CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2025-AER-034233

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year	Years		Day	Month	Year
Masked	PANAMA	Masked	Masked	Masked	78	Male			

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data)

1) Heart failure (Heart failure (10019279), Cardiac failure (10007554))
Not Recovered/Not Resolved/Ongoing

2) obstruction of the veins by fat (Fat embolism (10016246), Fat embolism (10016246))
Unknown

- ☐ PATIENT DIED
- ☑ LIFE THREATENING
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- ☑ RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY
- ☐ CONGENITAL ANOMALY
- ☑ OTHER MEDICALLY IMPORTANT CONDITION

II. SUSPECT DRUG(S)INFORMATION

14. SUSPECT DRUG(S)(include generic name)

1) Enzalutamide (Enzalutamide, Enzalutamide) (Suspect) (Verum) (40 Milligram, Capsule)(Unknown)

Cont..

20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☑ NA

15. DAILY DOSE(S)

1) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)

16. ROUTE(S) OF ADMINISTRATION

1) Oral

21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☑ NA

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) prostate cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (10/May/2022 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

1)ENALAPRIL(ENALAPRIL)(Unknown)

Cont..

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

Name : Astellas Pharma Global Development, Inc.
2375 Waterview Drive
Northbrook, IL, 60062-6111, UNITED STATES OF AMERICA

Study Information
Study Name: Enzalutamide Patient Support Progr (Cont..)
EudraCT Number:
Protocol No.: Enzalutamide_Astellas PSP
Center No.:
Subject Id :

24.REPORT NULLIFIED	24b. MFR CONTROL NO.
☐ YES ☐ NO	2025-AER-034233
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
19/Jun/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
23/Jun/2025	☑ INITIAL ☐ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) (Continuation...)

Event Description :

This report from study case was received by Astellas business partner Adium, on 19-Jun-2025 from patient, consumer (patient's wife) and was received at Astellas from Adium on 20-Jun-2025, which referring to a 78 Year(s) old Male patient in PANAMA, enrolled in post-marketing study: Enzalutamide Patient Support Program who was on Xtandi (enzalutamide), Capsule (160 milligram(s), 1 every 1 Day). Indication for use was Prostate cancer. The patient-initiated treatment on 10-May-2022.

Study no: Enzalutamide_Astellas PSP, Open-label study

The patient received enzalutamide for prostate cancer according to the following dosage regimen: 10-May-2022 - (ongoing): Oral 160 mg, once daily. Action taken with enzalutamide was dose not changed.

The patient received Eligard (leuprorelin acetate) for prostate cancer according to the following dosage regimen: 10-May-2022 - (ongoing): subcutaneous 45 mg, once in 6 months. Action taken with leuprorelin acetate was dose not changed.

On an unknown date, patient experienced moderate heart failure and obstruction of the veins by fat. The patient received oral route - Enalapril for heart failure.

The outcome of event heart failure was not recovered/not resolved, outcome of event obstruction of the veins by fat was unknown.

On an unknown date in May-2025, the patient had severe lower extremity edema. Patient received topical skin creams and antibiotics for lower extremity edema.

Patient's wife reported that due to his heart failure, which is indicated to be due to vein obstruction by fat, he is experiencing significant edema in his lower limbs, making it difficult for him to walk due to the swelling of his legs and feet. Batch and expiration date of the medication was not reported.

Medical history was not reported.

Past medications were not reported.

Concomitant medication included ENALAPRIL.

No relevant lab data was reported.

The patient and patient's wife assessed the following events with respect to enzalutamide and leuprorelin acetate:
- Heart failure (Seriousness: serious (Life threatening, Disability/Incapacity, Causality: Not related)
- Obstruction of the veins by fat (Seriousness: Non serious, Causality: Not related)

Consent to contact patient and patient's wife for follow-up information was denied.

No additional information was available.

Tracking of changes:
19-Jun-2025: Initial information was received.

Company Remarks (Sender's Comments) :

Event Information:
Fat embolism was assessed as Serious due to Other Medically Important Condition.
Heart failure was assessed as Serious due to Disability/Permanent Damage and Life Threatening.

Other Medically Important Condition is based on nature of the event and manifestation into life threatening Heart failure.
Life Threatening is based on threat to life considering the baleful nature of the event.

obstruction of the veins by fat was coded as Fat embolism due to closest available MedDRA term.

Product: Enzalutamide
Astellas assessed Heart failure as Not Related, since associated Fat embolism provides more plausible alternative explanation for the event in this elderly patient with underlying malignancy. Fat embolism assessed as Not Related as based on the information available, a reasonable possibility to suggest a relationship between the suspect drug and the event cannot be established. Complications due to underlying advance malignancy constitutes a more plausible alternative explanation for the event in this patient with advanced age. With the available information medical assessment has been done, however, upon receiving further information case will be reassessed.

14.SUSPECT DRUG(S) (Continuation...)

Continuation Sheet for CIOMS report

Product-Reaction Level

1) Drug : Enzalutamide (Enzalutamide)
Active Substance : 1) Enzalutamide
Coding Class : Verum
Drug Characterization : Suspect
Form Strength : 1) 40 Milligram
Form of Admin : 1) Capsule
Lot Number : 1) Unknown
Daily Dose : 1) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)
Route of Admin : 1) Oral
Indications : 1) prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 10/May/2022 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Heart failure (Heart failure - 10019279, Cardiac failure - 10007554)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) obstruction of the veins by fat (Fat embolism - 10016246, Fat embolism - 10016246)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Heart failure
CORE UnLabeled
IB UnLabeled
2) obstruction of the veins by fat
CORE UnLabeled
IB UnLabeled

2) Drug : ELIGARD
Active Substance : 1) LEUPRORELIN ACETATE
Drug Characterization : Suspect
Form Strength : 1) 45 Milligram
Form of Admin : 1) Injection
Lot Number : 1) Unknown
Daily Dose : 1) 0.25 milligram(s) (45 milligram(s), 1 in 6 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 10/May/2022 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Heart failure (Heart failure - 10019279, Cardiac failure - 10007554)
Causality as per reporter : Not Related
Causality as per Mfr : Not assessed
DeChallenge : Not applicable
ReChallenge : Not Applicable
2) obstruction of the veins by fat (Fat embolism - 10016246, Fat embolism - 10016246)
Causality as per reporter : Not Related
Causality as per Mfr : Not assessed
DeChallenge : Not applicable
ReChallenge : Not Applicable

15. DAILY DOSE(S) (Continuation...)

Dosage Text :

Drug 1 :Enzalutamide

1) 160 milligrams daily

Drug 2 :ELIGARD

Continuation Sheet for CIOMS report

1) Injection, powder, lyophilized , for solution/injectable suspension

22.CONCOMITANT DRUG(S) (Continuation...)

1). Drug	:	ENALAPRIL
Active Substance	:	1) ENALAPRIL
Form Strength	:	
Form of Admin	:	1) Unknown
Daily Dose	:	
Route of Admin	:	1) Unknown
Indications	:	1) Drug use for unknown indication [10057097 - Drug use for unknown indication]

24a. NAME AND ADDRESS OF MANUFACTURER (Continuation...)

Study # :Enzalutamide_Astellas PSP