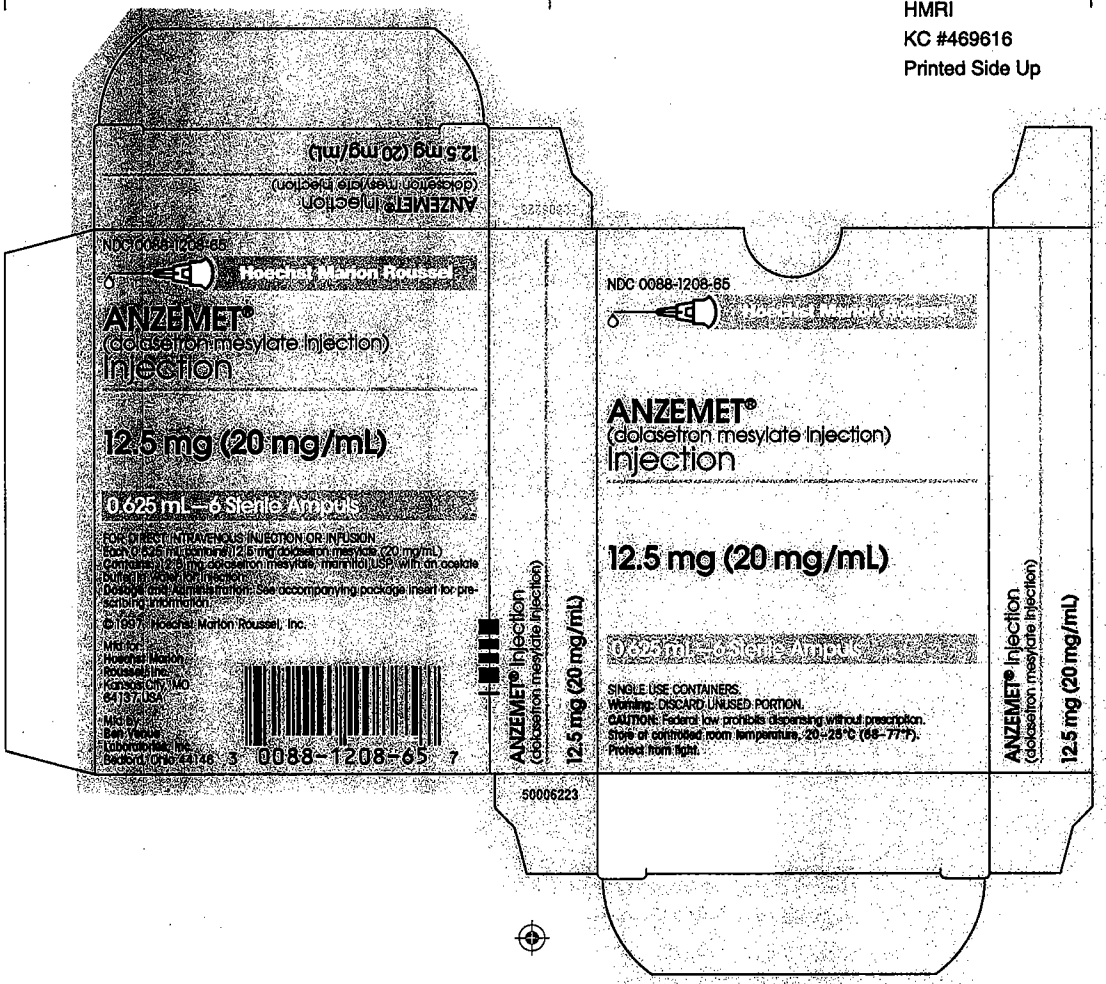
APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

HMRI
KC #469616
Printed Side Up



MAR 22 2002

APPROVED

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

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

Indicates No Varnish/Varnish Area
DOES NOT PRINT

DIE IS FPO

Lot
Exp

H1208-65

NDC 0088-1208-65

Anzemet®

12.5mg
(20mg/mL)

dolasetron mesylate injection

Injection

SINGLE-USE CONTAINERS.
WARNING: DISCARD UNUSED PORTION

6 Sterile Ampuls
0.625 mL

Aventis

Anzemet® Injection
dolasetron mesylate injection
12.5mg (20mg/mL)

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.

℞ **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

3 0088-1208-65 7

50056634

Anzemet® Injection
dolasetron mesylate injection
12.5mg (20mg/mL)

Anzemet® Injection
dolasetron mesylate injection
12.5mg (20mg/mL)

MAR 22 2002

APPROVED

APPROVED

MAR 22 2002

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

APPROVALS:

FUNCTIONAL

PROOFREADING

REGULATORY

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

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

APPROVALS

FUNCTIONAL

PROOFREADING

REGULATORY

NDC 0088-1206-32

℞ ONLY

Anzemet® Injection 100mg (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 22 200

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%

NDC 0088-1206-32

Anzemet® Injection **100**mg (20mg/mL)

dolasetron mesylate injection

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

Lot Exp

One 5mL Sterile Vial

Mfd for: **Aventis Pharmaceuticals Inc.**
Made in Italy 50056635

200%

NDC 0088-1206-32

Anzemet® Injection **100**mg (20mg/mL)

dolasetron mesylate injection

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

Lot Exp

One 5mL Sterile Vial

Mfd for: **Aventis Pharmaceuticals Inc.**
Made in Italy 50056635

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

APPROVED

MAR 22 2002

DIE IS FPO

NDC 0088-1206-32

Anzemet®
Injection
dolasetron mesylate injection
100 mg (20mg/mL)

Anzemet® Injection
dolasetron mesylate injection

℞ **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

50060619

3 0088-1206-32 5

NDC 0088-1206-32

Anzemet®
Injection
dolasetron mesylate injection
100 mg
(20mg/mL)

SINGLE-USE CONTAINER.
WARNING: DISCARD UNUSED PORTION.

One 5mL Sterile Vial Aventis

Lot

Exp

NDC 0088-1206-32

Anzemet®
Injection
dolasetron mesylate injection
100 mg
(20mg/mL)

One 5mL Sterile Vial Aventis

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

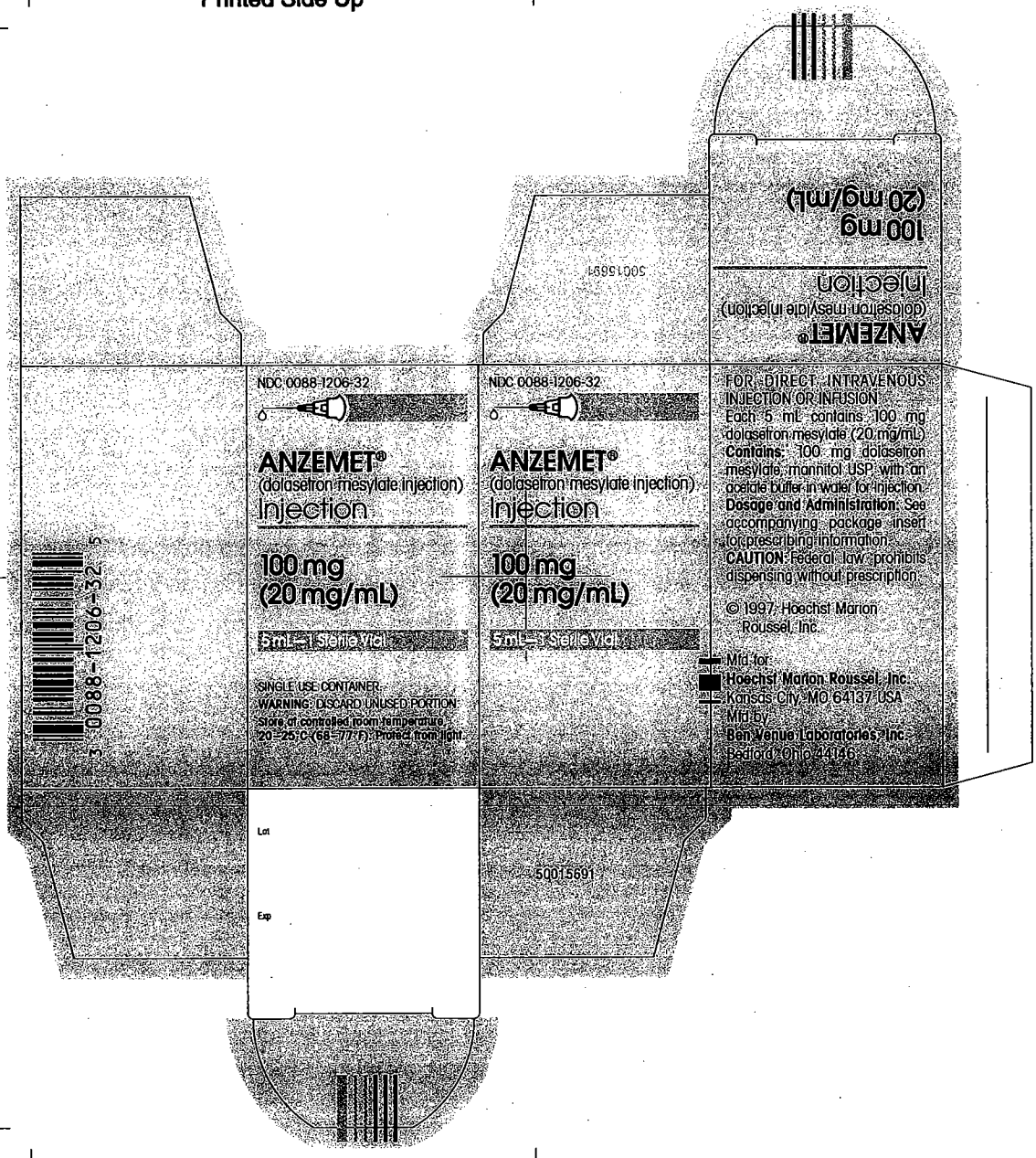
PROOFREADING

REGULATORY

APPROVED

MAR 22 2007

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

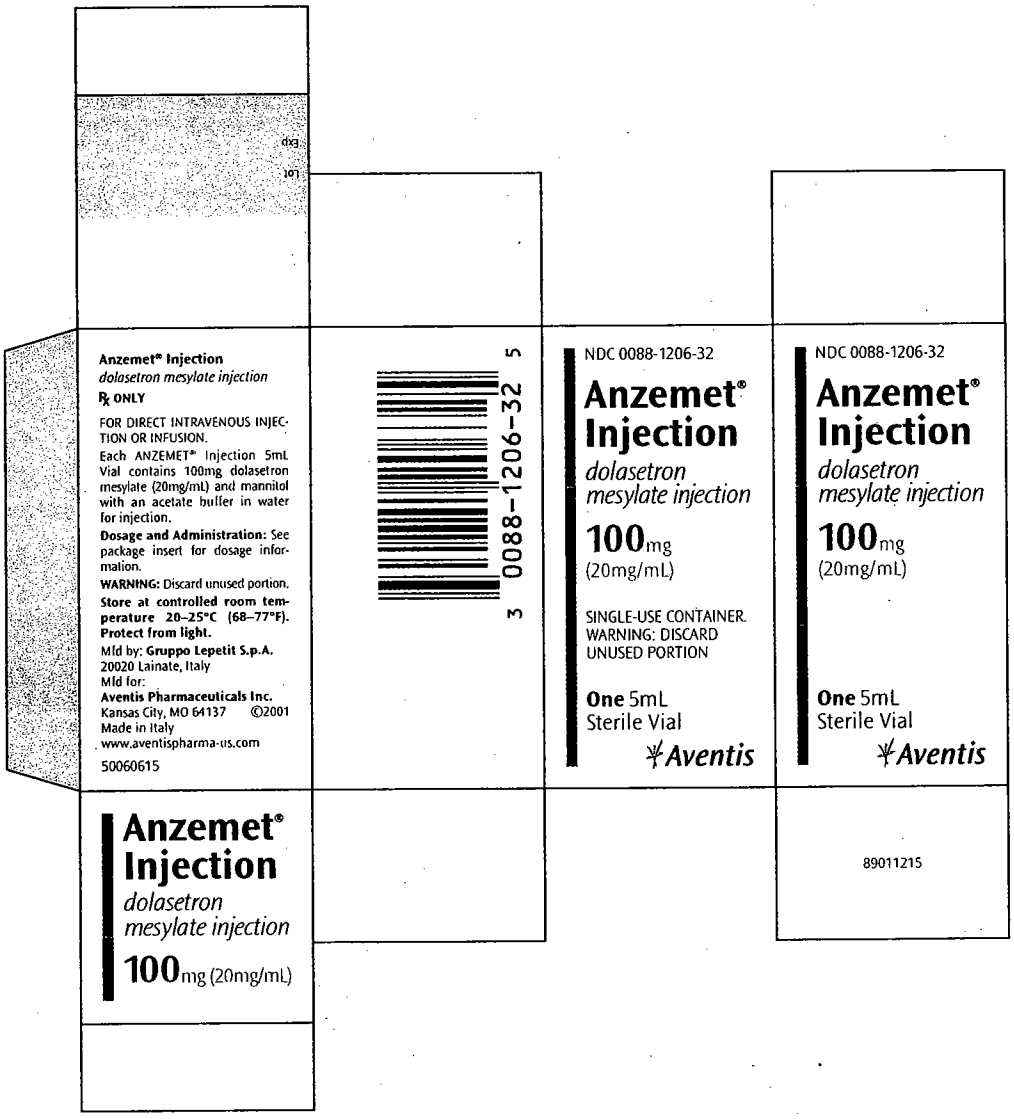
REGULATORY

DOES NOT PRINT VARNISH/NO VARNISH AREA

APPROVED

MAR 22 2002

DIE IS FPO



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

APPROVED

MAR 22 200

Anzemet®
dolasetron mesylate injection
Injection
100 mg (20mg/mL)

Anzemet® Injection
dolasetron mesylate injection

FOR DIRECT INTRAVENOUS INJECTION OR INFUSION.

Each ANZEMET® Injection 5 mL vial contains 100 mg dolasetron mesylate (20mg/mL), mannitol USP, with an acetate buffer in water for injection.

℞ **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

50056633

3 0088-1206-32 5

Lot

Exp

NDC 0088-1206-32

Anzemet®

dolasetron mesylate injection

Injection

100 mg (20mg/mL)

SINGLE-USE CONTAINER.
WARNING: DISCARD UNUSED PORTION

One 5mL Sterile Vial

Aventis

NDC 0088-1206-32

Anzemet®

dolasetron mesylate injection

Injection

100 mg (20mg/mL)

One 5mL Sterile Vial

Aventis

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."