

North Central Cancer Treatment Group

N0272: Phase I/II Trial of Imatinib Mesylate; (Gleevec; STI571) in Treatment of Recurrent Oligodendroglioma and Mixed Oligoastrocytoma

Addendum 9 – September 14, 2007

Summary

- This addendum is in response to Jeannette Wick's August 6, 2007, notice regarding updated pharmaceutical information for STI571 (imatinib). Novartis Pharmaceuticals has indicated that when the current supply of STI571 (imatinib) is expended, no further supplies of capsules will be available. STI571 will only be provided in 100 mg tablets.
- Administrative/editorial changes.

Replacement pages are included. Please incorporate into the protocol and keep this addendum with your protocol.

Title page Revised to reflect Addendum 9 and updated NCI version date.

Section 8.0 **Dosage Modification Based on Adverse Events**
Page 23: Novartis Pharmaceuticals will now only be providing STI571 in tablet form. Therefore, the first sentence Footnote #1 in Section 8.2 has been revised as follows:
Adjusted to the nearest 100 mg, since imatinib is only available in 100 mg capsules tablets.

Section 14.0 **Translational Research and Pharmacologic Studies on Tissue Specimens**
Page 40: Contact information in the last column for Paraffin Tissues has been updated as follows:
To: NCCTG
Operations Office
ATTN: NCCTG
~~Research Coordinator~~ **PC Office**
RO_FF_03_24-CC/NW Clinic
200 First Street, SW
Rochester, MN 55905

Section 15.0 **Drug Information**
Page 41: Novartis Pharmaceuticals will now only be providing STI571 in tablet form. Therefore, the first paragraph in Section 15.1 and the entire Section 15.2 have been revised as follows:
15.1 Imatinib mesylate (Gleevec, Novartis; STI571; NSC 716051) is 4-[(4-Methyl-1-piperazinyl) methyl]-N-[4-methyl-3-[[4-(3-pyridinyl)-2-pyrimidinyl]amino]-phenyl]benzamide methanesulfonate. ~~The drug is provided as imatinib mesylate, equivalent to 100 mg of imatinib free base, with a molecular formula is C₂₉H₃₁N₇O-CH₄SO₃ and a relative molecular mass of 589.7. Imatinib mesylate is a white, off white, yellowish or brownish powder. It is very soluble in water and freely soluble in aqueous buffers ≤pH 5.0 but is less soluble to insoluble in neutral/alkaline aqueous buffers. In non-aqueous solvents, the drug substance is soluble DMSO, slightly soluble in ethanol and methanol, but is insoluble in less polar solvents such as acetone, acetonitrile or isopropanol. Imatinib (STI571) is available in very dark yellow to brownish orange, round, biconvex tablets with NVR on one side and SA and a score on the other. They contain 100~~

mg imatinib with microcrystalline cellulose, crospovidone, hypomellose, colloidal silicone dioxide, and magnesium stearate. Each bottle contains 100 tablets.

15.2 Preparation and storage

Storage: ~~The capsules should be stored at room temperature not to exceed 25°C (77°)~~ **Store tablets at room temperature not to exceed 30° (86°F) in the original package.**

Stability: Shelf life testing of the intact bottles is on-going. Current data support a shelf life of ~~3~~ **five** years.

~~Imatinib is supplied in orange to grayish orange opaque hard gelatin capsule gelatin capsules which contain a common dry powder blend filled in capsule shells of size 1 (100 mg dosage strength), with "NVR SI" printed in red ink, and contains 100 mg of imatinib free base. Drug will be supplied to the investigational pharmacy in bottles of 60 capsules. Imatinib should be stored at 25° C (77°F); excursions permitted to 15–30°C (59–86°F). [See USP Controlled Room Temperature] and dispensed in a tight container.~~

Section 17.0

Page 57:

Pathology Considerations

Contact information in Section 17.2 has been updated as follows:


NCCTG Operations Office

ATTN: NCCTG ~~Research Coordinator~~ **PC Office**

RO_FF_03_24-CC/NW Clinic

200 First Street, SW

Rochester, MN 55905

	DEPARTMENT OF HEALTH & HUMAN SERVICES	Public Health Service National Institutes of Health National Cancer Institute Bethesda, Maryland 20892 6130 Executive Blvd. Executive Plaza North Room 7149 Rockville, Maryland 20852 Phone 301-496-5725 Fax 301-402-4870 wickj@mail.nih.gov
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August 8, 2007

Notice to Principal Investigators using STI571 (imatinib) (NSC #716051)

To whom it may concern;

Novartis Pharmaceuticals has notified us that when our current supply of STI571 (imatinib) is expended, no further supplies of capsules will be available. They will provide only 100 mg tablets in the future. Thus, your protocol must be amended.

Please amend your protocol, removing reference to capsules and replacing it with tablets throughout the protocol. In the drug supply section, please use the following information to make appropriate changes:

How Supplied: Imatinib (STI571) is available in very dark yellow to brownish orange, round, biconvex tablets with NVR on one side and SA and a score on the other. They contain 100 mg imatinib with microcrystalline cellulose, crospovidine, hypomellose, colloidal silicone dioxide and magnesium stearate. Each bottle contains 100 tablets.

Storage: Store tablets at room temperature not to exceed 30° (86°F) in the original package.

Stability: Shelf life testing of the intact bottles is on-going. Current data support a shelf life of five years.

Please submit a protocol amendment reflecting the changes to the pharmaceutical information by August 22, 2007. The amendment cover letter must state, "This amendment is in response to Jeannette Wick's June 10, 2002 notice regarding updated

pharmaceutical information for STI571 (imatinib).” If you have questions or need further information, please contact me at 301-496-5725.

Sincerely,

Jeannette Y. Wick, R.Ph., MBA
Clinical Research Pharmacist
Pharmaceutical Management Branch, CTEP, DCTD

cc: Anthony Murgo, MD
Jan Cassedei, Ph.D.
Drug file: STI571 (NSC 716051)