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

MEDWATCH
3500A Facsimile

For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting
Philip Morris Products S.A.

Relsys International, Inc., FDA Facsimile Approval: 20-APR-2007

Mfr Report # PMI001159
UF/Importer Report #
FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier (b) (6) In confidence
2. Age at Time of Event: 88 Years or Date of Birth: (b) (6)
3. Sex: ☐ Female ☒ Male
4. Weight: 165.8 lbs or 75.2 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: (b) (6) (mm/dd/yyyy)
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)
☐ Disability or Permanent Damage
☐ Congenital Anomaly/Birth Defect
☐ Other Serious (Important Medical Events)

3. Date of Event (mm/dd/yyyy): (b) (6)
4. Date of This Report (mm/dd/yyyy): 12/12/2016

5. Describe Event or Problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)
Death (Cause unknown) [Death]

Case Description:
Verbatim: Death

Clinical study ZRHR-ERS-09-EXT-US: A 26-week extension study to determine the biological and functional changes in healthy smokers who switched from conventional cigarettes (CC) to Tobacco Heating System 2.2 (THS 2.2) compared to those who continued to smoke CC in the ZRHR-ERS-09-US study.

INITIAL INFORMATION RECEIVED ON 15-SEP-2016:

This report was received from an Investigator and it concerned an 88-year-old Caucasian male subject (Initials: (b) (6), ID
continued in additional info section...

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.)
Race: Caucasian
#1 --/--/1941 to UNK, Historical Condition, Tobacco user (Since the age of 13 years, on an average of 20 units (1 pack) daily)
#2 Ongoing, Current Condition, Gastrooesophageal reflux disease
#3 Ongoing, Current Condition, Hypertension

Form Generated by Argus Safety Web v6.0.3

C. SUSPECT PRODUCT(S)

1. Name (Give labeled strength & mfr/labeler)
#1. Conventional cigarette (N/A) N/A
#2. Tobacco Heating System 2.2 (N/A) N/A

2. Dose, Frequency & Route Used
#1. 20 DF, UNK, Respiratory
#2. 39 THS in total, Respiratory

3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. --/--/1941 to Ongoing
#2. 12/28/2015 to 01/04/2016

4. Diagnosis for Use (Indication)
#1. Tobacco user (Tobacco user)
#2. Tobacco user (Tobacco user)

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☒ Doesn't Apply

6. Lot #
#1.
#2.

7. Exp. Date
#1.
#2.

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☒ Doesn't Apply

9. NDC# or Unique ID

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
1) Omeprazole (Omeprazole) --/--/2012 to UNK
2) Aspirin (Acetylsalicylic acid) 02/16/2016 to UNK
continued in additional info section...

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Philip Morris Products S.A.
Quai Jean Renaud 5
Neuchâtel, 2000 SWITZERLAND

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 (mm/dd/yyyy): 11/30/2016

5. (A)NDA #
IND # N/A
STN #
PMA/510(k) #
Combination Product ☐ Yes
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #
ZRHR-ERS-09-EXT-US

7. Type of Report (Check all that apply)
☐ 5-day ☐ 30-day
☐ 7-day ☐ Periodic
☐ 10-day ☐ Initial
☒ 15-day ☒ Follow-up #3

9. Manufacturer Report Number
PMI001159

8. Adverse Event Term(s)
Death

E. INITIAL REPORTER

1. Name and Address
UNITED STATES
Name and address withheld.

Phone # Withheld

2. Health Professional?
☒ Yes ☐ No

3. Occupation
Physician

4. Initial Reporter Also Sent Report to FDA
☐ Yes ☐ No ☐ Unk

MEDWATCH
3500A Facsimile (Back) **(Continued)**

Mfr Report # PMI001159
UF/Importer Report #
FDA Use Only

ADDITIONAL INFORMATION

B5. EVENT DESCRIPTION (Continued)

Number: 08084, weight: 75.2 kg, height: 164 cm) who had been enrolled in the above mentioned clinical study.

His medical history included obesity, acid reflux and hypertension. The subject was taking oral omeprazole at the dosage of 20 mg daily since 2012 for acid reflux, oral aspirin (acetylsalicylic acid) at the dosage of 81 mg daily since 16-Feb-2016 for cardiac prophylaxis, oral losartan at the dosage of 50 mg daily since 14-Jul-2016 for hypertension and oral gabapentin at the dosage of 300 mg daily from 28-Apr-2016 to 08-Jul-2016 for pinched nerve.

It was reported that the subject had not returned calls and his diary entry had not been completed in over a month. The subject's obituary was found: the subject died due to unknown cause on 1(b) (6) The autopsy was not performed.

The investigational site was not able to contact anyone to obtain further information because the subject did not provide an emergency contact.

The Investigator considered the reported event of death to be unrelated to the use of THS 2.2.

FOLLOW UP INFORMATION RECEIVED ON 28-SEP-2016:

It was clarified that obesity was captured in the subject's medical history due to his weight at screening.

The subject started smoking conventional cigarettes in 1941, at the age of 13 years, on an average of 20 units (1 pack) daily.

On 28-Dec-2015, the subject was enrolled into the study. During the run-in period, the subject used a total of 39 THS (daily amount not specified).

On 04-Jan-2016, he was randomized to Conventional Cigarettes arm. After randomization, the subject continued smoking 20 units (1 pack) daily.

THS use was stopped after the run-in period. The subject smoked conventional cigarettes throughout the study.

It was not possible to clarify the cause of the death, which remained unknown, since the subject did not leave any emergency contact to the site.

The Investigator confirmed that the reported event was not related to THS, not related to conventional cigarettes consumption or to any study procedures.

FOLLOW UP INFORMATION RECEIVED ON 14-NOV-2016:

The Investigator clarified that "obesity" was captured in the subject's medical history because he was asked to do so by the Clinical Research Associate.

FOLLOW UP INFORMATION RECEIVED ON 30-NOV-2016:

The Investigator clarified that "Obesity" was removed from the subject's medical history.

No further information is expected. Case closed.

Case Comment:
The reported event of Death was assessed as serious (fatal).

The reported event of Death is unexpected, as per the Reference Safety Information (i.e. the Investigator's Brochure).

The Investigator considered the reported event of Death as being not related to the use of THS 2.2, not related to conventional cigarette smoking or to study procedures. In agreement with the Investigator's causality assessment, the reported event of Death is assessed as not related to the use of THS. 2.2. The Sponsor has also assessed the reported event of Death as being not related to the consumption of conventional cigarettes and not related to any study procedures.

MEDWATCH
3500A Facsimile (Back) **(Continued)**

Mfr Report #
PMI001159
UF/Importer Report #
FDA Use Only

C10. CONCOMITANT MEDICAL PRODUCTS (Continued)

3) Losartan (Losartan potassium) 07/14/2016 to UNK
4) Gabapentin (Gabapentin) 04/28/2016 to 07/08/2016