

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20850

CHEMISTRY REVIEW(S)

K. Burgiovanni

SEP 21 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-850 **CHEMISTRY REVIEW #:** 6 **REVIEW DATE:** September 21, 1998

<u>SUBMISSION:</u>	<u>TYPE:</u>	<u>DOCUMENT DATE:</u>
Amendment	1S NDA	September 10, 1998 September 17, 1998

<u>CDER ORIGINAL NDA DATE:</u>	<u>ASSIGNED DATE:</u>
September 29, 1997	September 30, 1997

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:

Boehringer Ingelheim Pharmaceuticals, Inc.
a Subsidiary of
Boehringer Ingelheim Corporation
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877

DRUG PRODUCT NAME:

Proprietary: Micardis®
Nonproprietary/USAN: telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S

PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of telmisartan tablets

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

DOSAGE FORM: tablet

STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

DISPENSED: Rx

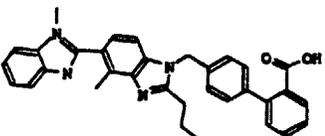
NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.

Micardis® (telmisartan) tablets

Page 2

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

<p>BE Number: 0183482AA</p> <p>CAF Number: 144701484</p> <p>Formula: C(33)H(30)N(4)O(2)</p> <p>Mol. Wt.: 514.00</p>	 <p>The chemical structure of Telmisartan is shown. It consists of a biphenyl core. One phenyl ring is substituted at the 2-position with a carboxylic acid group (-COOH). The other phenyl ring is substituted at the 1-position with a propyl group (-CH2CH2CH3) and at the 4-position with a dimethylbenzimidazol-2-yl group (-N(CH3)2C5H3N).</p>
<p>NAME: TELMISARTAN</p>	

The above graphic is from the CHEM-X database.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND

DMF

DMF

DMF

prov

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above and are acceptable.

RELATED DOCUMENTS: IND
CONSULTS:

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

VALIDATION: A validation package was sent, respectively, to laboratories in St. Louis and Philadelphia on June 17, 1998. Each laboratory confirmed receipt.

ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable as of March 27, 1998. Compliance judged the three packagers acceptable as of September 17, 1998.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted an amendment, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product.

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Dr. Emmanuel Fadiran has reviewed the biopharmaceutics and dissolution section and has rendered an opinion as discussed in review #5. Recently a Q of [redacted] was agreed upon.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for telmisartan in 40 and 80mg tablet strengths.

This amendment provides the names of three packaging firms located in this country, that BI wants to use for packaging the completed blister and package insert. Two are new and one was submitted in the original application.

NDA 20-850

Page 4

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

CONCLUSIONS & RECOMMENDATIONS:

This reviewer recommends approval for the telmisartan NDA as far as Chemistry is concerned. The only outstanding issue is the interest in lower dosage strengths.

cc: Orig. NDA 20-850
HFD-110/Division File
HFD-110/ CBerninger
HFD-110/ KBongiovanni, PM
Stoneham, Massachusetts District Office
HFD-810/ CHoiberg/JSimmons
R/D Init by: KSrinivasachar/

file name: c:\nda-rev\20850r6.doc

IS/ 9-21-98

IS/

Carl J. Berninger, Ph.D.,

AUG 24 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-850 CHEMISTRY REVIEW #: 5 REVIEW DATE: August 24, 1998

**SUBMISSION: TYPE: DOCUMENT DATE:
Amendments 1S NDA July 10, 1998**

June 17, 1998

June 19, 1998

**CDER ORIGINAL NDA DATE:
September 29, 1997**

**ASSIGNED DATE:
September 30, 1997**

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:

**Boehringer Ingelheim Pharmaceuticals, Inc.
a Subsidiary of
Boehringer Ingelheim Corporation
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877**

DRUG PRODUCT NAME:

**Proprietary: Micardis®
Nonproprietary/USAN: telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S**

**PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of telmisartan tablets**

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

DOSAGE FORM: tablet

STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

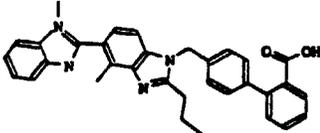
DISPENSED: Rx

NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

Page 2

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

<p>AT Number: 0183482AA</p> <p>DMF Number: 144701484</p> <p>Formula: C(33)H(30)N(4)O(2)</p> <p>Mol Wt: 514.00</p>	 <p>The chemical structure of Telmisartan is shown. It consists of a central benzimidazole ring system. One of the benzimidazole nitrogens is substituted with a methyl group. The 2-position of the benzimidazole ring is substituted with a propyl group. The 4-position of the benzimidazole ring is substituted with a 1,1'-biphenyl-2-carboxylic acid group. The biphenyl system is oriented such that the carboxylic acid group is on the same side as the propyl group.</p>
<p>NAME: TELMISARTAN</p>	

The above graphic is from the CHEM-X database.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND

DMF

DMF

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above and are acceptable.

RELATED DOCUMENTS: IND

CONSULTS:

VALIDATION: A validation package was sent, respectively, to laboratories in St. Louis and Philadelphia. Each laboratory confirmed receipt. The validation letter/forms are

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

attached to this review. The letter with the sample package sent to the Philadelphia District is dated June 17, 1998 and a copy of it is the entire amendment of that date. ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable as of March 27, 1998.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted an amendment, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product.

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Dr. Emmanuel Fadiran has reviewed the biopharmaceutics and dissolution section and has rendered an opinion.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for telmisartan in 40 and 80mg tablet strengths.

The July 10, 1998 amendment provides a response to the deficiencies communicated to the firm in our letter dated May 26, 1998.

CONCLUSIONS & RECOMMENDATIONS:

This reviewer recommends that this New Drug Application is approvable for Chemistry. Dr. Fadiran's Biopharmaceutics comment should be communicated to the firm.

cc: Orig. NDA 20-850
HFD-110/Division File
HFD-110/ CBerninger
HFD-110/ KBongiovanni, PM
Stoneham, Massachusetts District Office
HFD-810/ CHoiberg/JSimmons
R/D Init by: KSrinivasachar/
file name: c:\nda-rev\20850r5.doc

/S/

Carl J. Berninger, Ph.D.,

/S/
8-24-98

K. Bongiovanni

AUG 24 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-850 CHEMISTRY REVIEW #: 4 REVIEW DATE: August 20, 1998

**SUBMISSION: TYPE: DOCUMENT DATE:
Amendment 1S NDA July 15, 1998**

**CDER ORIGINAL NDA DATE: ASSIGNED DATE:
September 29, 1997 September 30, 1997**

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:

**Boehringer Ingelheim Pharmaceuticals, Inc.
a Subsidiary of
Boehringer Ingelheim Corporation
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877**

DRUG PRODUCT NAME:

**Proprietary: Micardis®
Nonproprietary/USAN: telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S**

**PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of telmisartan tablets**

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

DOSAGE FORM: tablet

STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

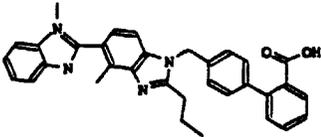
DISPENSED: Rx X OTC

NDA 20-850

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

Page 2

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

<p>ATC Number: 0183482AA</p> <p>DMF Number: 144701484</p> <p>Formula: C(33)H(30)N(4)O(2)</p> <p>Mol. Wt.: 514.00</p>	 <p>The image shows the chemical structure of Telmisartan, which consists of a benzimidazole ring system substituted with a methyl group and a propyl group, connected via a methylene bridge to a biphenyl ring system substituted with a propyl group and a carboxylic acid group.</p>
<p>NAME: TELMISARTAN</p>	

The above graphic is from the CHEM-X database.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND

DMF

DMF

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above and are acceptable.

RELATED DOCUMENTS: IND

CONSULTS:

VALIDATION: A validation package was sent, respectively, to laboratories in St. Louis and Philadelphia. Each laboratory confirmed receipt.

ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable as of March 27, 1998.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted an amendment, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product.

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Emmanuel Fadiran will review the biopharmaceutics and dissolution section and render an opinion. His review is in draft form as of this date.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for telmisartan in 40 and 80mg tablet strengths.

This amendment provides revised container labels for the box in which the blisters will be placed, and blister labels, in response to our deficiency letter dated July 9, 1998.

BI asks that we give chemistry approval, as soon as possible, for the immediate container and blister labels so that printing may proceed before the launch. BI is assuming approval this fall.

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

CONCLUSIONS & RECOMMENDATIONS:

All the labeling deficiencies have been corrected except one.

This change was communicated to the firm by Ms. Bongiovanni and should be included in the final letter.

After this one change is made, the external carton label and blister label is approved for Chemistry.

cc: Orig. NDA 20-850
HFD-110/Division File
HFD-110/ CBerninger
HFD-110/ KBongiovanni, PM
Stoneham, Massachusetts District Office
HFD-810/ CHOiberg/JSimmons
R/D Init by: KSrinivasachar/

file name: c:\nda-rev\20850r4.doc

JSI

Carl J. Berninger, Ph.D.,

8-21-98

JSI

JUN 26 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-850 CHEM. REVIEW #: 3 REVIEW DATE: June 25, 1998

**SUBMISSION: TYPE: DOCUMENT DATE:
Amendment 1S May 15, 1998
Amendment June 8, 1988**

**CDER ORIGINAL NDA DATE: ASSIGNED DATE:
September 29, 1997 September 30, 1997**

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:

Boehringer Ingelheim Pharmaceuticals, Inc.
a Subsidiary of
Boehringer Ingelheim Corporation
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877

DRUG PRODUCT NAME:

Proprietary: Micardis®
Nonproprietary/USAN: telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S

**PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of telmisartan tablets**

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

DOSAGE FORM: tablet

STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

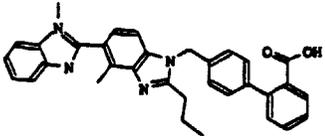
DISPENSED: x Rx OTC

NDA 20-850

Page 2

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

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

NI Number: 0183482AA	
CAF Number: 144701484	
Formula: C(33)H(30)N(4)O(2)	
Mol. Wt.: 514.00	
NAME: TELMISARTAN	

The above graphic is from the CHEM-X database.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND

DMF

DMF

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above.

RELATED DOCUMENTS: IND

CONSULTS:

VALIDATION: A validation package was sent, respectively, to laboratories in St. Louis and Philadelphia. Each laboratory confirmed receipt.

ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable as of March 27, 1998.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted an amendment, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product.

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Emmanuel Fadiran will review the biopharmaceutics and dissolution section and render an opinion. His review is in draft form as of this date.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for telmisartan in 40 and 80mg tablet strengths.

These amendments provide immediate container labels (original and updated) for the box in which the blisters will be placed, blister labels, MSDS, and drug substance stability data.

BI asks that we give chemistry approval, as soon as possible, for the immediate container labels and blister labels so that printing may proceed before the launch. BI is assuming approval this fall.

CONCLUSIONS & RECOMMENDATIONS:

This reviewer recommends the changes listed in the Deficiencies/Comment section of this review.

cc: Orig. NDA 20-850
HFD-110/Division File
HFD-110/ CBerninger
HFD-110/ KBohgiovanni, PM
Stoneham, Massachusetts District Office
HFD-810/ CHOiberg/JSimmons
R/D Init by: KSrinivasachar/

/S/

Carl J. Berninger, Ph.D.,

/S/

file name: c:\nda-rev\20850r3.doc

6-25-98

NID 08/10/1998
JUN 16 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
= **Review of Chemistry, Manufacturing, and Controls**

NDA #: 20-850 **CHEM. REVIEW #:** 2 **REVIEW DATE:** June 10, 1998

SUBMISSION: **TYPE:** **DOCUMENT DATE:**
Amendment 1S March 3, 1998

CDER DATE: **ASSIGNED DATE:**
March 4, 1998 March 4, 1998

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:
Boehringer Ingelheim Pharmaceuticals, Inc.
a Subsidiary of
Boehringer Ingelheim Corporation
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877

DRUG PRODUCT NAME:
Proprietary: Micardis®
Nonproprietary/USAN: telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S

PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of telmisartan tablets

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

DOSAGE FORM: tablet

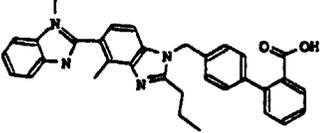
STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

DISPENSED: x Rx OTC

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

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

<p>EC Number: 0183482AA</p> <p>CAF Number: 144701484</p> <p>Formula: C(33)H(30)N(4)O(2)</p> <p>Mol Wt.: 514.00</p>	 <p>The image shows the chemical structure of Telmisartan, a dual angiotensin II receptor antagonist. It features a central benzimidazole ring system with a methyl group at the 2-position and a propyl group at the 2'-position. This central system is connected via a methylene bridge to a biphenyl ring system, which has a carboxylic acid group at the 2-position.</p>
<p>NAME: TELMISARTAN</p>	

The above graphic is from the CHEM-X Service.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND/

DMF

DMF

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above.

RELATED DOCUMENTS: IND/

CONSULTS:

VALIDATION: A validation package was sent, respectively, to laboratories in St. Louis and Philadelphia. Each laboratory confirmed receipt.

Boehringer Ingelheim Pharmaceuticals, Inc.
Micardis® (telmisartan) tablets

ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable. See review #1.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted an amendment, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product.

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Emmanuel Fadiran will review the biopharmaceutics and dissolution section and render an opinion.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for telmisartan in 40 and 80mg tablet strengths.

This amendment provides additional information as to name and address of manufacturer, flow chart and narrative description, in-process control procedures, material quality control, impurities, analytical validation, and batch analysis.

CONCLUSIONS & RECOMMENDATIONS:

NOT APPROVABLE

No additional deficiencies were found. The deficiencies noted in the "List" should be corrected by the firm, but are not of a nature to impede approval as far as the manufacturing and controls portion of this application is concerned.

cc: Orig. NDA 20-850
HFD-110/Division File
HFD-110/CBerninger
HFD-110/KBongiovanni, PM
Stoneham, Massachusetts District Office
HFD-810/CHoiberg/JSimmons
R/D Init by: KSrinivasachar/

file name: c:\nda-rev\20850r2.doc

JS/
Carl J. Berninger, Ph.D.,

JS/

6-15-98

DW EDWARDS
MAY 4 1998

DIVISION OF CARDIO-RENAL DRUG PRODUCTS

Review of Chemistry, Manufacturing, and Controls

NDA #: 20-850 CHEM. REVIEW #: 1 REVIEW DATE: April 30, 1998

SUBMISSION: TYPE: DOCUMENT DATE:

Original NDA 1S September 26, 1997
Amendment No. 3 October 28, 1997 (confirmation of trade name)

CDER DATE: ASSIGNED DATE:

September 29, 1997 September 30, 1997

ORIGINAL: yes

NAME & ADDRESS OF APPLICANT:

Boehringer Ingelheim Pharmaceuticals, Inc.
90 Ridgebury Road
P. O. Box 368
Ridgefield, Connecticut 06877

DRUG PRODUCT NAME:

Proprietary: Micardis®
Nonproprietary/USAN: Telmisartan (INN and USAN)
Code Name/#: BIBR 277 SE; BI-BR277; BIBR0277SE
Chem.Type/Ther.Class: 1S

PATENT STATUS: U. S. Patent Number 5,591,762; expiration date, January 7, 2014;
covers the formulation, composition, and/or method of use of Telmisartan tablets...

PHARMACOL.CATEGORY/INDICATION: Antihypertensive

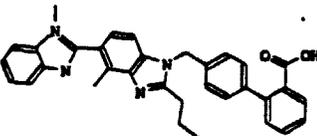
DOSAGE FORM: tablet

STRENGTHS: 40 and 80 mg

ROUTE OF ADMINISTRATION: oral

DISPENSED: x Rx OTC

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

BE Number: 0183482AA DMF Number: 144701484 Formula: C(33)H(30)N(4)O(2) Weight: 514.00	
NAME: TELMISARTAN	

The above graphic is from the CHEM-X Service.

CHEMICAL NAME: 4'-[(1,4'-dimethyl-2'-propyl-[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid

SUPPORTING DOCUMENTS:

IND

DMF

DMF

DMF

DMF

DMF

DMF

All the DMFs referenced in the submission are given above.

RELATED DOCUMENTS: IND

CONSULTS:

VALIDATION: When we are sure there are no more changes needed in the regulatory methods, validation will be requested.

ESTABLISHMENT EVALUATION: A completed EES request was sent to Compliance on November 5, 1997, after the POC was designated by BI Regulatory Affairs. Both facilities were judged acceptable.

BRAND NAME: Firm proposed Micardis™ and the Labeling and Nomenclature Committee found no reason to object, as of May 22, 1997. A second request for trademark review was submitted to the committee and again the committee found no reason to object, as of 2/18/98.

The firm submitted amendment No. 3, dated October 28, 1997, to inform us that they plan to use the brand name Micardis™ for this drug product. Satisfactory

STATISTICS: Review of drug product stability data. The drug substance and drug product are stable enough not to need a formal Statistical review.

MICROBIOLOGY: This drug substance is entirely synthetic, thus a Microbiological Consult is not needed.

BIOPHARMACEUTICS: Emmanuel Fadiran will review the biopharmaceutics and dissolution section and render an opinion.

ENVIRONMENTAL ASSESSMENT: The submitted request for exemption is acceptable.

REMARKS/COMMENTS:

Boehringer Ingelheim Pharmaceuticals is requesting NDA approval for Telmisartan in 40 and 80mg tablet strengths.

This NDA is unusual in that for each section, short summaries are given and then the full laboratory signed report. Generally the firm provides only summary information, not the actual laboratory report which gives the details.

CONCLUSIONS & RECOMMENDATIONS:

NOT APPROVABLE

The deficiencies noted in the "List" should be corrected by the firm, but are not of a nature to impede approval as far as the manufacturing and controls portion of this application is concerned.

- cc: Orig. NDA 20-850
- HFD-110/Division File
- HFD-110/CBerninger
- HFD-110/ KBongiovanni, PM
- District
- HFD-810/CHoiberg/JSimmons

/S/

Carl J. Berninger, Ph.D.,

R/D Init by: J. Short/

file name: c:\nda-rev\20850r1x.doc

IS/ 5/1/98