

U.S. Department of Health and Human Services
Food and Drug Administration

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

Mfr Report # CA042-09-0137(2)
UF/Importer Report #
FDA Use Only

MEDWATCH

FORM FDA 3500A (10/05)

A. PATIENT INFORMATION			
1. Patient Identifier M-A In confidence	2. Age at Time of Event: 68 Y or _____ Date of Birth: 05/17/1940	3. Sex <input checked="" type="checkbox"/> Female or <input type="checkbox"/> Male	4. Weight _____ lbs or 79.8 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 Adverse Event (Check all that apply)			
<input type="checkbox"/> Death: _____ (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) 03/20/2009		4. Date of This Report (mm/dd/yyyy) 05/15/2009	

5. Describe Event or Problem

A 68 year-old Caucasian female subject (#440-0005) experienced septic arthritis suspicion while enrolled in An Open-Label, Phase II Study of Weekly ABI-007 as First Line Therapy for Patients with Metastatic Breast Cancer. The subject received the first dose of treatment with ABI-007 (100 mg/m²) on 17-Sep-2008. The last dose of ABI-007 (100 mg/m²) prior to the onset of the serious adverse event was received on 17-Mar-2009.

On 19-Mar-2009, two days after the last dose of study drug, the subject was hospitalized for suspected septic arthritis. On this date the subject presented to the emergency room with an approximate three day history of pain, edema and redness on the right foot and was subsequently admitted. In the emergency room the subject's temperature was noted to be 39 degrees C. Treatment was provided with cefazolin, ciprofloxacin and piperacillin/tazobactam. At the time of this report the event is ongoing.

ABI-007 was interrupted on 24-Mar-2009 due to this event.

Cont...

6. Relevant Tests/Laboratory Data, Including Dates	
19-Mar-2009 C reactive protein - 289 mg/L (reference range <10)	
20-Mar-2009 Uric Acid - 121 umol/L (reference range 150-360) WBC - 6.52 x 10 ⁹ /L (reference range 4.20-10.20)	
Cont...	

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)	
Concurrent Disease: Hypertension[10020772] Hypothyroidism[10021114] Arthrosis[10003416] Pulmonary embolism[10037377] Pulmonary metastases[10037420] Corneal ulcer[10048492] Hemicolectomy[10019460]	

C. SUSPECT PRODUCT(S)			
1. Name (Give labeled strength & mfr/labeler) #1 ABI-007 (Abraxane [®] for Injectable Suspension (paclitaxel) #2 _____ Cont...			
2. Dose, Frequency & Route Used #1 (100 mg/m ²), Intraveno- #2 _____		3. Therapy Dates (If unknown, give duration) from/to (or best estimate) #1 09/17/2008 - ongoing #2 _____	
4. Diagnosis for Use (Indication) #1 Breast cancer[10006187] #2 _____		5. Event Abated After Use Stopped or Dose Reduced? #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	
6. Lot # #1 UNK #2 _____		7. Exp. Date #1 UNK #2 _____	
8. Event Reappeared After Reintroduction? #1 <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply #2 UNK <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Doesn't Apply			
9. NDC # or Unique ID			
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)			
1) DIOVAN (VALSARTAN) ???/??/1988 - ONGOING			
2) TIAZAC (DILTIAZEM HYDROCHLORIDE) ???/??/2006 - ONGOING			
3) SYNTHROID (LEVOTHY-ROXINE SODIUM) ??/??/1978 - ONGOING			
4) TYLENOL (PARACETAM- Cont...			

G. ALL MANUFACTURERS			
1. Contact Office - Name/Address (and Manufacturing Site for Devices) Abraxis BioScience 11755 Wilshire Blvd., Ste 2000 Los Angeles, CA 90025 USA (Initial Unit)		2. Phone Number Cont...	
4. Date Received by Manufacturer (mm/dd/yyyy) 05/07/2009		5. (A)NDA # _____ IND # 55,974 STN # _____ PMA/510(k) # _____ Combination Product <input type="checkbox"/> Yes Pre-1938 <input type="checkbox"/> Yes OTC Product <input type="checkbox"/> Yes	
6. If IND, Give Protocol # CA042		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 <input checked="" type="checkbox"/> Health Professional <input type="checkbox"/> User Facility <input type="checkbox"/> Company Representative <input type="checkbox"/> Distributor <input type="checkbox"/> Other:	
7. Type of Report (Check all that apply) <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 # 2			
9. Manufacturer Report Number CA042-09-0137(2)		8. Adverse Event Term(s) 1) INFLAMMATORY Cont...	

E. INITIAL REPORTER			
1. Name and Address Guy Cantin CH ^A : Saint-Sacrement Hospital 1050 Chemin Ste-Foy Quebec, G1S 4L8 CANADA		Phone # (418) 649-5741	

2. Health Professional? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No	3. Occupation Physician	4. Initial Reporter Also Sent Report to FDA <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Unk.
--	----------------------------	---

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

Continuation Sheet for FDA-3500A Form

Mfr. Report # : CA042-09-0137(2)

Page 2 of 4

Date of This Report : 05/15/2009

B. ADVERSE EVENT OR PRODUCT PROBLEM

B.5 Describe Event or Problem (Cont...)

The subject's medical history was relevant for hypertension, hypothyroidism, arthrosis and pulmonary embolism on 24-Feb-2009 (refer to CA042-09-0089).

Concomitant medications were not reported.

The investigator reported the event of septic arthritis suspicion was probably related to the study drug.

FOLLOW-UP INFORMATION RECEIVED ON 16-APR-2009:

The event term was revised to probable gout arthritis. The onset date for the event was revised to 20-Mar-2009. An ultrasound, x-ray, and computed tomography of the foot were performed (dates not reported) and revealed an infection of the foot. While hospitalized the subject developed a urinary tract infection that was deemed not to be a serious adverse event. Additional treatment was provided with ertapenem and naprosyn. The event was considered resolved with sequelae on 31-Mar-2009.

After stopping ABI-007 the event did not abate.

Concomitant medications included valsartan, diltiazem hydrochloride, levothyroxine sodium, paracetamol, heparin, warfarin sodium, morphine, hydromorphone hydrochloride, docusate sodium, senna and pantoprazole sodium.

The investigator reported that the event of probable gout arthritis was possibly related to the study drug.

FOLLOW-UP INFORMATION RECEIVED ON 21-APR-2009:

On 21-Mar-2009, an x-ray of the right ankle and foot was performed. In the right ankle there were no signs of erosive arthritis or osteitis. In the right foot there were calcifications at the Achilles tendon attachment point. There were signs of arthrosis at the metatarsal-phalangeal joint of the first toe and between the scaphoid and cuneiforms. The x-ray revealed no signs of osteitis. Also on this date a three-phase bone scintigraphy of the ankles and feet was performed which was strongly suggestive of an infectious process on the right tarsus. A labeled white cell scan was strongly suggestive of an infectious tarsal affliction. On 23-Mar-2009, a surface echograph of the right foot was done which revealed no indication of abscess or hematoma.

Additional medical history included pulmonary metastases, corneal ulcer and hemicolectomy.

FOLLOW-UP INFORMATION RECEIVED ON 7-May-2009:

The event term was revised to inflammatory arthritis/pseudo gout. Per the Investigator, the revised diagnosis was based on the excellent response after treatment with naproxen. Laboratory values were notable for a C reactive protein of 289 mg/L on 19-Mar-2009 (reference range <10). On 20-Mar-2009, the uric acid was 121 umol/L (reference range 150-360) and the white blood cell count was $6.51 \times 10^9/L$ (reference range 4.20-10.20).

B.6 Relevant Tests/Laboratory Data, Including Dates (Cont...)

21-Mar-2009

x-ray of the right ankle- no signs of erosive arthritis or osteitis. In the right foot there were calcifications at the Achilles tendon attachment point. There were signs of arthrosis at the metatarsal-phalangeal joint of the first toe and between the scaphoid and cuneiforms. The x-ray revealed no signs of osteitis.

three-phase bone scintigraphy of the ankles and feet - strongly suggestive of an infectious process on the right tarsus.

labeled white cell scan - strongly suggestive of an infectious tarsal affliction

23-Mar-2009 - surface echograph of the right foot revealed no indication of abscess or hematoma.

C. SUSPECT PRODUCT(S) (Cont...)

Continuation Sheet for FDA-3500A Form

Mfr. Report # : CA042-09-0137(2)

Page 3 of 4

Date of This Report : 05/15/2009

Seq No. : 1
C.1 Suspect Product : ABI-007 (Abraxane® for Injectable Suspension
(paclitaxel protein-bound
particles) (albumin-bound)) (PACLITAXEL)
C.2 Dose, Frequency & Route Used : 1) (100 mg/m2), Intravenous

C.10 Concomitant Medical Products and Therapy Dates

Seq No. : 1
Concomitant Medical Product : DIOVAN (VALSARTAN)
Dose, Frequency & Route Used : 1) 80 mg, Oral
Diagnosis for Use (Indication) : 1) Hypertension [10020772]

Seq No. : 2
Concomitant Medical Product : TIAZAC (DILTIAZEM HYDROCHLORIDE)
Dose, Frequency & Route Used : 1) 300 mg, Oral
Diagnosis for Use (Indication) : 1) Hypertension [10020772]

Seq No. : 3
Concomitant Medical Product : SYNTHROID (LEVOTHYROXINE SODIUM)
Dose, Frequency & Route Used : 1) 100 mg, Oral
Diagnosis for Use (Indication) : 1) Hypothyroidism [10021114]

Seq No. : 4
Concomitant Medical Product : TYLENOL (PARACETAMOL)
Dose, Frequency & Route Used : 1) Oral
Therapy Dates : 1) ??/??/2003 - ONGOING
Diagnosis for Use (Indication) : 1) Arthrosis [10003416]
2) Fever [10016558]

Seq No. : 5
Concomitant Medical Product : INOHEP (HEPARIN-FRACTION, SODIUM SALT)
Dose, Frequency & Route Used : 1) 15000 UT, Subcutaneous
Therapy Dates : 1) 02/24/2009 - ONGOING
Diagnosis for Use (Indication) : 1) Prophylaxis [10036898]

Seq No. : 6
Concomitant Medical Product : COUMADIN (WARFARIN SODIUM)
Dose, Frequency & Route Used : 1) 5-7.5 MG, Oral
Therapy Dates : 1) 02/24/2009 - ONGOING
Diagnosis for Use (Indication) : 1) Prophylaxis [10036898]

Seq No. : 7
Concomitant Medical Product : MORPHINE (MORPHINE)
Dose, Frequency & Route Used : 1) 5 mg, Oral
Therapy Dates : 1) 03/19/2009 - 03/25/2009
Diagnosis for Use (Indication) : 1) Pain foot [10033400]

Seq No. : 8
Concomitant Medical Product : DILAUDID (HYDROMORPHONE HYDROCHLORIDE)
Dose, Frequency & Route Used : 1) 1 mg, Intravenous
Therapy Dates : 1) 03/19/2009 - 03/19/2009
Diagnosis for Use (Indication) : 1) Pain foot [10033400]

Seq No. : 9
Concomitant Medical Product : COLACE (DOCUSATE SODIUM)
Dose, Frequency & Route Used : 1) 200 mg, Oral
Therapy Dates : 1) 03/22/2009 - 03/30/2009
Diagnosis for Use (Indication) : 1) Constipation [10010774]

Seq No. : 10
Concomitant Medical Product : SENOKOT (SENNA FRUIT)
Dose, Frequency & Route Used : 1) 17.2 mg, Oral
Therapy Dates : 1) 03/22/2009 - 03/30/2009
Diagnosis for Use (Indication) : 1) Constipation [10010774]

Seq No. : 11
Concomitant Medical Product : PANTOLOC (PANTOPRAZOLE SODIUM)
Dose, Frequency & Route Used : 1) 40 mg, Oral
Therapy Dates : 1) 03/26/2009 - ONGOING
Diagnosis for Use (Indication) : 1) Prophylaxis [10036898]

G. ALL MANUFACTURERS

G.2 Phone Number

Continuation Sheet for FDA-3500A Form

Page 4 of 4

Mfr. Report # : CA042-09-0137(2)

Date of This Report : 05/15/2009

(310) 883-1300

G.8 Adverse Event Term(s)

1) INFLAMMATORY ARTHRITIS/PSEUDOGOUT (Gouty arthritis, Gouty arthritis)

Company Comments:

A search of the database reveals that no serious, similar reports of septic arthritis have been received.

It is not possible to make an accurate assessment of causality given the limited information provided. The subject's immune status, as well as other co morbid conditions, may be contributory.

A search of the database reveals no other cases of gout arthritis.

Given the information provided, a causal link between the event and ABI-007 is unlikely. The onset of symptoms preceded the last dose of ABI-007. In addition, the presence of an infectious process is more likely in this setting, supported by the symptom of fever and findings on scintigraphy.

A search of the database is notable for one report of "Acute Inflammatory Arthritis" (CA023-06-0549) in a 71 year old female with metastatic breast cancer enrolled in a clinical trial. Four days after the first and only dose of ABI-007 and bevacizumab the subject experienced symptoms of inflammatory arthritis of multiple joints and was hospitalized ten days later. The event was deemed possibly related to ABI-007. An additional post marketing report of "Arthritis" (ABHIH-09-0009) was received regarding a 67 year old patient who experienced a worsening of osteoarthritis coincident with Abraxane therapy.

Given the final diagnosis of inflammatory arthritis consistent with resolution of symptoms following anti inflammatory medication and the absence of definitive alternative etiology, it is possible the event is causally linked to ABI-007 administration. An infectious etiology remains possible; antibiotic therapy was initiated at the onset of symptoms and may have contributed to the resolution of symptoms.