CIOMS FORM

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	GUATEMALA		PRIVACY		36 Years	Female	64.00 kg	17	JAN	2023

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)
Event Verbatim [LOWER LEVEL TERM] (Related symptoms if any separated by commas)

Other Serious Criteria: Medically Significant
Imuran and leukopenia [Off label use in unapproved indication]
Leucopenia/ low WBC, [Leucopenia]
Leucopenia/ low WBC [Condition aggravated]
low lymphocyte absolute count [Lymphocyte count decreased]

Case Description: Initial report was received on 30-MAY-2025.

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☐ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ OTHER

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)
#1) Imuran (Azathioprine) Unknown

(Continued on Additional Information Page)

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

15. DAILY DOSE(S)
#1) UNK

16. ROUTE(S) OF ADMINISTRATION
#1) Unknown

17. INDICATION(S) FOR USE
#1) Systemic lupus erythematosus (Systemic lupus erythematosus)

(Continued on Additional Information Page)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)
#1) 23-MAR-2023 / 16-JAN-2025

19. THERAPY DURATION
#1) 1 year 9 months 25 days

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)
#1) Hydroxychloroquine (Hydroxychloroquine sulfate) ; 23-MAR-2023 / Unknown
#2) Vortioxetine (Vortioxetine) ; 12-DEC-2023 / Unknown
#3) Deflazacorte (Deflazacort) ; 15-MAR-2024 / Ongoing
#4) Dapagliflozin (Dapagliflozin) ; 17-MAY-2024 / Unknown
#5) Prednisone (Prednisone) ; 13-AUG-2024 / Ongoing
#6) Betametasone Dipropionato (Betamethasone dipropionate) ; 15-NOV-2024 / Ongoing

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

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Current Condition	Systemic lupus erythematosus (Systemic lupus erythematosus)
2008 to Ongoing	Current Condition	Chronic sinusitis (Chronic sinusitis)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER
Aspen
Dublin, IRELAND

26. REMARKS
World Wide #: GT-SAMIL-GLO2025GT004496
Study ID: 2303007
Center ID: 2303

24b. MFR CONTROL NO.
GLO2025GT004496

25b. NAME AND ADDRESS OF REPORTER
NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

24c. DATE RECEIVED BY MANUFACTURER
30-MAY-2025

24d. REPORT SOURCE
☒ STUDY ☒ LITERATURE ☒ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT
09-JUN-2025

25a. REPORT TYPE
☒ INITIAL ☐ FOLLOWUP:

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Aspen central recipient was on 03-JUN-2025.

GLO2025GT004496 is a Report from Study report received from an Other Health Professional via Novartis (GT-002147023-NVSC2025GT047764) concerning a 36-Years-old Female patient who experienced Leukopenia, Condition aggravated, Lymphocyte count decreased while patient was on Imuran (Azathioprine) for the treatment of Systemic lupus erythematosus, Leukopenia. Off label use was also noted.

The events Leukopenia, Condition aggravated and Off label use were assessed as serious Medically Significant.

The patient was enrolled in the study on an unknown date.

The patient has medical history of Systemic lupus erythematosus (unknown date - ongoing), Chronic sinusitis (2008 - ongoing), Hyperinsulinaemia (17-May-2024 - ongoing), BNT162b2 (24-Jun-2022 - 24-Jun-2022), Upper respiratory tract infection (unknown date - ongoing), COVID-19 vaccine (27-Mar-2021 - 27-Mar-2021), COVID-19 vaccine (01-Jun-2021 - 01-Jun-2021) and COVID-19 vaccine (09-Dec-2021 - 09-Dec-2021).

Concomitant medication included Hydroxychloroquine (23-Mar-2023 - unknown date), Vortioxetine (12-Dec-2023 - unknown date), Deflazacorte (15-Mar-2024 - ongoing), Dapagliflozin (17-May-2024 - unknown date), Prednisone (13-Aug-2024 - ongoing) and Betametasone Dipropionato (15-Nov-2024 - ongoing).

The patient-initiated administration of Imuran for the treatment of Systemic lupus erythematosus, Leukopenia on 17-Jan-2023. Last drug administration date is not reported.

Co-suspect medication included: VAY736 Vs placebo for the treatment of Systemic lupus erythematosus, Leukopenia from 13-AUG-2024 to unknown date.

The patient experienced Serious Imuran and leukopenia (Off label use) on 17-Jan-2023, Serious Leucopenia/ low WBC, (Leukopenia) on 06-Jan-2025, Serious Leucopenia/ low WBC (Condition aggravated) on 06-Jan-2025 and non-serious low lymphocyte absolute count (Lymphocyte count decreased) on unknown date.

On 13 Aug 2024, the subject received blinded study medication. On 23 Mar 2023, the subject started co-suspect medication azathioprine (Imuran) (manufacturer Laboratorio Aspen (Aspen labs)) for the treatment of systemic lupus erythematosus and leukopenia at an unknown dose (route: unknown) Batch/Lot Number: Unknown and from 17 Jan 2025 at an unknown dose (route: unknown) Batch/Lot Number: Unknown. On 06 Jan 2025, 1 year 09 months 15 days after the first dose of blinded study medication, the subject developed "leucopenia" (leukopenia). The subject was treated with azathioprine (Imuran). The action taken with blinded study medication was reported as no change after the subject experienced leukopenia. On 16 Jan 2025, the dose of azathioprine was reduced to 50 mg bid due to low WBC, low lymphocyte absolute count. On the same date, the subject received most recent dose of co-suspect medication azathioprine (Imuran)). On 17 Jan 2023, the subject again started co-suspect medication azathioprine. The outcome of the event leukopenia was reported as condition unchanged. The diagnosed event leukopenia was considered non-serious by the investigator. The causality of leukopenia was reported as not suspected with blinded study medication. The causality of leukopenia to any other medication or non-drug therapy was reported as suspected. The causality of leukopenia with co-suspect azathioprine (Imuran) was suspected. Follow up report received on 27 Mar 2025: Added brand name (Imuran) and manufacturer details (Laboratorio Aspen (Aspen labs)) of co-suspect azathioprine. Follow up report received on 28 May 2025: Added treatment medication (azathioprine (Imuran)). Changed action taken for co-suspect medication azathioprine (from treatment temporarily interrupted to dose reduced).

Action taken with Imuran is Dose reduced.
Action taken with VAY736 Vs placebo id Dose not changed.

Off label use was reported as event outcome Unknown.
Leukopenia was reported as event outcome Not Recovered/Not Resolved/Ongoing.
Condition aggravated was reported as event outcome Not Recovered/Not Resolved/Ongoing.
Lymphocyte count decreased was reported as event outcome Unknown.

Causality
Imuran
Event: Off label use
Reporter's causality: Not Assessable
Company's causality: Not Assessable
Seriousness: Serious
Outcome: Unknown

Causality
Imuran
Event: Leukopenia
Reporter's causality: Related

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Company's causality: Not Assessable
Seriousness: Serious
Outcome: Not Recovered/Not Resolved/Ongoing

Causality
Imuran
Event: Condition aggravated
Reporter's causality: Related
Company's causality: Not Assessable
Seriousness: Serious
Outcome: Not Recovered/Not Resolved/Ongoing

Causality
Imuran
Event: Lymphocyte count decreased
Reporter's causality: Related
Company's causality: Not Assessable
Seriousness: Non-serious
Outcome: Unknown

13. Relevant Tests

On an unknown date: low WBC, low lymphocyte absolute count.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) Imuran (Azathioprine) Unknown; Regimen #1	UNK; Unknown	Systemic lupus erythematosus (Systemic lupus erythematosus) leukopenia (Leukopenia)	23-MAR-2023 / 16-JAN-2025; 1 year 9 months 25 days
#1) Imuran (Azathioprine) Unknown; Regimen #2	UNK; Unknown	Systemic lupus erythematosus (Systemic lupus erythematosus) leukopenia (Leukopenia)	17-JAN-2023 / Unknown; Unknown
#1) Imuran (Azathioprine) Unknown; Regimen #3	50 milligram, bid; Unknown	Systemic lupus erythematosus (Systemic lupus erythematosus) leukopenia (Leukopenia)	16-JAN-2025 / Unknown; Unknown

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
17-MAY-2024 to Ongoing	Current Condition	Hyperinsulinemia (Hyperinsulinaemia);
24-JUN-2022 to 24-JUN-2022	Historical Drug	BNT162B2 (BNT162b2); Drug Indication: COVID-19 prophylaxis (COVID-19 prophylaxis)
Unknown to Ongoing	Current Condition	Upper respiratory infection (Upper respiratory tract infection);
27-MAR-2021 to 27-MAR-2021	Historical Drug	COVID-19 vaccination (COVID-19 vaccine); Drug Indication: COVID-19 prophylaxis (COVID-19 prophylaxis)
01-JUN-2021 to 01-JUN-2021	Historical Drug	COVID-19 vaccination (COVID-19 vaccine); Drug Indication: COVID-19 prophylaxis (COVID-19 prophylaxis)
09-DEC-2021 to 09-DEC-2021	Historical Drug	COVID-19 vaccination (COVID-19 vaccine); Drug Indication:

ADDITIONAL INFORMATION

23. OTHER RELEVANT HISTORY continued

From/To Dates	Type of History / Notes	Description
		COVID-19 prophylaxis (COVID-19 prophylaxis)