EU Risk Management Plan for

RIULVY 174 mg gastro-resistant hard capsules

and

RIULVY 348 mg gastro-resistant hard capsules

(tegomil fumarate)

RMP version to be assessed as part of this application:

RMP version number: 1.0

Data lock point for this RMP: 16 September 2024

Date of final sign-off: 11 April 2025

Rationale for submitting an updated RMP: Not applicable.

Summary of significant changes in this RMP: Not applicable.

Other RMP versions under evaluation: Not applicable.

Details of the currently approved RMP: Not applicable.

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List of Abbreviations

ATC	Anatomical Therapeutic Chemical classification
EEA	European Economic Area
EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
GVP	Good Pharmacovigilance Practices
INN	International Non-proprietary Name
PML	Progressive Multifocal Leukoencephalopathy
PSUR	Periodic Safety Update Report
QPPV	Qualified Person for Pharmacovigilance
RMP	Risk Management Plan
RRMS	Relapsing Remitting Multiple Sclerosis
SmPC	Summary of Product Characteristics

Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance (INN or common name)	Tegomil fumarate.
Pharmacotherapeutic group (ATC Code)	*Immunosuppressants, other immunosuppressants* (L04AX10).
Marketing Authorisation Applicant	Neuraxpharm Pharmaceuticals S.L.
Medicinal products to which this RMP refers	2.
Invented names in the European Economic Area (EEA)	RIULVY 174 mg gastro-resistant hard capsules. RIULVY 348 mg gastro-resistant hard capsules.
Marketing authorisation procedure	Centralised Procedure (H0006427).
Brief description of the product	*Chemical class:* Tegomil fumarate is a derived fumarate ester drug.
	Summary of mode of action: The mechanism by which tegomil fumarate exerts therapeutic effects in multiple sclerosis is not fully understood. Tegomil fumarate acts via the major active metabolite, monomethyl fumarate. Preclinical studies indicate that monomethyl fumarate pharmacodynamic responses appear to be primarily mediated through activation of the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) transcriptional pathway. Dimethyl fumarate has been shown to up regulate Nrf2-dependent antioxidant genes in patients (e.g. NAD(P)H dehydrogenase, quinone one; [NQO1]).
	Important information about its composition: None.
Hyperlink to the Product Information	Please refer to the product information text in module 1.3.1.
Indications in the EEA	*Current:* Treatment of adult and paediatric patients aged 13 years and older with Relapsing Remitting Multiple Sclerosis (RRMS).
	Proposed: Not applicable.

Dosage in the EEA	*Current:* Treatment should be initiated under supervision of a physician experienced in the treatment of multiple sclerosis. The starting dose is 174 mg twice a day. After 7 days, the dose should be increased to the recommended maintenance dose of 348 mg twice a day. Temporary dose reduction to 174 mg twice a day may reduce the occurrence of flushing and gastrointestinal adverse reactions. Within 1 month, the recommended maintenance dose of 348 mg twice a day should be resumed.
	Proposed: Not applicable.
Pharmaceutical forms and strengths	*Current:* RIULVY 174 mg gastro-resistant hard capsules: each capsule contains 174 mg tegomil fumarate (corresponding to 120 mg dimethyl fumarate). RIULVY 348 mg gastro-resistant hard capsules: each capsule contains 348 mg (corresponding to 240 mg dimethyl fumarate).
	Proposed: Not applicable.
Is/will the product be subject to additional monitoring in the EU?	No.

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable since this module is not required for hybrid type of application.

Part II: Module SII - Non-clinical part of the safety specification

Not applicable since this module is not required for hybrid type of application.

Part II: Module SIII - Clinical trial exposure

Not applicable since this module is not required for hybrid type of application.

Part II: Module SIV - Populations not studied in clinical trials

Not applicable since this module is not required for hybrid type of application.

Part II: Module SV - Post-authorisation experience

Not applicable since this module is not required for hybrid type of application.

Part II: Module SVI - Additional EU requirements for the safety specification

Not applicable since this module is not required for hybrid type of application.

Part II: Module SVII - Identified and potential risks

Not applicable since this module is not required for hybrid type of application.

Part II: Module SVIII - Summary of the safety concerns

This summary of safety concerns has been obtained from the European Public Assessment Report (EPAR) -RMP for Tecfidera® Biogen Netherlands B.V. published on 19 August 2024 (version 17.0) on the European Medicines Agency (EMA) website.

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Progressive Multifocal Leukoencephalopathy (PML).
Important potential risks	• Malignancies. • Effects on pregnancy outcome.
Missing information	• Long term efficacy and safety. • Safety profile in patients with moderate to severe renal impairment.

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection:

Specific adverse reaction follow-up questionnaires for risk of PML and Malignancies

The objective of this activity is to detect any new risk factors or a change in the current understanding of these risks.

Data collection forms at different time points post-event (up to 24 months) are used for case reports of PML, to aid further characterisation of the event and identification of potential risk factors. These data collection forms aim to collect detailed information relating to suspected PML events in a standardised fashion, to enable timely and robust collection of data, thereby optimising risk evaluation.

Data collection forms are also used to enable timely and robust collection of malignancies, thereby optimising risk evaluation.

Details of the proposed follow up questionnaires are presented in Annex 4 in pdf version of RMP.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities will be conducted.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

No planned or on-going post-authorisation efficacy studies have been imposed.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

The safety information in the proposed product information is aligned to the reference medicinal product.

V.1 Routine Risk Minimisation Measures

Not applicable.

V.2 Additional Risk Minimisation Measures

Not applicable.

V.3 Summary of Risk Minimisation Measures

Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for RIULVY 174 mg gastro-resistant hard capsules and RIULVY 348 mg gastro-resistant hard capsules (tegomil fumarate)

This is a summary of the Risk Management Plan (RMP) for RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules. The RMP details important risks of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules, how these risks can be minimised, and how more information will be obtained about RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' risks and uncertainties (missing information).

RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules should be used.

This summary of the RMP for RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' RMP.

I. The medicine and what it is used for

RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules are authorised for the treatment of adult and paediatric patients aged 13 years and older with Relapsing Remitting Multiple Sclerosis (RRMS) (see SmPC for the full indication). It contains tegomil fumarate as the active substance and it is given by oral route of administration.

Further information about the evaluation of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' benefits can be found in RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage <*Pre-authorisation RMP (this line should be only edited by EMA): link to the EPAR summary landing page. Post-authorisation RMP (this line should be edited by the Applicant/MAH):* link to product's EPAR summary landing page on the EMA webpage.>

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules, together with measures to minimise such risks and the proposed studies for learning more about RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules' risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;

- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute ***routine risk minimisation measures***.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including Periodic Safety Update Report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute ***routine pharmacovigilance activities***.

If important information that may affect the safe use of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Progressive Multifocal Leukoencephalopathy (PML).
Important potential risks	• Malignancies. • Effects on pregnancy outcome.
Missing information	• Long term efficacy and safety. • Safety profile in patients with moderate to severe renal impairment.

II.B Summary of important risks

The safety information in the proposed product information is aligned to the reference medicinal product.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for RIULVY 174 mg gastro-resistant hard capsules and RIULVY 248 mg gastro-resistant hard capsules.

Part VII: Annexes

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Annex 4 – Specific adverse drug reaction follow-up forms

Specific adverse reaction follow-up questionnaires for risk of PML and Malignancies

Adverse event follow-up forms will be distributed for potential/confirmed events of PML and malignancies (see Part III [Pharmacovigilance Plan] of the EU RMP for details).

The follow up forms for distribution are provided in this Annex below:

- Multiple Sclerosis Suspect Progressive Multifocal Leukoencephalopathy Data Collection Tool.
- Multiple Sclerosis Confirmed Progressive Multifocal Leukoencephalopathy Data Collection Tool for Months 3 and 6.
- Multiple Sclerosis Confirmed Progressive Multifocal Leukoencephalopathy Data Collection Tool for Months 12 and 24.
- Malignancies Data Collection Tool.

NEURAXPHARM®	Multiple Sclerosis Suspect Progressive Multifocal Leukoencephalopathy Data Collection Tool	

Neuraxpharm Unique case ID#:_____

I. Patient Information

Patient name:_____ _____DOB (DD/MMM/YYYY):_____
Gender:_____ Height:_____ BMI:_____

II. Primary neurologist:

Name:_____ Email:_____
Address:_____ Phone:_____
Fax:_____

III. Treating physician (if different from primary neurologist):

Name:_____ Email:_____
Address:_____ Phone:_____
Fax:_____

IV. Primary Suspect product

Select the product you believe to be the Primary Suspect Product:
☐ DMF Neuraxpharm ☐ Other, please specify _____

Is this patient receiving Tysabri at an extended interval dosing (e.g.>4weeks)?

☐ Yes ☐ No

Provide additional details on the dosing and frequency of the Primary Suspect Product, including information on the use of multiple regimens:

Start date (DD/MMM/YYYY)	Stop date (DD/MMM/YYYY)	Dose	Frequency of dosing	Number of Infusions (Tysabri)	Lot/batch#

In your assessment, is the suspected PML related to the Primary Suspect product?
☐ Yes ☐ No

Neuraxpharm Unique case ID#:_____

V. Secondary Suspect Product (if applicable)

Select the product you believe to be the Secondary Suspect Product:

☐ DMF Neuraxpharm ☐ Other, please specify____

Provide additional details on the dosing and frequency of the Secondary Suspect Product, including information on the use of multiple regimens:

Start date (DD/MMM/YYYY)	Stop date (DD/MMM/YYYY)	Dose	Frequency of dosing	Number of Infusions (Tysabri)	Lot/batch#

In your assessment, is the suspected PML related to the Secondary Suspect product?

☐ Yes ☐ No

Since discontinuation of Neuraxpharm suspect product, is the patient being treated with other MS therapy?

☐ Yes ☐ No

If yes, specifiy_____

VI. Multiple Sclerosis History

1) MS diagnosis date:_____(DD/MMM/YYYY)

2) Provide the MS therapies used prior to Primary Suspect Product:

Medication	Dose	Route	Frequency	Start date (DD/MMM/YYYY)	Stop date (DD/MMM/YYYY)

3) Has the patient received prior immunosuppressant therapy, radiation therapy, antineoplastic or immunomodulatory therapy for a condition other than MS?

   ☐ Yes ☐ No

   If yes, list the drug and include the indication:_____

4) Is this patient immunocompromised from any other cause?

☐ Yes ☐ No

If yes, provide diagnosis:_____

5) Has the patient ever been or currently is enrolled in a Neuraxpharm Clinical Trial?

☐ Yes ☐ No

If yes, specify the trial number/name: Provide the patient's study ID:

VII. PML Suspicion

1) Indicate the reason(s) the patient is being evaluated for PML:

- Patient presented with clinical signs and symptoms? ☐ Yes ☐ No (Asymptomatic)

- Patient presented with radiological findings consistent with PML? ☐ Yes ☐ No

- Reason for MRI: (Check all that apply)

☐ MS standard of care ☐ PML surveillance ☐ Patient request ☐ Other:_____

2) List earliest presenting signs and symptoms that led to the evaluation for possible PML (even if identified in retrospect):

Symptoms	Date (DD/MMM/YYYY)

3) Provide copies of MRI reports. If not possible, provide detailed MRI results including lesion characteristics and location.

a. MRI at the time of the suspected PML diagnosis:

Date of MRI:_____(DD/MMM/YYYY)

Detailed description:

b. MRI prior to suspected PML diagnosis

Date of MRI:_____(DD/MMM/YYYY)

Detailed description:

(*Provide a CD of MRI DICOM images)*[1,2]

Neuraxpharm Unique case ID#:_____

4) Provide copies of CSF JCV DNA reports, if not possible provide details of lumbar puncture (LP) and CFS sample collection (provide all tests, even if multiple assays performed on a single puncture):

	Test 1	Test 2	Test 3
Date of LP (DD/MMM/YYYY)			
LP performed Pre-PLEX (if applicable)	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
CSF JCV DNA Result	☐Positive ☐Negative ☐Inconclusive	☐Positive ☐Negative ☐Inconclusive	☐Positive ☐Negative ☐Inconclusive
Quantitative (copies/mL)			
Laboratory name and Limit of Detection			

5) Has a CSF analysis been performed? (cell count, protein, glucose, albumin, various viral PCR testing, etc.)

☐ Yes ☐ No Date of test: _____(DD/MMM/YYYY)

Provide cell count:_____

6) Provide details of all serum anti-JCV antibody testing:

(Provide copies of the anti-JCV antibody test results)

Date of test: (DD/MMM/YYYY)	Result of test: (positive, negative, pending)	Index value available:	Index value:	Laboratory name:
	☐Positive ☐Negative ☐Pending	☐Yes ☐No		
	☐Positive ☐Negative ☐Pending	☐Yes ☐No		
	☐Positive ☐Negative ☐Pending	☐Yes ☐No		
	☐Positive ☐Negative ☐Pending	☐Yes ☐No		

7) Was a brain biopsy performed? ☐ Yes ☐ No

Neuraxpharm Unique case ID#:_____

Date of test: _____(DD/MMM/YYYY)

(If yes, provide a copy of the brain biopsy report.)

8) HIV status: ☐ Positive ☐ Negative ☐ unknown

Date of test:_____(DD/MMM/YYYY)

9) Was patient lymphopenic within 12 months prior to PML suspicion? ☐ Yes ☐ No

Date (DD/MMM/YYYY)	WBC	Lymphocyte (%)	Absolute Lymphocyte Count	Lymphocyte subset analysis: (CD4, CD8, CD4/CD8 ratio, etc.)	
					Not performed ☐
					Not performed ☐
					Not performed ☐
					Not performed ☐

VIII. Current treatment

1) Has the patient received steroids within the past 3 months? ☐ Yes ☐ No

Drug	Dose	Route	Frequency	Start date (DD/MMM/YYYY)	Stop date (DD/MMM/YYYY)	Reason for steroids

2) PML Treatment: (check all that apply)

Medication	Dose	Route	Frequency	Start date (DD/MMM/YYYY)	Start date (DD/MMM/YYYY)
☐Mefloquine					
☐Cidofovir					
☐Mirtazapine					
☐Other					
☐Other					

3) PLEX/IA:

Plasma exchange(PLEX): ☐Yes ☐No Inmunoadsorption (IA): ☐Yes ☐No

Neuraxpharm Unique case ID#:_____

Session	Date (DD/MMM/YYYY)	Volume
1		
2		
3		
4		
5		

IX. Patient's location

Patients current location: (check appropriate box)

☐ Hospital ☐Home ☐Nursing home
☐Intensive care Unit ☐ Hospice ☐ Rehabilitation facility ☐N/A (Patient is deceased)

If patient is deceased, provide the following information:

Date of death (DD/MMM/YYYY):_____

Reported cause of death:_____

Was an autopsy performed? ☐Yes ☐No

(If yes, provide anonymized copy of the autopsy report)

In your assessment, was the patient's death related to the Primary Suspect Product?

☐Yes ☐No

If applicable, in your assessment, was the patient´s death related to Secondary Suspect product?

☐Yes ☐No

X. Functional scores

- **Provide the patient's functional status scores on Primary Suspect Product prior to PML:**

EDSS: Date: (DD/MMM/YYYY)

Karnofsky score: Date: (DD/MMM/YYYY)

Modified ranking score: Date: (DD/MMM/YYYY)

- **At the time of PML suspicion:**

EDSS: Date: (DD/MMM/YYYY)

Neuraxpharm Unique case ID#:_____

Karnofsky score: Date: (DD/MMM/YYYY)

Modified ranking score: Date: (DD/MMM/YYYY)

Modified Rankin Score	
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

Karnofsky Performance Status Definitions/Criteria		
Able to carry on normal activity and to work; no special care needed	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not.
	20	Very sick; hospital admission necessary; active supportive treatment.
	10	Moribund; fatal processes progressing rapidly
	0	Dead

XI. Rule Out PML

1) Based on your evaluation, was PML ruled out? ☐Yes ☐No ☐ Still under investigation

Neuraxpharm Unique case ID#:_____

2) If PML was ruled out, provide the final diagnosis (if available):

3) Was the final diagnosis related to the Primary Suspect Product? ☐Yes ☐No

a) Was the final diagnosis related to the Secondary Suspect Product? (if applicable)

☐Yes ☐No

b) Provide the outcome for the final diagnosis:

☐Recovered ☐Recovered with sequelae ☐Not recovered ☐Unknown ☐Fatal

4) What MS therapy is planned or is the patient currently on?

Print name/title:_____

Signature: _____ Date: _____

1 Additionally include copies of the radiology reports for 6 months prior to PML suspicion.

Neuraxpharm Unique case ID#:_____

I. Patient Information

Patient initials:_____

DOB (DD/MMM/YYYY):_____

II. Is the Patient alive? ☐Yes ☐No

If yes, provide the patient´s current location (check appropriate box):

☐Hospital ☐Intensive care Unit ☐Nursing home
☐Home ☐Rehabilitation facility ☐Hospice

If no, provide the following information:

Date of death (DD/MMM/YYYY):_____

Reported cause of death:_____

Was an autopsy performed? ☐Yes ☐No

(If yes, provide anonymized copy of the autopsy report)

III. In your assessment, was the patient´s death related to one of the following products?

☐Yes ☐No
☐ DMF Neuraxpharm ☐ Other, please specify_____

IV. Functional Status -Post PML diagnosis: (please see table below)

EDSS (most recent): _____ Date (DD/MMM/YYYY)_____

Karnofsky (most recent):_____ Date (DD/MMM/YYYY)_____

Modified Rankin Score: _____ Date (DD/MMM/YYYY)_____

Neuraxpharm Unique case ID#:_____

Modified Rankin Score	
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

Karnofsky Performance Status Definitions/Criteria		
Able to carry on normal activity and to work; no special care needed	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not.
	20	Very sick; hospital admission necessary; active supportive treatment.
	10	Moribund; fatal processes progressing rapidly
	0	Dead

V. Test results <u>post PML diagnosis</u>: *(provide a copy of tests results)*

Provide copies of MRI reports, including most recent MRI report, and a CD with the MRI images, if not already provided. 1,2 If not possible, provide detailed MRI results including lesion characteristics and location:

Date of MRI: _____(dd/mmm/yyyy)

Detailed description:_____

Provide copies of CSF JCV DNA reports. If not possible, provide details of lumbar puncture (LP) and CSF sample collection (provide all tests, even if multiple assays are performed on a single puncture).

	Test 1	Test 2	Test 3
Date of LP (DD/MMM/YYYY)			
LP performed Pre-PLEX (if applicable)	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
CSF JCV DNA Result	☐Positive ☐Negative ☐Inconclusive	☐Positive ☐Negative ☐Inconclusive	☐Positive ☐Negative ☐Inconclusive
Quantitative (copies/mL)			
Laboratory name and Limit of Detection			

Date (DD/MMM/YYYY)	WBC	Lymphocyte (%)	Absolute Lymphocyte Count	Lymphocyte subset analysis: (CD4, CD8, CD4/CD8 ratio, etc.)	
					Not performed ☐
					Not performed ☐
					Not performed ☐
					Not performed ☐

VI. Is your patient currently on another therapy for Multiple Sclerosis? ☐Yes ☐No

If yes, what is the therapy?

Include start date and dosing regimen:

Provide patient's EDSS at time of new DMT onset:

VII. PML treatment:

Plasma Exchange (PLEX): ☐Yes ☐No Inmunoadsorption (IA): ☐Yes ☐No

Session	Date (DD/MMM/YYYY)	Volume
1		
2		
3		
4		
5		

Neuraxpharm Unique case ID#:_____

Medication	Dose	Route	Frequency	Start date (DD/MMM/YYYY)	Start date (DD/MMM/YYYY)
☐Mefloquine					
☐Cidofovir					
☐Mirtazapine					
☐Other					
☐Other					

VIII. PML Outcome:

a. What is the outcome of the patient's PML?

☐Recovered ☐Recovered with sequelae ☐Not recovered ☐Unknown ☐Fatal

Provide the date of the assessed outcome: (DD/MMM/YYYY)

IX. Was the patient been diagnosed with PML-IRIS?

☐Yes; onset date (DD/MMM/YYYY):_____ ☐No

a. Any new or worsening symptoms? ☐Yes ☐No

   If yes, specify the symptom: _____

   Onset date of IRIS symptoms:_____

b. Any contrast enhancements or MRI at time of PML-IRIS? ☐Yes ☐No

c. Any mass effect or edema on MRI? ☐Yes ☐No

X. PML-IRIS treatment:

a. Did the patient receive corticosteroids pre-PML-IRIS onset? ☐Yes ☐No

b. Did the patient receive corticosteroids post-PML-IRIS onset? ☐Yes ☐No

Specify all treatments the patient has received for PML-IRIS: (*including corticosteroids regimens*):

Medication	Dose	Route	Frequency	Start Date (DD/MMM/YYYY)	Stop Date (DD/MMM/YYYY)	Specify if treatment is pre- or post-PML-IRIS

Neuraxpharm Unique case ID#:_____

XI. PML-IRIS Outcome:

a. What is the outcome of the patient's PML-IRIS?

☐Recovered ☐Recovered with sequelae ☐Not recovered ☐Unknown ☐Fatal

Provide the date of the assessed outcome: (DD/MMM/YYYY)

b. What is the causality of the PML-IRIS to the following products?

☐Related ☐Non-related ☐Unknown

☐ DMF Neuraxpharm ☐ Other, please specify_____

Print name/title:_____

Signature: _____ Date: _____

1 Additionally include copies of the radiology reports for 6 months prior to PML suspicion.

Neuraxpharm Unique case ID#:_____

I. Patient Information

Patient initials:_____

DOB (DD/MMM/YYYY):_____

II. Is the Patient alive? ☐Yes ☐No

If yes, provide the patient´s current location (check appropriate box):

☐Hospital ☐Intensive care Unit ☐Nursing home
☐Home ☐Rehabilitation facility ☐Hospice

If no, provide the following information:

Date of death (DD/MMM/YYYY):_____

Reported cause of death:_____

Was an autopsy performed? ☐Yes ☐No

(If yes, provide anonymized copy of the autopsy report)

III. In your assessment, was the patient´s death related to Dimethyl Fumarate Neuraxpharm?

☐Yes ☐No

IV. Functional Status post-PML Diagnosis: (please see tables below)

EDSS (most recent): _____ Date (DD/MMM/YYYY)_____

Karnofsky (most recent):_____ Date (DD/MMM/YYYY)_____

Modified Rankin Score: _____ Date (DD/MMM/YYYY)_____

Modified Rankin Score	
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

Neuraxpharm Unique case ID#:_____

Karnofsky Performance Status Definitions/Criteria

Able to carry on normal activity and to work; no special care needed	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most personal needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not.
	20	Very sick; hospital admission necessary; active supportive treatment.
	10	Moribund; fatal processes progressing rapidly
	0	Dead

V. Test results <u>post PML diagnosis</u>: *(provide a copy of test results)*

Provide copies of MRI reports, including most recent MRI report, and a CD with the MRI images, if not already provided. [1,2] If not possible, provide detailed MRI results including lesion characteristics and location:

Date of MRI: _____(dd/mmm/yyyy)

Detailed description:_____

Date (DD/MMM/YYYY)	WBC	Lymphocyte (%)	Absolute Lymphocyte Count	Lymphocyte subset analysis: (CD4, CD8, CD4/CD8 ratio, etc.)	
					Not performed ☐
					Not performed ☐
					Not performed ☐
					Not performed ☐

VI. Is your patient currently on another therapy for Multiple Sclerosis? ☐Yes ☐No

If yes, what is the therapy?

Include start date and dosing regimen:

Provide patient's EDSS at time of new DMT onset:

Neuraxpharm Unique case ID#:_____

VII. PML Outcome:

a. What is the outcome of the patient's PML?

☐Recovered ☐Recovered with sequelae ☐Not recovered ☐Unknown ☐Fatal

Provide the date of the assessed outcome: (DD/MMM/YYYY)

VIII. PML-IRIS Outcome:

a. What is the outcome of the patient's PML-IRIS?

☐Recovered ☐Recovered with sequelae ☐Not recovered ☐Unknown ☐Fatal

Provide the date of the assessed outcome: (DD/MMM/YYYY)

b. What is the causality of the PML-IRIS to Dimethly Fumarate Neuraxpharm?

☐Related ☐Non-related ☐Unknown

Print name/title:_____

Signature: _____ Date: _____

1 Additionally include copies of the radiology reports for 6 months prior to PML suspicion.

NEURAXPHARM®	Malignancies data collection tool	

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Dimethyl Fumarate Neuraxpharm General Malignancy

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm general malignancy reports, please ask the follow-up questions below.

1. Please specify the patient' s type, stage, and grade of cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). Lf lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please indicate if the patient has a history of cancer.
5. Please provide any medical history risk factors the patient had for a general malignancy (e.g., family history of malignancies, radiation exposure, smoking, diabetes mellitus, etc.).
6. Please list all medications the patient has taken in the past 2 years.
7. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
8. Please provide all signs and symptoms related to the malignancy.
9. lf a tissue biopsy was performed, please provide the findings and the date it was performed.
10. Please provide results from all pathology or cytology studies.
11. Please provide results from all imaging studies.
12. Please provide results from physical examination.
13. lf the patient was hospitalized, please provide discharge report.
14. Please provide any treatments the patient received for the event.
15. Please provide outcome for event and date of resolution if applicable. lf the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Breast Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm breast cancer reports, please ask the follow up questions below.

1. Please specify the patient's type, stage, and grade of breast cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please provide any medical history risk factors the patient had for breast cancer (e.g., family history, hormone replacement therapy, breast cancer (BRCA) gene mutations, history of proliferative benign breast disease or breast carcinoma, etc.).
4. Please provide any social risk factors for breast cancer (e.g., smoking, alcohol consumption).
5. Please list the medications the patient has taken in the past 2 years.
6. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
7. If a tissue biopsy was performed, please provide the findings.
8. Please provide results from all imaging studies such as mammogram, ultrasound or magnetic resonance imaging (MRI).
9. Was the patient tested for estrogen receptor, progesterone receptor, or human epidermal growth factor receptor 2 (HER-2/neu) protein? lf so, please provide test results.
10. Please provide results from the physical exam.
11. If the patient was hospitalized, please provide discharge report.
12. Please provide any treatments the patient received for the event.
13. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Cervical Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm cervical cancer reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade of cervical cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please indicate if the patient has a history of cancer.
5. Please provide any medical history risk factors the patient had for cervical cancer (e .g., smoking, family history of cervical cancer, human papillomavirus (HPV) infection, or oral contraceptive use > 5 years, etc.).
6. Please indicate the dates if the patient received either the Cervarix or Gardasil HPV vaccination.
7. Please list the medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins, and herbs.
9. Please provide results and dates from all pathology or cytology studies.
10. Please provide results from all imaging studies.
11. Please provide results from physical examination.
12. If the patient was hospitalized, please provide discharge report.
13. Please provide any treatments the patient received for the event.
14. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Colon Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm colon cancer reports, please ask the follow up questions be low.

1. Please specify the patient's type, stage, and grade of colon cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please provide any medical history risk factors the patient had for colon cancer (e.g., family or personal history of colorectal cancer or adenomatous polyps, obesity, smoking, alcohol consumption, etc.).
5. Please list all medications the patient has taken in the past 2 years.
6. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
7. If a tissue biopsy was performed, please provide the findings and the date it was performed.
8. If tumor markers were analyzed, please provide the name of the marker(s) which were found and the date of the analysis.
9. Please provide results and dates from all pathology or cytology studies.
10. Please provide results from all imaging studies.
11. Please provide results from physical examination.
12. If the patient was hospitalized, please provide discharge report.
13. Please provide any treatments the patient received for the event.
14. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Endometrial Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm endometrial cancer reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade of endometrial cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please provide any medical history risk factors the patient had for endometria! cancer (e.g., personal or family history, diabetes, early menarche, late menopause, polycystic ovary syndrome, estrogen therapy, tamoxifen use, nulliparity, etc.).
4. Please list the medications the patient has taken in the past 2 years.
5. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
6. Please provide results from all pathology or cytology studies.
7. Please provide results from all imaging studies.
8. Please provide results from physical examination.
9. lf the patient was hospitalized, please provide discharge report.
10. Please provide any treatments the patient received for the event.
11. Please provide outcome for event and date of resolution if applicable. lf the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Lymphoma

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm lymphoma reports, please ask the follow up questions below.

1. Please specify the patient' s type and stage of lymphoma.
2. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
3. Please indicate if the patient has a history of cancer.
4. Please provide any medical history risk factors the patient had for lymphoma (e.g., family history, chromosomal abnormalities, transplantation, rheumatoid arthritis, etc.).
5. Please list the medications the patient has taken in the past 2 years.
6. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
7. lf a tissue biopsy was performed, please provide the findings.
8. Please provide results from all imaging studies.
9. Please provide results from physical examination.
10. Please provide results from all laboratory tests. Please include baseline values as well as reference ranges for any and all lab tests.
11. lf the patient was hospitalized, please provide discharge report.
12. Please provide any treatments the patient received for the event.
13. Please provide outcome for event and date of resolution if applicable. lf the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Melanoma

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm melanoma reports, please ask the follow up questions below.

1. Please specify the patient' s type, stage, and grade of melanoma.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please indicate if the patient has a history of cancer.
5. Please provide any medical history risk factors the patient had for melanoma (e.g., ultraviolet light exposure, family history of melanoma, pigmented lesions, etc.).
6. Please indicate if the patient has a family history of melanoma skin cancer and describe the family history.
7. Please list all medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
9. If a tissue biopsy was performed, please provide the findings and the date it was performed.
10. If tumor markers were analyzed, please provide the name of the marker(s) which were found and the date of the analysis.
11. Please provide results from all imaging studies.
12. Please provide results from physical examination.
13. If the patient was hospitalized, please provide discharge report.
14. Please provide any treatments the patient received for the event.
15. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Non-Melanoma

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm nonmelanoma reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade on non-melanoma skin cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please indicate if the patient was exposed to ultraviolet (UV) light, arsenic, or ionizing radiation.
5. Please provide any medical history risk factors the patient had for non-melanoma (e.g., family history or non-melanoma skin cancer, immunosuppression, genetic factors, etc.).
6. Please indicate if the patient has a family history of non-melanoma skin cancer and describe the family history.
7. Please list the medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
9. If a tissue biopsy was performed, please provide the findings and the date it was performed.
10. If tumor markers were analyzed, please provide the name of the marker(s) which were found and the date of the analysis.
11. Please provide results from all imaging studies.
12. Please provide results from physical examination.
13. If the patient was hospitalized, please provide discharge report.
14. Please provide any treatments the patient received for the event.
15. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Non-Small Cell Lung Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm non-small cell lung cancer reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade of non-small cell lung cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient was exposed to tobacco smoke, how many packs per year they smoke, if they currently smoke, if they are exposed to second-hand smoke, or if they have a remote history of smoking.
4. Please indicate if the patient had occupation or environmental exposure to hazardous chemicals (e.g., arsenic, chromium, asbestos, haloethers, radon gas, nickel, polycyclic aromatic hydrocarbons, etc.).
5. Please indicate if the patient has any other lung diseases, such as chronic obstructive pulmonary disease (COPD), lung fibrosis, tuberculosis, etc.
6. Please indicate if the patient has a family history of lung cancer and describe the family history.
7. Please list the medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
9. If a tissue biopsy was performed, please provide the findings and the date it was performed.
10. If tumor markers were analyzed, please provide the name of the marker(s) which were found and the date of the analysis.
11. Please provide results from all imaging studies.
12. Please provide results from physical examination.
13. Please provide the patient's pulmonary function test results and the date they were performed.
14. If the patient was hospitalized, please provide discharge report.
15. Please provide any treatments the patient received for the event.
16. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Prostate Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm prostate cancer reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade of prostate cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (date of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient has had any recent infections (bacterial, fungal, spirochetes, etc.).
4. Please indicate if the patient has a history of cancer.
5. Please indicate if the patient has a history of right or left sided heart failure.
6. Please provide any medical history risk factors the patient had for prostate cancer (e.g., family history, breast cancer (BRCA) 1 or BRCA 2 gene mutations, high testosterone levels, high insulin-like growth factor 1 levels, high intake of calcium, high fat diet, etc.).
7. Please list the medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
9. If a tissue biopsy was performed, please provide the findings.
10. Please provide results from all imaging studies.
11. Please provide results from physical examination.
12. Please provide the patient's prostate specific antigen (PSA) level and the date it was taken. Please include baseline values as well as reference ranges for any and all lab tests.
13. If the patient was hospitalized, please provide discharge report.
14. Please provide any treatments the patient received for the event.
15. Please provide outcome for event and date of resolution if applicable. If the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Renal Cell Carcinoma

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm renal cell carcinoma reports, please ask the follow-up questions below.

1. Please provide any medical history risk factors the patient had for renal cell carcinoma (e.g., family history, polycystic kidney disease, chronic hemodialysis, anemia, tuberous sclerosis, erythrocytosis, obesity, hypertension, etc.).
2. Please provide any available information on the histological type of cancer (e.g., clear cell vs papillary).
3. Please list the medications the patient has taken in the past 2 years.
4. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
5. Please provide the clinical signs and symptoms of the patient and the date at which each sign or symptom began.
6. Please provide the below laboratory results for the patient. Include reference ranges, baseline levels and levels for the treatment and management of the event.
    a. Liver function tests
    b. Renal function tests
    c. Coagulation profile
    d. Complete blood count with differentia!
    e. Creatinine Clearance (CrCl)
    f. Any other tests related to the diagnosis or management of renal cell carcinoma
7. Please provide results from urinalysis or state that it was not performed.
8. lf a tissue biopsy was performed, please provide the findings.
9. Please provide results from all imaging studies.
10. Please provide results from the physical exam.
11. lf the patient was hospitalized, please provide discharge report.
12. Please provide any treatments the patient received for the event.
13. Please provide outcome for event and <late of resolution if applicable. lf the patient recovered with sequelae, please describe the sequelae.

Dimethyl Fumarate Neuraxpharm Small Cell Lung Cancer

To provide consistency in our due diligence of Dimethyl Fumarate Neuraxpharm small cell lung cancer reports, please ask the follow-up questions below.

1. Please specify the patient's type, stage, and grade of small cell lung cancer.
2. Did the patient develop lymphopenia while on Dimethyl Fumarate Neuraxpharm? Please provide any available lymphocyte data (dlate of lab test, absolute lymphocyte count). If lymphocyte subset data (CD4, CD8) was checked, please provide. Please include baseline values as well as reference ranges for any and all lab tests.
3. Please indicate if the patient was exposed to tobacco smoke, how many packs per year they smoke, if they currently smoke, if they are exposed to second-hand smoke, or if they have a remote history of smoking.
4. Please indicate if the patient had occupation or environmental exposure to hazardous chemicals (e.g., arsenic, chromium, asbestos, haloethers, radon gas, nickel, polycyclic aromatic hydrocarbons, etc.).
5. Please indicate if the patient has any other lung diseases, such as chronic obstructive pulmonary disease (COPD), lung fibrosis, tuberculosis, etc.
6. Please indicate if the patient has a family history of lung cancer and describe the family history.
7. Please list the medications the patient has taken in the past 2 years.
8. Please provide any concomitant medications the patient is taking including prescription medications, over the counter (OTC), dietary supplements, vitamins and herbs.
9. If a tissue biopsy was performed, please provide the findings and the date it was performed.
10. If sputum cytology was performed, please provide the findings and the date it was performed.
11. If tumor markers were analyzed, please provide the name of the marker(s) which were found and the date of the analysis.
12. Please provide results from all imaging studies.
13. Please provide results from physical examination.
14. Please provide the patient's pulmonary function test results and the date they were performed. Please include baseline values as well as reference ranges for any and all results.
15. If the patient was hospitalized, please provide discharge report.
16. Please provide any treatments the patient received for the event.
17. Please provide outcome for event and date of resolution if applicable. If the event recovered with sequelae, please describe the sequelae.

Annex 6 – Details of proposed additional risk minimisation activities (if applicable)

Not applicable.