

Mfr report #  
 PRIUSA1999006496  
 UR/Dat report #  
 FDA Use Only

**A. Patient information**

1. Patient identifier: ?-?  
 2. Age at time of event: 40 yr  
 3. Sex:  female  male  
 4. Weight: UNK lbs or UNK kgs  
 Date of birth: ??/??/??

**B. Adverse event or product problem**

1.  Adverse event and/or  Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply):  
 death 22/222/22 (month/year)  
 life-threatening  
 hospitalization: initial or prolonged  
 disability  
 congenital anomaly  
 required intervention to prevent permanent impairment/damage  
 other:

3. Date of event (month/year): ??/??/??  
 4. Date of this report (month/year): 11/04/99

5. Describe event or problem

Report published in 1988 Annual Report of the American Association of Poison Control Centers National Data Collection System (case 159). A 40-year-old patient (sex unspecified) died following intentional misuse of acetaminophen with codeine. Exposure to medication was chronic.

Additional information received 4-Nov-99: This 40 year-old female presented to an emergency department comatose and in fulminant hepatic encephalopathy. She had reportedly taken an unknown amount of acetaminophen with codeine (#3) for chronic pain. Her vital signs were heart rate, 150; blood pressure, 70/50 mmHg (on dopamine); and respirations by ventilator. Initial labs included an acetaminophen level of 37 mcg/ml. Liver function tests were: AST, 3987 U/L; ALT, 1524 u/L; LDH, 20,030 u/L; CPK, 1225 u/L; total bilirubin, 1.5 mg/dL; alkaline phosphatase, 254 u/L; and ammonia, 197ug/dL. ABG's on 60% oxygen were pH, 7.24; PCO2, 37 mmHg; and PO2, 38 mmHg. The time of the last ingestion was not known. Five hours after the initial contact, the patient was minimally responsive to deep pain. Vital (Cont.)

6. Relevant tests/laboratory data, including dates

Acetaminophen level of 37 mcg/mL (Lab data cont.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Chronic pain

**C. Suspect medication(s)**

1. Name (give labeled strength & mfr/labeled, if known):  
 #1 TYLENOL W/CODEINE NO. 3 (tablet) (ACETAMINOPHEN/CODEINE)  
 #2

2. Dose, frequency & route used  
 #1 oral  
 #2

3. Therapy dates (if unknown, give duration) (month/year or best estimate)  
 #1 ??/??/??  
 #2

4. Diagnosis for use (indication)  
 #1 PAIN  
 #2

5. Event abated after use stopped or dose reduced  
 #1  yes  no  doesn't apply  
 #2  yes  no  doesn't apply

6. Lot # (if known)  
 #1  
 #2

7. Exp. date (if known)  
 #1  
 #2

8. Event reappeared after reintroduction  
 #1  yes  no  doesn't apply  
 #2  yes  no  doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)  
 No Concomitant Products Reported

**D. All manufacturers**

1. Contact office - name/address (& routing site for devices)  
 R.W. JOHNSON PHARM. RES. INST. USA  
 DIV. OF ORTHO PHARMACEUTICAL CORP.  
 920 U.S. Route 202  
 P.O. Box 300  
 Raritan NJ 08869  
 USA  
 ( Informing Unit )

2. Phone number  
 908-704-4504

3. Report source (check all that apply)  
 foreign  
 study  
 literature  
 consumer  
 health professional  
 user facility  
 company representative  
 distributor  
 other:

4. Date received by manufacturer (month/year)  
 11/04/99

5. (ANDA # 85-055)  
 IND #  
 PLA #  
 pre-1938  yes  
 OTC  yes  
 product

6. If IND, protocol #

7. Type of report (check all that apply)  
 5-day  15-day  
 10-day  periodic  
 initial  follow-up # 1

8. Adverse event term(s)  
 1) THERAPEUTIC RESPONSE INCREASED  
 2) HEPATIC NECROSIS  
 3) LIVER FATTY  
 4) PANCREATITIS  
 5) PULMONARY CONGESTION  
 6) CEREBRAL ATROPHY (Cont.)

9. Mfr. report number  
 PRIUSA1999006496

**E. Initial reporter**

1. Name, address & phone #  
 Dr. Toby Litovitz  
 National Capital Poison Center  
 Georgetown University Hospital  
 3800 Reservoir Road NW  
 Washington, DC 20007  
 USA

2. Health professional?  
 yes  no

3. Occupation  
 Physician

4. Initial reporter MRO sent report to FDA  
 yes  no  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.

920 P.O. Rar.



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Mfr. report #: PRIUSA1999006496

Date of this report: 11/04/99

B. Adverse event or product problem

B.5 Describe event or problem (Cont...)

signs were heart rate, 140; blood pressure, 110-120 mmHg/doppler; and respirations by ventilator. She had been administered activated charcoal and was receiving her loading dose of acetylcysteine. The dopamine had been discontinued. One dose of naloxone hydrochloride had been given. An IV of dextrose 5% in water with three ampules of bicarbonate at 50 mL per hour was infusing. A toxicology screen was pending. Approximately 24 hours after the initial contact, the patient remained comatose and tachycardic. Her vital signs were blood pressure, 120-130/60-70 mmHg; heart rate, 110 without dysrhythmias; and respirations by ventilator. She had been restarted on dopamine to maintain renal perfusion and continued to tolerate the acetylcysteine therapy. Two days after presentation to the emergency department, the patient expired. At autopsy, the patient was found to have hepatic centrilobular necrosis concurrent with acetaminophen toxicity. She also demonstrated fatty liver changes concurrent with alcohol abuse. Additional findings included acute pancreatitis, pulmonary congestion concurrent with ARDS, and degenerative cerebral changes.

B.6 Relevant tests/laboratory data, including dates (Cont...)

Lab Result:

Table with 5 columns: Sl. No., Test date, Test name, Test result, Normal value. Contains lab results for ALANINE AMINOTRANSFERASE, ALKALINE PHOSPHATASE, AMMONIA, ASPARTATE AMINOTRANSFERASE, BILIRUBIN, TOTAL, BLOOD GAS, PCO2, PO2, CREATINE KINASE, LACTIC DEHYDROGENASE, and PH.

G. All manufacturers

8. Adverse event term(s)

- 7) COMA
8) TACHYCARDIA
9) DRUG ABUSE

Source of report (Literature):

Seq No. : 1
Author : Toby Litovitz
Journal title : 1988 Annual Report of the American Association of Poison Control Centers National Data Collection System
Year : 89
Edition : 7(5)
Page number : From 495 To 545
Article title : American Journal of Emergency Medicine

