CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2025-AER-015757

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH			2a. AGE Years	3. SEX	4-6 REACTION ONSET		
		Day	Month	Year			Day	Month	Year
Masked	PANAMA	Masked	Masked	Masked	81	Male	09	Apr	2025

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

1) Hospitalization for cerebral ischemia (Cerebral ischemia (10008121), Cerebral ischaemia (10008120))
(09/Apr/2025 -) - Unknown
2) Completely unbalanced/decompensated (Chronic disease decompensation (10091880), Chronic disease decompensation (10091880))
(15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Elevated blood sugar/ Sugar 225 (Blood sugar increased (10005809), Blood glucose increased (10005557))
(15/Apr/2025 -) - Not Recovered/Not Resolved/Ongoing
4) fainting after xtandi ingestion (Fainting (10016169), Syncope (10042772))
(12/May/2025 -) - Unknown

Cont..

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) (01/Apr/2024 -)

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) LOW PRESSURE (10024895, Low blood pressure) (Continuing: Yes)

Cont..

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.

2025-AER-015757

24c. DATE RECEIVED BY MANUFACTURER

12/May/2025

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

DATE OF THIS REPORT

15/May/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...)

5) blood pressure in 64/34 (Blood pressure low (10005753), Hypotension (10021097)(12/May/2025 -) - Unknown)

6) Fever (Fever (10016558), Pyrexia (10037660) - Unknown)

Event Description :

This report from study case was received by Astellas business partner Adium, on 21-Apr-2025, from Consumer (Family member) in PANAMA and received at Astellas from Adium on 22-Apr-2025 referring to a 81 Year(s) old Male patient, 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 01-Apr-2024.

Study No: Enzalutamide_Astellas PSP; Open-Label study.

The patient received enzalutamide for a Prostate cancer according to the following dosage regimens: 01-Apr-2024 - (Ongoing): Oral 160mg once daily.

The patient received Eligard (leuprorelin acetate) for a Prostate cancer according to the following dosage regimens: 01-Apr-2024 - (Ongoing): subcutaneous 45mg every 6 months.

Action taken with enzalutamide and leuprorelin acetate treatment in response to events was no change (ongoing).

The Consumer (Family member) refers that on Thursday on 13-Mar-2025, a toe had to be amputated and that he will probably be discharged from the hospital tomorrow, 18-Mar-2025. The Consumer (Family member) reported that he was hospitalized due to elevated blood sugar and was completely decompensated 15-Apr-2025. The patient had not yet recovered for these events.

On an unknown date the patient had moderate fever. No treatment was required. On 12-May-2025 10:10 am the patient had Fainting after ingestion of Xtandi, Blood pressure was 64/34 and Sugar 225. The outcome of events was unknown. The patient's daughter mentioned that patient on 12-May-2025 admitted (hospital) due to presenting fever, low blood pressure, high sugar, mentioned that so far they have not been provided with information regarding the patient's condition, but comments that patient before was also hospitalized for a month from 09-Apr-2025 to 09-May-2025 in that month was performed a CT scan and an MRI, but through the MRI, the patient was diagnosed with cerebral ischemia (severe), although the patient's daughter says that she does not know since when it started since they found out through that exam (MRI). Family member reports that he was taken to the hospital and is under emergency observation until his doctor returns. The outcome of event Hospitalization for cerebral ischemia was unknown however stop date reported as 09-May-2025. It was reported that no treatment was required. The outcome of event Elevated blood sugar/sugar 225 was not recovered.

Patient's daughter mentions that patient still continues with both treatments (leuprorelin acetate and enzalutamide) only that due to her condition she has not been able to apply her leuprorelin acetate dose that corresponded to the month of May 2025, on 12-May-2025 patient's daughter refers that she did not even give time for the patient to take her enzalutamide dose (confusing information). Patient's daughter mentions that she does not have the information about when the patient's dose (leuprorelin acetate) was applied, she only indicates that it was 6 months ago, she also mentions that she does not have the information about the expiration date and lot number.

Diseases included Low blood pressure and Blood sugar increased.

Past medications were not reported.

Concomitant medications were not reported.

Lab data included:
15-Apr-2025: Blood sugar: elevated blood sugar
Apr-2025:an MRI: diagnosed with cerebral ischemia
Apr-2025: a CT scan: unknown result
12-May-2025: Blood pressure: 64/34 unknown unit, low
12-May-2025 10:10: blood sugar: 225 unknown unit

The Consumer (Family member) assessed the following events with respect to enzalutamide and leuprorelin acetate:
- Elevated blood sugar/sugar 225 (seriousness: Serious (Hospitalization and medical significant); causality: Not assessed)
- Completely unbalanced/decompensated (seriousness: Serious (Hospitalization and medical significant); causality: Not assessed)

The patient's daughter assessed the following events with respect to enzalutamide and leuprorelin acetate:
- Hospitalization for cerebral ischemia (seriousness: Serious (Life-threatening, Disability and Hospitalization); causality: Not assessed)
- fainting after Xtandi ingestion (seriousness: Serious (Hospitalization); causality: Related)
- blood pressure in 64/34 (seriousness: Serious (Hospitalization); causality: Not assessed)
- Fever (seriousness: Serious (Hospitalization); causality: Not assessed)
- Elevated blood sugar/sugar 225 (seriousness: Serious (Hospitalization and medical significant); causality: Related)

Consent to contact Consumer (Family member) and patient's daughter for follow-up information was denied.

Continuation Sheet for CIOMS report

No additional information was available.

Tracking of changes:
21-Apr-2025: Initial information was received. Initial Received Date on 17-Mar-2025, minimum required information was not obtained at the company, the terms were fulfilled on Latest Received Date on 21-Apr-2025.

Follow up case was received by Astellas business partner Adium, on 12-May-2025 and 13-May-2025 from Consumer (patient's daughter) in PANAMA and received at Astellas from Adium on 13-May-2025: Added lab data, medical history and events (Hospitalization for cerebral ischemia, fainting after Xtandi ingestion, blood pressure in 64/34 and fever). Updated event verbatim (from Elevated blood sugar to Elevated blood sugar/sugar 225) and clinical description.

Company Remarks (Sender's Comments) :

Event Information:
Cerebral ischemia was assessed as Serious due to Disability/Permanent Damage, Caused/Prolonged Hospitalization, Other Medically Important Condition and Life Threatening.
Blood sugar increased was assessed as Serious due to Caused/Prolonged Hospitalization and Other Medically Important Condition.
Fever, Chronic disease decompensation, Fainting and Blood pressure low were assessed as Serious due to Caused/Prolonged Hospitalization.

Other Medically Important Condition is based on nature of the events.
Life Threatening is based on threat to life considering the baleful nature of the event.

All events were coded to closest available LLTs in MedDRA.

Product: Enzalutamide
Astellas assessed Cerebral ischemia, Chronic disease decompensation, Blood sugar increased, Fainting, Blood pressure low and Fever as Not Related, as based on the information available, a reasonable possibility to suggest a relationship between the suspect drug and the events cannot be established. Elderly aged patient with underlying malignancy is a risk factor. Current conditions of low blood pressure and Blood sugar increased could alternately explain the events of Blood pressure low and Blood sugar increased. Chronic disease decompensation was likely secondary to Blood sugar increased. Concurrent Blood pressure low could be a risk factor for Fainting and Cerebral ischemia.

Additional Information (Continuation...)

Laboratory Data :

15-Apr-2025: Blood sugar: elevated blood sugar
Apr-2025:an MRI: diagnosed with cerebral ischemia
Apr-2025: a CT scan: unknown result
12-May-2025 10:10: Blood pressure: 64/34 unknown unit, low
12-May-2025 10:10: blood sugar: 225 unknown unit

Lab Result :

Test Name	Test Date	Test Result	Normal Value
BLOOD PRESSURE	12/May/2025 10:10:00		
BLOOD SUGAR	15/Apr/2025		
BLOOD SUGAR	12/May/2025 10:10:00		
CT SCAN	/Apr/2025		
MRI	/Apr/2025		

Test Result (Code) / Result Unstructured Data (free text) :

1) Test Name: BLOOD PRESSURE

Result Unstructured Data (free text) : 64/34, low
Test Date: 12/May/2025 10:10:00

2) Test Name: BLOOD SUGAR

Result Unstructured Data (free text) : elevated
Test Date: 15/Apr/2025

3) Test Name: BLOOD SUGAR

Continuation Sheet for CIOMS report

Result Unstructured Data (free text) : 225 unknown unit
Test Date: 12/May/2025 10:10:00

4) Test Name: CT SCAN

Result Unstructured Data (free text) : unknown result
Test Date: /Apr/2025

5) Test Name: MRI

Result Unstructured Data (free text) : cerebral ischemia
Test Date: /Apr/2025

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
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 : 01/Apr/2024 To :Continuing
Action(s) Taken With Drug	: Dose not changed

Causality

1) Hospitalization for cerebral ischemia (Cerebral ischemia - 10008121, Cerebral ischaemia - 10008120)

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

2) Completely unbalanced/decompensated (Chronic disease decompensation - 10091880, Chronic disease decompensation - 10091880)

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

3) Elevated blood sugar/ Sugar 225 (Blood sugar increased - 10005809, Blood glucose increased - 10005557)

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

4) fainting after xtandi ingestion (Fainting - 10016169, Syncope - 10042772)

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

5) blood pressure in 64/34 (Blood pressure low - 10005753, Hypotension - 10021097)

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

6) Fever (Fever - 10016558, Pyrexia - 10037660)

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

Labeling :

1) Hospitalization for cerebral ischemia	
CORE	UnLabeled
IB	UnLabeled
2) Completely unbalanced/decompensated	
CORE	UnLabeled
IB	UnLabeled

Continuation Sheet for CIOMS report

3) Elevated blood sugar/ Sugar 225

CORE	UnLabeled
IB	UnLabeled

4) fainting after xtandi ingestion

CORE	Labeled
IB	Labeled

5) blood pressure in 64/34

CORE	UnLabeled
IB	UnLabeled

6) Fever

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 : 01/Apr/2024 To :Continuing
Action(s) Taken With Drug	: Dose not changed

Causality

1) Hospitalization for cerebral ischemia (Cerebral ischemia - 10008121, Cerebral ischaemia - 10008120)

Causality as per reporter	: Not assessed
Causality as per Mfr	: Not assessed

2) Completely unbalanced/decompensated (Chronic disease decompensation - 10091880, Chronic disease decompensation - 10091880)

Causality as per reporter	: Not assessed
Causality as per Mfr	: Not assessed

3) Elevated blood sugar/ Sugar 225 (Blood sugar increased - 10005809, Blood glucose increased - 10005557)

Causality as per reporter	: Related
Causality as per Mfr	: Not assessed

4) fainting after xtandi ingestion (Fainting - 10016169, Syncope - 10042772)

Causality as per reporter	: Related
Causality as per Mfr	: Not assessed

5) blood pressure in 64/34 (Blood pressure low - 10005753, Hypotension - 10021097)

Causality as per reporter	: Related
Causality as per Mfr	: Not assessed

6) Fever (Fever - 10016558, Pyrexia - 10037660)

Causality as per reporter	: Not assessed
Causality as per Mfr	: Not assessed

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

Dosage Text :

Drug 2 :ELIGARD

1) Eligard 45 mg lyophilized for injectable suspension

23. OTHER RELEVANT HISTORY (Continuation...)

2) HIGH SUGAR (10005809 , Blood sugar increased) (Continuing : YES)

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

Study # :Enzalutamide_Astellas PSP