

Individual Safety Report



3308359-3-00-01

RES. INST. USA
use by user-facilities,
and manufacturers for
DATORY reporting

Approved by FDA on 08/25/98

LDN report #	PRIUSA1999002530
U7751a report #	
FDA Use Only	

FDA MEDICAL PRODUCTS REPORTING PROGRAM

Page 1 of 2

A. Patient information			
1. Patient identifier ? - ?	2. Age at time of event or Date of birth: 45 yr ??/??/??	3. Sex <input checked="" type="checkbox"/> female <input type="checkbox"/> male	4. Weight UNK lbs or UNK 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 checked="" type="checkbox"/> death ??/??/?? (month/yr)		<input type="checkbox"/> disability	
<input type="checkbox"/> life-threatening		<input type="checkbox"/> congenital anomaly	
<input checked="" type="checkbox"/> hospitalization - initial or prolonged		<input type="checkbox"/> required intervention to prevent permanent impairment/damage	
<input type="checkbox"/> other:			
3. Date of event (month/yr) ??/??/??	4. Date of this report (month/yr) 07/15/99		
5. Describe event or problem			
<p>Report published in 1998 Annual Report of Poison Control Centers Toxic Exposure Surveillance System (case 259) of a 45-year-old (sex unspecified) who died following ingestion of acetaminophen with codeine (dose, date unspecified) for an unknown reason. Chronicity is unknown for acetaminophen with codeine.</p> <p>Additional information received 08-Jul-99: This 45-year-old female diabetic was taking acetaminophen with codeine #3 for a long time for alleged back pain from trauma. It is unclear whether she took an overdose or excessive amount of acetaminophen with codeine. She was uncooperative, then lapsed into a coma. At the time of the initial call to the poison center her prothrombin time was 65 seconds with an INR of 5.6, SGOT 2,180, SGPT 1,972, total bilirubin 2.7, creatinine 1.5. The patient was awake, alert and cooperative, but denied any knowledge of medical problems other than back pain. She was started on N-acetylcysteine and activated charcoal, but liver enzymes progressed to get worse and her prothrombin time also increased. On day 2 her ammonia (Cont.)</p>			
6. Relevant tests/laboratory data, including dates			
<p>Additional information received 08-Jul-99: Day 1 prothrombin time 65 seconds, INR 5.6, SGOT 2,180, SGPT 1,972, total bilirubin 2.7, creatinine 1.5</p> <p>Day 2 ammonia level 155 mosm, SGOT 4,110, LDH 17,596, total bilirubin 3.36, vital signs "okay", intracranial pressure between 9 and 15 mL of water, heart rate 120 - 130, blood pressure 130 - 150/60 - 80, cardiac index 6.8, systemic vascular resistance 572, (Cont.)</p>			
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)			
<p>No Pat Profiles Rptd</p> <p>Additional information received 08-Jul-99: diabetes, chronic back pain from previous trauma; taking Tylenol for a long time.</p>			

C. Suspect medication(s)			
1. Name (give labeled strength & mfr/labeler, if known)			
#1 TYLENOL W/CODEINE NO. 3 (tablet) (ACETAMINOPHEN/CODEINE)			
#2			
2. Dose, frequency & route used		3. Therapy dates (if unknown, give duration) (month/yr or best estimate)	
#1 oral		#1 ??/??/?? - Stopped	
#2		#2	
4. Diagnosis for use (indication)		5. Event abated after use stopped or dose reduced	
#1 PAIN		#1 <input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> doesn't apply	
#2		#2 <input type="checkbox"/> yes <input type="checkbox"/> no <input type="checkbox"/> doesn't apply	
6. Lot # (if known)		7. Exp. date (if known)	
#1		#1	
#2		#2	
9. NDC # - for product problems only (if known)			
#1			
#2			
10. Concomitant medical products and therapy dates (exclude treatment of event)			
No Concomitant Products Reported			

G. All manufacturers		
1. Contact office - name/address (& mailing site for devices)		2. Phone number
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)		908-704-4504
3. Report source (check all that apply)		
<input type="checkbox"/> foreign		
<input type="checkbox"/> study		
<input checked="" 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:		
4. Date received by manufacturer (month/yr)	5. (ANDA #	
07/08/99	85-055	
6. If IND, protocol #	IND #	
	PLA #	
7. Type of report (check all that apply)	pre-1938 <input type="checkbox"/> yes	
<input type="checkbox"/> 5-day <input checked="" type="checkbox"/> 15-day	OTC product <input type="checkbox"/> yes	
<input type="checkbox"/> 10-day <input type="checkbox"/> periodic		
<input type="checkbox"/> initial <input checked="" type="checkbox"/> follow-up # 1		
9. Mfr. report number	8. Adverse event term(s)	
PRIUSA1999002530	1) HYPERTENSION INTRACRANIAL	
	2) COMA	
	3) PROTHROMBIN DECREASED	
	4) HEPATIC FAILURE	

I. Initial reporter			
1. Name, address & phone #			
Dr. Toby Litovitz American Association of Poison Control Centers 3201 New Mexico Ave, Suite 310 Washington, DC 20016 USA Phone # :202-362-7493			
2. Health professional?		3. Occupation	
<input checked="" type="checkbox"/> yes <input type="checkbox"/> no		Physician	
4. Initial reporter also reporting to FDA			
<input type="checkbox"/> yes <input type="checkbox"/> no <input checked="" type="checkbox"/> 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.

JUL 21 1999

DOS



3388359-3-00-02

B. Adverse event or product problem

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

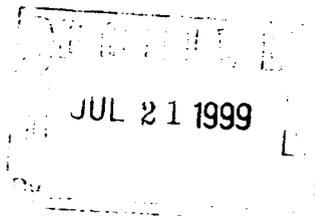
level was 155 mosm, SGOT 4,110, LDH 17,596. She was put on a liver failure protocol and given fresh frozen plasma, IV fluids and oxygen. Her total bilirubin at that time was 3.36, her vital signs were "okay". Late that day she became obtunded and there was great difficulty arousing her. She was transferred to an institution with capability of doing liver transplants. At the receiving hospital she was chemically paralyzed and sedated. An intracranial bolt was inserted and found an intracranial pressure between 9 and 15 mL of water, a Swan Ganz was inserted. Her heart rate was 120 - 130 with an occasional premature ventricular contraction, blood pressure 130 - 150/60 - 80, cardiac index was 6.8, systemic vascular resistance 572, central venous pressure was 13, pulmonary artery pressure was 30/20, wedge pressure was 16, cardiac output was 12. She was placed on renal profusion dose of dopamine and she was getting flesh, frozen plasma to attempt to correct her coagulopathy. At the receiving hospital N-acetylcysteine was discontinued, despite the urging from the poison center. They placed her on D-penicillamine suspecting Wilson's disease and copper toxicity. For reasons not explained to the poison center, she was considered to not be a liver transplant eligible patient. She continued unresponsive to painful stimuli, her liver enzymes, AST dropped to 1,481, ALT to 1,686. On day 3 the prothrombin time dropped to 22. Again, the poison center recommended IV N-acetylcysteine but the hospital refused. On day 4 her AST was down to 542, ALT 1,185, total bilirubin 7.6, creatinine 7.9. On day 5 net total bilirubin rose to 9, ammonia dropped to 79, lipase 1,520, prothrombin 23.2, creatinine 0.8. She continued unresponsive, required pressors to sustain her blood pressure and on day 10 she expired.

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

central venous pressure 13, pulmonary artery pressure 30/20, wedge pressure 16, cardiac output 12, AST 1,481, ALT 1,686
 Day 3 prothrombin time 22
 Day 4 AST 542, ALT 1,185, total bilirubin 7.6, creatinine 7.9
 Day 5 net total bilirubin 9, ammonia 79, lipase 1,520, prothrombin 23.2, creatinine 0.8

Source of report (Literature):

Seq No. : 1
 Author : Toby Litovitz
 Year : 99
 Article title : 1998 Annual Report of the American Association of Poison Control Centers Toxic Exposure Surveillance System



D88

JUL 23 1999