

SUSPECT ADVERSE REACTION REPORT												
	2021US010520											

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) Masked	1a. COUNTRY PANAMA	2. DATE OF BIRTH Day Masked	Month Masked	Year Masked	2a. AGE Years 79	3. SEX Male	4-6 REACTION ONSET Day 15	Month Feb	Year 2021	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
7+13 DESCRIBE REACTION(S) (including relevant tests/lab data) 1) Dizziness (Dizziness (10013573), Dizziness (10013573)) (08/Mar/2021 -) - Recovered/Resolved With Sequelae 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 -) - Not Recovered/Not Resolved/Ongoing 3) He feels his right hand asleep (Numbness in hand (10049681), Hypoaesthesia (10020937)) (/Jun/2023 -) - Not Recovered/Not Resolved/Ongoing 4) Hot flashes he feels in both feet and in the body (Hot flashes (10020407), Hot flush (10060800)) Not Recovered/Not Resolved/Ongoing										☐ PATIENT DIED ☐ LIFE THREATENING ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION ☐ RESULTS IN PERSISTENCE OR SIGNIFICANT DISABILITY/INCAPACITY ☐ CONGENITAL ANOMALY ☐ OTHER MEDICALLY IMPORTANT CONDITION
Cont..										

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name) 1) Enzalutamide (Enzalutamide, Enzalutamide) (Suspect) (Verum) (40 Milligram, Capsule) (L 2081024AE - 7309795173) (40 Milligram, Capsule) (L1939652AAC)		20. DID EVENT ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☐ NA
15. DAILY DOSE(S) 1) 40.0 milligram(s) (40 milligram(s), 1 in 1 Day) 2) 40.0 milligram(s) (40 milligram(s), 1 in 1 Day)		21. DID EVENT REAPPEAR AFTER REINTRODUCTION ☐ YES ☐ NO ☐ NA (NA : Not Applicable)
16. ROUTE(S) OF ADMINISTRATION 1) Oral 2) Oral		
17. INDICATION(S) FOR USE 1) prostate cancer [10060862 - Prostate cancer]		
18. THERAPY DATE(S) (from/to) 1) (15/Feb/2021 -)	19. THERAPY DURATION	

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 ☐ YES ☐ NO	24b. MFR CONTROL NO. 2021US010520		
24c. DATE RECEIVED BY MANUFACTURER 16/Jul/2025	24d. REPORT SOURCE ☒ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL		
DATE OF THIS REPORT 24/Jul/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) Fall (Fall (10016173), Fall (10016173)(25/Feb/2025 -) - Recovered/Resolved)

6) Pains that still bother him in the rib (Rib pain (10048722), Musculoskeletal chest pain (10050819)(14/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

7) Pains that still bother him in the shoulder (Shoulder pain (10040617), Arthralgia (10003239)(14/May/2025 -) - Not Recovered/Not Resolved/Ongoing)

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

9) wear and tear on the right knee when flexing the knee (Knee injury (10049032), Joint injury (10060820) - Not Recovered/Not Resolved/Ongoing)

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 numbers were L 2081024AE - 7309795173 and 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 28-Feb-2022 - (ongoing): Oral 40 mg, once daily. The expiry date reported 30-Apr-2024, and Feb-2026.

The patient received Eligard (leuporelin) for prostate cancer according to the following dosage regimens: 26-Mar-2019 - Apr-2023: unknown route, dose, and frequency and 28-Feb-2022 - (ongoing): Subcutaneous 45 mg every 6 months. (Last application: The patient continue to use it. The patient received it 1.5 months ago.)

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), wear and tear on the right knee when flexing the knee was no change. Action taken with Eligard (leuporelin) 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 (also reported never experienced dizziness).

The patient indicated that he also used the leuporelin 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 leuporelin 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 still have the irritation, especially in the morning.

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 (also reported as 14-May-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.

Continuation Sheet for CIOMS report

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.

At time of report on 16-Jul-2025 the patient reported the patient fingers still go numb. The patient can move hand, but when the patient touch or pick up something, the patient can't feel anything. The patient continued to experience hot flashes in the right foot near the knee. The patient feel pain in my right knee when the patient bend the knee, and it causes windpipe damage (the patient think that's what caused the patient to fall). The patient have not had any more falls. The patient still hurts, not every day, but it comes and goes. Shoulder pain still bothers the patient, not every day, but the pain comes and goes. The patient lower back also hurts. This pain started a week ago. The doctor said it's muscle pain.

On an unknown date the patient had wear and tear on the right knee when flexing the knee. The outcome was not recovered.

The patient had not yet recovered from the events (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. The outcome of event Hot flashes he feels in both feet and in the body and He feels his right hand asleep, Irritation in both elbows in the upper part (skin irritation) as if it were a rash was not recovered. The outcome of event Dizziness was Recovered / resolved with sequelae. The outcome of event fall was recovered.

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 (leuporelin):

- 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/Underdosing (seriousness: Not Reported; causality: Not Assessed)
- He feels his right hand asleep (seriousness: Non-serious; causality: Related)
- Fall (seriousness: Non-serious; causality: Related)
- 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: Related)
- wear and tear on the right knee when flexing the knee (seriousness: Non-serious; causality: Not Assessed)

The patient assessed the following events with respect to Eligard (leuporelin):

- 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/Underdosing (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)
- wear and tear on the right knee when flexing the knee (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 (leuporelin) 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.

Continuation Sheet for CIOMS report

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.

This information case was received by Astellas business partner Asofarma (a subsidiary of Tecnofarma S. A) on 16-Jul-2025 from a patient and was received at Astellas from Asofarma on 17-Jul-2025: Added even wear and tear on the right knee when flexing the knee. Updated enzalutamide therapy details, event Hot flashes he feels in both feet and in the body, He feels his right hand asleep, Irritation in both elbows in the upper part (skin irritation) as if it were a rash outcome from unknown to not recovered, Dizziness outcome from unknown to Recovered / resolved with sequelae, fall from not recovered to recovered, Updated verbatim from Patient took 40 mg Xtandi daily to Patient took 40 mg Xtandi daily/Underdosing, event He feels his right hand asleep, Pains that still bother him in the shoulder and Fall causality from not assessed to related and case description.

Company Remarks (Sender's Comments) :

Event Information:

Hot flashes, Knee injury, Underdose, Dizziness, Numbness in hand, Skin irritation, Fall, Rib pain and Shoulder pain were assessed as Non Serious. Non-Serious is 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.

Astellas assessed Knee injury as Not Related which had occurred during flexing the knee, need additional information on event for better assessment. 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. Underdose was assessed as Not Related, as it was due to human action.

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

Continuation Sheet for CIOMS report

Form of Admin : 2) 40 Milligram
 : 1) Capsule
 Lot Number : 2) Capsule
 : 1) L 2081024AE - 7309795173
 : 2) L1939652AAC
 Daily Dose : 1) 40.0 milligram(s) (40 milligram(s), 1 in 1 Day)
 : 2) 40.0 milligram(s) (40 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
 : 2) From : 28/Feb/2022 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 : Related
 Causality as per Mfr : Related
 DeChallenge : Not applicable
 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 : Related
 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 : Related
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 8) Patient took 40 mg xtandi daily/Underdosing (Underdose - 10057362, Underdose - 10057362)
 Causality as per reporter : Not assessed
 Causality as per Mfr : Not Related
 DeChallenge : Not applicable
 ReChallenge : Not Applicable
- 9) wear and tear on the right knee when flexing the knee (Knee injury - 10049032, Joint injury - 10060820)
 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

Continuation Sheet for CIOMS report

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/Underdosing	
CORE	UnLabeled
IB	UnLabeled
9) wear and tear on the right knee when flexing the knee	
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
	: 2) From : 28/Feb/2022 To :Continuing
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/Underdosing (Underdose - 10057362, Underdose - 10057362)
DeChallenge : Not applicable
ReChallenge : Not Applicable

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

Dosage Text :

Continuation Sheet for CIOMS report

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