CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 21-335/S-001

Chemistry Review(s)

DIVISION OF ONCOLOGY DRUG PRODUCTS
Original NDA Review of Chemistry, Manufacturing, and Controls

NDA #: 21-335 CHEMISTRY REVIEW #: 1 REVIEW DATE: November 19, 2001

SUBMISSION TYPE	DOC. DATE	CDER DATE	ASSIGNED DATE
Efficacy supplement –001	October 15, 2001	October 16, 2001	October 18, 2001

NAME & ADDRESS OF APPLICANT: Novartis Pharmaceuticals Co.
59 Route 10
East Hanover, NJ 07936-1080

DRUG PRODUCT NAME:
- Proprietary: Gleevec™ Capsule
- Nonproprietary/USAN: Imatinib Mesylate (This name was adopted by the USAN Council, a statement on 1/31/01 is attached.)
- Code Name/Number: STI 571 (CGP 57148B)
- Chem. Type/Ther. Class: 1P

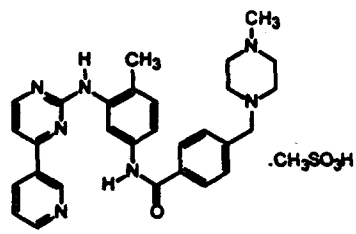
PHARMACOL. CATEGORY/INDICATION: Signal Transduction Inhibitor (Protein the Bcr-Abl Tyrosine Kinase Inhibitor)

DOSAGE FORM: Hard Gelatin Capsule
STRENGTHS: 50mg and 100mg/capsule
ROUTE OF ADMINISTRATION: Oral
DISPENSED: _x_ Rx ____ OTC

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA(M.F.), MOLECULAR WEIGHT(M.W.):

CAS Name: 4-[(4-Methyl-1-piperazinyl)methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]aminophenyl]benzamide methanesulfonate salt

INN: Imatinib mesylate
CAS Number: 220127-57-1 (for the free base: 152459-95-5)
Code Number: STI 571 (CGP 57148B)
M.F.: $C_{29}H_{31}N_7O.\ CH_4SO_3$
Salt/base ratio: 1.195 on anhydrous basis
M.W.: 493.6+96.1=589.7



REMARKS/COMMENTS:
See Review Notes.

CONCLUSIONS & RECOMMENDATIONS:
No change is noted in the package insert submitted in this supplement in terms of the Gleevec™ formulation, strength and packaging size . A request for a categorical exclusion from the preparation of the environmental assessment (EA) is adequate under 21 CFR 25.31(b). The EA exclusion request is granted. Approval of this efficacy supplement is recommended from the CMC viewpoints.

/S/

Sung K. Kim, Ph.D.,
Review Chemist, HFD-150

cc:
Orig. NDA 21-335
HFD-150/Division File
HFD-150/AStaten
HFD-150/SKim
HFD-150/RWood
HFD-810/HPatel
HFD-810/JSimmons
R/D Init. by:_____
Filename: N21335.SE1

Review Notes:
This efficacy supplement is to add a new indication for the use of Gleevec™ for the treatment of patients with unresectable and /or metastatic malignant gastrointestinal stromal tumors (GIST).

It is stated that the Gleevec™ formulation is the same as previously approved for CML. The dose and schedule are similar. A categorical exclusion from the preparation of an environmental assessment is requested under 21CFR 25.31 (b) stating that the estimated concentration of the substance at the point of entry into the aquatic environment will be less than 1 part per billion (ppb) and , to the best of its knowledge, no extraordinary circumstances exit which may significantly affect the quality of the human environmental and would thus require the preparation of at least an Environmental Assessment (EA).

Evaluation:
No change is noted in the submitted package insert regarding the strength and the package size of Gleevec. The EA exclusion request complies the condition described under 21 CFR 25.31(b).

No additional CMC information is needed concerning this efficacy supplement.
The EA exclusion request is granted.

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

/s/

Sung Kwang Kim
11/20/01 07:23:37 AM
CHEMIST

signed off on 11/19/01

Rebecca Wood
11/20/01 10:09:43 AM
CHEMIST