

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 021012

CHEMISTRY REVIEW(S)

Harapanhalli

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-012 **DATE REVIEWED:** July 12, 1999

REVIEW #: 3 **REVIEWER:** Ravi S. Harapanhalli, Ph.D.

<u>SUBMISSION</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment (BC)	25-JUN-1999	26-JUN-1999	26-JUN-1999
Labeling (N000BL)	12-FEB-1999	16-FEB-1999	23-FEB-1999
Labeling (N000BL)	08-JUN-1999	10-JUN-1999	15-JUN-1999

<u>PREVIOUS DOCS</u>	<u>DOC. DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	15-JUN-1997	17-JUN-1998	18-JUN-1998
AMENDMENT (BC)	07-AUG-1998	10-AUG-1998	13-AUG-1998
AMENDMENT (BC)	28-AUG-1998	31-AUG-1998	03-SEP-1998
AMENDMENT (BC)	22-SEP-1998	23-SEP-1998	24-SEP-1998
Amendment (BC)	28-JAN-1999	29-JAN-1999	16-FEB-1999
Amendment (AC)	05-FEB-1999	08-FEB-1999	16-FEB-1999
Amendment (BC)	21-MAY-1999	24-May-1999	24-May-1999
Deficiency letter	30-MAY-1999	30-MAY-1999	30-MAY-1999
Amendment (BC)	04-JUN-1999	04-JUN-1999	04-JUN-1999
Teleconference	21-JUN-1999	21-JUN-1999	21-JUN-1999

NAME & ADDRESS OF APPLICANT: DIATIDE, INC.,
9 Delta Drive
Londonderry, NH 03053
Contact: J. Kris Piper; (603) 437-8970

DRUG PRODUCT NAME
Proprietary: NeoTect™
Established: Kit for the preparation of Technetium Tc 99m Depreotide
Code Name/#: P829
Chem.Type/Ther.Class: Diagnostic radiopharmaceutical

PHARMACOL. CATEGORY/INDICATION: Diagnostic radiopharmaceutical for scintigraphic imaging of malignant tumors in the lung.

DOSAGE FORM: Sterile solution
STRENGTHS: 50 µg P829/20 mCi Tc 99m/ml saline POTENCY(IES)
ROUTE OF ADMINISTRATION: Intravenous

Rx/OTC:

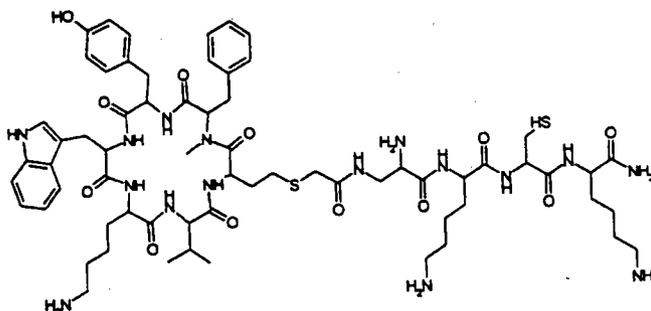
Rx OTC
 Yes No

SPECIAL PRODUCTS:

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:**

Chemical name: Cyclo(-L-homocysteinyl-N-methyl-L-phenylalanyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl),(1→1')-sulfide with 3-[(mercaptoacetyl)amino]-L-alanyl-L-lysyl-L-cysteinyl-L-lysine amide, trifluoroacetate salt.

CAS number: 161982-62-3
Molecular formula: $C_{65}H_{96}N_{16}O_{12}S_2$ (net)
Molecular weight: 1357.7
Structural formula:

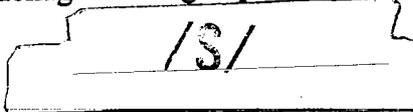


SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable): None
CONSULTS: None

REMARKS: The commitments and comments of review # 2 were communicated to Diatide on June 23, 1999. Diatide's responses dated June 25, 1999 were evaluated.

CONCLUSIONS & RECOMMENDATIONS: All responses were adequately addressed. The changes listed at the end should be made in the labeling. The NDA is recommended for approval. Methods validation package is being requested shortly.

 07/12/99
Ravi S. Harapanhalli, Ph.D.
Review Chemist, HFD-160/820

cc:
Org. NDA 21012
HFD-160/Division File
HFD-160/Harapanhalli
HFD-160/PharmTox/Baily
HFD-160/PM/JMoore
HFD-160/MO/Loewke
HFD-160/TEAMLEADER/Leutzinger
HFD-820/DIVISION DIRECTOR/Gibbs
R/D Init by: Leutzinger *eg*

 7/01/99

filename: c:\mydocuments\NDA21012.july12.doc

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-012 **DATE REVIEWED:** June 23, 1999

REVIEW #: 2 **REVIEWER:** Ravi S. Harapanhalli, Ph.D.

<u>SUBMISSION</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment (BC)	28-JAN-1999	29-JAN-1999	16-FEB-1999
Amendment (AC)	05-FEB-1999	08-FEB-1999	16-FEB-1999
Amendment (BC)	21-May-1999	24-May-1999	24-May-1999
Deficiency letter	30-MAY-1999	30-MAY-1999	30-MAY-1999
Amendment (BC)	04-JUN-1999	04-JUN-1999	04-JUN-1999
Teleconference	21-JUN-1999	21-JUN-1999	21-JUN-1999
Labeling (N000BL)	12-FEB-1999	16-FEB-1999	23-FEB-1999
Labeling (N000BL)	08-JUN-1999	10-JUN-1999	15-JUN-1999

<u>PREVIOUS DOCS</u>	<u>DOC. DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	15-JUN-1997	17-JUN-1998	18-JUN-1998
AMENDMENT (BC)	07-AUG-1998	10-AUG-1998	13-AUG-1998
AMENDMENT (BC)	28-AUG-1998	31-AUG-1998	03-SEP-1998
AMENDMENT (BC)	22-SEP-1998	23-SEP-1998	24-SEP-1998

NAME & ADDRESS OF APPLICANT: DIATIDE, INC.,
9 Delta Drive
Londonderry, NH 03053
Contact: J. Kris Piper; (603) 437-8970

DRUG PRODUCT NAME

Proprietary: NeoTect™
Established: Kit for the preparation of Technetium Tc 99m Depreotide
Code Name/#: P829
Chem.Type/Ther.Class: Diagnostic radiopharmaceutical

PHARMACOL. CATEGORY/INDICATION: Diagnostic radiopharmaceutical for scintigraphic imaging of malignant tumors in the lung.

DOSAGE FORM: Sterile solution
STRENGTHS: 50 µg P829/20 mCi Tc 99m/ml saline POTENCY(IES)
ROUTE OF ADMINISTRATION: Intravenous
Rx/OTC: Rx OTC

SPECIAL PRODUCTS:

 Yes X No

**CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA,
MOLECULAR WEIGHT:**

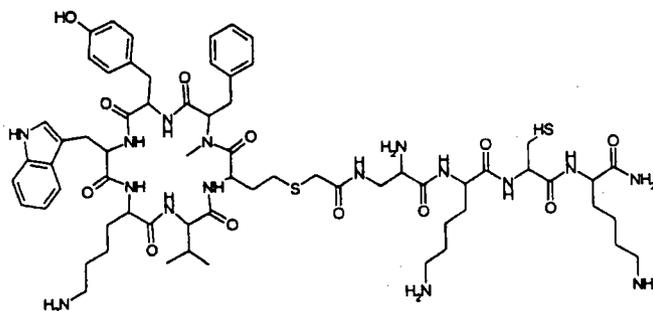
Chemical name: Cyclo(-L-homocysteinyl-N-methyl-L-phenylalanyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl),(1→1')-sulfide with 3-[(mercaptoacetyl)amino]-L-alanyl-L-lysyl-L-cysteinyl-L-lysine amide, trifluoroacetate salt.

CAS number: 161982-62-3

Molecular formula: $C_{65}H_{96}N_{16}O_{12}S_2$ (net)

Molecular weight: 1357.7

Structural formula:



SUPPORTING DOCUMENTS:

RELATED DOCUMENTS (if applicable): None

CONSULTS: None

REMARKS: Many deficiencies noted in the Agency's 'approvable' letter dated December 16, 1998 were resolved satisfactorily.

The issues were resolved through Diatide's submission dated June 04, 1999, and through the teleconference on June 21, 1999. The two labeling submissions dated February 12, 1999 and June 8, 1999 were also reviewed. DMF

which supports this NDA, was amended in response to Agency's deficiency letter. The amendment was not adequate, and the deficiency letter was sent [redacted]. However, the issues in the DMF were addressed in the NDA responses and hence were deemed not critical to the approval of this NDA.

CONCLUSIONS & RECOMMENDATIONS: The comments and commitments listed at the end should be communicated to the sponsor. The recommended changes should be made in the labeling. Methods validation package should be requested following the implementation of the revised specifications in the regulatory methods. The NDA is recommended for approval.

/S/ [redacted] 06/23/99
Ravi S. Harapanhalli, Ph.D.

/S/ [redacted] 6/23/99

DIVISION OF MEDICAL IMAGING AND RADIOPHARMACEUTICAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

NDA #: 21-012

DATE REVIEWED: October 26, 1998

REVIEW #: 1

REVIEWER: Ravi S. Harapanhalli, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
ORIGINAL	15-JUN-97	17-JUN-98	18-JUN-98
AMENDMENT (BC)	07-AUG-98	10-AUG-98	13-AUG-98
AMENDMENT (BC)	28-AUG-98	31-AUG-98	03-SEP-98
AMENDMENT (BC)	22-SEP-98	23-SEP-98	24-SEP-98

NAME & ADDRESS OF APPLICANT:

DIATIDE, INC.,
9 Delta Drive
Londonderry, NH 03053
Contact: J. Kris Piper; (603) 437-8970

DRUG PRODUCT NAME

Proprietary:
Established:
Code Name/#:
Chem. Type/Ther. Class:

NeoTect™
Kit for the preparation of Technetium Tc 99m Depreotide
P829
Diagnostic

PHARMACOL. CATEGORY/INDICATION:

Diagnostic radiopharmaceutical for scintigraphic imaging of malignant tumors in the lung.

DOSAGE FORM:

Sterile solution

STRENGTHS: 50 µg P829/20 mCi Tc 99m/ml saline POTENCY(IES)

ROUTE OF ADMINISTRATION:

Intravenous

Rx/OTC: Rx OTCSPECIAL PRODUCTS: Yes No

(If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical name: Cyclo(-L-homocysteinyl-N-methyl-L-phenylalanyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl),(1→1')-sulfide with 3-[(mercaptoacetyl)amino]-L-alanyl-L-lysyl-L-cysteinyl-L-lysine amide, trifluoroacetate salt.

CAS number: 161982-62-3

Molecular formula: C₆₅H₉₆N₁₆O₁₂S₂ (net)

Molecular weight: 1357.7

Structural formula:

CONCLUSIONS & RECOMMENDATIONS:

NDA 21-012 was reviewed for CMC/

Based on these major issues, together with those of lesser importance, we recommend that NDA 21-012 be "approvable."

DMF [redacted] NDA 21012 [redacted]

**APPEARS THIS WAY
ON ORIGINAL**

[redacted] /S/ 11/19/98
Ravi S. Harapanhalli, Ph.D.
Review Chemist, HFD-160/820

- cc:
- Org. NDA 21012
- HFD-160/Division File
- HFD-160/Harapanhalli/21 Sept. 1998
- HFD-160/Pharm-Tox/Bailey
- HFD-160/ Biopharm/Choi
- HFD-160/MO/Loewke
- HFD-160/Stat/Mucci
- HFD-160/PM/Ferre-Hockensmith
- HFD-160/TEAMLEADER/Leutzinger
- HFD-820/DIVISION DIRECTOR/Gibbs
- R/D Init by: TEAMLEADER

[redacted] /S/ 11/24/98

filename: NDA21012.1

**APPEARS THIS WAY
ON ORIGINAL**