CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2025-AER-009987

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	85	Male		Jan	2025

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

1) Stroke (Stroke (10042244), Cerebrovascular accident (10008190))
(/Jan/2025 -) - Not Recovered/Not Resolved/Ongoing
2) Deterioration of his body due to his age, he was losing mobility (General physical health deterioration (10049438), General physical health deterioration (10049438))
Unknown
3) Deterioration of his body due to his age, he was losing mobility (Mobility decreased (10048334), Mobility decreased (10048334))
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)(40 Milligram, Capsule)(Unknown)(40 Milligram, Capsule)(Unknown)

Cont..

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)	1) Oral
2) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)	2) 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) (01/Dec/2023 -)	

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) HIGH PRESSURE (10005750, Blood pressure increased) (- /Jan/2025) (Continuing: No)

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-009987
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
16/Apr/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
21/Apr/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 spontaneous case was received by Astellas business partner Adium, on 17-Feb-2025, from a consumer (patient's son) in PANAMA and was received at Astellas from Adium on 18-Feb-2025, concerning an 85 years old male patient, enrolled in post-marketing study: Enzalutamide Patient Support Program who was on Xtandi (enzalutamide), Capsule. The patient-initiated treatment on 01-Dec-2023.

Study ID: Study ID: Enzalutamide_Astellas PSP; Open-Label study (ASOFARMA A TU LADO).

The patient received enzalutamide for prostate cancer with following dosage regimens: 01-Dec-2023 (also reported as 29-Nov-2023) - (stop date not reported): Oral, 160 mg once daily, (start date not reported) (reported as 29-Nov-2023) - 12-Jan-2025 (also reported as 02-Jan-2025): Oral, 160 mg once daily and 12-Feb-2025 (also reported as Mar-2025) - (ongoing): Oral, 160 mg once daily.

Action taken with enzalutamide was dose not changed.

The patient received Eligard (leuprorelin acetate) for prostate cancer with following dosage regimen: 01-Dec-2023 - (ongoing): subcutaneous, 45 mg every 6 months.

Action taken with Eligard was dose not changed.

The patient's son stated that on 29-Nov-2023, the patient began using leuprorelin acetate and enzalutamide, and approximately a month and a half later, he started using a bone medication. For this reason, the patient received leuprorelin acetate and the bone medication every 6 months. There was no expiration date or lot number provided for the enzalutamide and leuprorelin acetate medications. The patient continued with leuprorelin acetate 45mg lyophilized for injectable suspension and had discontinued treatment with enzalutamide 40mg capsules.

The patient's son reported that the patient was hospitalized for one month from 12-Jan-2025 (also reported as 02-Jan-2025) to 12-Feb-2025 due to a stroke which started approximately on 10-Jan-2025 or 15-Jan-2025 (he does not remember well) and as a result, the patient currently cannot move his hands or feet, have difficulty swallowing, and speaks little. Approximately 4 to 5 days ago, the patient was discharged from the hospital and 15 days ago, he underwent a gastro procedure (unspecified). For this reason, the patient must eat via a tube placed in his stomach. The patient's son was not aware of how severe the stroke would be, and consequently, the patient was unable to attend his scheduled appointment on 22-Jan-2025. Since the patient was discharged, the urologist had not contacted the patient's son, despite his attempts to reach him via chat. The son wishes to consult about how the patient, who has difficulty swallowing, might take the enzalutamide pill. The patient's son reported that he would attempt to contact the urologist again on 17-Feb-2025, to check if he will respond. He commented that the patient was due for his leuprorelin acetate application, as the last application was approximately 6 months ago around the navel (no date provided).

Upon follow up, patient's son reported that he did not have lot number information and laboratory and diagnostic test results for the event. He also reported that patient had never stopped taking enzalutamide 160 mg daily. He mentioned that he only stopped taking it when he was hospitalized from 12-Jan-2025 to 12-Feb-2025. Reporter stated that the patient had suffered from high blood pressure all his life, until Jan-2025 when he stopped taking medication for the condition. It was reported that the patient received physical therapy twice a week because of the deterioration of his body due to his age, he was losing mobility. It was reported that the patient only receives physical therapy 3 times a week for stroke treatment which started on 20-Feb-2025 and since the patient cannot swallow much, he was fed through a gastro which was done by the urological center at the end of Jan-2025 to early Feb-2025. Regarding stroke it was reported that patient was stable, but patient's son believed he would not have (improvement) and was not recovered. Patient's son did not know if enzalutamide was related to the stroke patient had, because the doctors did not indicate anything about this information. The outcome of event stroke was reported as not resolved and outcome of events Deterioration of his body due to his age, he was losing mobility (General physical health deterioration, mobility decreased) was unknown.

Upon follow up, patient's son recalled that the patient started using enzalutamide 29-Nov-2023 and was discontinued from enzalutamide on 02-Jan-2025, the day he was hospitalized for a stroke (son's words - inconsistent information). Patient's wife mentioned that the patient took the last dose of enzalutamide the same day he was hospitalized approximately on 12-Jan-2025, in Feb-2025 the patient was discharged and in Mar-2025 he resumed enzalutamide only that she does not remember the exact date (wife's words - inconsistent information).

Patient's wife mentioned that patient was bedridden at home due to the stroke, she referred that patient cannot swallow or chew, for that reason she gives him his medicines and special milk by means of a bottle.

Medical history included blood pressure increased (patient has suffered from high blood pressure all his life, until Jan-2025 when he stopped taking medication for the condition).

Past Medications included eye drops, vitamins, OMACOR and NORVASC (currently he no longer takes any of these medications).

Concomitant medications included unspecified bone medication and 2 unspecified medications. The patient's son reported that the patient was receiving a medication (name not provided) to strengthen his bones because he was told that enzalutamide can erode the bones (treatment ongoing). He also mentions that the patient takes medications (name not provided) for hip pain; the patient's son is unaware if the pain is caused by prostate cancer that has spread to the hip.

No relevant lab data was reported.

Continuation Sheet for CIOMS report

The patient's son assessed the following events with respect to enzalutamide and leuprorelin acetate:
- Stroke (seriousness: serious (Hospitalization and Disability); causality: Not Assessed)
- Deterioration of his body due to his age, he was losing mobility (General physical health deterioration, mobility decreased) (seriousness: Not reported; causality: Not Assessed)

The patient's wife assessed the following event with respect to enzalutamide and leuprorelin acetate:
- Stroke (seriousness: serious (Hospitalization and Disability); causality: Not Assessed)

The causality analysis is performed by Pharmacovigilance of Asofarma Centroamérica y Caribe using the data received from the source document. The notifier does not provide the causal relationship between the adverse event(s) and the medication(s).

Consent to contact consumer (patient's son) for follow-up information was provided and patient's wife was unknown.

Tracking of changes:
17-Feb-2025: Initial information was received.

This spontaneous case was received by Astellas business partner Adium, on 03-Apr-2025, from a consumer and was received at Astellas from Adium on 04-Apr-2025: Events Deterioration of his body due to his age, he was losing mobility (General physical health deterioration, mobility decreased) added. Medical history, past drugs details, enzalutamide therapy details, event details (onset date, hospitalization dates, treatment) and narrative were updated.

This spontaneous case was received by Astellas business partner Adium, on 16-Apr-2025, from a consumer and was received at Astellas from Adium on 16-Apr-2025: Narrative description was updated.

Company Remarks (Sender's Comments) :

Event Information:
Stroke was assessed as Serious due to Disability/Permanent Damage and Caused/Prolonged Hospitalization.
General physical health deterioration and Mobility decreased were assessed as Non Serious.
Non-Serious is based on events not meeting ICH seriousness criteria.

Deterioration of his body due to his age, he was losing mobility was coded as General physical health deterioration and as Mobility decreased due to closest available LLTs in MedDRA.

Product: Enzalutamide
Astellas assessed Stroke, General physical health deterioration and Mobility decreased as Not Related, based on the clinically relevant information currently available for this individual case and the evidence is not sufficient to suggest a relationship between the suspect therapy and the reported adverse events. Complication due to advance underlying metastatic cancer with elderly age constitutes a more plausible alternative explanation for the reported events. Mobility decreased was secondary to elderly age and General physical health deterioration.

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

Product-Reaction Level

1) Drug	:	Enzalutamide (Enzalutamide)
Active Substance	:	1) Enzalutamide
Coding Class	:	Verum
Drug Characterization	:	Suspect
Form Strength	:	1) 40 Milligram 2) 40 Milligram 3) 40 Milligram
Form of Admin	:	1) Capsule 2) Capsule 3) Capsule
Lot Number	:	1) Unknown 2) Unknown 3) Unknown
Daily Dose	:	1) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day) 2) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day) 3) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)
Route of Admin	:	1) Oral 2) Oral 3) Oral
Indications	:	1) Prostate cancer [10060862 - Prostate cancer]

Continuation Sheet for CIOMS report

Therapy Dates : 1) From : 01/Dec/2023 To :Continuing
2) From : To :12/Jan/2025
3) From : 12/Feb/2025 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Stroke (Stroke - 10042244, Cerebrovascular accident - 10008190)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Deterioration of his body due to his age, he was losing mobility (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Deterioration of his body due to his age, he was losing mobility (Mobility decreased - 10048334, Mobility decreased - 10048334)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Stroke
CORE UnLabeled
IB UnLabeled
2) Deterioration of his body due to his age, he was losing mobility
CORE UnLabeled
IB UnLabeled
3) Deterioration of his body due to his age, he was losing mobility
CORE UnLabeled
IB UnLabeled

2) Drug : ELIGARD
Active Substance : 1) LEUPRORELIN ACETATE
Drug Characterization : Suspect
Form Strength : 1) 45 Milligram
Form of Admin : 1) Suspension for 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 : 01/Dec/2023 To :Continuing
Action(s) Taken With Drug : Dose not changed

Causality

1) Stroke (Stroke - 10042244, Cerebrovascular accident - 10008190)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Deterioration of his body due to his age, he was losing mobility (General physical health deterioration - 10049438, General physical health deterioration - 10049438)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) Deterioration of his body due to his age, he was losing mobility (Mobility decreased - 10048334, Mobility decreased - 10048334)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Study # :Enzalutamide_Astellas PSP

Continuation Sheet for CIOMS report

Past Therapy (ies)

Product Name	:	Omacor
Indication	:	Drug use for unknown indication (10057097)
Start Date	:	
Stop Date	:	

Product Name	:	NORVASC
Indication	:	Drug use for unknown indication (10057097)
Start Date	:	
Stop Date	:	