CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2021US010520

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	79	Male	15	Feb	2021

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

1) Dizziness (Dizziness (10013573), Dizziness (10013573))
(08/Mar/2021 -) - Unknown
2) Irritation in both elbows in the upper part (skin irritation) as if it were a rash (Skin irritation (10040880), Skin irritation (10040880))
(06/Jun/2023 -) - Unknown
3) He feels his right hand asleep (Numbness in hand (10049681), Hypoaesthesia (10020937))
(/Jun/2023 -) - Unknown
4) Hot flashes he feels in both feet and in the body (Hot flashes (10020407), Hot flush (10060800))
(Asked but Unknown -) - 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)(40 Milligram, Capsule)(L1939652AAC)

Cont..

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

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
1) 40.0 milligram(s) (40 milligram(s), 1 in 1 Day) 2) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)	1) Oral 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) (15/Feb/2021 -)	

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.)

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	2021US010520
24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
19/May/2025	☑ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL
DATE OF THIS REPORT	25a. REPORT TYPE
27/May/2025	☐ INITIAL ☑ FOLLOWUP

= Continuation attached sheet(s)..

Continuation Sheet for CIOMS report

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

5) Fall (Fall (10016173), Fall (10016173)(25/Feb/2025 -) - Not Recovered/Not Resolved/Ongoing)

6) Pains that still bother him in the rib (Rib pain (10048722), Musculoskeletal chest pain (10050819)(//2025 -) - Not Recovered/Not Resolved/Ongoing)

7) Pains that still bother him in the shoulder (Shoulder pain (10040617), Arthralgia (10003239)(//2025 -) - Not Recovered/Not Resolved/Ongoing)

8) Patient took 40 mg xtandi daily (Underdose (10057362), Underdose (10057362)(15/Feb/2021 -) - Unknown)

Event Description :

This Patient Support Program case was received by Astellas business partner, Tecnofarma S.A., from received from a Consumer or other non health professional in PANAMA on 18-Mar-2021 and received at Astellas from Tecnofarma S.A., on 19-Mar-2021, concerning a 79 Year(s) old (reported 81 years-old; now reported as 83 Year(s) old) Male patient, enrolled in post-marketing study: Enzalutamide Patient Support Program who was on Xtandi (enzalutamide), Capsule (40 milligram(s), 1 every 1 Day). Indication for use was Prostate cancer. The lot number was L1939652AAC. The patient initiated treatment on 15-Feb-2021.

Study No: Enzalutamide_Astellas PSP; Open-Label study.

The patient received enzalutamide for prostate cancer according to the following dosage regimens: 15-Feb-2021 - (stop date not provided): Oral, 40 mg, once daily and (start date not provided) (start date also reported as 15-Feb-2021) - (ongoing): Oral 160 mg, once daily.

The patient received Eligard (leuprorelin) for prostate cancer according to the following dosage regimens: 26-MarR-2019 - Apr-2023: unknown route, dose, and frequency and (start date not provided - (ongoing): Subcutaneous 45 mg every 6 months.

Action taken with enzalutamide in response to events (dizziness, hot flashes he feels in both feet and in the body and patient took 40 mg Xtandi daily) was unknown and in response to events (irritation in both elbows in the upper part (skin irritation) as if it were a rash, fall and He feels his right hand asleep, Pains that still bother him in the rib and Pains that still bother him in the shoulder) was no change. Action taken with Eligard (leuprorelin) treatment in response to the events was no change.

Since 15-Feb-2021, the patient took 40 mg enzalutamide daily, which was considered as underdose. Since 08-Mar-2021 the patient had dizziness.

The patient indicated that he also used the leuprorelin medication (he does not provide a start date) but his last application was in Apr-2023, he does not have the lot number and expiration date of the leuprorelin medication, the doctor was the one who applied it and he discarded the box. The patient reported that on 06-Jun-2023, he started with irritation in both elbows in the upper part (skin irritation) as if it were a rash. On 08-Jun-2023 he would go to the doctor for a consultation and to be prescribed some medication. He does not currently use any medication for this symptom. The patient comments that two weeks ago on 06-May-2023 he had the same irritation mentioned above, but he applied a cocoa cream and it had disappeared.

The patient refers that the event "irritation in both elbows in the upper part (skin irritation) as if it were a rash" was not related to the enzalutamide medication, that probably these symptoms were due to the heat, the patient commented that he no longer went to consult with the physician that was scheduled for 08-Jun-2023, because the day after the event was reported he no longer had irritation. The patient refers that the irritation on both elbows in the upper part (skin irritation) was not similar to some kind of eruption, which was like a rash. It was reported that the drug enzalutamide was prescribed by his physician for prostate cancer.

The patient had an appointment with his physician, the patient consulted him about some hot flashes he feels in both feet and in the body (sensation of heat), the physician commented to the patient that it was due to the side effects of the enzalutamide medication, that it was normal to feel these symptoms and that it would soon pass.

Patient refers that 4 to 5 days ago, he does not remember the date, he feels his right hand asleep (numbness in hand), it does not cause his malaise, but it causes his discomfort because when he grabs an object, he does not feel that he is holding it in his hand. He has not consulted with his doctor about this symptom because he has not had an appointment, but he will do so on Tuesday, 04-Jul-2023.

Patient mentions that, on 25-Feb-2025, he suffered a fall leaving the bathroom, he refers that at the moment he left the bathroom he grabbed a lever or curtain rods (it is unknown what exactly he is referring to), he mentions that the reason for the fall was because the carpet moved causing him to fall, patient refers that he was conscious, although he comments that because of the fall he hurt his right and left hand, since the patient comments that he placed both hands in front of him so that his head would not hit the toilet, he also comments that in his stomach in the part of the left rib he received the blow on the tip of the toilet, which is a pain that he still has, for this reason he cannot go out to the street to request his next box of Xtandi, he will probably request it on Tuesday. On 25-Feb-2025 the patient went to the emergency hospital where he had an x-ray, which revealed that there was no fracture, but he did have pain. Patient agrees to be contacted and treating physician for future follow-up.

On 19-May-2025, the patient reported that, from the fall of 25-Feb-2025, he still did not feel recovered because he still had pains that still bother him in the rib and shoulder so he must rest constantly, but he walks and performs his activities, he mentions that he managed not to hit his face. Patient agrees to be contacted and treating physician for future follow-up.

The patient had not yet recovered from the events (Fall, Pains that still bother him in the rib and Pains that still bother him in the shoulder). The outcome of the other events were unknown.

Continuation Sheet for CIOMS report

Medical history was not reported.

Past medications were not reported.

Concomitant medication included Contractile plus 4mg: take 1tablet every 12 hours, for pain.

Lab data included:
On 25-Feb-2025, X-RAY: no fracture.

The consumer assessed the following event with respect to enzalutamide and Eligard (leuprorelin):
- Dizziness (seriousness: Non-serious; causality: Not Assessed)

The patient assessed the following events with respect to enzalutamide:
- Hot flashes he feels in both feet and in the body (seriousness: Non- serious; causality: Related)
- Irritation in both elbows in the upper part (skin irritation) as if it were a rash (seriousness: Non-serious; causality: Not related)
- Patient took 40 mg Xtandi daily (seriousness: Not Reported; causality: Not Assessed)
- He feels his right hand asleep (seriousness: Non-serious; causality: Not Assessed)
- Fall (seriousness: Non-serious; causality: Not Assessed)
- Pains that still bother him in the rib (seriousness: Non-serious; causality: Not Assessed)
- Pains that still bother him in the shoulder (seriousness: Non-serious; causality: Not Assessed)

The patient assessed the following events with respect to Eligard (leuprorelin):
- Hot flashes he feels in both feet and in the body (seriousness: Non- serious; causality: Not Assessed)
- Irritation in both elbows in the upper part (skin irritation) as if it were a rash (seriousness: Non-serious; causality: Not Assessed)
- Patient took 40 mg Xtandi daily (seriousness: Not Reported; causality: Not Assessed)
- He feels his right hand asleep (seriousness: Non-serious; causality: Not Assessed)
- Fall (seriousness: Non-serious; causality: Not Assessed)
- Pains that still bother him in the rib (seriousness: Non-serious; causality: Not Assessed)
- Pains that still bother him in the shoulder (seriousness: Non-serious; causality: Not Assessed)

Consent to contact Patient for follow-up information was provided and denied for the consumer.

Tracking of changes:
18-Mar-2021: Initial information was received.

Follow-up information received on 26-Apr-2021. Confirmation of country of incidence, non-significant information.

This patient support program case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 08-Jun-2023 from a patient and was received at Astellas from Asofarma on 08-Jun-2023. The patient was enrolled in Astellas sponsored patient support program titled "ASOFARMA A TU LADO": Added the enzalutamide therapy details (additional dosage regimen, lot number and expiration dates), co-suspect Eligard (leuprorelin) details, new event of irritation in both elbows in the upper part (skin irritation) as if it were a rash. Updated the report type from spontaneous to sponsored study, action taken with suspect drugs and narrative description.

This patient support program case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 20-Jun-2023 from a patient and was received at Astellas from Asofarma on 20-Jun-2023: New event "hot flashes he feels in both feet and in the body" added, event details of "irritation in both elbows in the upper part (skin irritation) as if it were a rash" (outcome, causality) and narrative was updated.

This patient support program case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 29-Jun-2023 from a patient and was received at Astellas from Asofarma on 30-Jun-2023: Added new event He feels his right hand asleep, event outcome and causality of Hot flashes he feels in both feet and in the body. Updated clinical information.

On 12-Jul-2023 and 13-Jul-2023 confirmation was received that no additional information was available.

On 31-Jul-2023 confirmation was received that no additional information was available.

This information case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 27-Feb-2025 from a patient and was received at Astellas from Asofarma on 28-Feb-2025: concomitant medications, Irritation in both elbows in the upper part (skin irritation) as if it were a rash event onset date, lab data, outcome (Hot flashes he feels in both feet and in the body and Irritation in both elbows in the upper part (skin irritation) as if it were a rash) and case description updated.
New event fall added.

This patient support program case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 19-May-2025 from a patient and was received at Astellas from Asofarma on 20-May-2025: New events (Pains that still bother him in the rib and Pains that still bother him in the shoulder) added, patient's age updated, consent to contact patient for follow-up information updated from no to yes and case description updated.

Company Remarks (Sender's Comments) :

Continuation Sheet for CIOMS report

Event Information:
Hot flashes, Underdose, Dizziness, Numbness in hand, Skin irritation, Rib pain, Shoulder pain and Fall were assessed as Non-Serious due to no patient jeopardy reported/ as event does not meet the ICH seriousness criteria.

All the events coded to closest available LLT per MEDDRA.

Product: Enzalutamide
Astellas assessed Dizziness, Skin irritation, Numbness in hand and Hot flashes as Related based on temporal association. Elderly age and underlying malignancy could be confounders for Dizziness and Numbness in hand. Exposure to heat is a confounder for Skin irritation. Eligard is confounder for the events. Underdose was assessed as Not Related, as it was due to human action. Astellas assessed Fall as not related as there is no evidence that drug caused the fall. Elderly age and concurrent dizziness are risk factors. Events Rib pain and Shoulder pain were assessed as not related as these were due to fall in this elderly patient.

Additional Information (Continuation...)

Laboratory Data :

25-Feb-2025: X-Ray: no fracture

Lab Result :

Test Name	Test Date	Test Result	Normal Value
X-RAY	25/Feb/2025		

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

1) Test Name: X-RAY

Result Unstructured Data (free text) : no fracture
Test Date: 25/Feb/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
  2) 40 Milligram
- Form of Admin : 1) Capsule
  2) Capsule
- Lot Number : 1) Unknown
  2) L1939652AAC
- Daily Dose : 1) 40.0 milligram(s) (40 milligram(s), 1 in 1 Day)
  2) 160.0 milligram(s) (160 milligram(s), 1 in 1 Day)
- Route of Admin : 1) Oral
  2) Oral
- Indications : 1) prostate cancer [10060862 - Prostate cancer]
- Therapy Dates : 1) From : 15/Feb/2021 To :Unknown
- Action(s) Taken With Drug : Unknown

Causality

1) Dizziness (Dizziness - 10013573, Dizziness - 10013573)
- Causality as per reporter : Not assessed
- Causality as per Mfr : Related

2) Irritation in both elbows in the upper part (skin irritation) as if it were a rash (Skin irritation - 10040880, Skin irritation - 10040880)
- Causality as per reporter : Not Related
- Causality as per Mfr : Related
- DeChallenge : Not applicable
- ReChallenge : Not Applicable

3) He feels his right hand asleep (Numbness in hand - 10049681, Hypoaesthesia - 10020937)
- Causality as per reporter : Not assessed
- Causality as per Mfr : Related
- DeChallenge : Not applicable

Continuation Sheet for CIOMS report

ReChallenge : Not Applicable

4) Hot flashes he feels in both feet and in the body (Hot flashes - 10020407, Hot flush - 10060800)
Causality as per reporter : Related
Causality as per Mfr : Related

5) Fall (Fall - 10016173, Fall - 10016173)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) Pains that still bother him in the rib (Rib pain - 10048722, Musculoskeletal chest pain - 10050819)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) Pains that still bother him in the shoulder (Shoulder pain - 10040617, Arthralgia - 10003239)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) Patient took 40 mg xtandi daily (Underdose - 10057362, Underdose - 10057362)
Causality as per reporter : Not assessed
Causality as per Mfr : Not Related
DeChallenge : Not applicable
ReChallenge : Not Applicable

Labeling :

1) Dizziness
CORE UnLabeled
IB UnLabeled

2) Irritation in both elbows in the upper part (skin irritation) as if it were a rash
CORE UnLabeled
IB UnLabeled

3) He feels his right hand asleep
CORE UnLabeled
IB UnLabeled

4) Hot flashes he feels in both feet and in the body
CORE Labeled
IB UnLabeled

5) Fall
CORE Labeled
IB Labeled

6) Pains that still bother him in the rib
CORE UnLabeled
IB UnLabeled

7) Pains that still bother him in the shoulder
CORE UnLabeled
IB UnLabeled

8) Patient took 40 mg xtandi daily
CORE UnLabeled
IB UnLabeled

2) Drug : ELIGARD
Active Substance : 1) LEUPRORELIN ACETATE
Drug Characterization : Suspect
Form Strength : 1) 45 Milligram
2) 45 Milligram
Form of Admin : 1) Injection
2) Injection
Lot Number : 1) Unknown
2) Unknown
Daily Dose : (45 milligram(s))
Route of Admin : 1) Unknown
2) Subcutaneous
Indications : 1) Prostate cancer [10060862 - Prostate cancer]
Therapy Dates : 1) From : 26/Mar/2019 To :/Apr/2023

Continuation Sheet for CIOMS report

Action(s) Taken With Drug : Dose not changed

Causality

1) Dizziness (Dizziness - 10013573, Dizziness - 10013573)
DeChallenge : Not applicable
ReChallenge : Not Applicable

2) Irritation in both elbows in the upper part (skin irritation) as if it were a rash (Skin irritation - 10040880, Skin irritation - 10040880)
DeChallenge : Not applicable
ReChallenge : Not Applicable

3) He feels his right hand asleep (Numbness in hand - 10049681, Hypoaesthesia - 10020937)
DeChallenge : Not applicable
ReChallenge : Not Applicable

4) Hot flashes he feels in both feet and in the body (Hot flashes - 10020407, Hot flush - 10060800)
DeChallenge : Not applicable
ReChallenge : Not Applicable

5) Fall (Fall - 10016173, Fall - 10016173)
DeChallenge : Not applicable
ReChallenge : Not Applicable

6) Pains that still bother him in the rib (Rib pain - 10048722, Musculoskeletal chest pain - 10050819)
DeChallenge : Not applicable
ReChallenge : Not Applicable

7) Pains that still bother him in the shoulder (Shoulder pain - 10040617, Arthralgia - 10003239)
DeChallenge : Not applicable
ReChallenge : Not Applicable

8) Patient took 40 mg xtandi daily (Underdose - 10057362, Underdose - 10057362)
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Dosage Text :

Drug 2 :ELIGARD

1) UNK UNK, unknown freq.

2) 45 mg, every 6 months ongoing

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

Study # :Enzalutamide_Astellas PSP