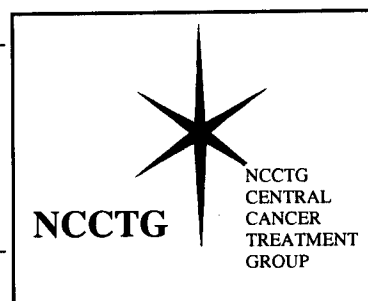


---

**Operations Office**

Telephone (507) 266-3853

---



**Date:** March 14, 2003

**To:** NCCTG Primary Clinical Research Associates

**From:** Linda S. Long

**Re:** N0177, Pilot and Phase II Trial of OSI-774 and Radiation in Glioblastoma Multiforme Patients

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with OSI-774 for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

AE\_2003000295

Please note that all risks currently cited in the NCCTG consent form can not be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

**Please submit this adverse event to your Institutional Review Board.**

If you have any questions concerning this communication, please contact Linda S. Long at 507-266-3853.

lsl  
enclosure



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

National Institutes of Health  
National Cancer Institute

**DATE:** February 26, 2003  
**FROM:** Janet Dancey, M.D., Investigational Drug Branch, CTEP, DCTD, NCI  
**SUBJECT:** OSI-774 IND Safety Report  
**TO:** Investigators Using OSI-774, IND 63,383

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 by an investigator conducting a clinical trial in conjunction with Genentech and OSI Pharmaceuticals for the CTEP-sponsored investigational agent, OSI-774 (IND 63,383).

Please complete the following:

- 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.

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

CTEP's evaluation of this IND Safety Report in light of previous experience with OSI-774 does not require a change in the clinical protocols for this agent at this time.

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

The MedWatch form that describes the following adverse event is attached:

A 55-year-old male with glioblastoma multiforme experienced pulmonary fibrosis after being treated with OSI-774. Approximately 3 months after treatment initiation, the patient was diagnosed with pneumonia and treatment was withheld. A chest computerized tomography (CT) scan was performed to rule out any pulmonary pathology prior to resuming treatment with OSI-774. Approximately 1 month later, a chest CT scan showed mediastinal lipomatosis and extensive bilateral pulmonary fibrosis with a confluent area of pulmonary fibrosis suggested involving the left lung.

**CONFIDENTIAL**

OSI Pharmaceuticals  
For use by user-facilities,  
distributors and manufacturers for  
**MANDATORY** reporting

# MED WATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Mfr report # <b>2003000295</b>
UP/Dist report # 
FDA Use Only

A. Patient information			
1. Patient identifier RJG In confidence	2. Age at time of event: 55 Years or Date of birth: 09/29/1947	3. Sex <input type="checkbox"/> female <input checked="" type="checkbox"/> male	4. Weight lbs or 94 kgs
B. Adverse event or product problem			
1. <input checked="" type="checkbox"/> Adverse event and/or <input type="checkbox"/> Product problem (e.g., defects/malfunctions)			
2. Outcomes attributed to a adverse event (check all that apply)			
<input type="checkbox"/> death (month/day/yr)		<input type="checkbox"/> disability	
<input type="checkbox"/> life-threatening		<input type="checkbox"/> congenital anomaly	
<input type="checkbox"/> hospitalization - initial or prolonged		<input type="checkbox"/> required intervention to prevent permanent impairment/damage	
		<input checked="" type="checkbox"/> other: <u>Medica-Cont...</u>	
3. Date of event (month/day/yr) 01/23/03	4. Date of this report (month/day/yr) 02/19/03		
5. Describe event or problem			
<p><b>PULMONARY FIBROSIS (Pulmonary fibrosis)</b></p> <p>This 55-year-old male was enrolled in an investigator sponsored study. The patient has glioblastoma multiforme. Protocol therapy consisted of erlotinib 150 mg po QD commencing on 27-Sep-2002. Protocol therapy was held on 27-Dec-2002. Other significant history included a pneumonia on 26-Dec-2002 and a chest CT to rule out any pulmonary pathology prior to resuming erlotinib.</p> <p>On 23-Jan-2003 a chest CT showed mediastinal lipomatosis and extensive bilateral pulmonary fibrosis with a confluent area of pulmonary fibrosis suggested involving the left lung.</p> <p>The investigator considered the event to be possibly related to erlotinib.</p>			
6. Relevant tests/laboratory data, including dates			
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)			
Past Disease: PNEUMONIA			

C. Suspect medication(s)			
1. Name (give labeled strength & mfr/labeler, if known)			
#1 Erlotinib HCl (Tablets)		Cont...	
#2		#2	
2. Dose, frequency & route used		3. Therapy dates (if unknown, give duration)	
#1 150 mg (QD), Oral		#1 09/27/02 - 12/27/02	
#2		#2	
4. Diagnosis for use (indication)		5. Event abated after use stopped or dose reduced	
#1 GLOBLASTOMA MULTIFORME		#1 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply	
#2		#2 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply	
6. Lot # (if known)		7. Exp. date (if known)	
#1 Unk		#1 Unk	
#2		#2	
8. Event reappeared after reintroduction			
#1 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply			
#2 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply			
9. NDC # - for product problems only (if known)			
#1			
#2			
10. Concomitant medical products and therapy dates (exclude treatment of event)			
1) MINOXIDIL			
2) VERAPAMIL			
3) GLYCERYL TRINITRATE			
4) ACETYLSALICYLIC			
Cont			
G. All manufacturers			
1. Contact office - name/address (& mfg site for devices)		2. Phone number	
OSI Pharmaceuticals Boulder Safety 2860 Wilderness Place Boulder, CO 80301 USA ( Informing Unit )		303-444-5893	
4. Date received by manufacturer (month/day/yr)		5. (A) NDA #	
02/07/03		IND # 53,728	
6. If IND, protocol #		PLA #	
Unk		pre-1938 <input type="checkbox"/> yes	
7. Type of report (check all that apply)		OTC product <input type="checkbox"/> yes	
<input type="checkbox"/> 5-day <input checked="" type="checkbox"/> 15-day			
<input type="checkbox"/> 10-day <input type="checkbox"/> periodic			
<input checked="" type="checkbox"/> Initial <input type="checkbox"/> follow-up #			
9. Mfr. report number		8. Adverse event term(s)	
2003000295		1) PULMONARY FIBROSIS (Pulmonary fibrosis)	
E. Initial reporter			
1. Name & address		phone #	
Cathy Brewer Taussig Cancer Center 9500 Euclid Avenue Cleveland, OH 44195 USA		216-445-5368	
2. Health professional?		3. Occupation	
<input checked="" type="checkbox"/> yes <input type="checkbox"/> no		Study Coordinator	
4. Initial reporter also sent report to FDA			
		<input type="checkbox"/> yes <input checked="" type="checkbox"/> no <input type="checkbox"/> unk	

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

OSI Pharmaceuticals  
Boulder Safety  
2860 Wilderness Place  
Boulder, CO 80301  
USA

Continuation Sheet for FDA-3500A Form

Page 2 of 2

Mfr. report # : 2003000295

Date of this report : 02/19/03

**B. Adverse event or product problem**

**B.2 Outcome attributed to adverse event (Cont...)**

Other : Medically significant

**C. Suspect medication (Cont...)**

Seq No. : 1  
C.1 Suspect medication : Erlotinib HCl (Tablets)

**C10. Concomitant medical products**

Seq No. : 4  
Concomitant Medical Product : ACETYLSALICYLIC ACID

Seq No. : 5  
Concomitant Medical Product : DEXAMETHASONE

Seq No. : 6  
Concomitant Medical Product : GABAPENTIN

Seq No. : 7  
Concomitant Medical Product : FAMOTIDINE

Seq No. : 8  
Concomitant Medical Product : ALPRAZOLAM

Seq No. : 9  
Concomitant Medical Product : MINOCYCLINE

Seq No. : 10  
Concomitant Medical Product : CEFALEXIN

Seq No. : 11  
Concomitant Medical Product : CHERACOL