

CENTER FOR DRUG EVALUATION AND RESEARCH

21-397
Application Number **21-423**
21-424

CHEMISTRY REVIEW(S)

NDA 21-397

Neurontin (gabapentin) Capsules

Pfizer Inc.

Michael C. Theodorakis, Ph.D.

Division of New Drug Chemistry II (HFD-820)

**Division of Anesthetic, Drug Abuse and Critical Care Drug
Products (HFD-170)**

Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	5
The Executive Summary.....	9
I. Recommendations	9
A. Recommendation and Conclusion on Approvability.....	9
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable...9	
II. Summary of Chemistry Assessments.....	9
A. Description of the Drug Product(s) and Drug Substance(s)	9
B. Description of How the Drug Product is Intended to be Used.....	9
C. Basis for Approvability or Not-Approval Recommendation	10
III. Administrative.....	10
A. Reviewer's Signature	10
B. Endorsement Block	10
C. CC Block.....	10
Chemistry Assessment.....	11
I. DRUG SUBSTANCE.....	11
1. Description & Characterization.....	11
a. Description.....	11
b. Characterization / Proof Of Structure.....	11
2. Manufacturer	11
3. Synthesis / Method Of Manufacture.....	11

a.	Starting Materials - Specs & Tests.....	11
b.	Solvents, Reagents, etc.	11
c.	Flow Chart.....	11
d.	Detailed Description.....	11
4.	Process Controls.....	11
a.	Reaction Completion / Other In-Process Tests.....	11
a.	Preparation.....	12
6.	Regulatory Specifications / Analytical Methods.....	12
a.	Drug Substance Specifications & Tests.....	12
b.	Purity Profile.....	13
c.	Microbiology.....	13
7.	Container/Closure System For Drug Substance Storage ...	13
8.	Drug Substance Stability.....	13
II.	<u>DRUG PRODUCT</u>	14
1.	<u>Components/Composition:</u>	14
2.	<u>Specifications & Methods For Drug Product Ingredients</u>	16
a.	<u>Active Ingredient(s):</u>	16
b.	<u>Inactive Ingredients</u>	17
3.	Manufacturer	17
4.	Methods Of Manufacturing And Packaging.....	17
a.	Production Operations	17
b.	In-Process Controls & Tests.....	17
c.	Reprocessing Operations.....	17
5.	Regulatory Specifications And Methods For Drug Product:.....	17
a.	Sampling Procedures.....	17
b.	Regulatory Specifications And Methods.....	17
6.	<u>Container/Closure System:</u>	20
7.	<u>Microbiology:</u>	20
8.	Drug Product Stability:.....	20

III. INVESTIGATIONAL FORMULATIONS: 20

IV. ENVIRONMENTAL ASSESSMENT:..... 20

V. METHODS VALIDATION: 21

VI. LABELING: 21

VII. ESTABLISHMENT INSPECTION:..... 22

VIII. DRAFT DEFICIENCY LETTER..... 23

**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary Section

Chemistry Review Data Sheet

1. NDA 21-397
2. REVIEW # 1
3. March 3, 2002
4. Michael C. Theodorakis, Ph.D.

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
N/A Original application	

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	07-AUG-2001
Amendment (BZ), Labeling	20-DEC-2001
Amendment (BZ), Labeling	14-JAN-2002
Amendment (BZ), Labeling	11-FEB-2002

7. NAME & ADDRESS OF APPLICANT:

Parke-Davis Pharmaceuticals Inc.
 Name: Subsidiary of Pfizer Inc.

 Pfizer Inc.
 Address: 235 East 42nd Street
 New York, N.Y. 10017
 Representat Drusilla Scott, Ph. D.
 ive: Director

 Telephone: 734-622-1819

8. DRUG PRODUCT NAME/CODE/TYPE:

Executive Summary Section

- a) Proprietary Name: Neurontin Capsules
- b) Non-Proprietary Name gabapentin capsules
- c) Code Name/# :
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type : 6
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

Type 6 NDA:

10. PHARMACOL. CATEGORY:

11. DOSAGE FORM:

Capsules

12. STRENGTH/POTENCY:

100, 300, and 400 mg/capsule

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

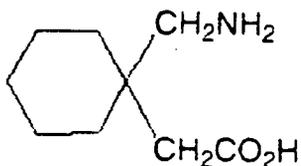
SPOTS product - Form Completed

Not a SPOTS product

Executive Summary Section

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

Gabapentin is described as 1-(aminomethyl) cyclohexaneacetic acid with a molecular formula of $C_9H_{17}NO_2$ and a molecular weight of 171.24. The structural formula of gabapentin is



Gabapentin is a white to off-white crystalline solid. It is freely soluble in water and both basic and acidic aqueous solutions.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS

¹ Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 -Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Executive Summary Section

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-235; approved	Neurontin (gabapentin) Capsules
NDA	20-882; approved	Neurontin (gabapentin) Tablets
NDA	21-129; approved	Neurontin (gabapentin) Oral Solution
NDA	21-216; approved pediatric	Neurontin (gabapentin) Oral Solution
NDA	21-397; Type 6 under review	Neurontin (gabapentin) Capsules
NDA	21-423; Type 6 under review	Neurontin (gabapentin) Tablets
NDA	21-424; Type 6 under review	Neurontin (gabapentin) Oral Solution
IND	28,454 (SN 423)	Neurontin (gabapentin) Capsules
IND	52,719	Neurontin (gabapentin) Capsules
IND	57,813	Neurontin (gabapentin) Oral Solution
IND	58,148	Neurontin (gabapentin) Capsules
IND	60,622	Neurontin (gabapentin) Capsules

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES			
Pharm/Tox			
Biopharm			
LNC			
Methods Validation			
OPDRA			
EA			
Microbiology			

Executive Summary Section

The Chemistry Review for NDA 21-397

The Executive Summary:

I. Recommendations

A. Recommendation and Conclusion on Approvability:

It is recommended that approval be granted to this NDA.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable:

No Phase IV commitments were made.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

This is a Type 6 NDA. All information about the manufacture and controls of the drug substance, gabapentin, is included in the approved NDA 20-235, Neurontin (gabapentin) Capsules.

Similarly, all information about the drug product is included in NDA 20-235.

The inactive ingredients for the capsules are lactose, cornstarch, and talc. The 100 mg capsule shell contains gelatin and titanium dioxide. The 300 mg capsule shell contains gelatin, titanium dioxide, and yellow iron oxide. The 400 mg capsule shell contains gelatin, red iron oxide, titanium dioxide, and yellow iron oxide. The imprinting ink contains FD&C Blue No.2 and titanium dioxide.

B. Description of How the Drug Product is Intended to be Used

The capsules will be available in bottles of 100 capsules and in unit-dose configuration of 50 capsules.

It is given orally with or without food to treat

Therapy may be initiated as a single 300 mg dose on Day 1, 600 mg/day (in 2 divided doses) on Day 2, and 900

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

/s/

Michael Theodorakis
5/13/02 04:00:32 PM
CHEMIST

Dale Koble
5/13/02 04:17:52 PM
CHEMIST

**APPEARS THIS WAY
ON ORIGINAL**

**THIS SECTION
WAS
DETERMINED
NOT
TO BE
RELEASABLE**

12 pages

NDA 21-423

Neurontin (gabapentin) Tablets

Pfizer Inc.

Michael C. Theodorakis, Ph.D.

Division of New Drug Chemistry II (HFD-820)

**Division of Anesthetic, Drug Abuse and Critical Care Drug
Products (HFD-170)**

Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	5
The Executive Summary.....	9
I. Recommendations	9
A. Recommendation and Conclusion on Approvability.....	9
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable...9	
II. Summary of Chemistry Assessments.....	9
A. Description of the Drug Product(s) and Drug Substance(s)	9
B. Description of How the Drug Product is Intended to be Used.....	9
C. Basis for Approvability or Not-Approval Recommendation	10
III. Administrative.....	10
A. Reviewer's Signature	10
B. Endorsement Block	10
C. CC Block.....	10
Chemistry Assessment.....	11
I. DRUG SUBSTANCE.....	11
1. Description & Characterization.....	11
a. Description.....	11
b. Characterization / Proof Of Structure.....	11
2. Manufacturer	11
3. Synthesis / Method Of Manufacture.....	11

a.	Starting Materials - Specs & Tests.....	11
b.	Solvents, Reagents, etc.....	11
c.	Flow Chart.....	11
d.	Detailed Description.....	11
4.	Process Controls.....	11
a.	Reaction Completion / Other In-Process Tests.....	11
a.	Preparation.....	12
6.	Regulatory Specifications / Analytical Methods.....	12
a.	Drug Substance Specifications & Tests.....	12
b.	Purity Profile.....	13
c.	Microbiology.....	13
7.	Container/Closure System For Drug Substance Storage	13
8.	Drug Substance Stability.....	13
II.	DRUG PRODUCT.....	14
1.	<u>Components/Composition:</u>	14
2.	<u>Specifications & Methods For Drug Product Ingredients</u>	16
a.	<u>Active Ingredient(s):</u>	16
b.	<u>Inactive Ingredients</u>	17
3.	Manufacturer	17
4.	Methods Of Manufacturing And Packaging.....	17
a.	Production Operations	17
b.	In-Process Controls & Tests	17
c.	Reprocessing Operations.....	17
5.	Regulatory Specifications And Methods For Drug Product:.....	17
a.	Sampling Procedures	17
b.	Regulatory Specifications And Methods.....	18
6.	<u>Container/Closure System:</u>	18
7.	<u>Microbiology:</u>	18
8.	Drug Product Stability:.....	18

III. INVESTIGATIONAL FORMULATIONS: 18

IV. ENVIRONMENTAL ASSESSMENT: 18

V. METHODS VALIDATION: 20

VI. LABELING: 20

VII. ESTABLISHMENT INSPECTION: 20

VIII. DRAFT DEFICIENCY LETTER 21

**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary Section

Chemistry Review Data Sheet

1. NDA 21-423
2. REVIEW # 1
3. March 3, 2002
4. Michael C. Theodorakis, Ph.D.
5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
N/A Original application	

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	07-AUG-2001
Amendment (BZ), Labeling	20-DEC-2001
Amendment (BZ), Labeling	14-JAN-2002
Amendment (BZ), Labeling	11-FEB-2002

7. NAME & ADDRESS OF APPLICANT:

Parke-Davis Pharmaceuticals Inc.
Name: Subsidiary of Pfizer Inc.

Pfizer Inc.
Address: 235 East 42nd Street
New York, N.Y. 10017

Representative: Drusilla Scott, Ph. D.
ive: Director

Telephone: 734-622-1819

8. DRUG PRODUCT NAME/CODE/TYPE:

Executive Summary Section

- a) Proprietary Name: Neurontin Tablets
- b) Non-Proprietary Name gabapentin tablets
- c) Code Name/# :
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type : 6
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

Type 6 NDA:

10. PHARMACOL. CATEGORY:

11. DOSAGE FORM:

Tablets

12. STRENGTH/POTENCY:

600, and 800 mg/tablet

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

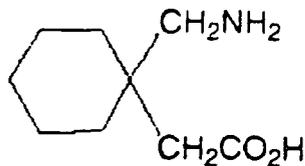
_____ SPOTS product - Form Completed

Not a SPOTS product

Executive Summary Section

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

Gabapentin is described as 1-(aminomethyl) cyclohexaneacetic acid with a molecular formula of $C_9H_{17}NO_2$ and a molecular weight of 171.24. The structural formula of gabapentin is



Gabapentin is a white to off-white crystalline solid. It is freely soluble in water and both basic and acidic aqueous solutions.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS

¹ Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 -Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Executive Summary Section

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-235; approved	Neurontin (gabapentin) Capsules
NDA	20-882; approved	Neurontin (gabapentin) Tablets
NDA	21-129; approved	Neurontin (gabapentin) Oral Solution
NDA	21-216; approved pediatric	Neurontin (gabapentin) Oral Solution
NDA	21-397; Type 6 under review	Neurontin (gabapentin) Capsules
NDA	21-423; Type 6 under review	Neurontin (gabapentin) Tablets
NDA	21-424; Type 6 under review	Neurontin (gabapentin) Oral Solution
IND	28,454 (SN 423)	Neurontin (gabapentin) Capsules
IND	52,719	Neurontin (gabapentin) Capsules
IND	57,813	Neurontin (gabapentin) Oral Solution
IND	58,148	Neurontin (gabapentin) Capsules
IND	60,622	Neurontin (gabapentin) Capsules

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES			
Pharm/Tox			
Biopharm			
LNC			
Methods Validation			
OPDRA			
EA			
Microbiology			

Executive Summary Section

The Chemistry Review for NDA 21-397

The Executive Summary:

I. Recommendations

A. Recommendation and Conclusion on Approvability:

It is recommended that approval be granted to this NDA.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable:

No Phase IV commitments were made.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

This is a Type 6 NDA. All information about the manufacture and controls of the drug substance, gabapentin, is included in the approved NDA 20-882, Neurontin (gabapentin) Tablets.

Similarly, all information about the drug product is included in NDA 20-882.

The inactive ingredients for the tablets are poloxamer 407, copolyvidonum, cornstarch, magnesium stearate, hydroxypropyl cellulose, talc, candelilla wax and purified water. The imprinting ink for the 600 mg tablets contains synthetic black iron oxide, pharmaceutical shellac, pharmaceutical glaze, propylene glycol, ammonium hydroxide, isopropyl alcohol and n-butyl alcohol. The imprinting ink for the 800 mg tablets contains synthetic yellow iron oxide, synthetic red iron oxide, hydroxypropyl methylcellulose, propylene glycol, methanol, isopropyl alcohol and deionized water.

B. Description of How the Drug Product is Intended to be Used

The tablets will be available in bottles of 100 and 500 tablets and in unit-dose configuration of 50 tablets.

Executive Summary Section

It is given orally with or without food to treat

Therapy may be initiated as a single 300 mg dose on Day 1, 600 mg/day (in 2 divided doses) on Day 2, and 900 mg/day (in 3 divided doses) on Day 3. The maximum daily dose is 3600 mg (in 3 divided doses). Clinical efficacy was demonstrated at doses of 1800 to 3600 mg/day.

C. Basis for Approvability or Not-Approval Recommendation

This is an approved drug product under NDA 20-882. The NDA under review is a Type 6 NDA that provides for a new indication. The environmental assessment has showed that the new indication will result to an appreciable amount of gabapentin being introduced into the environment.

This was acceptable and it was based on the following assumptions. The amount of total worldwide gabapentin production was estimated to be _____ . This number exceeded by _____ the actual world wide total production of gabapentin. The second assumption was that the total worldwide production of gabapentin would be disposed in the US water supply. This would have resulted in a concentration (known as expected introduction concentration (EIC)) of _____ . This would have been far smaller than the minimum inhibitory concentration (MIC) for gabapentin which is 1000 ppm.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

Review Chemist/MCTheodorakis/March 12, 2002
Team Leader/DLKoble/
PM/KCompton/

C. CC Block

**THIS SECTION
WAS
DETERMINED
NOT
TO BE
RELEASABLE**

11 pages

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

/s/

Michael Theodorakis
5/13/02 04:09:26 PM
CHEMIST

Dale Koble
5/13/02 04:22:20 PM
CHEMIST

**APPEARS THIS WAY
ON ORIGINAL**

Table of Contents

Table of Contents	2
Chemistry Review Data Sheet.....	5
The Executive Summary.....	9
I. Recommendations	9
A. Recommendation and Conclusion on Approvability.....	9
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable...	9
II. Summary of Chemistry Assessments.....	9
A. Description of the Drug Product(s) and Drug Substance(s)	9
B. Description of How the Drug Product is Intended to be Used.....	9
C. Basis for Approvability or Not-Approval Recommendation	10
III. Administrative.....	10
A. Reviewer's Signature	10
B. Endorsement Block	10
C. CC Block.....	10
Chemistry Assessment.....	11
I. DRUG SUBSTANCE.....	11
1. Description & Characterization.....	11
a. Description.....	11
b. Characterization / Proof Of Structure.....	11
2. Manufacturer	11
3. Synthesis / Method Of Manufacture.....	11

a.	Starting Materials - Specs & Tests.....	11
b.	Solvents, Reagents, etc.	11
c.	Flow Chart.....	11
d.	Detailed Description.....	11
4.	Process Controls.....	11
a.	Reaction Completion / Other In-Process Tests.....	11
a.	Preparation.....	12
6.	Regulatory Specifications / Analytical Methods.....	12
a.	Drug Substance Specifications & Tests.....	12
b.	Purity Profile.....	13
c.	Microbiology.....	13
7.	Container/Closure System For Drug Substance Storage ...	13
8.	Drug Substance Stability.....	13
II.	DRUG PRODUCT.....	14
1.	<u>Components/Composition:</u>	14
2.	<u>Specifications & Methods For Drug Product Ingredients</u> 15	
a.	<u>Active Ingredient(s):</u>	15
b.	<u>Inactive Ingredients</u>	16
3.	Manufacturer	16
4.	Methods Of Manufacturing And Packaging.....	16
a.	Production Operations	16
b.	In-Process Controls & Tests.....	16
c.	Reprocessing Operations.....	16
5.	Regulatory Specifications And Methods For Drug Product:.....	16
a.	Sampling Procedures	16
b.	Regulatory Specifications And Methods.....	17
6.	<u>Container/Closure System:</u>	18
7.	<u>Microbiology:</u>	18
8.	Drug Product Stability:.....	18

III. INVESTIGATIONAL FORMULATIONS: 18

IV. ENVIRONMENTAL ASSESSMENT: 18

V. METHODS VALIDATION: 19

VI. LABELING: 19

VII. ESTABLISHMENT INSPECTION: 20

VIII. DRAFT DEFICIENCY LETTER 21

**APPEARS THIS WAY
ON ORIGINAL**

Executive Summary Section

Chemistry Review Data Sheet

1. NDA 21-424
2. REVIEW # 1
3. March 3, 2002
4. Michael C. Theodorakis, Ph.D.

5. PREVIOUS DOCUMENTS:

<u>Previous Documents</u>	<u>Document Date</u>
N/A Original application	

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	07-AUG-2001
Amendment (BZ), Labeling	20-DEC-2001
Amendment (BZ), Labeling	14-JAN-2002
Amendment (BZ), Labeling	11-FEB-2002

7. NAME & ADDRESS OF APPLICANT:

Parke-Davis Pharmaceuticals Inc.
 Name: Subsidiary of Pfizer Inc.

 Pfizer Inc.
 Address: 235 East 42nd Street
 New York, N.Y. 10017
 Representat Drusilla Scott, Ph.D.
 ive: Director
 Telephone: 734-622-1819

8. DRUG PRODUCT NAME/CODE/TYPE:

Executive Summary Section

- a) Proprietary Name: Neurontin Oral Solution
- b) Non-Proprietary Name gabapentin oral solution
- c) Code Name/# :
- d) Chem. Type/Submission Priority (ONDC only):
 - Chem. Type : 6
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

Type 6 NDA:

10. PHARMACOL. CATEGORY:

11. DOSAGE FORM:

Oral solution

12. STRENGTH/POTENCY:

50 mg/mL; 250 mg/5 mL;
470 mL bottle

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED: Rx OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

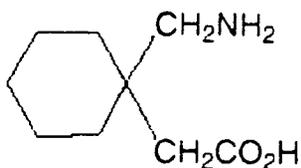
_____ SPOTS product - Form Completed

Not a SPOTS product

Executive Summary Section

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

Gabapentin is described as 1-(aminomethyl)cyclohexaneacetic acid with a molecular formula of C₉H₁₇NO₂ and a molecular weight of 171.24. The structural formula of gabapentin is



Gabapentin is a white to off-white crystalline solid. It is freely soluble in water and both basic and acidic aqueous solutions.

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS

¹ Action codes for DMF Table:

1 - DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 -Type 1 DMF

3 - Reviewed previously and no revision since last review

4 - Sufficient information in application

5 - Authority to reference not granted

6 - DMF not available

7 - Other (explain under "Comments")

² Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

Executive Summary Section

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA	20-235; approved	Neurontin (gabapentin) Capsules
NDA	20-882; approved	Neurontin (gabapentin) Tablets
NDA	21-129; approved	Neurontin (gabapentin) Oral Solution
NDA	21-216; approved pediatric	Neurontin (gabapentin) Oral Solution
NDA	21-397; Type 6 under review	Neurontin (gabapentin) Capsules
NDA	21-423; Type 6 under review	Neurontin (gabapentin) Tablets
NDA	21-424; Type 6 under review	Neurontin (gabapentin) Oral Solution
IND	28,454 (SN 423)	Neurontin (gabapentin) Capsules
IND	52,719	Neurontin (gabapentin) Capsules
IND	57,813	Neurontin (gabapentin) Oral Solution
IND	58,148	Neurontin (gabapentin) Capsules
IND	60,622	Neurontin (gabapentin) Capsules

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES			
Pharm/Tox			
Biopharm			
LNC			
Methods Validation			
OPDRA			
EA			
Microbiology			

Executive Summary Section

The Chemistry Review for NDA 21-397

The Executive Summary:

I. Recommendations

A. Recommendation and Conclusion on Approvability:

It is recommended that approval be granted to this NDA.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable:

No Phase IV commitments were made.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

This is a Type 6 NDA. All information about the manufacture and controls of the drug substance, gabapentin, is included in the approved NDA 21-129, Neurontin (gabapentin) Oral Solution.

Similarly, all information about the drug product is included in NDA 21-129.

The inactive ingredients for the oral solution are glycerin, xylitol, purified water and artificial cool strawberry anise flavor.

B. Description of How the Drug Product is Intended to be Used

The oral solution will be available in bottles of 470 mL and the concentration will be 50 mg/mL.

It is given orally with or without food to treat

Therapy may be initiated as a single 300 mg dose on Day 1, 600 mg/day (in 2 divided doses) on Day 2, and 900 mg/day (in 3 divided doses) on Day 3. The maximum daily dose is 3600 mg (in 3 divided doses). Clinical efficacy was demonstrated at doses of 1800 to 3600 mg/day.

Executive Summary Section

C. Basis for Approvability or Not-Approval Recommendation

This is an approved drug product under NDA 21-129. The NDA under review is a Type 6 NDA that provides for a new indication. The environmental assessment has showed that the new indication will result to an appreciable amount of gabapentin being introduced into the environment.

This was acceptable and it was based on the following assumptions. The amount of total worldwide gabapentin production was estimated to be, _____ This number exceeded by _____ the actual world wide total production of gabapentin. The second assumption was that the total worldwide production of gabapentin would be disposed in the US water supply. This would have resulted in a concentration (known as expected introduction concentration (EIC)) of _____ This would have been far smaller than the minimum inhibitory concentration (MIC) for gabapentin which is 1000 ppm.

III. Administrative**A. Reviewer's Signature****B. Endorsement Block**

Review Chemist/MCTheodorakis/March 12, 2002
Team Leader/DLKoble/
PM/KCompton/

C. CC Block

**THIS SECTION
WAS
DETERMINED
NOT
TO BE
RELEASABLE**

1/1 Pages

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

/s/

Michael Theodorakis
5/13/02 04:56:37 PM
CHEMIST

Dale Koble
5/13/02 05:01:25 PM
CHEMIST

**APPEARS THIS WAY
ON ORIGINAL**