SUSPECT ADVERSE REACTION REPORT

2022US042124

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	82	Male			

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

1) Thrombosis (Thrombosis (10043607), Thrombosis (10043607))
(Asked but Unknown -) - Unknown
2) Has had joint problems (discomfort in joints) (Discomfort in joints (10013088), Musculoskeletal discomfort (10053156))
(Asked but Unknown -) - Unknown

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ 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..

15. DAILY DOSE(S)

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

16. ROUTE(S) OF ADMINISTRATION

1) Oral

17. INDICATION(S) FOR USE

1) Prostate cancer [10060862 - Prostate cancer]

18. THERAPY DATE(S) (from/to)

1) (21/Jul/2022 -)

19. THERAPY DURATION

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

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

(NA : Not Applicable)

III. CONCOMITANT DRUG(S) AND HISTORY

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

No concomitants used/reported

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

1) PARKINSON'S DISEASE (10061536, Parkinson's disease) (Continuing: Yes)

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 ☐ YES ☐ NO

24b. MFR CONTROL NO.

2022US042124

24c. DATE RECEIVED BY MANUFACTURER

20/Jun/2025

24d. REPORT SOURCE ☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL

DATE OF THIS REPORT

25/Jun/2025

25a. REPORT TYPE ☐ 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 Patient Support Program case was received by Astellas business partner, Tecnofarma S.A., on 23-Nov-2022 from patient and patient's daughter and was received at Astellas from Tecnofarma S.A. on 24-Nov-2022, referring to an 82 years old male patient who experienced thrombosis and has had joint problems (discomfort in joints) during Xtandi (enzalutamide) treatment. The patient was enrolled in Astellas sponsored patient support program titled "ASOFARMA A TU LADO".

No other suspect medications were reported.

Current condition included Parkinson's disease.

The patient concomitantly received an unspecified injection every 3 months for prostate cancer. Patient's daughter does not know the name because she does not live with the patient.

The patient received enzalutamide for prostate cancer according to the following dosage regimen: 21-Jul-2022 - (ongoing): Oral 160 mg, once daily. The patient's daughter does not have information on the lot number and expiration date of enzalutamide.

It was reported that the patient was bedridden because he suffered from Parkinson's disease and it was then more advanced, the patient's daughter says that he suffered from it long before the prostate cancer, but the patient was already 82 years old and Parkinson's was a degenerative disease. The patient's daughter says that since an unknown date, the patient has had joint problems (discomfort in joints) because he also had thrombosis, so then he was not mobilized if it was not necessary.

Upon follow up it was reported that the patient remains bedridden, where he performs all his daily needs with the assistance of a caregiver. He has active movements in his lower and upper limbs, converses well, and eats his daily meals without problems. Patient's age as of 20-Jun-2025 was reported as 85 years.

No lab test information was provided.

Action taken with enzalutamide treatment was no change (ongoing).

The outcome of thrombosis and has had joint problems (discomfort in joints) was reported as unknown.

The patient and patient's daughter assessed the following events with respect to enzalutamide:
- Thrombosis (seriousness: serious (Disability/Permanent Damage); causality: Not Assessed)
- Has had joint problems (discomfort in joints) (seriousness: serious (Disability/Permanent Damage); causality: Not Assessed)

No additional information was available.

On 09-Dec-2022, confirmation was received that no additional information was available.

Follow up information was received from Astellas business partner Adium on 20-Jun-2025 from patient's daughter and was received at Astellas from Adium on 23-Jun-2025: Enzalutamide start date, events seriousness updated to serious (Disability/Permanent Damage) and outcome updated from not recovered to unknown for both events. Narrative description updated.

Company Remarks (Sender's Comments) :

Event Information:
Thrombosis was assessed as Serious due to Disability/Permanent Damage and Other Medically Important Condition.
Discomfort in joints was assessed as Serious due to Disability/Permanent Damage.

Other Medically Important Condition is based on nature of the event.

Events were coded with closest available MedDRA terms.

Product: Enzalutamide
Astellas assessed Thrombosis and Discomfort in joints as Not Related based on the information available, a reasonable possibility to suggest a relationship between the suspect drug and the event cannot be established. The risk factor for Thrombosis includes the underlying malignancy, due to hypercoagulable state complications in this elderly patient. Discomfort in joints is confounded by the concurrent event of Thrombosis and elderly age of patient.

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

Product-Reaction Level

Continuation Sheet for CIOMS report

1) Drug	:	Enzalutamide (Enzalutamide)
Active Substance	:	Enzalutamide
Coding Class	:	Verum
Drug Characterization	:	Suspect
Form Strength	:	40 Milligram
Form of Admin	:	Capsule
Lot Number	:	Unknown
Daily Dose	:	160.0 milligram(s) (160 milligram(s), 1 in 1 Day)
Route of Admin	:	Oral
Indications	:	Prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	From : 21/Jul/2022 To :Continuing
Action(s) Taken With Drug	:	Dose not changed

Causality

1) Thrombosis (Thrombosis - 10043607, Thrombosis - 10043607)

Causality as per reporter	:	Not assessed
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

2) Has had joint problems (discomfort in joints) (Discomfort in joints - 10013088, Musculoskeletal discomfort - 10053156)

Causality as per reporter	:	Not assessed
Causality as per Mfr	:	Not Related
DeChallenge	:	Not applicable
ReChallenge	:	Not Applicable

Labeling :

1) Thrombosis	
CORE	UnLabeled
IB	UnLabeled
2) Has had joint problems (discomfort in joints)	
CORE	UnLabeled
IB	UnLabeled

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

Study # :Enzalutamide_Astellas PSP