

CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 21-208

CHEMISTRY REVIEW(S)

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: November 21, 2000

CHEMISTRY REVIEW: #7

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	November 13, 2000	November 13, 2000	November 17, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

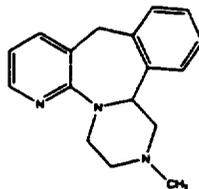
DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION: Depression
DOSAGE FORM: Orally Disintegrating Tablets
STRENGTHS: 15, 30 and 45 mg
ROUTE of ADMINISTRATION: oral
DISPENSED: RX OTC
SPECIAL PRODUCTS: Yes No

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine
USAN name: Mirtazapine
Chemical Formula: C₁₇H₁₉N₃
Molecular Weight: 265.36
Laboratory Code: none listed
Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
_____	_____	_____	Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
_____	_____	_____	Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
_____	_____	_____	Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
_____	_____	_____	Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____: Remeron® (mirtazapine) Tablets, depression Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: acceptable on 08-10-00
 CFN 2211109: acceptable on 02-01-00
withhold recommendation on 10-27-00
 Site removed from application 10-30-00.
 See review #6 for details

CFN 9610343: acceptable on 02-07-00
 CFN 9610349: acceptable on 10-27-00
 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: acceptable on 08-25-00
 CFN 1421954: acceptable on 08-01-00

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, we recommend **Approval** for application 21-208.

Sherita D. McLamore, Ph.D.
Review Chemist

Robert Seevers, Ph.D.
Chemistry Team Leader

cc:
Orig. NDA 21-208
HFD-120/Division File
HFD-810/CHoiberg
HFD-180/JSimmons
HFD-120/SMcLamore
HFD-120/RSeevers
HFD-120/PDavid

Filename: C:\WINDOWS\DESKTOP\Reviews\NDA's\NDA21208-VII.doc

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Jan 13 2000

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: June 8, 2000

CHEMISTRY REVIEW: #1

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Initial Submission	December 30, 1999	January 3, 2000	February 3, 2000
Amendment	February 17, 2000	February 18, 2000	February 18, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

HARMACOLOGICAL CATEGORY/INDICATION:

Depression

DOSE FORM:

Orally Disintegrating Tablets

STRENGTHS:

15, 30 and 45 mg

ROUTE of ADMINISTRATION:

oral

DISPENSED:

RX OTC
 Yes No

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine

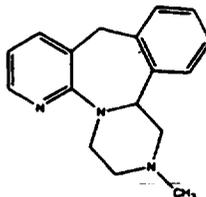
USAN name: Mirtazapine

Chemical Formula: C₁₇H₁₉N₃

Molecular Weight: 265.36

Laboratory Code: none listed

Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Inadequate Reviewed by S. McLamore	06-05-00	November 19, 1999

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. Remeron® (mirtazapine) Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: pending
 CFN 2211109: acceptable on 02-01-00
 CFN 9610343: acceptable on 02-07-00
 CFN 9610349: pending
 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: pending
 CFN 1421954: pending

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

Microbiology Consult

n/a

COMMENTS:

1. Remeron Orally Disintegrating Tablets are currently not marketed in any country.
2. Mirtazapine, which is marketed as a racemate, is an antidepressant agent that belongs to the piperazino-azepine group of compounds.
3. NDA 20-415 is referenced for the drug substance, mirtazapine.
4. Mirtazapine was approved for use in Remeron® (mirtazapine) Tablet as a solid oral dosage form for the treatment of depression (NDA 20-415, approved 14-June-96). To date, there is no USP monograph available.

5. On July 15, 1999, the applicant requested _____ (mirtazapine) Tablets as the trade name for the drug product. The request was denied by the agency on November 3, 1999. The applicant filed an appeal on December 6, 1999 and the decision is pending.
6. The dosage form is an orally disintegrating tablet available as a 15-, 30-, and 45 mg tablet, dosing once a day.

**APPEARS THIS WAY
ON ORIGINAL**

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, the application is Approvable with specific comments to be communicated to the firm (see draft letter comments at the end of this review).

/S/

Sherita D. McLamore, Ph.D.
Chemist

06-08-00

/S/

Robert Seevers, Ph.D.
Chemistry Team Leader

6/13/00

Orig. NDA 21-208
HFD-120/Division File
HFD-810/CHOiberg
HFD-180/JSimmons
HFD-120/SMcLamore
HFD-120/RSeevers
HFD-120/PDavid

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**APPEARS THIS WAY
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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: August 15, 2000

CHEMISTRY REVIEW: #2

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	July 13, 2000	July 17, 2000	July 18, 2000
Amendment	July 21, 2000	July 24, 2000	July 26, 2000
Amendment	July 27, 2000	July 24, 2000	July 26, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION:

Depression

DOSAGE FORM:

Orally Disintegrating Tablets

STRENGTHS:

15, 30 and 45 mg

ROUTE of ADMINISTRATION:

oral

DISPENSED:

RX OTC
 Yes No

SPECIAL PRODUCTS:CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine

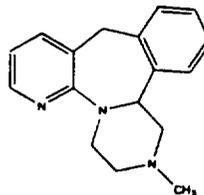
USAN name: Mirtazapine

Chemical Formula: C₁₇H₁₉N₃

Molecular Weight: 265.36

Laboratory Code: none listed

Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
			Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
			Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____, Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: inspection scheduled
 CFN 2211109: acceptable on 02-01-00
 CFN 9610343: acceptable on 02-07-00
 CFN 9610349: assigned inspection to IB
 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: assigned inspection to IB
 CFN 1421954: inspection performed

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

**APPEARS THIS WAY
ON ORIGINAL**

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, the application is **Approvable** with specific comment to be communicated to the applicant.

/S/

8-15-00

Sherita D. McLamore, Ph.D.
Review Chemist

/S/

8/16/00

Robert Seevers, Ph.D.
Chemistry Team Leader

- cc:
 Orig. NDA 21-208
 HFD-120/Division File
 HFD-810/CHOiberg
 HFD-180/JSimmons
 HFD-120/SMcLamore
 HFD-120/RSeevers
 HFD-120/PDavid

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
 Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: August 15, 2000

CHEMISTRY REVIEW: #3

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	August 14, 2000	August 14, 2000	August 14, 2000
Amendment	August 28, 2000	August 29, 2000	August 29, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
 375 Mt. Pleasant Avenue
 West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION:

Depression
 Orally Disintegrating Tablets

DOSAGE FORM:

15, 30 and 45 mg

STRENGTHS:

oral

ROUTE of ADMINISTRATION:

RX OTC
 Yes No

DISPENSED:

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine

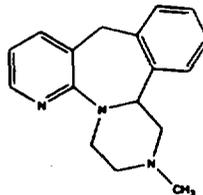
USAN name: Mirtazapine

Chemical Formula: C₁₇H₁₉N₃

Molecular Weight: 265.36

Laboratory Code: none listed

Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
			Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
			Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron[®] (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____ Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: acceptable on 08-10-00
 CFN 2211109: acceptable on 02-01-00
 CFN 9610343: acceptable on 02-07-00
 CFN 9610349: inspection scheduled
 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: acceptable on 07-25-00
 CFN 1421954: acceptable on 08-01-00

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

**APPEARS THIS WAY
ON ORIGINAL**

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, the application be Approved pending an acceptable recommendation from EES for CFN 9610349

ISI

9-06-00

Sherita D. McLamore, Ph.D.
Review Chemist

ISI
D.D. 11/1/00

9/11/00

Robert Seevers, Ph.D.
Chemistry Team Leader

- cc:
- Orig. NDA 21-208
- HFD-120/Division File
- HFD-810/CHoiberg
- HFD-180/JSimmons
- HFD-120/SMcLamore
- HFD-120/RSeevers
- HFD-120/PDavid

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: October 20, 2000

CHEMISTRY REVIEW: #5

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	October 5, 2000	October 10, 200	October 13, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION:

Depression

DOSAGE FORM:

Orally Disintegrating Tablets

STRENGTHS:

15, 30 and 45 mg

ROUTE of ADMINISTRATION:

oral

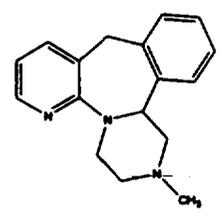
DISPENSED:

RX OTC
 Yes No

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine
USAN name: Mirtazapine
Chemical Formula: C₁₇H₁₉N₃
Molecular Weight: 265.36
Laboratory Code: none listed
Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
			Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
		International	Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____ Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: acceptable on 08-10-00
 CFN 2211109: acceptable on 02-01-00
 CFN 9610343: acceptable on 02-07-00
 CFN 9610349: inspection scheduled
 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: acceptable on 08-25-00
 CFN 1421954: acceptable on 08-01-00

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

**APPEARS THIS WAY
ON ORIGINAL**

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, the application is **Approvable** with specific comment to be communicated to the applicant.

1/5/

10-20-00

Sherita D. McLamore, Ph.D.
Review Chemist

1/5/

10/27/00

Robert Seevers, Ph.D.
Chemistry Team Leader

- cc:
- Orig. NDA 21-208
- HFD-120/Division File
- HFD-810/CHOiberg
- HFD-180/JSimmons
- HFD-120/SMcLamore
- HFD-120/RSeevers
- HFD-120/PDavid

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: September 27, 2000

CHEMISTRY REVIEW: #4

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Amendment	August 30, 2000	September 5, 2000	September 7, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary: [redacted]
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION:

Depression

DOSAGE FORM:

Orally Disintegrating Tablets

STRENGTHS:

15, 30 and 45 mg

ROUTE of ADMINISTRATION:

oral

DISPENSED:

RX OTC
 Yes No

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine

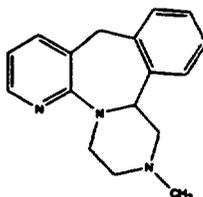
USAN name: Mirtazapine

Chemical Formula: C₁₇H₁₉N₃

Molecular Weight: 265.36

Laboratory Code: none listed

Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
			Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
			Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____ Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

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 CFN 2211109: acceptable on 02-01-00
 CFN 9610343: acceptable on 02-07-00
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 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: acceptable on 07-25-00
 CFN 1421954: acceptable on 08-01-00

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

**APPEARS THIS WAY
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CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, the application be Approved pending an acceptable recommendation from EES for CFN 9610349

ISI

[Signature] 9-27-00
Sherita D. McLamore, Ph.D.
Review Chemist

[Signature] 10/16/00
Robert Seevers, Ph.D.
Chemistry Team Leader

- cc:
- Orig. NDA 21-208
- HFD-120/Division File
- HFD-810/CHOiberg
- HFD-180/JSimmons
- HFD-120/SMcLamore
- HFD-120/RSeevers
- HFD-120/PDavid

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DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
Review of Chemistry, Manufacturing, and Controls

NDA NUMBER: 21-208

DATE REVIEWED: October 30, 2000

CHEMISTRY REVIEW: #6

REVIEWER: Sherita McLamore, Ph.D.

<u>SUBMISSION TYPE</u>	<u>DOCUMENT DATE</u>	<u>CDER DATE</u>	<u>ASSIGNED DATE</u>
Fax	October 30, 2000	n/a	October 30, 2000
Fax	October 27, 2000	n/a	October 30, 2000

NAME and ADDRESS of APPLICANT:

Organon Inc.
375 Mt. Pleasant Avenue
West Orange, New Jersey 07052

DRUG PRODUCT NAME:

Proprietary:
Non proprietary/USAN: Mirtazapine
Code Name/Number: ORG3770
Chem. Type/Ther. Class: 3S

PHARMACOLOGICAL CATEGORY/INDICATION:

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DOSAGE FORM:

Orally Disintegrating Tablets

STRENGTHS:

15, 30 and 45 mg

ROUTE of ADMINISTRATION:

oral

DISPENSED:

RX OTC
 Yes No

SPECIAL PRODUCTS:

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA:

CA name: 1,2,3,4,10,14b-hexahydro-2-methyl-pyrazino[2, 1-a]pyrido[2, 3-c][2]benzazepine

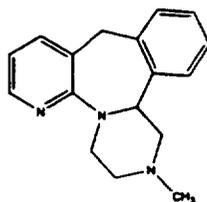
USAN name: Mirtazapine

Chemical Formula: C₁₇H₁₉N₃

Molecular Weight: 265.36

Laboratory Code: none listed

Chemical Structure:



SUPPORTING DOCUMENTS:

TYPE/ NUMBER	SUBJECT	HOLDER/ SPONSOR	STATUS	REVIEW DATE	LETTER DATE
			Adequate Reviewed by J. C. Leaks	1-17-00	November 29, 1999
			Adequate Reviewed by S. McLamore	8-11-00	November 19, 1999
			Adequate Reviewed by S. McLamore	7-26-00	June 30, 2000
		ai nd	Adequate Reviewed by S. McLamore	7-26-00	August 6, 2000

RELATED DOCUMENTS:

1. NDA 20-415: Remeron® (mirtazapine) Tablets, depression, Organon, Approved June 14, 1996
2. _____) Tablets, depression
Organon

OTHER REQUESTS:

Establishment Evaluation Request 7 sites

CFN 2133545: acceptable on 08-10-00
 CFN 2211109: acceptable on 02-01-00
withhold recommendation on 10-27-00
 CFN 9610343: acceptable on 02-07-00
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 CFN 2529406: acceptable on 02-01-00
 CFN 9610342: acceptable on 08-25-00
 CFN 1421954: acceptable on 08-01-00

Methods Validation Pending

The following test methods will be submitted to the FDA laboratories after all review issues are resolved: identification and assay by HPLC; determination of related substances; content uniformity testing by UV and dissolution.

**APPEARS THIS WAY
ON ORIGINAL**

*Site removed from application 10-30-00. See review for details

CONCLUSIONS and RECOMMENDATIONS:

From a CMC perspective, we recommend Approval for application 21-208.

/S/

10-30-00

Sherita D. McLamore, Ph.D.
Review Chemist

/S/

10/24/00

Robert Seevers, Ph.D.
Chemistry Team Leader

- cc:
- Orig. NDA 21-208
- HFD-120/Division File
- HFD-810/CHOiberg
- HFD-180/JSimmons
- HFD-120/SMcLamore
- HFD-120/RSeevers
- HFD-120/PDavid

Filename: C:\WINDOWS\DESKTOP\Reviews\NDA's\NDA21208-VI.doc

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WAS
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NOT
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