

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

**NDA 21-938 (GIST)
NDA 21-968 (MRCC)**

Chemistry Review(s)

NDA 21-938

SUTENT™
(Sunitinib malate) 12.5, 25 and 50 mg capsules

Pfizer Inc.

Chengyi Liang, Ph.D.
HFD-150 Division of Oncology Drug Products



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Chemistry Review Data Sheet

1. NDA #: 21-938



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- 2. CHEM. REVIEW #: 1
- 3. REVIEW DATE: Jan. 24, 2006
- 4. REVIEWER: Chengyi Liang, Ph.D.

5. PREVIOUS DOCUMENTS

Previous Documents

Document Date

None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed

Documnent Date

Original	08-10-2005
Amendment (BC)	10-06-2005
Amendment	01-10-2006
Amendment	01-23-2006

7. NAME & ADDRESS OF APPLICANT:

Name:

Pfizer Inc
10777 Science Center Dr.
San Diego, CA 92121

Representative:

NA

Telephone:

NA

8. DRUG PRODUCT NAME/CODE/TYPE:

- a. Proprietary: Sutent
- b. Nonproprietary Name/USAN: Sunitinib Malate
- c. Code Name/#: SU011248 L-malate
- d. Chem. Type/Submission Priority
 - Chem. Type 1
 - Submission Priority P

9. LEGAL BASIS FOR SUBMISSION:

Fulfilled PDUFA filing requirements

10. PHARMACOL. CATEGORY/INDICATION:

11. DOSAGE FORM:

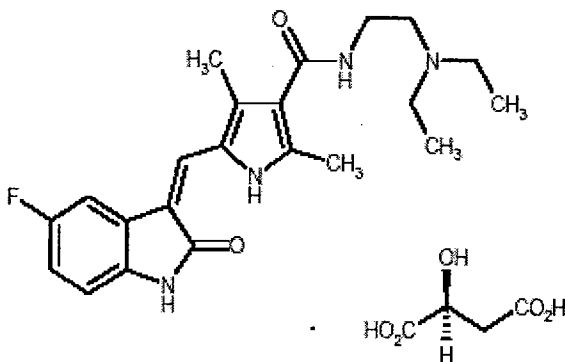
Capsules

12. STRENGTHS/POTENCY:

12.5, 25 and 50 mg

13. ROUTE OF ADMINISTRATION: Oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM)
No

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



IUPAC: (Z)-N-[2-(Diethylamino)ethyl]-5-[(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (S)-2-hydroxysuccinate

CAS: N-[2-(Diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide, compound with (S)-2-hydroxybutanedioic acid

USAN Chemical Name:

1. Butanedioic acid, hydroxy-, (2S)-, compound with N-[2-(diethylamino)ethyl]-5-[(Z)-(5-fluoro-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide (1:1)
2. N-[2-Diethylamino)ethyl]-5-[(Z)-(5-fluoro-2-oxo-1,2-dihydro-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-pyrrole-3-carboxamide hydrogen (2S)-2-hydroxybutanedioate

Molecular formula $C_{22}H_{27}FN_4O_2 \cdot C_4H_6O_5$

MW 532.57



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17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
	III			3	adequate	D. Christodoulou	8/9/99
	III			3	adequate	Raymond Frankewich	4/29/02
	III			3	adequate	J. Salemme	3/7/03
	III			3	adequate	D. Klein	2/9/01

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")

18. STATUS:

Consults/CMC Related Reviews	Recommendation	Date	Reviewer
EES	Acceptable	9-26-2005	Office of Compliance
DMETS	Acceptable	12-7-2005	Felicia Duffy
Methods Validation	May be requested post approval	1/24/2006	Chengyi Liang
EA	Categorical exclusion is acceptable	6/6/2005	Chengyi Liang
Microbiology	N/A		

The Chemistry Review for NDA 21-938

The Executive Summary

Chengyi Liang, Ph.D.
Jan. 2006

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA is recommended for approval from the standpoint of CMC. A number of deficiencies related to the drug substance and drug product have been satisfactorily addressed. The Office of Compliance has given an overall acceptable recommendation.

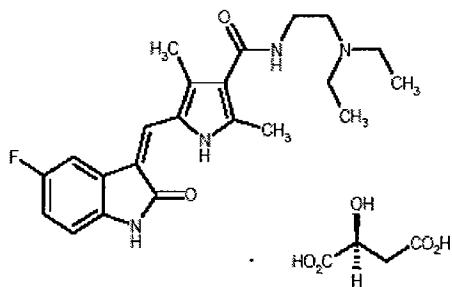
B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

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

SUTENT™ (sunitinib malate), an oral multi-tyrosine kinase receptor inhibitor, is the malate salt of sunitinib. Sunitinib malate is described chemically as butanedioic acid, hydroxy-, (2S)-, compound with *N*-[2-(diethylamino)ethyl]-5-[(*Z*)-(5-fluoro-1,2-dihydro-2-oxo-3*H*-indol-3-ylidene)methyl]-2,4-dimethyl-1*H*-pyrrole-3-carboxamide (1:1). The molecular formula is $C_{22}H_{27}FN_4O_2 \cdot C_4H_6O_5$ and has the following structural formula:



The DS is a fine, yellowish crystalline powder and is soluble in water and ethanol.

SUTENT (sunitinib malate) capsules is manufactured [

] and supplied as printed hard gelatin capsules containing sunitinib malate equivalent to 12.5 mg, 25 mg and 50 mg of sunitinib respectively together with mannitol, croscarmellose sodium, povidone (K-25) and magnesium stearate as inactive ingredients.

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

Sunitinib malate is a small molecule, multi-tyrosine kinase receptor's inhibitor that selectively targets and intracellularly blocks the signaling pathways of receptor tyrosine kinases (RTKs). It is being submitted for the treatment of malignant gastrointestinal stromal tumors



(GIST) after failure of imatinib mesylate treatment, and for the treatment of metastatic renal cell carcinoma (mRCC) after failure of prior cytokine-based therapy.

The recommended daily dose of DP is orally 50 mg per day.

C. Basis for Approvability Recommendation

A number of minor deficiencies related to the drug substance and drug product have been satisfactorily addressed by the applicant. This application is recommended for approval from the standpoint of chemistry, manufacturing and controls.

III. Administrative

A. Reviewer's Signature

Chengyi Liang, Ph.D., Review Chemist

Nallaperumal Chidambaram, Ph.D.
Chemistry Team Leader

B. Endorsement Block

Chemist Name/Date: Chengyi Liang, Ph.D.

Chemistry Team Leader Name/Date: Nallaperumal Chidambaram, Ph.D.

Project ManagerName/Date: Christy Cottrell

C. CC Block

CC:

Orig. NDA 21-938

HFD-150 Division File

HFD-150/CLiang

HFD-150/NChidambaram

HFD-150/CCottrell

Chemistry Review Data Sheet

66 Page(s) Withheld



 § 552(b)(4) Trade Secret / Confidential

 § 552(b)(5) Deliberative Process

 § 552(b)(4) Draft Labeling

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

/s/

Chengyi Liang
1/25/2006 03:13:54 PM
CHEMIST

Nallaperumal Chidambaram
1/25/2006 05:10:20 PM
CHEMIST