CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

2025-097086(0)

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
Unknown	GUATEMALA	Unknown	Unknown	Unknown	60	Male	24	Jun	2025

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

MedDRA Version : v.28.0

1) SJOGREN'S SYNDROME (Sjogren's syndrome (10040767), Sjogren's syndrome (10040767))
(24/Jun/2025 -) - Unknown

2) HYPERTHYROIDITIS (Hyperthyroidism (10020850), Hyperthyroidism (10020850))
(24/Jun/2025 -) - Unknown

3) GRADE 3 RASH (Rash (10037844), Rash (10037844))
(24/Jun/2025 -) - 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) OPDIVO (NIVOLUMAB) (Suspect) (Solution for injection)(Unknown)

Cont..

15. DAILY DOSE(S)

(100 milligram(s))

16. ROUTE(S) OF ADMINISTRATION

1) Intravenous (not otherwise specified)

17. INDICATION(S) FOR USE

1) Acral melanoma [10000583 - Acral lentiginous melanoma]

18. THERAPY DATE(S) (from/to)

1) (06/May/2025 - 24/Jun/2025)

19. THERAPY DURATION

1) 50.00 Days

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.)

MedDRA Version : v.28.0

1) ACRAL MELANOMA ON THE LEFT FOOT AND WITH RECURRENCE IN THE LUNG (10000583, Acral lentiginous melanoma) (Continuing: Yes)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

Name : BMS
UNITED STATES OF AMERICA
aepbusinessprocess@bms.com

24.REPORT NULLIFIED

☐ YES ☐ NO

24b. MFR CONTROL NO.

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24c. DATE RECEIVED BY MANUFACTURER

04/Jul/2025

24d. REPORT SOURCE

☐ STUDY ☐ LITERATURE ☑ HEALTH PROFESSIONAL

DATE OF THIS REPORT

11/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...)

Event Description :

This report was received by business partner Adium Pharma S.A. (formerly Tecnofarma) (reference number: GT-ADIUM-GT-0213-20250704) on 04-Jul-2025 and forwarded to BMS on 07-Jul-2025. The spontaneous case was reported by a Physician and describes the occurrence of SJOGREN'S SYNDROME ("SJOGREN'S SYNDROME") and HYPERTHYROIDISM ("HYPERTHYROIDITIS") in a 60-year-old male patient who received NIVOLUMAB solution for injection and IPILIMUMAB solution for injection for Acral lentiginous melanoma. An additional non-serious event is detailed below.

Acral lentiginous melanoma on an unknown date was listed as CONCURRENT CONDITION.

On 06-MAY-2025, the patient started intravenous NIVOLUMAB 100mg, 10mg/ml 100 MG x 1 INY x 1 FCO and intravenous IPILIMUMAB 50mg, 50mg/10ml 50 MG X 1 INY X 1 FCO. On 24-JUN-2025, SJOGREN'S SYNDROME (seriousness criterion: medical significance), HYPERTHYROIDISM (seriousness criterion: medical significance), RASH ("grade 3 rash") and PAROTITIS ("parotitis") occurred. The patient was treated with steroids. NIVOLUMAB and IPILIMUMAB were interrupted.

The patient was undergoing treatment for acral melanoma on the left foot with recurrence in the lung. He was undergoing the third cycle of NIVOLUMAB/IPILIMUMAB when he presented with SJOGREN'S SYNDROME, PAROTITIS, grade 3 RASH, and HYPERTHYROIDISM. The patient felt very ill, so he attended a consultation where the application of the fourth dose was suspended and treatment with steroids was started to reduce the adverse event.

The reporter considered SJOGREN'S SYNDROME, HYPERTHYROIDISM, RASH to be related to NIVOLUMAB and IPILIMUMAB.

The physician agreed to be contacted for future follow-ups.

Company Remarks (Sender's Comments) :

This patient presented with Sjogren's syndrome and hyperthyroiditis (hyperthyroidism) seven weeks after initiation of therapy with nivolumab and ipilimumab. The events were treated with steroids. Based on the expected latency period and the increased predisposition of overlapping immune mediated events following ICI combination therapy, the reported events are assessed as related to nivolumab and ipilimumab owing to their immune mediated mechanism of action.

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

Product-Reaction Level

1) Drug	:	OPDIVO
Active Substance	:	1) NIVOLUMAB
Drug Characterization	:	Suspect
Form of Admin	:	1) Solution for injection
Lot Number	:	1) Unknown
Daily Dose	:	(100 milligram(s))
Route of Admin	:	1) Intravenous (not otherwise specified)
Indications	:	1) Acral melanoma [10000583 - Acral lentiginous melanoma]
Therapy Dates	:	1) From : 06/May/2025 To :24/Jun/2025
Therapy Duration	:	1) 50.00 Days
Action(s) Taken With Drug	:	Drug Interrupted

Causality

1) SJOGREN'S SYNDROME (Sjogren's syndrome - 10040767, Sjogren's syndrome - 10040767)		
Causality as per reporter	:	Related
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable
2) HYPERTHYROIDITIS (Hyperthyroidism - 10020850, Hyperthyroidism - 10020850)		
Causality as per reporter	:	Related
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable
3) GRADE 3 RASH (Rash - 10037844, Rash - 10037844)		
Causality as per reporter	:	Related
Causality as per Mfr	:	Related
DeChallenge	:	Not applicable

Labeling :

1) SJOGREN'S SYNDROME	
CORE	Labeled

Continuation Sheet for CIOMS report

2) HYPERTHYROIDITIS
CORE Labeled
3) GRADE 3 RASH
CORE Labeled

2) Drug : Yervoy
Active Substance : 1) IPILIMUMAB
Drug Characterization : Suspect
Form of Admin : 1) Solution for injection
Lot Number : 1) Unknown
Daily Dose : (50 milligram(s))
Route of Admin : 1) Intravenous (not otherwise specified)
Indications : 1) Acral melanoma [10000583 - Acral lentiginous melanoma]
Therapy Dates : 1) From : 06/May/2025 To :24/Jun/2025
Therapy Duration : 1) 50.00 Days
Action(s) Taken With Drug : Drug Interrupted

Causality

1) SJOGREN'S SYNDROME (Sjogren's syndrome - 10040767, Sjogren's syndrome - 10040767)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Unknown
2) HYPERTHYROIDITIS (Hyperthyroidism - 10020850, Hyperthyroidism - 10020850)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Unknown
3) GRADE 3 RASH (Rash - 10037844, Rash - 10037844)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Unknown

Labeling :

1) SJOGREN'S SYNDROME
CORE UnLabeled
2) HYPERTHYROIDITIS
CORE Labeled
3) GRADE 3 RASH
CORE Labeled

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

Dosage Text :
Drug 1 :OPDIVO
1) 10mg/ml 100 MG x 1 INY x 1 FCO

Drug 2 :YERVOY
1) 50mg/10ml 50 MG X 1 INY X 1 FCO

Primary Reporter:
Physician
GUATEMALA