CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2025-AER-030164

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	GUATEMALA	Masked	Masked	Masked	76	Male		Feb	2025

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

1) Intense heat (Feeling hot (10016334), Feeling hot (10016334))
(/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
2) Excessive sweating (Excess sweating (10015590), Hyperhidrosis (10020642))
(/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing
3) Intense hot flashes (Hot flashes (10020407), Hot flush (10060800))
(/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing

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..

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)

Cont..

16. ROUTE(S) OF ADMINISTRATION

1) Oral

Cont..

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

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Spinal cancer (prostate cancer metastasized in the area of the spine) [10036909 - Prostate cancer metastatic]

Cont..

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (20/May/2024 -)	

III. CONCOMITANT DRUG(S) AND HISTORY

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

1)BICALUTAMIDE(BICALUTAMIDE)(Capsule)(19/Mar/2024 -)

Cont..

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

1) ABNORMAL TOTAL PROSTATE ANTIGEN (10058012, Prostatic specific antigen abnormal) (/Jan/2024 - 18/May/2024) (Continuing: No)

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	24b. MFR CONTROL NO.
☐ YES ☐ NO	2025-AER-030164
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
19/Aug/2025	☑ STUDY ☐ LITERATURE ☑ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
25/Aug/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 23-May-2025 and 28-May-2025 from patient, Nurse and was received at Astellas from Adium on 30-May-2025 and 02-Jun-2025, concerning a 76 Year(s) old Male patient in GUATEMALA, 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 metastatic. The patient initiated treatment on 20-May-2024.

Study No.: Enzalutamide_Astellas PSP; Blinding Technique: Open-Label

The patient received enzalutamide for Spinal cancer (prostate cancer metastasized in the area of the spine) with following dosage regimen: (20-May-2024) - (stop date not provided): Oral, 160 mg once daily.

Action taken with enzalutamide was unknown.

The patient received Eligard (leuprorelin acetate) (Injection, powder, lyophilized, for suspension) for Prostate cancer with following dosage regimen: (09-Feb-2024) - (stop date not provided): Subcutaneous, 22.5 mg every 3 months.

Action taken with leuprorelin acetate was unknown.

The patient received Prolia (denosumab) (pre-filled syringe) for Spinal cancer (prostate cancer metastasized in the area of the spine) with following dosage regimen: (20-May-2024) - (stop date not provided): 120 mg every 3 months via unknown route.
Action taken with denosumab was unknown.

The patient received leuprorelin acetate (Injectable Powder, for suspension) for Prostate cancer with following dosage regimen: (23-May-2024) - (2025): 45 mg every 6 months, frequency via subcutaneous route. (Lot number: L14177A1, Expiration Date: Jul-2025)
Action taken with leuprorelin acetate was drug withdrawn for Intense hot flashes and Excessive sweating.
Action taken with leuprorelin acetate was unknown Intense heat.

The patient reported that he received the first dose of leuprorelin acetate on Friday, 09-Feb-2024 and mentioned that on Saturday (09-Feb-2024), he experienced significant pain in the lower limbs, as well as a headache. The patient states that in the days prior, he already had flu-like symptoms.

On Monday, 12-Feb-2024, follow-up was conducted via phone, with the patient reporting feeling better. He was taking acetaminophen 1 g every 6 hours.

The patient reported that since 08-Mar-2024, he has been experiencing burning in the stomach, mentioning that he cannot digest anything as it causes spasms and burning in the stomach. Additionally, he mentioned that he underwent radiation therapy last week. The patient was asked if he was taking any gastric protectants, and he reported that he has not taken any, so it was suggested that he consult with his treating physician. The patient reports feeling better and that he has been able to eat better.

On 23-May-2025, The patient support nurse from the patient support programme reported that the patient on 09-Feb-2024 was given the first dose of Leuprorelin acetate medication and for the last 2 months, no date, the patient has chills and for the last 15 days, no date, he has permanent pain in his spine, comments that on 20-May-2024 he went for a consultation with the treating doctor who told the patient that the chills were caused by the Leuprorelin acetate medication and the pain in the spine is caused by the prostate cancer because it metastasised in the area of the spine, which is why it causes pain and the patient's treating doctor referred him to another doctor to treat the pain. He commented that the treating doctor prescribed the drugs Tramacet for spinal pain, Enzalutamide and Prolia for spinal cancer (the patient is not enrolled in the PSP with the drugs Enzalutamide) and Prolia, he is only enrolled with Leuprorelin acetate.

The nurse mentioned that before starting Leuprorelin acetate treatment in January 2024, the patient had a total prostate antigen test and the results showed 900 ng/ml, so the doctor prescribed the Leuprorelin acetate drug.

On 17-May-2024, the total prostate antigen test was carried out and on 18 May 2024 the results were 0 ng/ml, so the doctor told the patient that thanks to the Leuprorelin acetate drug he had made great progress.

The patient support nurse in the patient support programme stated in the call that the patient's Leuprorelin acetate treatment start date was 19-Mar-2024, but the date placed was the one in the CRM.

On 23-May-2024 the patient was given the Leuprorelin acetate 45 mg drug and not the 22.5 mg drug that was given in the first dose. Leuprorelin acetate 45 mg at a dose of 45 mg every 6 months, from 23 May 2024, for the indication prostate cancer (lot: L14177A1, expiry date: July-2025).

On an unknown date on Feb-2025, patient experienced Intense heat.

On 28-May-2025, patient reported, he had Intense hot flashes and excessive sweating (Moderate) (Feb-2025), so by his own decision he discontinued Leuprorelin acetate 45 mg treatment.

Outcome of Intense heat, Excessive sweating and Intense hot flashes were not resolved.

Continuation Sheet for CIOMS report

On 19-Aug-2025, the patient indicates that, based on a medical decision and his own decision, he omitted treatment with Leuprorelin acetate and underwent surgery in early August, but does not specify the type of surgery.

Diseases included Flu-like symptoms, Cardiac disorder, Prostatic specific antigen abnormal, Prostate cancer, Pain on lower thigh, Headache, Dyspepsia, Abdominal spasm, Chills, Pain in spine and Prostate cancer metastatic.

Patient 16 years ago, does not refer to exact date, was diagnosed with heart problems, but never obtained medication to treat heart problem.

Past medications were not reported.

Concomitant medication included BICALUTAMIDE, ACETAMINOPHEN and TRAMACET [PARACETAMOL;TRAMADOL HYDROCHLORIDE].

Lab data included:
In Jan-2024, PSA: 900 nanogram per millliiter.
On 18-May-2024, PSA: results were 0 ng/m.

The patient and nurse assessed the following events with respect to enzalutamide, prolia and leuprorelin acetate (Injection, powder, lyophilized, for suspension):
- Intense heat (Seriousness: Non serious, Causality: Not Assessed)
- Excessive sweating (Seriousness: Non serious, Causality: Not Assessed)
- Intense hot flashes (Seriousness: Non serious, Causality: Not Assessed)

The patient assessed the following events with respect to leuprorelin acetate (Injectable Powder, for suspension):
- Intense heat (Seriousness: Non serious, Causality: Not Assessed)
- Excessive sweating (Seriousness: Non serious, Causality: related)
- Intense hot flashes (Seriousness: Non serious, Causality: related)

Consent to contact patient for follow-up information was denied and for nurse was not provided.

Tracking of changes:
23-May-2025: Initial information was received.

Follow-up information received by Astellas business partner, Adium, on 19-Aug-2025, from patient and was received at Astellas from Adium on 20-Aug-2025: Narrative description was updated.

Company Remarks (Sender's Comments) :

Event Information:
Feeling hot, Excess sweating and Hot flashes were assessed as Non Serious.

Non-Serious is based on events did not meet any ICH seriousness criteria.

All events were coded to their respective MedDRA terms to reflect the medical essence of the reported events appropriately.

Product: Enzalutamide
Astellas assessed Feeling hot, Excess sweating and Hot flashes as Related based on plausible temporal relationship. Eligard is a potential confounder for events. With the available information medical assessment has been done, however, upon receiving further information case will be reassessed.

Additional Information (Continuation...)

Laboratory Data :

In Jan-2024, PSA: 900 nanogram per millliiter.
On 18-May-2024, PSA: results were 0 ng/m.

Lab Result :

Test Name	Test Date	Test Result	Normal Value
PSA	/Jan/2024	900 nanogram per millliiter	
PSA	18/May/2024		

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

2) Test Name: PSA

Continuation Sheet for CIOMS report

Result Unstructured Data (free text) : results were 0 ng/ml
Test Date: 18/May/2024

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) Spinal cancer (prostate cancer metastasized in the area of the spine) [10036909 - Prostate cancer metastatic]
Therapy Dates : 1) From : 20/May/2024 To :Unknown
Action(s) Taken With Drug : Unknown

Causality

1) Intense heat (Feeling hot - 10016334, Feeling hot - 10016334)
Causality as per reporter : Not assessed
Causality as per Mfr : Related
ReChallenge : Not Applicable
2) Excessive sweating (Excess sweating - 10015590, Hyperhidrosis - 10020642)
Causality as per reporter : Not assessed
Causality as per Mfr : Related
ReChallenge : Not Applicable
3) Intense hot flashes (Hot flashes - 10020407, Hot flush - 10060800)
Causality as per reporter : Not assessed
Causality as per Mfr : Related
ReChallenge : Not Applicable

Labeling :

1) Intense heat
CORE UnLabeled
IB UnLabeled
2) Excessive sweating
CORE UnLabeled
IB UnLabeled
3) Intense hot flashes
CORE Labeled
IB UnLabeled

2) Drug : ELIGARD
Active Substance : 1) LEUPRORELIN ACETATE
Drug Characterization : Suspect
Form Strength : 1) 22.5 Milligram
Form of Admin : 1) Suspension for injection
Lot Number : 1) Unknown
Daily Dose : 1) 0.25 milligram(s) (22.5 milligram(s), 1 in 3 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Prostate cancer [10007113 - Cancer of prostate]
Therapy Dates : 1) From : 09/Feb/2024 To :Unknown
Action(s) Taken With Drug : Unknown

Causality

1) Intense heat (Feeling hot - 10016334, Feeling hot - 10016334)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
2) Excessive sweating (Excess sweating - 10015590, Hyperhidrosis - 10020642)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
3) Intense hot flashes (Hot flashes - 10020407, Hot flush - 10060800)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed

Continuation Sheet for CIOMS report

3) Drug : PROLIA
Active Substance : 1) DENOSUMAB
Drug Characterization : Suspect
Form Strength : 1) 60 Milligram
Form of Admin : 1) Injection
Lot Number : 1) L14177A1
Daily Dose : 1) 1.333 milligram(s) (120 milligram(s), 1 in 3 Month)
Route of Admin : 1) Unknown
Indications : 1) Spinal cancer (prostate cancer metastasized in the area of the spine) [10036909 - Prostate cancer metastatic]
Therapy Dates : 1) From : 20/May/2024 To :Unknown
Action(s) Taken With Drug : Unknown

Causality

1) Intense heat (Feeling hot - 10016334, Feeling hot - 10016334)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
2) Excessive sweating (Excess sweating - 10015590, Hyperhidrosis - 10020642)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
3) Intense hot flashes (Hot flashes - 10020407, Hot flush - 10060800)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed

4) Drug : ELIGARD
Active Substance : 1) LEUPRORELIN ACETATE
Drug Characterization : Suspect
Form Strength : 1) 45 Milligram
Form of Admin : 1) Powder for suspension for injection
Lot Number : 1) L14177A1
Daily Dose : 1) 0.25 milligram(s) (45 milligram(s), 1 in 6 Month)
Route of Admin : 1) Subcutaneous
Indications : 1) Prostate cancer [10007113 - Cancer of prostate]
Therapy Dates : 1) From : 23/May/2024 To ://2025
Action(s) Taken With Drug : Drug withdrawn

Causality

1) Intense heat (Feeling hot - 10016334, Feeling hot - 10016334)
Causality as per reporter : Not assessed
Causality as per Mfr : Not assessed
2) Excessive sweating (Excess sweating - 10015590, Hyperhidrosis - 10020642)
Causality as per reporter : Related
Causality as per Mfr : Not assessed
3) Intense hot flashes (Hot flashes - 10020407, Hot flush - 10060800)
Causality as per reporter : Related
Causality as per Mfr : Not assessed

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

Dosage Text :

Drug 2 :ELIGARD

1) Injection, powder, lyophilized, for suspension

Drug 3 :PROLIA

1) 2 pre-filled syringes of 120 mg every 3 months

Drug 4 :ELIGARD

1) Injectable Powder, for suspension

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

1). Drug : BICALUTAMIDE
Active Substance : 1) BICALUTAMIDE
Form Strength :
Form of Admin : 1) Capsule
Daily Dose : 1) 1.0 dosage form (1 dosage form, 1 in 1 Day)

Continuation Sheet for CIOMS report

Route of Admin	:	1) Unknown
Indications	:	1) prostate cancer [10060862 - Prostate cancer]
Therapy Dates	:	1) From : 19/Mar/2024 To : Unknown
Dosage Text	:	1) Ongoing

2). Drug	:	ACETAMINOPHEN
Active Substance	:	1) PARACETAMOL
Form Strength	:	
Form of Admin	:	1) Unknown
Daily Dose	:	1) 4.0 gram(s) (1 gram(s), 1 in 6 Hour)
Route of Admin	:	1) Unknown
Indications	:	1) drug use for unknown indication [10057097 - Drug use for unknown indication]

3). Drug	:	TRAMACET [PARACETAMOL;TRAMADOL HYDROCHLORIDE]
Active Substance	:	1) PARACETAMOL 2) TRAMADOL HYDROCHLORIDE
Form Strength	:	
Form of Admin	:	1) Capsule
Daily Dose	:	1) 3.0 dosage form (1 dosage form, 1 in 8 Hour)
Route of Admin	:	1) Unknown
Indications	:	1) spinal pain [10072005 - Spinal pain]
Therapy Dates	:	1) From : 20/May/2024 To : Unknown
Dosage Text	:	1) 37.5 mg / 325 mg

23. OTHER RELEVANT HISTORY (Continuation...)

2) PAIN IN THE LOWER LIMBS (10033475 , Pain on lower thigh) (10/Feb/2024 -) (Continuing : NO)

3) HEADACHE (10019211 , Headache) (10/Feb/2024 -) (Continuing : NO)

4) BURNING IN THE PIT OF THE STOMACH (10013946 , Dyspepsia) (08/Mar/2024 -) (Continuing : YES)

5) ABDOMINAL SPASM (10051889 , Abdominal spasm) (08/Mar/2024 -) (Continuing : YES)

6) FLU-LIKE SYMPTOMS (10016797 , Flu-like symptoms) (Continuing : NO)

7) HEART PROBLEMS (10061024 , Cardiac disorder) (Continuing : YES)

8) PROSTATE CANCER (10060862 , Prostate cancer) (Continuing : YES)

9) CHILLS (10008531 , Chills) (Continuing : YES)

10) SPINE PAIN (10052060 , Pain in spine) (Continuing : YES)

11) SPINAL CANCER (PROSTATE CANCER METASTASIZED IN THE AREA OF THE SPINE) / METASTASIS (10036909 , Prostate cancer metastatic) (Continuing : YES)

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

Study # :Enzalutamide_Astellas PSP