Individual Safety Report

3626129-3-00-01

PHARM. RES. INST. USA
For use by user-facilities, stributors and manufacturers for
MANDATORY reporting

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Approved by FDA on 09/25/98

Mfr report # PRIUSA2000001665

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient identifier: [redacted] in confidence
2. Age at time of event: or 69 yr
   Date of birth: 11/15/1930
3. Sex: [x] female [ ] male
4. Weight: UNK lbs or unk UNK kgs

B. Adverse event or product problem

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

2. Outcomes attributed to adverse event (check all that apply)
   - [ ] death (mo/day/yr)
   - [ ] life-threatening
   - [ ] hospitalization - initial or prolonged
   - [ ] disability
   - [ ] congenital anomaly
   - [ ] required intervention to prevent permanent impairment/damage
   - [x] other: Med signif

3. Date of event (mo/day/yr): 02/14/00
4. Date of this report (mo/day/yr): 11/09/00

5. Describe event or problem

A 69 year-old woman, with allergies to penicillin and codeine, received LEVAQUIN (levofloxacin) PO (dose unspecified) on 11-Feb-00 for treatment of pneumonia. Concomitant medication included digoxin, acetylsalicylic acid, metronidazole, levothyroxine sodium, sertraline hydrochloride, and docusate. The patient developed elevated serum transaminase levels. No further information provided.

Additional information received 16-Mar-00: copy of hospital adverse drug experience form: date of event: 14-Feb-00. Diagnosis: acute hepatitis. Other observations: malaise, dyspnea, tachycardia, increased liver function tests, increased bilirubin, increased INR.
Suspect drug(s): acetaminophen (vs viral induced) or levofloxacin.
Other concomitant drugs: sertraline, loratadine, lorazepam, levothyroxine, vitamin E, vitamin C, calcium, famotidine.
Relevant lab values: 14-Feb-00: ammonia: 102; lactic acid: 7.2. 15-Feb-00: BUN: 36; AST: 15,046; ALT: 9072; INR: 3.48.
16-Feb-00: total bilirubin: 2.8; alk phos: (Cont.)

6. Relevant tests/laboratory data, including dates

Additional information received 16-Mar-00:
14-Feb-00: ammonia: 102; lactic acid: 7.2
15-Feb-00: BUN: 36; AST: 15,046; ALT: 9072; INR: 3.48
16-Feb-00: total bilirubin: 2.8; alk phos: 131

Additional information received 5-Apr-00:

AST (normal range 14-59): 15-Feb: 15,046; (Cont.)

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

Allergy
Allergic to penicillin and codeine

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #1 LEVAQUIN(tablet)(LEVOFLOXACIN)
   #2 TYLENOL(PARACETAMOL)
   (Cont.)

2. Dose, frequency & route used
   #1 unk, oral
   #2 1000 mg, 3 in 1 daily, oral

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
   #1 02/11/00 - Stopped
   #2 ??/???/??

4. Diagnosis for use (indication)
   #1 PNEUMONIA, ORGANISM UNSPECIFIED
   #2 UNKNOWN

5. Event abated after use stopped or dose reduced
   #1 [x] 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 [x] 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)
    1) SYNTHROID(LEVOTHYROXINE SODIUM)
    2) ZOLOFT(SERTRALINE HYDROCHLORIDE)
    3) LORATADINE(LORATA-
    (Cont.)

G. All manufacturers

1. Contact office - name/address (& mfring 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
   - [x] health professional
   - [ ] user facility
   - [ ] company representative
   - [ ] distributor
   - [ ] other:

4. Date received by manufacturer (mo/day/yr): 02/15/00

5. (A)NDA # 20-634
   IND #
   PLA #
   pre-1938 [ ] yes
   OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
   - [ ] 5-day
   - [ ] 15-day
   - [ ] 10-day
   - [x] periodic
   - [x] Initial
   - [ ] follow-up #

8. Adverse event term(s)
   1) CARDIAC FAILURE
   2) HEPATITIS
   3) PROTHROMBIN DECREASED
   4) MALAISE
   5) DYSPNOEA
   6) TACHYCARDIA

9. Mfr. report number: PRIUSA2000001665

E. Initial reporter

1. Name, address & phone #
   [redacted]

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2. Health professional? [x] yes [ ] no
3. Occupation: Pharmacis
4. Initial reporter also sent report to FDA [ ] yes [ ] no [x] 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.

3500A Facsimile

MEDWATCH Safety Report

3626129-3-00-02

HARM. RES. INST. USA

For use by user-facilities, ributors and manufacturers for **MANDATORY** reporting

Approved by FDA on 09/15/95

Mfr report # PRIUSA2000001665

USF/Dist report #

FDA Use Only

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

A. Patient information

1. Patient identifier — In confidence
2. Age at time of event: or Date of birth:
3. Sex: ☐ female ☐ male
4. Weight: ____ lbs or ____ kgs

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 (mo/day/yr)
   - ☐ life-threatening
   - ☐ hospitalization - initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other:
3. Date of event (mo/day/yr)
4. Date of this report (mo/day/yr)
5. Describe event or problem
6. Relevant tests/laboratory data, including dates
7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   #3 TYLENOL PM(TYLENOL PM)
   #4
2. Dose, frequency & route used
   #3 1 in 1 night(s), oral
   #4
3. Therapy dates (from/to (or best estimate)) (if unknown, give duration)
   #3 ??/???/??
   #4
4. Diagnosis for use (indication)
   #3 UNKNOWN
   #4
5. Event abated after use stopped or dose reduced
   #3 ☐ yes ☐ no ☐ doesn't apply
   #4 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   #3
   #4
7. Exp. date (if known)
   #3
   #4
8. Event reappeared after reintroduction
   #3 ☐ yes ☐ no ☐ doesn't apply
   #4 ☐ yes ☐ no ☐ doesn't apply
9. NDC # - for product problems only (if known)
10. Concomitant medical products and therapy dates (exclude treatment of event)

G. All manufacturers

1. Contact office - name/address (& mfring site for devices)
2. Phone number
3. Report source (check all that apply)
   - ☐ foreign
   - ☐ study
   - ☐ literature
   - ☐ consumer
   - ☐ health professional
   - ☐ user facility
   - ☐ company representative
   - ☐ distributor
   - ☐ other:
4. Date received by manufacturer (mo/day/yr)
5. (A)NDA # ____ IND # ____ PLA # ____ pre-1938 ☐ yes OTC product ☐ yes
6. If IND, protocol #
7. Type of report (check all that apply)
   - ☐ 5-day ☐ 15-day
   - ☐ 10-day ☐ periodic
   - ☐ initial ☐ follow-up # ____
8. Adverse event term(s)

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9. Mfr. report number

E. Initial reporter

1. Name, address & phone #
2. Health professional? ☐ yes ☐ no
3. Occupation
4. Initial reporter also sent report to FDA ☐ yes ☐ no ☐ unk

3500A Facsimile

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

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

Individual Safety Report
3626129-3-00-03

Mfr. report # : PRIUSA2000001665

Date of this report : 11/09/00

B. Adverse event or product problem

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

131.
Was drug discontinued? No, acetaminophen continued Q12H PRN.
Action taken: put on vancomycin, imipenem, ciprofloxacin to cover pneumonitis, serum toxicity tests, lactulose and vitamin K.

Additional information received 5-Apr-00 from pharmacist: patient's age at time of event: 69 years (date of birth: 15-Nov-30).

LFT improved during course of hospital stay 15-Feb through 23-Feb-00. AST (normal range 14-59): 15-Feb: 15,046; 16-Feb: 4,946; 17-Feb: 1136; 18-Feb: 673; 19-Feb: 257; 20-Feb: 130; 21-Feb: 96; 22-Feb: 69; 23-Feb: 72. ALT (normal range 9-72): 15-Feb: 9072; 16-Feb: 5681; 17-Feb: 2868; 18-Feb: 2275; 19-Feb: 1502; 20-Feb: 947; 21-Feb: 858; 22-Feb: 564; 23-Feb: 435.

Patient was discharged on 23-Feb-00.

Per physician note: rapid decline in AST from 15,046 to 673 in three days was most consistent with severe congestive heart failure, right congestion.

Acetaminophen was discontinued on 16-Feb-00.

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

16-Feb: 4,946; 17-Feb: 1136; 18-Feb: 673; 19-Feb: 257; 20-Feb: 130; 21-Feb: 96; 22-Feb: 69; 23-Feb: 72. ALT (normal range 9-72): 15-Feb: 9072; 16-Feb: 5681; 17-Feb: 2868; 18-Feb: 2275; 19-Feb: 1502; 20-Feb: 947; 21-Feb: 858; 22-Feb: 564; 23-Feb: 435.

C. Suspect medication (Cont...)

Seq No.	: 2
C.1 Suspect medication	: TYLENOL(PARACETAMOL)
C.2 Dose, frequency & route used	: 2) 650 mg, 1 in 12 hour(s), oral
C.3 Therapy Dates (or duration)	: 2) ??/???/?? - 02/16/00

C10. Concomitant medical products

Seq No.	: 1
Concomitant Medical Product	: SYNTHROID(LEVOTHYROXINE SODIUM)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 2
Concomitant Medical Product	: ZOLOFT(SERTRALINE HYDROCHLORIDE)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 3
Concomitant Medical Product	: LORATADINE(LORATADINE)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 4
Concomitant Medical Product	: LORAZEPAM(LORAZEPAM)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 5
Concomitant Medical Product	: VITAMIN E(TOCOPHEROL)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 6
Concomitant Medical Product	: VITAMIN C(ASCORBIC ACID)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 7
Concomitant Medical Product	: CALCIUM(CALCIUM)
Dose, frequency & route used	: 1) unk, unknown
Seq No.	: 8
Concomitant Medical Product	: FAMOTIDINE(FAMOTIDINE)

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USA

Individual Safety Report

3626129-3-00-04

Continuation Sheet for FDA-3500A Form

Mfr. report # : PRIUSA2000001665

Date of this report : 11/09/00

Dose, frequency & route used : 1) unk, unknown

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