

**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>63383</b>	2. AGENT NAME <b>OSI-774 (erlotinib; Tarceva®)</b>	3. DATE <b>August 19, 2009</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b>
		7. FAX NUMBER <b>301-402-0428</b>
8. PROTOCOL NUMBER (AE #) <b>6980 (AE# 1670060)</b>		
9. PATIENT IDENTIFICATION <b>0019</b>	10. AGE <b>56</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient is a 56-year-old male with adenocarcinoma of the rectum who experienced grade 3 edema of the lower extremities and grade 3 asteatotic eczema of the lower extremities while on a phase I/II trial utilizing the investigational agent erlotinib in combination with cetuximab. He began the investigational therapy on April 17, 2009, and received his last dose of erlotinib on July 2, 2009 (Cycle 4, Day 14), and his last dose of cetuximab on June 19, 2009 (Cycle 4, Day 1). On June 26, 2009, the patient did not return to the clinic for a scheduled dose of cetuximab but he continued to receive erlotinib. On July 2, 2009, he presented to the clinic complaining of severe, painful, weeping bilateral lower extremity edema and small, scattered, cracked lesions on both legs for which he was admitted to the hospital. The consulting dermatologist diagnosed asteatotic eczema on both lower extremities due to severe lower extremity edema. The patient also had an acniform rash on his face, chest and arms possibly related to cetuximab. He received minocycline, clobetasol cream and emollients for the eczema and Lasix® for the edema. The patient developed a fever that evening and was started on vancomycin for empirical coverage of a possible cellulitis superinfection. On July 3, 2009, his urine culture tested positive for a urinary tract infection with sensitivity to doxycycline. The vancomycin was discontinued and the patient continued on minocycline for his urinary tract infection and drug eruptions. He was discharged on July 6, 2009, and continued on lovenox and minocycline at home. He was to return for a re-evaluation with his oncologist on July 10, 2009. 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 =21 Days</b> <b>Erlotinib 100 mg PO daily on Days 8-21 of cycle 1, then on Days 1-21 of all subsequent cycles</b>		
14. DATES OF TREATMENT <b>The patient began the investigational therapy on April 17, 2009, and received the last dose of erlotinib on July 2, 2009 (Cycle 4, Day 5).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using erlotinib = 2848. There have been 6 other cases of edema of the lower extremity and no other case of asteatotic eczema of bilateral lower extremity reported to the NCI through AdEERS as serious adverse events for erlotinib.</b>		
16. COMMENTS <b>Also administered on this protocol:</b> <b>Cetuximab: 250 mg/m<sup>2</sup> IV over 60-120 min weekly</b> <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 21CFR312.32(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>		