

# 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)

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Mfr report #	WAES 0711USA01780
UF/Dist report #	
FDA Use On	

A. Patient information			
1. Patient identifier Unk AN 61508 in confidence	2. Age at time of event: or 67 years Date of Birth: 08/27/1940	3. Sex <input type="checkbox"/> Female <input checked="" type="checkbox"/> Male	4. Weight 189 pounds

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 11/17/2007 (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) 11/05/2007	4. Date of this report (mm/dd/yyyy) 02/25/2009

5. Describe event or problem  
This is in follow-up to report(s) previously submitted on 11/15/2007; 11/29/2007; 12/13/2007; 11/5/2008

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 67 year old white male with Non-small cell lung cancer (NSCLC) of squamous cell carcinoma (diagnosed 27-JUN-2007, stage T2, N2, M1, stage IV on 11-AUG-2007), gastroesophageal reflux disease, seasonal allergic rhinitis, chronic obstructive pulmonary disease, hypertension, alopecia and a history of radiotherapy (total dose 3500 cGy from (20-AUG-2007 to 10-SEP-2007), anorexia, imbalance, and oral thrush who entered a study, title as stated above. On 12-OCT-2007, the patient was randomized and placed on blinded therapy of vorinostat capsule, PO, 400 mg or placebo once a day

(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: Radiotherapy; Anorexia; Balance impaired NOS; Oral candidiasis CONCURRENT CONDITIONS: Gastroesophageal reflux disease; Seasonal allergic rhinitis; Chronic obstructive pulmonary disease; Hypertension; Alopecia; Sores mouth; Dysgeusia; Anorexia; Pain; Nausea
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C. Suspect medication(s)			
1. Name (Give labeled strength & mfr/labeler) # 1 CAP 0683-blinded therapy Unk # 2 (Continued on Additional Page)			
2. Dose, frequency & route used # 1 Unk/Unk/PO # 2		3. Therapy dates (if unknown, give duration) from/to (or best estimate) # 1 10/12/2007 - 10/15/2007 # 2	
4. Diagnosis for use (indication) # 1 Squamous cell carcinoma # 2		5. Event abated after use stopped or dose reduced. yes no N/A unk # 1 <input type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> # 2 <input type="checkbox"/> <input type="checkbox"/> <input 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 type="checkbox"/> <input type="checkbox"/> <input checked="" type="checkbox"/> <input type="checkbox"/> # 2 <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>	
9. NDC # or Unique ID Unknown			
10. Concomitant medical products and therapy dates (excluded treatment of event) EMEND 10/12/2007-11/05/2007 MARINOL 10/25/2007-11/05/2007 (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) 10/27/2008	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:
6. If IND, protocol # 056009	5. (A)NDA # IND # 58915 STN # PMA/ 510(k) # Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC product <input type="checkbox"/> Yes
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# 4	9. Mfr. report number WAES 0711USA01780

8. Adverse event term(s) NON-SMALL CELL LUNG CANCER
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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

for 14 days of a 25 day cycle for the treatment of non-small cell lung cancer, squamous cell carcinoma. Concomitant study therapy included carboplatin 6 AUC IV (dose =800 mg) and paclitaxel 200 mg/m2 (dose= 400 mg). Other concomitant therapy included risperidone, dexamethasone (manufacturer unknown), famotidine (manufacturer unknown), loratadine, fluticasone propionate, megestrol acetate, acetaminophen (TYLENOL), aprepitant (MSD), diphenhydramine/ mycostatin/ fluocinolone acetonide/ tetracycline (klacks solution) and prochlorperazine maleate, dronabinol (MARINOL).

The study drug was interrupted from 16-OCT-2007 to 18-OCT-2007. On 25-OCT-2007, the patient was given marinol 2.5 mg and prochlorperazine 5 mg twice daily for treatment of dysgeusia and anorexia. On 26-OCT-2007 to 01-NOV-2007, therapy with study drug was interrupted again. On 01-NOV-2007, the physician decided that the patient should stop study medication (reason not reported). On 05-NOV-2007, the patient presented to the clinic with confusion and anorexia. The patient was admitted to the hospital for progression of non small cell lung cancer (grade 5). Therapy with study therapy was held due to dehydration grade 2 (also reported as discontinued on 05-NOV-2008). On 05-NOV-2007, an MRI brain(sm) results were improved, no significant edema. On 08-NOV-2007, a lumbar puncture was negative. See laboratory data section for additional laboratory findings. The patient was treated with megestrol acetate, dexamethasone and risperidone. It was noted that a PET scan performed 06-AUG-2007 confirmed CNS metastases, therefore preexisting condition prior to enrollment on the study. A neurological exam was done and the patient was found to have progressive disease. On 09-NOV-2008 an 10-NOV-2008, it was reported that both potassium and calcium were low (potassium was 3.3 both days and calcium was 8.0 on 09-NOV-2008 and 8.4 on 10-NOV-2008). On 09-NOV-2008 and 10-NOV-2008, pulse oximetry was performed it was reported as 91% and 95% on room air, respectively, hemoglobin was low at 8.2 and red blood cell count (RBC) was low. A Psychiatrist did not find any psychiatric disorder. The investigator never could prove the exact cause of confusion, except that ultimately due to the cancer and radiation treatment with or without some chemotherapy affect. He recovered somewhat and then was discharged on 10-NOV-2007 to a Hospice program. Discharge diagnosis was metastatic lung cancer. The patient presented to the clinic on 12-NOV-2007 and was entered into hospice. On 17-NOV-2007, the patient died. The cause of death was progression of NSCLC, grade 5. The patient's death was due disease of metastatic lung cancer as reported by the investigator.

During the study, the patient experienced the following NSAEs: dysgeusia grade 1 (11-OCT-2007), diarrhea grade 1 (25-OCT-2007), dehydration grade 2 (01-NOV-2007), lower extremity edema grade 1 (01-NOV-2007), fatigue grade 1 (01-NOV-2007), anxiety grade 1 (05-NOV-2007), shortness of breath grade 1 (05-NOV-2007), weakness grade 2 (05-NOV-2007), weight loss grade 2 (05-NOV-2007), asthenia grade 2 (05-NOV-2007), weight decreased grade 2 (05-NOV-2007), dyspnoea respiratory grade 1 (05-NOV-2007).

The reporting investigator felt that low potassium (grade 3) (NSAE), and the patient's death due to progression of NSCLC, (grade 5) were not related to study therapy of vorinostat or placebo, carboplatin, or paclitaxel.

This is an amended report. For the paclitaxel entry on the therapy screen the dose was changed from 200 mg/m[2] IV to 400 mg IV.

This report was inadvertently sent to the FDA on 05-NOV-2008. This report no longer meets the criteria for expedited submission to the FDA.

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>
positron emission tomography Comment: to confirm CNS metastases	08/06/2007			
spinal tap Comment: lumbar puncture - negative	11/08/2007			

## LABORATORY RESULTS

<u>Tests</u>	<u>Date</u>	<u>Value</u>	<u>Unit</u>	<u>Normal Range</u>
hemoglobin Comment: abnormal - low	11/06/2007	8.2		
red blood cell count Comment: abnormal	11/06/2007	2.9		
hemoglobin Comment: abnormal	11/07/2007	10.3		

red blood cell count Comment: abnormal	11/07/2007	3.57	
hemoglobin Comment: abnormal	11/08/2007	10.4	
serum calcium Comment: abnormal	11/08/2007	8.4	
serum potassium	11/08/2007	3.3	3.5 - 5.1
red blood cell count Comment: abnormal	11/08/2007	3.61	
hemoglobin Comment: abnormal	11/09/2007	10.2	
pulse oximetry Comment: room air	11/09/2007	91 %	
serum calcium Comment: abnormal	11/09/2007	8.0	
serum potassium	11/09/2007	3.3	3.5 - 5.1
red blood cell count Comment: abnormal	11/09/2007	3.56	
hemoglobin Comment: abnormal	11/10/2007	10.6	
pulse oximetry Comment: room air	11/10/2007	95 %	
serum calcium Comment: abnormal	11/10/2007	8.4	
serum potassium	11/10/2007	3.3	
red blood cell count Comment: abnormal	11/10/2007	3.66	

C. Suspect medication(s)

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

- #1 CAP 0683-blinded therapy Unk
- #2 carboplatin Unk
- #3 paclitaxel Unk

2. Dose, frequency & route used

- #1 Unk/Unk/PO
- #2 800 mg/Unk/IV
- #3 400 mg/Unk/IV

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

- #1 10/19/2007 - 10/25/2007
- #2 10/19/2007 - 10/19/2007
- #3 10/19/2007 - 10/19/2007

4. Diagnosis for use (indication)

- #1 Squamous cell carcinoma
- #2 Squamous cell carcinoma
- #3 Squamous cell carcinoma

5. Event abated after use stopped or dose reduced

	YES	NO	N/A	UNK
#1			X	
#2			X	
#3			X	

6. Lot # (if known)

- #1
- #2
- #3

## 7. Exp date (if known)

#1  
#2  
#3

## 8. Event reappeared after reintroduction

	YES	NO	N/A	UNK
#1			X	
#2			X	
#3			X	

## C. Suspect medication(s)

## 10. Concomitant medical products and therapy dates (exclude treatment of event)

TYLENOL	08/17/2007 - Cont
[therapy unspecified]	09/12/2007 - 11/05/2007
dexamethasone	11/05/2007 - 11/05/2007
dexamethasone	11/06/2007 - Cont
famotidine	10/??/2007 - Cont
fluticasone propionate	10/??/2007 - Cont
loratadine	10/??/2007 - Cont
megestrol acetate	11/05/2007 - Cont
prochlorperazine maleate	10/11/2007 - 11/05/2007
risperidone	11/09/2007 - 11/09/2007