

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)

MedWatch

The FDA Medical Products Reporting Program

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Mfr report #	WAES 0806USA01374
UF/Dist report #	
	FDA Use Onl

A. Patient information

1. Patient identifier Confidential AN 60010 in confidence	2. Age at time of event: or 42 years Date of Birth: 01/01/1966	3. Sex <input checked="" type="checkbox"/> Female <input type="checkbox"/> Male	4. Weight 79 lbs
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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 checked="" type="checkbox"/> Death 06/23/2008 (mm/dd/yyyy)	<input type="checkbox"/> Disability or Permanent Damage
<input type="checkbox"/> Life-threatening	<input type="checkbox"/> Congenital Anomaly/Birth Defect
<input checked="" type="checkbox"/> Hospitalization-initial or prolonged	<input type="checkbox"/> Other Serious(Important Medical Events)
<input type="checkbox"/> Required Intervention to Prevent Permanent Impairment/Damage (Devices)	
3. Date of event (mm/dd/yyyy) 06/04/2008	4. Date of this report (mm/dd/yyyy) 02/27/2009

5. Describe event or problem
This is in follow-up to report(s) previously submitted on 11/24/2008; 1/7/2009; 2/5/2009

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 42 year old Asian female with a history of tubal ligation and with adenocarcinoma, who on 26-MAY-2008 was randomized to a study, title as above.

On 26-MAY-2008 the patient was placed on therapy with blinded therapy with either vorinostat, capsule, 400 mg or placebo administered on days 1-14 of cycle 1 (cycle equivalent to 25 days) for the treatment of non-small cell lung cancer (diagnosed 17-APR-2008; current staging (26-MAY-2008): T4/N3/M1; overall stage IV).

(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.)

MEDICAL HISTORY: Tubal ligation
CONCURRENT CONDITIONS: Adenocarcinoma; Premedication; Prophylaxis

C. Suspect medication(s)

1. Name (Give labeled strength & mfr/labeler) # 1 CAP 0683-blinded therapy Unk # 2 carboplatin 574 mg (Continued on Additional Page)	
2. Dose, frequency & route used # 1 Unk/Unk/PO # 2 574 mg/1X/IV	3. Therapy dates (if unknown, give duration) from/to (or best estimate) # 1 05/26/2008 - 06/06/2008 # 2 05/30/2008 - 05/30/2008
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 checked="" type="checkbox"/> <input type="checkbox"/>
6. Lot # # 1 # 2	7. Exp. Date # 1 # 2
8. Event reappeared after reintroduction. 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 checked="" type="checkbox"/> <input type="checkbox"/>	
9. NDC # or Unique ID Unknown	
10. Concomitant medical products and therapy dates (excluded treatment of event) ATIVAN 05/30/2008 - 06/01/2008 DECMAX 05/29/2008 - 05/29/2008 (Continued on Additional Page)	

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
4. Date received by manufacturer (mm/dd/yyyy) 02/17/2009	5. (A)NDA # IND # 58915 STN # PMA/ 510(k) # Combination Product <input type="checkbox"/> Yes <input type="checkbox"/> No Pre-1938 <input type="checkbox"/> Yes <input type="checkbox"/> No OTC product <input type="checkbox"/> Yes <input type="checkbox"/> No
6. If IND, protocol # 0560079	9. Mfr. report number WAES 0806USA01374
7. Type of report <input type="checkbox"/> 5-day <input type="checkbox"/> 30-day <input type="checkbox"/> 7-day <input type="checkbox"/> Periodic <input type="checkbox"/> 10-day <input type="checkbox"/> Initial <input checked="" type="checkbox"/> 15-day <input checked="" type="checkbox"/> Follow-up# 3	3. Report source (check all that apply) <input checked="" type="checkbox"/> foreign <input checked="" type="checkbox"/> study <input type="checkbox"/> literature <input type="checkbox"/> consumer health professional <input type="checkbox"/> user facility <input type="checkbox"/> company representative <input type="checkbox"/> distributor <input type="checkbox"/> other:

8. Adverse event term(s)
NEUTROPENIA; THROMBOCYTOPENIA; GASTROENTERITIS; DEATH

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

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

Concomitant study therapy included carboplatin, AUC equivalent to 6 (574 mg) and paclitaxel, 200 mg/m² (240 mg) both administered intravenously on 30-MAY-2008.

Other concomitant therapy included: dexamethasone (DECMAX), granisetron hydrochloride (GRANISSET) and dexamethasone (manufacturer unknown) for premedication for paclitaxel, ranitidine hydrochloride (RANTAC) and omeprazole (OMEZ), for vomiting prophylaxis, lorazepam (ATIVAN) for postchemotherapy medication, promethazine hydrochloride (PHENERGAN) and "effecorlin" for allergic reaction prophylaxis.

On 04-JUN-2008, at 17:00, the patient developed gastroenteritis (grade 3), with watery diarrhea seven to eight times with no blood, the patient was not taking any medication which would lead to bleeding. Stool and urine culture shows no pathogen isolated. On 07-JUN-2008, at 13:00, the patient developed neutropenia (grade 4) and thrombocytopenia (grade 2). On 07-JUN-2008, the patient was hospitalized for neutropenia (grade 4), gastroenteritis (grade 3) and thrombocytopenia (grade 2). The patient was afebrile. On 07-Jun-2008 blood neutrophil count was 17 %, blood platelet count was 55000/cumm, serum sodium test was 129 meq/L and white blood cell count was 1160/cumm. Blood pressure was 90/70, pulse was 100/minutes, respiratory rate was 24/minutes and temperature was 99. The patient also had dehydration (grade 2). Study therapy was interrupted. The patient was treated with IV pints, piperacillin sodium (+) tazobactam sodium (ZOSYN), nitroimidazole (FLAGYL), amikacin, benzydamine hydrochloride (TANTUM), filgrastim (NUFIL SAFE), loperamide hydrochloride (IMODIUM), dextrose in normal saline (2 pints), normal saline (2 pints) and ringer's lactate (2 pints) with "kesol" added to each pint and ceftazidime (CEFTUM). On 09-Jun-2008, white blood cell count was 4510/cumm, blood neutrophil count was 42 percent and blood platelet count was 24,000/cumm. On 09-JUN-2008, the patient recovered from neutropenia (grade 4), gastroenteritis (grade 3) and recovered with sequelae from thrombocytopenia (grade 2) and was discharged from the hospital. On 09-JUN-2008 the patient experienced thrombocytopenia (grade 4) and the outcome was unknown. It was also reported that there was no diarrhea, no fever, and the patient was clinically better so she was discharged on 09-JUN-2008. All treatments were given for 3 days. Discharge diagnoses were neutropenia (grade 4), thrombocytopenia (grade 2) and gastroenteritis. On 20-JUN-2008, the patient was discontinued from study medication due to progressive disease. The patient was lost to follow-up. The patient's family reported to the investigator that the patient died 23-JUN-2008 at home. She was not on any treatment. There was no autopsy performed and the cause of death was unknown. The patients family did not mention any signs and symptoms after the hospital discharge.

The reporting investigator felt that gastroenteritis (grade 3) was related to blinded study therapy. Neutropenia (grade 4) and thrombocytopenia (grade 2) were not related to blinded study therapy and were related to carboplatin and paclitaxel. Dehydration (grade 2) was not related to paclitaxel and carboplatin. Death cause unknown was reported to be not related to study therapy, paclitaxel and carboplatin.

The patient was placed on the following treatment medications during the study: benzydamine hydrochloride (TANTUM) for oral ulcer prophylaxis, cyanocobalamin (+) iron polymaltose (+) pyridixone (OROFER SYRUP) for nutritional support and for the treatment of dehydration.

This is an amended report, the unit measure of "/cumm" was added to the narrative and the laboratory data table.

Additional information is not expected.

6. Relevant tests/laboratory data, including dates

DIAGNOSTIC TEST

Tests	Date	Value Unit	Normal Range
blood pressure measurement	06/07/2008	90/70	

LABORATORY RESULTS

Tests	Date	Value Unit	Normal Range
stool culture Comment: no pathogen isolated	06/04/2008		
urine culture Comment: no pathogen isolated	06/04/2008		
WBC count	06/07/2008	1160 /cumm	4000 - 11000
body temp	06/07/2008	99	
neutrophil count	06/07/2008	17 percent	40 - 75
platelet count	06/07/2008	55000 /cumm	150000 - 400000

serum creatinine
Comment: results not reported

serum potassium
Comment: results not reported

serum sodium
respiratory rate measurement
total heartbeat count
WBC count
neutrophil count
platelet count

06/07/2008
06/07/2008
06/07/2008
06/09/2008
06/09/2008
06/09/2008

129 meq/L
24 /min
100 /min
4510 /cumm
42 percent
24,000 /cumm
136 - 142
4000 - 11000
40 - 75
150000 - 400000

C. Suspect medication(s)

1. Name (Give labeled strength & mfr/labeler)

#3 paclitaxel 240 mg

2. Dose, frequency & route used

#3 240 mg/1X/IV

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

#3 05/30/2008 - 05/30/2008

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)

GRANISET 05/30/2008 - 05/30/2008
OMEZ 05/30/2008 - 06/03/2008
RANTAC 05/30/2008 - 05/30/2008
dexamethasone 05/30/2008 - 05/30/2008
promethazine hydrochloride 05/30/2008 - 05/30/2008