

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

**TO: Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA**

**FAX: 301-796-9845**

1. IND NUMBER <b>74019</b>	2. AGENT NAME <b>Sunitinib malate (SU011248 L-malate; Sutent®)</b>	3. DATE <b>June 25, 2010</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>Pamela Harris, MD –Senior Investigator for Investigational Therapeutics 1, Investigational Drug Branch, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b>
		7. FAX NUMBER <b>301-402-0428</b>
8a. PROTOCOL NUMBER (AE #) <b>ADVL0612 (AE# 1842265)</b>	8b. AE GRADE: AE <b>Grade 4: Hypoxia</b> <b>Grade 4: Hemorrhage, CNS</b>	
9. PATIENT IDENTIFICATION <b>800231</b>	10. AGE <b>8 yrs</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient is an 8-year-old male with thalamic/midbrain glioblastoma multiforme who experienced grade 4 hypoxia and a grade 4 cerebral hemorrhage while on a phase 1 study utilizing the investigational agent sunitinib malate. He began the investigational therapy on June 8, 2010, and received his last dose of sunitinib malate on June 23, 2010 (Cycle 1, Day 16). On June 21, 2010 (Cycle 1, Day 14), the patient was neurologically stable during a routine clinic visit, however, he developed a pentamidine reaction with asymptomatic hypotension which necessitated hospitalization and IV fluids. The patient responded to therapy, and he was discharged the next day. On June 24, 2010 (Cycle 1, Day 17), the patient developed a headache, and eventually became less responsive and dyspneic. He was admitted to the local hospital, intubated and placed on mechanical ventilation as he was apneic. A CT scan of the head revealed an acute hemorrhage filling most of the fourth ventricle and extending inferiorly to the base of the skull and superiorly to the level of the foramen of Monro with a new mass in the floor of the fourth ventricle. The patient remains on mechanical ventilation in the ICU. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE: <b>Cycle = 42 Days</b> <b>Sunitinib malate: 15 mg/m<sup>2</sup> PO daily as powder, Days 1-28</b>		
14. DATES OF TREATMENT <b>The patient started the investigational therapy on June 8, 2010, and received the last dose of sunitinib malate on June 23, 2010, (Cycle 1, Day 16).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using sunitinib malate = 2503</b> <b>There have been 15 other cases of hypoxia and 2 other cases of cerebral hemorrhage reported to the NCI through AdEERS as serious adverse events for sunitinib malate.</b>		
16. COMMENTS: <b>AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR 312.32(d)(2).</b> <b>DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.</b>		