



**DATE:** August 4, 2010

**FROM:** Pamela J. Harris, M.D., Investigational Drug Branch, CTEP, DCTD, NCI

**SUBJECT:** Sunitinib Malate (SU011248 L-malate; Sutent®) NCI IND Safety Report, AE# 1274440

**TO:** Investigators Using Sunitinib (NSC 736511)

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. Please find attached a copy of an IND Safety Report recently submitted to the FDA for the CTEP-sponsored investigational agent sunitinib.

The following must be completed by all investigators using sunitinib under NCI IND 74019:

- Send a copy of the IND Safety Report to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of the IND Safety Report in your protocol file.

If your study is not covered under IND 74019, it is strongly recommended that you follow the instructions above.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

Based on CTEP's assessment of the current information in light of previous experience with sunitinib, there does not appear to be a change in the risk-benefit ratio for sunitinib studies; therefore, CTEP is not requiring a protocol amendment at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The attached Adverse Events Assessments describe the adverse event(s) (synopsis provided below), relevant previous experience under this IND and/or NSC, and the total number of patients enrolled in trials under this IND and/or NSC.

A 50-year-old male with metastatic follicular thyroid carcinoma experienced grade 4 laryngeal edema while on a phase 2 trial utilizing the investigational agent sunitinib.

**ADVERSE EVENTS ASSESSMENT**

IND 74019 NSC 736511 Sunitinib malate (SU011248 L-malate; Sutent®) AE: 1274440	ADVERSE EXPERIENCE REPORT NO. IND Safety Report: #1 Event: Gr. 4: Edema, larynx Protocol: 7735
--	---

The patient is a 50-year-old male with metastatic follicular thyroid carcinoma who experienced laryngeal edema while on a phase 2 trial utilizing the investigational agent sunitinib. He began the first course of treatment on October 23, 2007, receiving sunitinib 50 mg PO daily for 4 weeks, every 6 weeks. He received his last dose of sunitinib on March 11, 2010 (Cycle 20, Day 28).

The patient was diagnosed with metastatic follicular thyroid carcinoma in November 2005 and is status post thyroidectomy, radioactive iodine, and radiation therapy. He began the investigational therapy with sunitinib on October 23, 2007.

On March 17, 2010 (Cycle 20, Day 34), the patient presented to the ER with stridor, dyspnea and dysphagia for solids and liquids. The patient had had previous intermittent episodes of stridor which resolved with halting sunitinib; however, this episode was worse than usual. The patient underwent laryngoscopy and was found to have significant vocal cord stenosis and supraglottic and infraglottic edema. He initially improved with racemic epinephrine and Decadron® but later became more stridorous and was intubated. He was taken to the operating room on March 19, 2010, to undergo a tracheotomy for bilateral vocal cord paralysis. A CT scan of the neck was consistent with scar tissue and possibly recurrent tumor overlying and adjacent to the entire anterior tracheal wall. It was felt that the the patient's tracheotomy would be long-term because of his vocal cord paralysis, which was likely not reversible at this point. The tracheotomy and tracheobronchoscopy were well tolerated. The patient was sent to the intensive care unit in stable condition with a stable airway. He remained stable during the hospitalization and passed a swallow study. The patient and his wife received instructions on how to use a tracheostomy. The patient was discharged on March 27, 2010 in stable condition.

The patient's past medical history is significant for hypertension. Medications taken at the time of the event included omega-3 fatty acids with vitamin E, a multivitamin, olmesartan/hydrochlorothiazide, and Synthroid®.

There has been one other case of laryngeal edema, specifically supraglottic edema (grade 2, possibly related), and one case of laryngeal obstruction/airway stenosis (grade 4, unrelated) reported to the NCI as serious adverse events through AdEERS under the sunitinib NSC and/or IND.

There have been 2,645 patients enrolled in NCI-sponsored clinical trials under the sunitinib IND and/or NSC.

In this case, it is thought that a possible relationship exists between the adverse event and sunitinib.

	<b>Laryngeal edema</b>
<b>Sunitinib</b>	Possible
<b>Follicular thyroid carcinoma</b>	Unlikely

Date: 8/3/10

Signature: 

Pamela Harris, M.D.  
(IDB Monitor for sunitinib)

If this assessment is changed, we will notify your office.

cc: Cynthia Barbitsch, R.Ph.  
David V. Woo, Ph.D.  
Pfizer, Inc.