

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-350

CHEMISTRY REVIEW(S)



NDA 21-350

TRIGLIDE[®]
(fenofibrate tablets)

SkyePharma Inc.

Elsbeth Chikhale, Ph.D.
Division of Metabolic and Endocrine Drug Products



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Chemistry Review Data Sheet

1. NDA 21-350
2. REVIEW #: 3
3. REVIEW DATE: 29-APR-2005
4. REVIEWER: Elsbeth Chikhale, Ph.D.
5. PREVIOUS DOCUMENTS: CMC Review #1, dated April 10, 2002
CMC Review #2, dated December 6, 2004

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Incomplete response to December 14, 2004 letter	28-JAN-2005
Amendment to Incomplete response ¹	3-MAR-2005
Amendment to Incomplete response ²	3-MAR-2005
Amendment to Incomplete response ³	15-APR-2005
Amendment to Incomplete response ⁴	27-APR-2005

¹applicant's responses to the Agency's information request

²applicant's responses to the Agency's information request

³applicant's responses to the Agency's information request

⁴applicant's correction to monograph 672-5

7. NAME & ADDRESS OF APPLICANT:

Name: SkyePharma Inc.

Address: 10450 Science Center Drive
San Diego, CA 92121

Representative:

Telephone: (858) 625-2424

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: TRIGLIDE*
- b) Non-Proprietary Name (USAN): Fenofibrate tablet
- c) Code Name/#: N/A
- d) Chem. Type/Submission Priority:
 - Chem. Type: 3
 - Submission Priority: S

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

This is a 505(b)(2) resubmission / complete response to deficiency letter

10. PHARMACOL. CATEGORY:

Lipid Altering Agent II

11. DOSAGE FORM: tablets

12. STRENGTH/POTENCY: 50 mg/tablet and 160 mg/tablet

13. ROUTE OF ADMINISTRATION: oral

14. Rx/OTC DISPENSED: Rx OTC

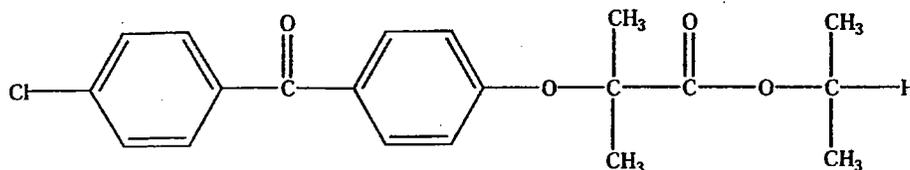
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product Form Completed (for Egg Lecithin, one of the excipients)

Not a SPOTS product

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

2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid-1-methylethyl ester



$C_{20}H_{21}ClO_4$

Molecular Weight: 360.8



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
500	II			3	Adequate	12/ 30/03	Reviewed by M. Shaikh
	IV			1	Adequate	4/4/02	Review by Yvonne Yang, Ph.D.
	III			f 3	Adequate	10/6/03	Reviewed by William Timmer, Ph.D.
	III			1, 4	N/A		

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 relevant 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)

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CHEMISTRY REVIEW



Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA (Abbott)	19-304	Fenofibrate capsules
NDA (Abbott)	21-656	Fenofibrate tablets
NDA (Reliant Pharma)	21-695	Fenofibrate capsules
NDA (Abbott)	21-203	Fenofibrate tablets
NDA (Cipher Pharma)	21-612	Fenofibrate capsules
IND (RTP)	60,743	Fenofibrate tablets

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Acceptable EER	12/7/04	Elsbeth Chikhale, Ph.D.
Biopharm	Dissolution specifications acceptable	4/12/05	Wei Qiu, Ph.D.
Methods Validation	Adequate for release and stability studies	12/6/04	Elsbeth Chikhale, Ph.D.
ODS	Triglide: Acceptable	9/28/04	Tia M. Harper-Velazquez, Pharm.D.
EA	Acceptable	12/6/04	Elsbeth Chikhale, Ph.D.

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On Original

The Chemistry Review for NDA 21-350

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 21-350 is **recommended for approval** from the standpoint of chemistry, manufacture and controls. The submitted stability data support 18 months of expiry for the 160 mg tablets (as proposed) and 12 months of expiry for the 50 mg tablets

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

None

II. Summary of Chemistry Assessments

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

1) Drug Product

The drug product, described in this 505(b)(2) NDA, is an immediate release uncoated tablet for oral administration. The product is intended to be used for the treatment of hypercholesterolemia and treatment of hypertriglyceridemia (Fredrickson Type IV and V). The drug product comes in a 50 mg and a 160 mg strength and is packaged in  bottles containing 90 tablets/bottle. The proposed storage is controlled room temperature. The original NDA was submitted on 6/22/01 and was found approvable from a CMC standpoint on 4/24/02. The main deficiency was the instability of the drug product. The applicant reformulated the drug product and filed a resubmission on 3/31/04. This application was found approvable on 12/14/04 and had biopharmaceutics, CMC and regulatory deficiencies. The CMC deficiencies mainly pertained to the drug product specifications and their impact on the drug product quality. Responses to each CMC deficiency were provided in amendments dated 1/28/05, 3/4/05, 4/15/05 and 4/27/05. The submitted stability data support a 12 months expiration date for the 50 mg tablets and a 18 month expiry date for the 160 mg tablets.

2) Drug Substance

Fenofibrate is a fibric acid derivative with lipid altering properties. It is a white or almost white crystalline powder, insoluble in water. Fenofibric acid is the active metabolite of fenofibrate, and is responsible for the pharmacological activity. The drug substance is stable for 5 years at room temperature (DMF  review #2, dated 5/27/03). The applicant suggests that the particle size of the drug substance is important for the bioavailability. Therefore, the drug substance particle size is controlled in the drug substance itself, as well as in the tablet formulation.

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

Patients should receive this drug product in combination with an appropriate lipid-lowering diet. The bioavailability of the drug product is optimized when taken with food. The initial dose is 50 mg or 160 mg per day (1 tablet per day). Per the proposed label, the dosage should be individualized according to the patient's response, measured at 4 to 8 week intervals. The maximum daily dose is 160 mg/day.



C. Basis for Approvability or Not-Approval Recommendation

This NDA is recommended for approval from the CMC standpoint. The applicant has satisfactorily responded to all CMC deficiencies.

III. Administrative

A. Reviewer's Signature

Elsbeth Chikhale, Ph.D.

Signatures attached in DFS.

15 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

Withheld Track Number: Chemistry- /

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

/s/

Elsbeth Chikhale
5/2/05 09:05:45 AM
CHEMIST

Mamta Gautam-Basak
5/2/05 09:15:33 AM
CHEMIST

Concur, minor comment on storage statement to be forwarded.



NDA 21-350

TRIGLIDE[®]
(fenofibrate tablets)

SkyePharma Inc.

Elsbeth Chikhale, Ph.D.
Division of Metabolic and Endocrine Drug Products



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2. Specifications for drug product ingredients	13
3. Manufacturer	16
4. Method of Manufacturing and Packaging	17
5. Regulatory Specifications for the drug product	23
6. Container/closure system	30
7. Stability of Drug Product	33
C. Investigational Formulations	43
D. Environmental Impact Analysis Report	43
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F. Labeling	44
G. Establishment Inspection	44
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Chemistry Review Data Sheet

1. NDA 21-350
2. REVIEW #: 2
3. REVIEW DATE: 6-DEC-2004
4. REVIEWER: Elsbeth Chikhale, Ph.D.
5. PREVIOUS DOCUMENTS: CMC Review #1, dated April 10, 2002

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Resubmission (RS)	31-MAR-2004
Amendment to RS ¹	19-MAY-2004
Amendment to RS ²	30-JUL-2004
Amendment to RS ³	26-OCT-2004
Amendment to RS ⁴	16-NOV-2004

- 1) applicant's responses to the Agency's information request
- 2) applicant's responses to the Agency's information request
- 3) applicant's responses to the Agency's information request
- 4) applicant's responses to the Agency's information request

7. NAME & ADDRESS OF APPLICANT:

Name: SkyePharma Inc.

Address: 10450 Science Center Drive
San Diego, CA 92121

Representative:

Telephone: (858) 625-2424

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: TRIGLIDE®
- b) Non-Proprietary Name (USAN): Fenofibrate tablet
- c) Code Name/#: N/A
- d) Chem. Type/Submission Priority:

- Chem. Type: 3
- Submission Priority: S

Chemistry Review Data Sheet

9. LEGAL BASIS FOR SUBMISSION:

This is a 505(b)(2) resubmission.

10. PHARMACOL. CATEGORY:

Lipid Altering Agent II

11. DOSAGE FORM: tablets

12. STRENGTH/POTENCY: 50 mg/tablet and 160 mg/tablet

13. ROUTE OF ADMINISTRATION: oral

14. Rx/OTC DISPENSED: Rx OTC

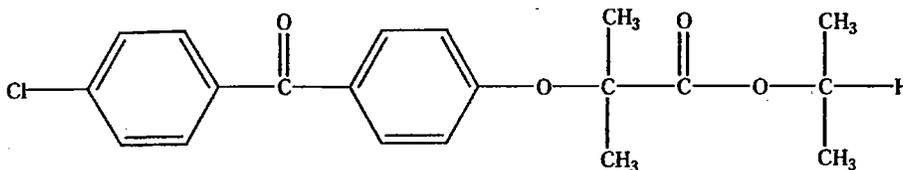
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product Form Completed (for Egg Lecithin, one of the excipients)

Not a SPOTS product

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

2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid-1-methylethyl ester



$C_{20}H_{21}ClO_4$

Molecular Weight: 360.8



CHEMISTRY REVIEW



Chemistry Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
[REDACTED]	II	[REDACTED]	[REDACTED]	3	Adequate	12/ 30/03	Reviewed by M. Shaikh
[REDACTED]	IV	[REDACTED]	[REDACTED]	1	Adequate	4/4/02	Review by Yvonne Yang, Ph.D.
[REDACTED]	III	[REDACTED]	[REDACTED]	1	Adequate	3/ 11/02	Review by Don Klein, Ph.D., DMF strike force
[REDACTED]	III	[REDACTED]	[REDACTED]	1	Adequate	3/27/02	Reviewed by Elsbeth Chikhale, Ph.D.
[REDACTED]	III	[REDACTED]	[REDACTED]	3	Adequate	10/6/03	Reviewed by William Timmer, Ph.D.
[REDACTED]	III	[REDACTED]	[REDACTED]	4	N/A		

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 relevant 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)



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Chemistry Review Data Sheet

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA (Abbott)	19-304	Fenofibrate capsules
NDA (Abbott)	21-656	Fenofibrate tablets
NDA (Reliant Pharma)	21-695	Fenofibrate capsules
NDA (Abbott)	21-203	Fenofibrate tablets
NDA (Cipher Pharma)	21-612	Fenofibrate capsules
IND (RTP)	60,743	Fenofibrate tablets

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EES	Pending EER	12/6/04	Elsbeth Chikhale, Ph.D.
Biopharm	Approvable	11/29/04	Wei Qiu, Ph.D.
Methods Validation	Adequate	12/6/04	Elsbeth Chikhale, Ph.D.
ODS	Triglide: Acceptable	9/28/04	Tia M. Harper-Velazquez, Pharm.D.
EA	Acceptable	12/6/04	Elsbeth Chikhale, Ph.D.

Appears This Way
On Original

The Chemistry Review for NDA 21-350

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 21-350 is **approvable** from the standpoint of chemistry, manufacture and controls, pending satisfactory response to deficiencies. See draft letter with list of deficiencies and information requests to be forwarded to the sponsor.

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

None

II. Summary of Chemistry Assessments

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

1) Drug Product

The drug product, described in this 505(b)(2) NDA, is an immediate release uncoated tablet for oral administration. The product is intended to be used for the treatment of hypertriglyceridemia (Fredrickson Type IV and V). The drug product comes in a 50 mg and a 160 mg strength and is packaged in [REDACTED] bottles (commercial distribution)

[REDACTED]. The proposed storage is controlled room temperature. The original NDA was submitted on 6/22/01 and was found approvable from a CMC standpoint on 4/24/02. The main deficiency was the instability of the drug product. The reformulated drug product exhibits better stability properties, however, there is still a major stability problem that limits the shelf life of this drug product, i.e., the drug product [REDACTED] upon extended storage [REDACTED] of storage at accelerated conditions. [REDACTED]

[REDACTED] The submitted stability data support a [REDACTED] expiration date for the commercial (bottle) package [REDACTED]

2) Drug Substance

Fenofibrate is a fibric acid derivative with lipid altering properties. It is a white or almost white crystalline powder, insoluble in water. Fenofibric acid is the active metabolite of fenofibrate, and is responsible for the pharmacological activity. The drug substance is stable for 5 years at room temperature (DMF [REDACTED] review #2, dated 5/27/03). The applicant suggests that the particle size of the drug substance is important for the bioavailability. Therefore, the drug substance particle size is controlled in the drug substance itself, as well as in the tablet formulation.

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

Patients should receive this drug product in combination with an appropriate lipid-lowering diet. The bioavailability of the drug product is optimized when taken with food. The initial dose is 50 mg or 160 mg per day (1 tablet per day). Per the proposed label, the dosage should be individualized according to the patient's response, measured at 4 to 8 week intervals. The maximum daily dose is 160 mg/day.



C. Basis for Approvability or Not-Approval Recommendation

This NDA is approvable, because of the following deficiencies:

- The application lacks sufficient evidence that the drug product used in the bioequivalence (BE) study (Lipanthyl 200M) is the same drug product from CMC perspective, as the reference listed drug, Tricor 200 mg capsule (Abbott's NDA 19-304).
- The drug product specification is not adequate to assess the drug product quality and raise a safety concern [REDACTED] and efficacy concern [REDACTED].
 - A) The applicant has not provided an adequate response to our communicated safety concern regarding the appearance of [REDACTED] which indicates the formation of an undetermined amount of unknown impurity.
 - B) In addition, the applicant proposes to revise the moisture content acceptance criteria to NMT [REDACTED] which could result in [REDACTED] of the tablets and potential damage to the tablets when taken from the container closure system, therefore raising an efficacy concern.
 - C) Furthermore, as discussed in the Clinical Pharmacology and Biopharmaceutics review by Wei Qui, Ph.D., dated 11/29/04, a change in medium used in the proposed dissolution method is recommended.
- The proposed shelf life is not supported by sufficient stability data.
- The facilities are pending a satisfactory GMP status as of 12/6/04.

III. Administrative

A. Reviewer's Signature

Elsbeth Chikhale, Ph.D.

Signatures attached in DFS.

37 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

Withheld Track Number: Chemistry-2

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

/s/

Elsbeth Chikhale
12/6/04 04:30:23 PM
CHEMIST

Sheldon Markofsky
12/6/04 04:39:05 PM
CHEMIST
Signed by S. Markofsky, Acting Chemistry Team Leader, for
Mamta Gautam-Basak.



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Chemistry Review Data Sheet

1. NDA 21-350
2. REVIEW #: 1
3. REVIEW DATE: 10-APR-2002
4. REVIEWER: Elsbeth Chikhale, Ph.D.
5. PREVIOUS DOCUMENTS: NA

6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original	22-JUN-2001
Amendment to original ¹	18-SEP-2001
Amendment to original ²	16-OCT-2001
Amendment to original ³	9-NOV-2001
Amendment to original ⁴	28-DEC-2001
Amendment to original ⁵	25-FEB-2002
Amendment to original ⁶	1-MAR-2002
Amendment to original ⁷	25-MAR-2002
Amendment to original ⁸	10-APR-2002

- 1) The 9-18-01 amendment provided for a request for a teleconference to discuss addition of a manufacturing site.
- 2) The 10-16-01 amendment provided for a notification about the sponsor's intend to institute a site change
- 3) The 11-9-01 amendment provided a communication indicating that the manufacturing sites are not ready for inspection, and that the sponsor will notify the Agency when the sites are ready.
- 4) The 12-28-01 amendment provided for addition of a new manufacturing facility, and the Agency was notified that an inspection could be scheduled
- 5) The 2-25-02 amendment provided for letters of authorization for DMFs
- 6) The 3-1-02 amendment provided manufacturing site status information
- 7) The 3-25-02 amendment provided updated package insert
- 8) The 4-10-02 amendment provided updated carton/container labels

7. NAME & ADDRESS OF APPLICANT:

Name: RTP Pharma Inc.

Address: 1000 Chemin du Golf, Verdun, Quebec, Canada H3E 1H4

Representative: Cato Research Ltd.

Telephone: (919) 361-2286

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: Pending
 b) Non-Proprietary Name (USAN): Fenofibrate tablet
 c) Code Name/#: N/A
 d) Chem. Type/Submission Priority:
- Chem. Type: 3
 - Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION:

This is a 505(b)(2) submission. The listed drug is Tikor®, fenofibrate capsules, micronized, 200 mg, Abbott, NDA 19-304

10. PHARMACOL. CATEGORY:

Lipid Altering Agent II

11. DOSAGE FORM: tablet

12. STRENGTH/POTENCY: 50 mg/tablet and 160 mg/tablet

13. ROUTE OF ADMINISTRATION: oral

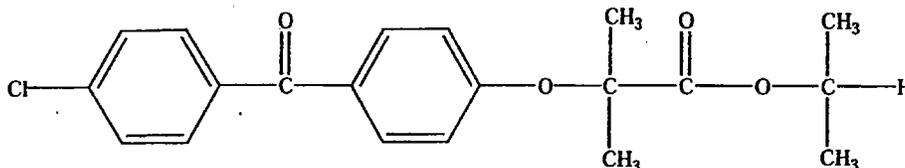
14. Rx/OTC DISPENSED: Rx OTC15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

SPOTS product Form Completed (for Egg Lecithin, one of the excipients)

Not a SPOTS product

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

2-[4-(4-chlorobenzoyl)phenoxy]-2-methyl-propanoic acid-1-methylethyl ester





CHEMISTRY REVIEW



Chemistry Review Data Sheet

$C_{20}H_{21}ClO_4$
Molecular Weight: 360.8

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYP E	HOLDER	ITEM REFERENCE D	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
	II			1	Inadequate	April 8, 2002	
	IV			1	Adequate	April 4, 2002	Review by Yvonne Yang, Ph.D.
	III			1	Adequate	March 11, 2002	Review by Don Klein, Ph.D., DMF strike force
	III			1	Adequate	March 27, 2002	

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)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
NDA (Abbott)	19-304	Fenofibrate capsules
NDA (Abbott)	21-203	Fenofibrate tablets
IND (RTP)	60,743	Fenofibrate tablets



CHEMISTRY REVIEW



Chemistry Review Data Sheet

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	NA		
EES	Pending		
Pharm/Tox	Approval pending labeling changes	10-15-01	Indra Antonipillai, Ph.D.
Biopharm	Approval, except for dissolution method and specifications, and pending labeling changes	3-11-02	Wei Qiu, Ph.D.
LNC			
Methods Validation			
ODS	Does not recommend use of the proposed names: ██████████ ██████████	2-22-02	Hye-Joo Kim, Pharm.D.
EA	Satisfactory		
Microbiology	NA		

*Decision by DMEDP still pending

*Appears This Way
On Original*

The Chemistry Review for NDA 21-350

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

NDA 21-350 is **approvable** from the standpoint of chemistry, manufacture and controls, pending satisfactory response to deficiencies. See draft letter with list of deficiencies and information requests to be forwarded to the sponsor.

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

None

II. Summary of Chemistry Assessments

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

1) Drug Product

The drug product, described in this 505(b)(2) NDA, is an immediate release uncoated tablet for oral administration. The product is intended to be used for the treatment of hypertriglyceridemia (Fredrickson Type IV and V). The drug product comes in a 50 mg and a 160 mg strength and is

The proposed storage is at 2-8°C (refrigerator temperature), but an expiry date can not yet be granted until more satisfactory stability data are provided.

2) Drug Substance

Fenofibrate is a fibric acid derivative with lipid altering properties. It is a white crystalline powder, insoluble in water. Fenofibric acid is the active metabolite of fenofibrate, and is responsible for the pharmacological activity. Fenofibrate is the drug substance in two already approved drug products (NDA 19-304 and 21-203). However, the sponsor of these two NDAs (Abbott) uses a different manufacturer for fenofibrate than the one used for this NDA. Information on the drug substance, fenofibrate, is provided in DMF [REDACTED]. A letter of authorization to allow the Agency to review this DMF was provided. The DMF was found inadequate to support this NDA and a letter to the DMF holder describing the deficiencies will be sent.

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

Patients should receive this drug product in combination with an appropriate lipid-lowering diet. The drug product should be taken with food to optimize the bioavailability. The initial dose is 50 mg or 160 mg per day (1 tablet per day). The dosage should be individualized according to the patient's response, measured at 4 to 8 week intervals. The maximum daily dose is 160 mg/day.

C. Basis for Approvability or Not-Approval Recommendation

This NDA is approvable. Among others, the main deficiencies for this NDA are as follows:

- DMF [REDACTED] for the drug substance is inadequate
- Insufficient (not enough lots and not enough time points) stability data were provided
- Since the sponsor has changed the manufacturing site for the drug product, site specific stability data are required.

III. Administrative**A. Reviewer's Signature**

Elsbeth Chikhale, Ph.D.

24 Page(s) Withheld

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Draft Labeling

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/s/

Elsbeth Chikhale
4/9/02 04:16:52 PM
CHEMIST

Sheldon Markofsky
4/10/02 11:40:46 AM
CHEMIST