SUSPECT ADVERSE REACTION REPORT

2025-097086(1)

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) PNEUMONIA (Bacterial pneumonia, unspecified (10004051), Pneumonia bacterial (10060946))
Unknown

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

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

4) 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..

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

15. DAILY DOSE(S)

(100 milligram(s))

16. ROUTE(S) OF ADMINISTRATION

1) Intravenous (not otherwise specified)

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

(NA : Not Applicable)

17. INDICATION(S) FOR USE

1) Acral melanoma [10000583 - Acral lentiginous melanoma]

18. THERAPY DATE(S) (from/to)	19. THERAPY DURATION
1) (06/May/2025 - 24/Jun/2025)	1) 50 Days

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	24b. MFR CONTROL NO.
☐ YES ☐ NO	2025-097086(1)
24c. DATE RECEIVED BY MANUFACTURER: 04/Aug/2025	24d. REPORT SOURCE: ☐ STUDY ☐ LITERATURE ☑ HEALTH PROFESSIONAL
DATE OF THIS REPORT: 11/Aug/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-Aug-2025 and forwarded to BMS on 04-Aug-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.

This spontaneous case was received on 4-Jul-2025, via an electronic form through the Jazz Safety tool from a company employee who was provided with information by a physician regarding a 60-year-old male patient being treated with the following medications: Opdivo 10mg/ml solution for intravenous infusion and Yervoy 50mg/10ml solution for intravenous infusion, both medications for the indication: Acral melanoma.

The last administration date of NIVOLUMAB and IPILIMUMAB was 24-Jun-2025.

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 withdrawn.

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 physician reports: The patient was covered by social security. Physician have not yet been able to evaluate him, as he was hospitalized with pneumonia requiring intensive care. This is not associated with the use of the medication.
The doctor reports: They will communicate further information through this medium as it becomes available.

On an unknown date, the patient experienced PNEUMONIA BACTERIAL (seriousness criteria: life-threatening and hospitalization).

The reporter considered SJOGREN'S SYNDROME, HYPERTHYROIDISM, RASH to be related to NIVOLUMAB and IPILIMUMAB, but saw no causal relationship between PNEUMONIA BACTERIAL and NIVOLUMAB and no causal relationship between PNEUMONIA BACTERIAL and IPILIMUMAB.

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

The above narrative is a summary of all previous and newly received information.
The most recent follow-up on 04-Aug-2025 included

Adverse event pneumonia bacterial added with seriousness criteria life-threatening and hospitalization. Action taken with nivolumab and ipilimumab updated. Causality assessment for pneumonia bacterial added. Narrative information updated.

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 for Acral lentiginous melanoma. Patient also had life-threatening pneumonia on an unspecified duration after receiving therapy with nivolumab and ipilimumab. The events Sjogren's syndrome and hyperthyroiditis 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 Sjogren's syndrome and hyperthyroiditis are assessed as related to nivolumab and ipilimumab owing to their immune mediated mechanism of action. Immunocompromised state associated with underlying melanoma is a risk factor for pneumonia and is considered not related to nivolumab and ipilimumab therapy.

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]

Continuation Sheet for CIOMS report

Therapy Dates : 1) From : 06/May/2025 To :24/Jun/2025
Therapy Duration : 1) 50 Days
Action(s) Taken With Drug : Drug withdrawn

Causality

1) PNEUMONIA (Bacterial pneumonia, unspecified - 10004051, Pneumonia bacterial - 10060946)
Causality as per reporter : Not Related
Causality as per Mfr : Not Related
DeChallenge : Unknown
ReChallenge : Not Applicable
2) SJOGREN'S SYNDROME (Sjogren's syndrome - 10040767, Sjogren's syndrome - 10040767)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
3) HYPERTHYROIDITIS (Hyperthyroidism - 10020850, Hyperthyroidism - 10020850)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
4) GRADE 3 RASH (Rash - 10037844, Rash - 10037844)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable

Labeling :

1) PNEUMONIA
CORE Labeled
2) SJOGREN'S SYNDROME
CORE Labeled
3) HYPERTHYROIDITIS
CORE Labeled
4) 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 Days
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Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Unknown
4) GRADE 3 RASH (Rash - 10037844, Rash - 10037844)
Causality as per reporter : Related
Causality as per Mfr : Related
DeChallenge : Not applicable
ReChallenge : Unknown

Continuation Sheet for CIOMS report

Labeling :

1) PNEUMONIA	
CORE	Labeled
2) SJOGREN'S SYNDROME	
CORE	UnLabeled
IB	
3) HYPERTHYROIDITIS	
CORE	Labeled
IB	
4) 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