

MedWatch

The FDA Medical Products Reporting Program

Merck Human Health Division

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

Merck Facsimile of FDA Form 3500A
Approved by FDA (10/21/1993)

Mfr report #	WAES 0712USA09142
UF/Dist report #	
	FDA Use On

Page 1

A. Patient information

1. Patient identifier Unk AN 61514 in confidence	2. Age at time of event: or 46 years Date of Birth: 04/29/1961	3. Sex <input checked="" type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight 173 pounds
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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 adverse event (check all that apply) <input type="checkbox"/> Death (mm/dd/yyyy) <input type="checkbox"/> Life-threatening <input checked="" type="checkbox"/> Hospitalization-initial or prolonged <input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices) <input type="checkbox"/> Disability or Permanent Damage <input type="checkbox"/> Congenital Anomaly/Birth Defect <input type="checkbox"/> Other Serious (Important Medical Events)
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3. Date of event (mm/dd/yyyy)	12/21/2007	4. Date of this report (mm/dd/yyyy)	03/09/2009
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5. Describe event or problem
This is in follow-up to report(s) previously submitted on 1/2/2008; 1/3/2008; 2/13/2008; 2/27/2008; 3/6/2008; 3/27/2008; 4/15/2008; 9/10/2008; 9/24/2008; 12/16/2008; 2/9/2009; 2/26/2009

A Phase II/III Randomized, Double-Blind Study of Paclitaxel plus Carboplatin in Combination with Vorinostat (MK-0683) or Placebo in Patients with Stage IIIB (with pleural effusion) or Stage IV Non-Small-Cell Lung Cancer (NSCLC)

Initial and follow-up information has been received from an investigator concerning a 46 year old white female with Chronic obstructive pulmonary disease (COPD), pain, anorexia, nausea, fatigue and a sleep disorder who was randomized on 07-DEC-2007 to a study, title as stated above. On 10-DEC-2007, the patient was placed on cycle one blinded study therapy, capsule, of either vorinostat 400 mg or placebo, administered daily for 14 days every 3 weeks, for the treatment of non-small cell lung cancer (diagnosed 23-OCT-2007, current staging T3,N2,M1, stage

(Continued on Additional Page)

6. Relevant tests/laboratory data, including dates Refer to Additional Page
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7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
CONCURRENT CONDITIONS: Pain; Sleep disorder; Nausea; Anorexia; Fatigue; Chronic obstructive pulmonary disease; Premedication; Tobacco user

C. Suspect medication(s)

1. Name (Give labeled strength & mfr/labeler) # 1 CAP 0683-blinded therapy Unk # 2 carboplatin Unk (Continued on Additional Page)
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2. Dose, frequency & route used # 1 Unk/Unk/PO # 2 600 mg/1X/IV	3. Therapy dates (if unknown, give duration) from/to (or best estimate) # 1 12/10/2007 - 12/20/2007 # 2 12/13/2007 - 12/13/2007
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4. Diagnosis for use (indication) # 1 Non-small cell lung cancer # 2 Non-small cell lung cancer	5. Event abated after use stopped or dose reduced. yes no N/A unk # 1 <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> # 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
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6. Lot # # 1 # 2	7. Exp. Date # 1 # 2	8. Event reappeared after reintroduction. yes no N/A unk # 1 <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> # 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/>
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9. NDC # or Unique ID Unknown

10. Concomitant medical products and therapy dates (excluded treatment of event) BENADRYL 12/13/2007-12/13/2007 DECADRON (DEXAMETHASONE) 12/13/2007-12/13/2007
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G. All manufacturers

1. Contact office - name/address Merck Human Health Division Merck & Co., Inc. P.O. Box 4 West Point, Pa. 19486-0004 Attn: World Wide Product Safety	2. Phone Number (215) 652-8071	3. Report source (check all that apply) <input type="checkbox"/> foreign <input checked="" type="checkbox"/> study <input type="checkbox"/> literature <input type="checkbox"/> consumer <input checked="" type="checkbox"/> health professional <input type="checkbox"/> user facility <input type="checkbox"/> company representative <input type="checkbox"/> distributor <input type="checkbox"/> other:
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4. Date received by manufacturer (mm/dd/yyyy)	02/26/2009	5. (A)NDA # IND # 58915
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6. If IND, protocol # 0560084	STN # PMA/ 510(k) #
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7. Type of report <input type="checkbox"/> 5-day <input type="checkbox"/> 7-day <input type="checkbox"/> 10-day <input checked="" type="checkbox"/> 15-day <input type="checkbox"/> 30-day <input type="checkbox"/> Periodic <input type="checkbox"/> Initial <input checked="" type="checkbox"/> Follow-up# 12	Combination Product Pre-1938 OTC product <input type="checkbox"/> Yes <input type="checkbox"/> Yes <input type="checkbox"/> Yes
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9. Mfr. report number WAES 0712USA09142
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8. Adverse event term(s) FEBRILE NEUTROPENIA

E. Initial reporter

1. Name, address & phone #

2. Health professional? <input checked="" type="checkbox"/> YES <input type="checkbox"/> NO	3. Occupation	4. Initial reporter also sent report to FDA. <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> unk
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FDA

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

B. Adverse event or product problem**5. Describe event or problem**

IV). Concomitant study therapy included carboplatin, 600 mg (AUC equivalent to 6), administered IV on day 3 and paclitaxel, 200 mg/m² (364 mg), administered IV on day 3; both initiated on 13-DEC-2007. Concomitant therapy included clonazepam (KLONOPIN), dronabinol (MARINOL), fentanyl (DURAGESIC), metoclopramide hydrochloride (REGLAN), dexamethasone (MSD), ranitidine hydrochloride (ZANTAC), diphenhydramine hydrochloride (BENADRYL) for pre-medication and acetaminophen (+) oxycodone hydrochloride (ENDOCET). On 21-DEC-2007, cycle 1 day 11, the patient developed neutropenic fever and shortness of breath and presented to an emergency room with increased shortness of breath. Other symptoms were weakness, cough with productive sputum and complaint of fever for 2 days. The patient's temperature was 99.2, white blood cell (WBC) count was 1.1, platelet count was 91,000 and breath sounds were decreased bilaterally with few scattered rhonchi. Blood pressure (BP) on admission was 116/82, heart rate was 124 beats/minute. The patient was hospitalized with the diagnosis of neutropenic fever (grade 3) and respiratory distress. No chest x-ray was done on day of admission. On 21-DEC-2007, study therapy was interrupted due to neutropenic fever. A Chest x-ray was performed on 25-DEC-2007 and revealed pleural effusion. Sputum cultures revealed gram positive cocci and therapy with intravenous cefepime and levofloxacin (LEVAQUIN) was initiated. The patient was placed on reverse isolation and therapy with filgrastim (NEUPOGEN), 480 mcg injection, daily. Oxygen support at 2L/min via nasal cannula, albuterol sulfate (+) ipratropium bromide (DUONEB) with mucomyst added and IV fluids were administered. On 24-DEC-2007, the patient had no further complaints, WBC count was stable at 15. On 24-DEC-2007, the patient was discharged to home. No blood cultures were drawn according to the discharge summary. The discharge diagnoses were reported as lung cancer, COPD, tobacco abuse and neutropenic fever. The patient was reported to be recovered from the febrile neutropenia on 25-DEC-2007. On 27-DEC-2007 the patient returned to the clinic for follow-up. She was improved after antibiotics and steroid therapy. The patient was scheduled to return on 03-JAN-2008 for next chemotherapy treatment.

The investigator felt that neutropenic fever (grade 3) was related to blinded study therapy and study therapy with carboplatin; neutropenic fever (grade 3) was not related to therapy with paclitaxel.

Additional information is not expected.

6. Relevant tests/laboratory data, including dates**DIAGNOSTIC TEST**

<u>Tests</u>	<u>Date</u>	<u>Value</u> <u>Unit</u>	<u>Normal Range</u>
blood pressure measurement	12/21/2007	116/82	
chest X-ray	12/25/2007		
Comment: pleural effusion			

LABORATORY RESULTS

<u>Tests</u>	<u>Date</u>	<u>Value</u> <u>Unit</u>	<u>Normal Range</u>
absolute neutrophil count	12/20/2007	500	2000 - 7800
WBC count	12/21/2007	1100 K/uL	4100 - 10900
body temp	12/21/2007	99.2	
platelet count	12/21/2007	91000 K/uL	140000 - 440000
blood culture	12/21/2007		
Comment: gram + cocci			
sputum culture	12/21/2007		
Comment: gram + cocci			
total heartbeat count	12/21/2007	124 beats/min	
WBC count	12/24/2007	15	
WBC count	12/25/2007	0.2	

C. Suspect medication(s)**1. Name (Give labeled strength & mfr/labeler)**

#3 paclitaxel Unk

2. Dose, frequency & route used

#3 364 mg/1X/IV

3. Therapy dates (if unknown, give duration) from/to (or best estimate)

#3 12/13/2007 - 12/13/2007

4. Diagnosis for use (indication)

#3 Non-small cell lung cancer

5. Event abated after use stopped or dose reduced

	YES	NO	N/A	UNK
#3				X

6. Lot # (if known)

#3

7. Exp date (if known)

#3

8. Event reappeared after reintroduction

	YES	NO	N/A	UNK
#3				X

C. Suspect medication(s)

10. Concomitant medical products and therapy dates (exclude treatment of event)	
DURAGESIC	11/28/2007 - 02/11/2008
ENDOCET	11/01/2007 - Cont
KLONOPIN	11/08/2007 - Cont
MARINOL	12/03/2007 - Cont
REGLAN	12/03/2007 - Cont
ZANTAC	12/13/2007 - 12/13/2007