Annex 4 - Specific adverse drug reaction follow-up forms

This annex contains the specific adverse event targeted follow-up checklists used to collect additional data for the following Gilenya RMP risks:

Targeted follow-up checklists:

Identified risk: Bradyarrhythmia (including conductiondefects and bradycardia complicated by hypotension) occurring post first dose

Gilenya Cardiac rate and rhythm disorders checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed for first dose events and/or other events.

Event description:

Did the patient experience any symptoms? ☐ No ☐ Yes *(please specify)*

Did the patient receive treatment for the event? ☐ No ☐ Yes *(please specify)*

Were any of the following diagnostic tests performed? Check all that apply and please specify which test(s), dates and results

☐ ECG (*please include baseline*) ☐ Echocardiogram

☐ Holter monitor (*please include baseline*) ☐ Coronary angiography

☐ Blood tests (*e.g. electrolytes*) ☐ Electrophysiology study (EPS)

☐ Stress test ☐ Others (*please specify*)

☐ Cardiac biomarkers (specify e.g., creatinine kinase-MB, troponin)

☐ None of the above

Patient history:

Did the patient have a history of any of the following prior to the start of the suspect drug? **Check all that apply**

☐ ECG abnormalities *(please specify)* ☐ Syncope

☐ Valvular disease *(please specify)* ☐ Symptomatic bradycardia

☐ Pacemaker (specify if temporary or permanent)

☐ Cardiovascular disease (e.g. angina, CAD, MI, CHF)

☐ Wolff-Parkinson-White syndrome (*please specify*)

☐ Other (e.g. COPD, sleep apnea, hyperthyroidism) (*please specify)*

☐ Congenital heart disease ☐ None of the above

Was the patient taking any of the following drugs? **Check all that apply**

☐ Antipsychotics/Antidepressants ☐ Theophylline

☐ Beta blockers ☐ Drugs of abuse (*e.g. cocaine*)

☐ Cholinomimetics *(e.g. metoclopramide)* ☐ Others (*please specify*)

☐ Antiarrhythmics (e.g. quinidine, digoxin, beta-blockers, calcium channel blockers)

☐ Anticonvulsants (e.g. phenytoin, gabapentin, topiramate)

☐ Calcium channel blockers (dihydropyridine or non-)

☐ None of the above

First dose observation (FDO) period: Please provide details of events occurring during/post FDO.

- First dose of Gilenya: Date: ____/____/____Time: _____
- Heart rate at baseline: Date: ____/____/____Time: _____Rate: _____ bpm
- The minimum heart rate measured during the event: _____ bpm
- The time interval between the first dose of Gilenya (*fingolimod*) and the minimum heart rate: _____ minutes / hours / days / weeks (*please specify units*)
- ECGs performed at time of event? If yes, please provide details on any abnormalities noted other than bradycardia.
- Did the patient receive any treatment for the event?

☐ Yes – pharmacological (*e.g. atropine, please specify*)

☐ Yes – non-pharmacological (*e.g. IV fluids, please specify*)

☐ No

Vital signs during observation period (*hourly heart rate and BP*):

Identified risk: Liver transaminase elevation

Liver injury checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Event Description:

1. Diagnosis and date of diagnosis_____
2. Did the patient present with any of the following signs or symptoms? **Check all that apply:**

☐ Jaundice	☐ Ascites	☐ Asterixis (flapping tremor)
☐ Dark urine	☐ Fever	☐ Altered mental status
☐ Pale stool	☐ Fatigue	☐ Abdominal pain (specify location)
☐ Pruritus	☐ Bleeding (specify location)	☐ Anorexia
☐ Nausea	☐ Spider angiomata	☐ Variceal Bleeding
☐ Caput medusa	☐ Peripheral edema	☐ Fetor hepaticus
☐ Gynecomastia	☐ Muscle wasting	☐ Other (specify)
☐ None		

3. Were any of the following diagnostic tests performed?

►If yes, please specify the dates and results including reference range and pre- and post-treatment values:

- ☐ Liver function tests
- ☐ Serology & PCR testings for Hepatitis A, B, C &/or E virus
- ☐ Autoantibody tests
- ☐ Abdominal or hepatobiliary ultrasound (with or without Doppler's)
- ☐ Abdominal CT scan
- ☐ Liver biopsy
- ☐ Liver transplant (planned or completed)
- ☐ Other (specify)
- ☐ None

4. Does the patient have a history of any of the following prior to the start of the suspect drug? Check all that apply and include date(s) of onset as well as status (i.e. active/inactive) and details:

☐ Previously elevated liver enzymes ☐ Tattoos

☐ Hepatitis ☐ Transfusion or blood product administration
☐ Other hepatobiliary disease or dysfunction ☐ Gilbert's disease
☐ Autoimmune disease (specify type) ☐ Alcohol intake (quantify if possible)
☐ Active or chronic pancreatitis ☐ Drug abuse
☐ Diabetes mellitus (Type I or II) ☐ Foreign travel
☐ Non-alcoholic steatohepatitis ☐ Active gall bladder disease
☐ Cirrhosis ☐ Portal hypertension
☐ Ascites ☐ Variceal bleeding/esophageal varices
☐ Spider angiomata ☐ Thrombocytopenia
☐ None ☐ Other (specify)

5. Has the patient recently (i.e. within the past 6 months) taken any of the following? **Check all that apply:**

☐ Sulfonamides ☐ Furosemide ☐ ACE Inhibitors
☐ Valproic acid ☐ NSAIDS (e.g. ibuprofen) ☐ Estrogens (oral contraceptives)
☐ Metronidazole ☐ Acetaminophen/Paracetamol ☐ Amiodarone
☐ COX II inhibitors (e.g.celecoxib) ☐ Tetracycline ☐ Steroids
☐ Thiazide diuretics ☐ 6-Mercaptopurine ☐ Statins
☐ Nicotinic acid ☐ Methotrexate ☐ Other (specify)
☐ None

Identified risk: Macular edema

S1P Modulator Macular edema checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Relevant medical history (concurrent and pre-existing conditions)

(Please specify medical condition and date of onset)

☐ Eye diseases (e.g., uveitis, optic neuritis) ▶If yes (specify)

☐ Intraocular surgery▶If yes (provide type and date of surgery)

☐ Diabetes mellitus ▶If yes, provide:

- Date of diagnosis
- Was there evidence of retinopathy prior to starting the drug?☐ Yes, grade _☐ No

☐ Other (specify)

☐ None

Has the patient recently (i.e. within the past 6 months) taken any other medications?

☐ Yes (specify) ☐ No

Event description:

1. Date of diagnosis: ____/____/____
2. Was macular edema diagnosed in☐ Left eye☐ Right eye☐ Both eyes
3. Did the patient experience any symptoms due to the macular edema? ☐ Yes (list the symptoms) ☐ No
4. Were any of the following diagnostic tests performed? ▶If yes, please specify the dates and results at baseline (i.e. pre-Gilenya®) and at the time of the event

☐ Fundoscopy

☐ Optical Coherence Tomography (OCT)

☐ Fluorescein angiography (FA)

☐ Visual acuity

☐ Other: _____

Course of the event after diagnosis:

5. Details of any treatment prescribed for the macular edema:

Right eye☐ Photocoagulation / Laser☐ Intravitreal steroid injection☐ Surgery

☐ Other (specify)☐ None

Left eye☐ Photocoagulation / Laser☐ Intravitreal steroid injection☐ Surgery

☐ Other (specify)☐ None

6. Current status of the macular edema

☐ Resolved☐ Improving☐ Unchanged☐ Deteriorated

☐ Results of tests performed (e.g., fundoscopy, Optical coherence tomography (OCT), FA, specify the dates and results)

7. Current status of vision impairment related to macular edema (if any)?

☐ Resolved☐ Improving☐ Unchanged☐ Deteriorated

☐ Visual acuity (specify the dates and results)

Important Identified Risk: Opportunistic infections including PML, VZV, herpes viral infections other than VZV, fungal infection

Suspected Progressive Multifocal Leukoencephalopathy checklist

Did the patient present with any of the following signs or symptoms? Check all that apply.
☐ Hemiparesis☐ Cognitive impairment☐ Weakness☐ Headaches
☐ Hemianopia☐ Personality changes☐ Aphasia☐ None of the above
☐ Brainstem deficits ☐ Dysarthria☐ Visual impairment☐ Others (*please specify*)
☐ Clumsiness/ Cerebellar deficits☐ Sensory deficits☐ Fever_____

Was brain MRI/MRA performed? ☐ **Yes** *(provide report and/or summarize below)* ☐ **No** ☐ **Unknown**

Results:_____
_____
_____
_____

CSF JCV analysis ☐ **Yes** *(provide results below)* ☐ **No** ☐ **Unknown**

Type of test (PCR, JCV antibody)	Test date	Result

Please include results of other relevant tests

Type of test	Test date	Result
JCV (serum or urine)		
Anti JCV antibody index		
Absolute lymphocyte count		
WBC – including lymphocyte subsets (e.g., CD4, CD8)		
Brain biopsy		
Other		

Patient History:

Does the patient have a history of any immunosuppressive disorders prior to the start of the suspect drug (eg, HIV infection; malignancy, e.g., leukemia, lymphoma, myeloproliferative diseases; sarcoidosis; other disturbances of the immune system, e.g., history of low CD4/CD8 ratio; other)? ☐ Yes *(summarize below)* ☐ No ☐ Unknown

Immune disorder	Date of onset	Status (active, inactive)	Other details

List prior MS therapies:

Drug	Dose	Start date	Stop date

Has the patient taken any of the following medications in the past or currently? Check all that apply and include dates of starting and completing and indication the medication in the space below.
☐ Chemotherapy/ Cytoreductive therapy *please specify*☐ Corticosteroids *specify dose and duration*
☐ Other immunosuppressant drugs *please specify*☐ Radiation therapy
☐ None of the above

Additional details:

Varicella Zoster Virus (VZV) infections checklist

Event Description

1. Confirm the type of varicella zoster virus infection:

☐ Primary infection (e.g. varicella/chickenpox) ☐Reactivation (e.g. herpes zoster/shingles) ☐Unknown/undetermined

2. Specify diagnosis (including complications, if any), the date the diagnosis was made (e.g. radiculitis, post-herpetic neuralgia, polyneuritis, facial paralysis, etc.) and current clinical status.

3. Infection location:

Skin: ☐ Yes☐ No☐ Unknown

If yes, provide clinical description and specify the involved dermatome(s):

If yes, any complication?☐ Eye ☐ Ear ☐ Post-herpetic neuralgia

Disseminated infection: ☐ Yes☐ No☐ Unknown

If yes: ☐ Cutaneous dissemination; ☐ CNS dissemination ☐ Visceral dissemination.

If applicable: CNS:☐ Meningitis ☐ Myelitis ☐ Encephalitis ☐ Vasculitis

☐ Other (*please specify*)

Other: ☐ Yes (*please specify*)☐ No☐ Unknown

4. Treatment for this event, including response (please provide treatment drugs, dose, route and dates of treatment)

5. Were any of the following diagnostic tests performed? ►**If yes, please specify the dates and results.**

Serum/blood	**CSF**	**Vesicles/skin lesion**
☐ VZV IgM/IgG	☐ VZV PCR	☐ VZV PCR
☐ VZV PCR	☐ Other (specify)	☐ Other (specify)
☐ Other (specify)	☐ None	☐ None
☐ None		

Patient history

6. Does the patient have a history of VZV exposure (infection and/or vaccination)?

History of varicella (*please provide date and/or age of the patient*)☐Yes☐No☐ Unknown

History of shingles (*please provide number of episodes (if recurrent), date and/orage of the patient*) ☐ Yes☐ No☐ Unknown

Varicella vaccination (*please provide number of doses, date and/or age of the patient at the time of vaccination*).☐ Yes☐ No☐ Unknown

Shingles vaccination (*please provide date and/or age of the patient at the time of vaccination*). ☐ Yes☐ No☐ Unknown

7. Has the patient recently (i.e. within the past 6 months) taken any immunosuppressive therapies? (*specify dose and duration of therapy*)

☐ Corticosteroids	☐ Yes	☐ No	☐ Unknown
☐ Other immunosuppressive or immunomodulator therapies	☐ Yes	☐ No	☐ Unknown
☐ Cytotoxics	☐ Yes	☐ No	☐ Unknown
☐ Other	☐ Yes	☐ No	☐ Unknown
☐ None	☐ Yes	☐ No	☐ Unknown

Cryptococcal Meningitis for Multiple Sclerosis Products

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed.

Part I: Critical Information – Please provide the following

Approximate onset date of symptoms that led to the diagnosis: _____

Action taken with fingolimod/siponimod: ☐Discontinued ☐Continued ☐Unknown
Event Outcome: ☐Complete recovery ☐Recovered with sequelae ☐Condition improving ☐ Condition unchanged ☐Condition deteriorating ☐Fatal ☐Unknown

What were the initial presenting symptom(s)?
☐ Subacute Headache☐ Nausea/Vomiting☐ Others (*please specify*)
☐ Confusion☐ Seizure(s)_____
☐ Lethargy ☐ Cranial nerve palsies_____
☐ Coma☐ Papilledema
☐ Fever☐ Neck stiffness ☐ None of the above

CBC (specifically absolute lymphocyte counts):

Test	Date	Result (please provide units)

Please indicate Cryptococcus diagnostic testing:
CSF cryptococcus antigen test ☐ Positive (titer)☐ Negative☐ Not done
Serum cryptococcus antigen test ☐ Positive (titer)☐ Negative☐ Not done
India inkmicroscopy ☐ Positive☐ Negative☐ Not done
Fungal culture results:_____

Part II: Additional Information that is helpful if available

Anti-Cryptococcal Treatment:

Drug	Dose	Start and stop dates of therapy

Patient History, Concurrent Conditions, and Relevant Therapy:

Does the patient have a history of any of the following prior to the start of fingolimod/Siponimod?

Check all that apply and please include date(s) of onset as well as status (i.e. active/ inactive) and details
☐ HIV Infection☐ Malignancy (e.g. Leukemia, Lymphoma, Myeloproliferative disease)
☐ Sarcoidosis☐ Other disturbances of the immune system (e.g. history of low CD4/CD8 ratio)
☐ Close contact with birds☐ Contact with eucalyptus trees ☐Other relevant history *(please specify)*☐ None of the above

_____

How long has the patient had Multiple Sclerosis (years/months or specific date of diagnosis) _____

List all MS treatments and duration:

Drug	Dose	Start and stop dates of therapy

List all concomitant or prior immunosuppressive therapies (e.g., monoclonal antibodies, cancer chemotherapy or cytoreductive treatments, corticosteroids, radiation therapy):

Drug/Intervention	Dose	Start and Stop dates of therapy

Identified risk: Skin cancer (Basal cell carcinoma, Kaposi's sarcoma, Malignant melanoma, Merkel cell carcinoma, Squamous cell carcinoma)

S1P Modulator and Skin Cancer checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed.

1. Event description:

☐ Diagnosis and date of diagnosis

☐ Signs /symptoms

☐ Location and clinical description of the skin lesion

☐ Biopsy results

2. Patient history prior to the start of the drug:

Does the patient have a history of skin cancer?

☐ Squamous cell carcinoma ☐ Basal cell carcinoma ☐ Melanoma ☐ Other (specify)

☐ None

►If yes, provide:
- Source of diagnosis (biopsy/ clinical only)
- Date of diagnosis
- Location of the lesion and treatment

Has the patient previously been treated with immunosuppresors/ immunomodulators?

☐ Yes ☐ No

►If yes, please provide the following information:
- Reason (MS or other than MS -specify)
- Drug generic name
- Treatment duration
- Dose

Is the patient a smoker?

☐ Yes ☐ No

►If yes, provide:
- Smoking duration in years
- Number cigarettes a day

3. Please select one item in each column of the table below to identify the patient's skin type (Fitzpatrick 1975)

Skin type	Sunburn Tendency	Tan tendency	Skin, hair and eye color

I	☐ Always sunburns	☐ Never tans	☐ White skin, freckles, blond or red hair, blue or green eyes
II	☐ Usually sunburns	☐ Sometimes tans	☐ White skin, blond hair, blue or green eyes
III	☐ Seldom sunburns	☐ Usually tans	☐ White skin, usually dark hair, brown eyes
IV-VI	☐ Never sunburns	☐ Always tans darkly.	☐ Brown to dark skin/ brown or black hair brown eyes

Identified Risk: Reproductive toxicity; Missing information: Lactating women

Multiple sclerosis- Pregnancy baseline FU checklist

- Please enter dates in DD/MM/YY format
- If the mother experienced an adverse event during pregnancy, please complete Adverse Event Report Form

1. To be populated by Novartis Country Organization		
Report type: ☐ study ☐ spontaneous	for study case:	Study number: Centre number: Patient number:
Country:		

2. Parental demographics		
Who took the drug? ☐ Mother ☐ Father		
	Mother	**Father** (required only if father took the drug)
Race/ Ethnicity:	☐ Asian ☐ Black ☐ Caucasian ☐ Hispanic ☐ Other, specify:	☐ Asian ☐ Black ☐ Caucasian ☐ Hispanic ☐ Other, specify:
Date of birth:		
Age	years	years
Height:	unit: ☐ cm ☐ in	unit: ☐ cm ☐ in
Weight	unit: ☐ kg ☐ lb (at LMP)	unit: ☐ kg ☐ lb

3. Maternal information	
Date of last menstrual period (LMP):	Expected date of delivery (EDD):
Method of EDD calculation: ☐ LMP ☐ Ultrasound ☐ Other, specify:	
Number of fetuses:	

4a. Suspected Novartis medication taken during or just before pregnancy									
Medication name	Dose/ times a day	Route of administration	Indication	If exact dates are unknown, enter gestation period, e.g. '2 weeks prior to last menstrual period'		Exposure by trimester*: enter yes, No, UNK (unknown)			
				Start date	Stop Date	Pre**	1st	2nd	3rd

4b. Other medications taken by the mother during pregnancy (including over-the-counter products)									

* 1st: week 0-12 2nd: week 13-26 3rd: week 27 onwards
** "Pre" refers to washout period of drug after stopping the medicine: for fingolimod = 8 weeks (2months), siponimod = 10 days, ofatumumab = 6 months

5. Contraception

Was contraception used? ☐ Yes ☐ No ☐ Unknown

Method of contraception

☐ oral contraceptive, specify name:

☐ intra-uterine device ☐ transdermal ☐ subcutaneous implant

☐ condom ☐ spermicide ☐ other, specify:

Do you think there was a failure in contraception? ☐ Yes ☐ No ☐ Unknown

Cause/reason for failure:

6. Prenatal tests

Prenatal test name	Test date	Abnormal results?			Test result (specify any abnormality)
		Yes	No	Not available	
		☐	☐	☐	
		☐	☐	☐	
		☐	☐	☐	

7. Maternal risk factors or conditions that may affect the outcome of the current pregnancy

☐ Smoking	
☐ Alcohol	
☐ Recreational drugs	Specify drugs used:
☐ Hypertension	
☐ Heart disease	Specify disease:

☐ Seizure	
☐ Diabetes	Specify type:
☐ Eclampsia	
☐ Pre-eclampsia	
☐ Thyroid disorder	Specify disorder:
☐ Infections	Specify infection:
☐ Environmental or occupational exposure	Specify exposure:
☐ History of infertility	
☐ Fertility treatment	Specify treatment:
☐ Autoimmune disease	Specify:
☐ Other	Specify:

8. Multiple sclerosis (MS) history

Duration of MS disease :

Is the patient mobile? ☐ Yes ☐ No EDSS:

Relapse just before or during current pregnancy

☐ Yes, date: ☐ No ☐ Unknown

Treatment given for the relapse (e.g. corticosteroid):

Current course of MS

☐ Primary progressive ☐ Secondary progressive

☐ Relapsing remitting ☐ Other, specify:

9. Previous obstetric history (provide details on all previous pregnancies below, including abortion or stillbirth)

Total number of prior pregnancies:

#	Gestation weeks at end of pregnancy	Outcome of pregnancy		Fetal/neonatal abnormalities or complications
1		☐ live birth ☐ spontaneous abort.	☐ therapeutic abort. ☐ elective termination	
2		☐ live birth ☐ spontaneous abort.	☐ therapeutic abort. ☐ elective termination	
3		☐ live birth ☐ spontaneous abort.	☐ therapeutic abort. ☐ elective termination	
4		☐ live birth ☐ spontaneous abort.	☐ therapeutic abort. ☐ elective termination	

10. Family history

Fetal malformations or other poor pregnancy outcomes (e.g. congen. anomaly or mental retardation) in the immediate family	Family side	Relationship

1		☐ maternal ☐ paternal	
2		☐ maternal ☐ paternal	
3		☐ maternal ☐ paternal	

11. Any additional comments:

12. In order for us to maintain complete product safety information, we would like to obtain additional medical details concerning this case therefore, with patient consent, we would like to contact the treating physician(s) concerning this report. If you agree, please provide the following information:	
Role:	Name, Address, phone number, email:
☐ Obstetrician ☐ Midwife ☐ other specialist, specify:	

13. Reporter Information		
Name, Address:		
Phone number:		
Reporter type: ☐ Obstetrician ☐ Other physician ☐ Non-healthcare professional ☐ Paediatrician ☐ Midwife ☐ other, specify:		
Date:	Signature:	

Please contact Novartis as soon as possible after the pregnancy has ended.

Multiple Sclerosis–Pregnancy Outcome (Estimated Date of Delivery+ one month) Follow-up Checklist

- Please enter dates in DD/MM/YY format
- If the mother experienced an adverse event during pregnancy, please complete Adverse Event Report Form

1. To be populated by Novartis Country Organization		
Report type: ☐ study ☐ spontaneous	for study case:	Study number: Centre number: Patient number:
Country:		

2a. Suspected Novartis medication taken during or just before pregnancy									
Medication name	Dose/ times a day	Route of administration	Indication	If exact dates are unknown, enter gestation period, e.g. '2 weeks prior to last menstrual period'		Exposure by trimester*: enter yes, No, UNK (unknown)			
				Start date	Stop Date	Pre**	1st	2nd	3rd
2b. Other medications taken by the mother during pregnancy (including over-the-counter products)									

* 1st: week 0-12 2nd: week 13-26 3rd: week 27 onwards
** "Pre" refers to washout period of drug after stopping the medicine: for fingolimod = 8 weeks (2months), siponimod = 10 days, ofatumumab = 6 months

3. Prenatal tests					
Prenatal test name	Test date	Abnormal results?			Test result (specify any abnormality)
		Yes	No	Not available	
		☐	☐	☐	
		☐	☐	☐	
		☐	☐	☐	

Pregnancy outcome		
☐ **4. Live birth**	Date of birth:	Gestation weeks at birth:
	Timing of delivery: ☐ Full-term (between 37 and 42 weeks of gestation) ☐ Premature (before 37 completed weeks of gestation) ☐ Post-mature (after 42 weeks of gestation)	
	Normal (healthy) baby ☐ Yes ☐ No	
	Neonate demographics (at birth): Sex: ☐ male ☐ female Length: unit: ☐ cm ☐ in ☐ percentile: Weight: unit: ☐ kg ☐ lb ☐ percentile: Head circumference: unit: ☐ cm ☐ in Small for gestational age: ☐ Yes☐ No Apgar scores: 1 min : 5 mins : 10 mins :	
	Is the baby still alive?☐ Yes ☐ No, date of death: Cause of death and autopsy result (if available):	
☐ **5.Termination** (up to 22 completed weeks gestation)	Date of termination:	Gestation weeks at termination:
	Type of termination: ☐ spontaneous abortion / miscarriage ☐ induced termination ☐ therapeutic reason (maternal or fetal complication) ☐ elective termination	
	Medical problems: ☐ Blighted ovum ☐ Molar pregnancy / Hydatidiform mole ☐ Ectopic pregnancy ☐ Other, specify:	
☐ **6.Stillbirth** (after 22 completed weeks gestation)	Date of stillbirth:	Gestation weeks at stillbirth:
	Was an autopsy performed? ☐ Yes ☐ No ☐Unknown If yes, please provide the result attached to this form and give brief details here:	

7. Anomalies in the baby or fetus
Were any anomalies noted for the baby or fetus? ☐ Yes ☐ No ☐Unknown
Describe all anomalies:
Were any of the anomalies of known genetic origin: ☐ No ☐ Yes please specify:
If there were congenital malformation was at least one major? (i.e. requires medical or surgical treatment, has serious adverse effect on health/development or has significant cosmetic impact): ☐ Yes ☐ No, only minor ☐None ☐ Unknown

8. Delivery/Labour
Mode of delivery: ☐ Normal delivery ☐ Caesarean section ☐ Others, specify:

9. Complication during or after delivery
☐ None ☐ Intrauterine death ☐ Other, specify:

10. Causal relationship
What is the causal relationship between reported medication and **the outcome of the pregnancy?** ☐ Not suspected ☐ Suspected ☐ Not assessable

11. Any additional comments:

12. In order for us to maintain complete product safety information, we would like to obtain additional medical details concerning this case therefore, with patient consent; we would like to contact the treating physician(s) concerning this report. If you agree, please provide the following information:	
Role:	Name, Address, phone number, email:
☐ Obstetrician ☐ Midwife ☐ Other specialist, specify:	

13. Reporter Information	
Name, Address:	
Phone number:	
Reporter type: ☐ Obstetrician ☐ Other physician ☐ Non-healthcare professional ☐ Paediatrician ☐ Midwife ☐ other, specify:	
Date:	Signature:

Multiple Sclerosis- – Infant Health status follow-UP During first year following drug exposure in pregnancy

- Please enter dates in DD/MM/YY format

1. To be populated by Novartis Country Organization		
Report type: ☐ study ☐ spontaneous	for study case:	Study number: Centre number: Patient number:
Country:		

2. Infant Demographics		
Status ☐ living	Infant date of birth:	Infant gender:
	Date of measurement:	Infant age at measurement(in months):
	Weight: unit: ☐ kg ☐ lb ☐ percentile specify:	
	Length: unit: ☐ cm ☐ in ☐ percentile specify:	
	Head circumference: unit: ☐ cm ☐ in	
☐ deceased	Date of death:	Infant age at death in months:
	Cause of death (please provide autopsy report if available):	

3. Infant Health Status		
Have any congenital malformations been identified since birth? ☐ Yes ☐ No ☐ Unknown	If yes, please specify:	Diagnosis date:
Did malformations reported at or since birth resolve by themselves? ☐ Yes ☐ No ☐ Unknown	If no, please indicate the details including any medical intervention or surgical treatment:	
Has the infant experienced infection requiring hospitalization?	Please specify diagnosis, labs and infection site if known:	Event start date and end date:

☐ Yes ☐ No ☐ Unknown	Treatment given and outcome:	

4. Breastfeeding
Is the infant breast-fed? (Including partially) ☐ yes, currently ☐ has been weaned, date or infant age at weaning: ☐ no ☐ unknown

5. Developmental Delay			
Has the doctor diagnosed the child with any developmental delay?	☐ Yes ☐ No ☐ Unknown	Age at diagnosis (in months):	If yes, is it: ☐ physical ☐ mental/cognitive Please provide more details:

6. Infant Vaccination		
Has the baby received all vaccinations as recommended?	☐ Yes ☐ No ☐ Unknown	**If No,** please provide details:
Has the child had any reaction after vaccination that needed medical care/ to be seen by a doctor?	☐ Yes ☐ No ☐ Unknown	If yes, Please specify:

7. Any additional comments:

8. In order for us to maintain complete product safety information, we would like to obtain additional medical details concerning this case therefore, with patient consent; we would like to contact the treating physician(s) concerning this report. If you agree, please provide the following information:	
Role:	Name, Address, phone number, email:
☐ Pediatrician ☐ General physician ☐ Other specialist, specify:	

9. Reporter Information	
Name, Address:	
Phone number:	
Reporter type: ☐ Obstetrician ☐ Other physician ☐ Non-healthcare professional ☐ Paediatrician ☐ Midwife ☐ other, specify:	
Date:	Signature:

Identified Risk: Convulsions

Seizures checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed.

EVENT DESCRIPTION: Did the patient present with any of the following signs/symptoms? Check/circle all that apply and please describe

Aura

☐ Visual disturbance ☐ Headache ☐ Nausea/Abdominal Sensation

☐ Depression/irritability/ sleep disruption ☐ Déjà vu/ jamais vu/ smell/ sound/taste

☐ Fear/ Panic

☐ Changes in bodily sensations, ability to interact, unfamiliarity with outside world

☐ No Aura

☐ Dizziness/lightheadedness

Post-ictal: ☐ Memory loss ☐ Confusion ☐ Weakness ☐ Somnolence ☐ Lethargy

Classification of current seizure: Please check all that apply

Generalized Seizures (produced by the entire brain)

Seizure classification	Symptoms
☐ "Grand Mal" or Generalized tonic-clonic	☐ Unconsciousness, convulsions, muscle rigidity
☐ Absence	☐ Brief loss of consciousness
☐ Myoclonic	☐ Sporadic (isolated), jerking movements
☐ Clonic	☐ Repetitive, jerking movements
☐ Tonic	☐ Muscle stiffness, rigidity
☐ Atonic	☐ Loss of muscle tone

Focal Seizures (produced by a small area of the brain)

Seizure classification	Symptoms
☐ Aura (formerly simple somatosensory)	☐ Jerking, muscle rigidity, spasms, head-turning
☐ Motor	☐ Unusual sensations affecting either the vision, hearing, smell taste or touch
☐ Autonomic	☐ Memory or emotional disturbances
	☐ Dyscognitive (formerly complex) ☐ Automatisms such as lip smacking, chewing,

fidgeting, walking and other repetitive, involuntary but coordinated movements

☐ Focal seizure secondarily generalized

☐ Symptoms initially associated with a preservation of consciousness that evolves into a loss of consciousness and convulsions

Were the seizures witnessed? ☐ Unknown ☐ No ☐ Yes *(please describe and if possible, include type and duration)*

Were any of the following diagnostic tests performed? Check all that apply and please specify which test(s), dates and results

☐ Neurological investigations (e.g. EEG, CT scan, MRI scan, PET, SPECT, video-EEG, lumbar puncture) ☐ Other (specify)

☐ General investigations (e.g. CBC, blood chemistry, urinalysis, alcohol screen, toxic screen)
☐ None of the above

Did the patient have a prior history of seizure? If yes, please provide classification and description:

_____

_____

_____

Relevant medical history (concurrent and pre-existing conditions)

(Please specify medical condition and date of onset)

☐ Temporary condition (exposure to drugs, drug withdrawal, high fever, abnormal sodium, calcium or glucose levels)

☐ Genetic disease or familial predisposition

☐ Idiopathic seizures

☐ Use of barbiturates/benzodiazepines

☐ Drugs of abuse (e.g. Cocaine)

☐ Brain tumor or other structural brain lesion (e.g. bleeding)

☐ Congenital brain defects

☐ Kidney or liver failure

☐ Traumatic brain injury, stroke, or a transient ischemic attack

☐ Peri or postpartum brain injury

☐ Phenylketonuria (PKU)

☐ Stopping alcohol after drinking heavily on most days

☐ Dementia (e.g. Alzheimer's disease)

☐ Sleep disorders

☐ Infections (brain abscess, meningitis, encephalitis, neurosyphilis, AIDS)

☐ Illness resulting in brain deterioration

☐ Psychiatric disorders

☐ Hyperventilation

☐ Emotional stress

☐ Migraines with focal symptoms or aura

☐ Menstrual cycle *(please specify (e.g. day 1, ovulation, second half cycle)*

☐ None

Was the patient taking any of the following drugs? Check all that apply

☐ Antibiotics (e.g., penicillin, ampicillin, carbenicillin, cephalosporin)☐ Antidepressants (e.g. bupropion, tricyclics)

☐ Analgesics (e.g., Fentanyl, mefenamic acid, tramadol, meperidine)☐ Drugs of abuse

☐ Antineoplastic agents (e.g., busulfan, carmustine, chlorambucil, methotrexate)

☐ Phenothiazines

☐ Antipsychotic medications (e.g. chlorpromazine, haloperidol, clozapine, atypicals)

☐ Metoclopramide

☐ Bronchial agents (e.g., aminophylline, theophylline)

☐ Lithium

☐ Sympathomimetics (e.g., ephedrine, phenylpropanolamine, terbutaline)

☐ General/local anesthetics (e.g., enflurane, ketamine, methohexital, bupivacaine, lidocaine, procaine)

☐ OTC and/or natural remedies (please specify)

☐ Immunosuppressants (steroids, cyclosporine)

☐ Anticonvulsants

☐ None of the above

Potential risks: Other malignant neoplasms; Lymphoma

Malignancy & Neoplasm checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided.

Description of the event (malignancy / neoplasm):

- Diagnosis/date of diagnosis
- Symptoms
- Location
- Is the cancer localized? If not, please provide details on further locations:
- Location of biopsy site(s) and result (**for lymphomas, please provide lymph node biopsy or an English summary as well as gene rearrangement studies if performed):**
- Histological typing of cancer including immunophenotyping and molecular profile (please provide a copy of report or an English summary**):**
- Staging of the neoplasm:
- Status of patient/Current treatment plan:

Were any of the following diagnostic tests performed? Check all that apply and specify which test(s), dates and results

☐ Biopsies
☐ Bone marrow aspiration
☐ Blood test, urine test, biomarkers
☐ Imaging tests (e.g. x-ray, CT scan, MRI scan, PET scan, mammogram, PSA screening)
☐ Exploratory surgery (planned or completed)
☐ EBV serology test
☐ Other viral serology tests (e.g. HIV, HCV)
☐ None of the above

Relevant medical history (concurrent and pre-existing conditions)

(Please specify medical condition and date of onset)

Check all that apply and provide details as applicable:

☐ Infection ☐ UV exposure, PUVA/UVB
☐ Smoking ☐ Alcohol abuse
☐ Personal history of malignancy ☐ Family history of malignancy
☐ Immunosuppression condition (e.g. HIV, transplantation) ☐ Immunosuppression therapy
☐ Autoimmune disease (e.g. psoriasis, Sjogren Syndrome, rheumatoid arthritis)
☐ Exposure to carcinogens (environmental, occupational) ☐ None of the above

Cervical dysplasia/cervical cancer checklist

A. Event description:

Current diagnosis _____ Date ___/____/_____

PAP results (date) _____ ☐ Not done ☐ Unknown

Biopsy results (date) _ _____ ☐ Not done ☐ Unknown

Current HPV results, genotype_____ Test date ___/____/_____

B. Patient history

1. How often has the subject had PAP tests? ___ Date of last PAP test (before current one): ___ / ___ / ___
   a. Was it normal? ☐ Yes ☐ No ☐ Unknown
   b. If not normal: What were PAP results? _____ ☐ Not done ☐ Unknown
      What were biopsy results?_____ ☐ Not done ☐ Unknown
2. When was the last normal PAP test (date)? _____ ☐ Not done ☐ Unknown
3. Has the patient ever been tested for HPV(Human papilloma virus) ☐Yes☐No☐Unknown
   a. HPV test results and genotype _____ ☐Unknown

1. Has the patient been vaccinated for HPV?

   ☐ Yes: Date: ____/____/____

   ☐ No

   ☐ Don't know

2. Smoking status:

   ☐ Current smoker How long _____

   ☐ Never smoked

   ☐ Smoked in past: How long ____ Quit date_____

6. Has the patient ever used contraceptive pills?

   ☐ Yes How long _____

   ☐ No

9. Is there a family history of cervical cancer?

   ☐ Yes: Relationship: _____

   ☐ No

   ☐ Don't know

10. Has the patient had a sexually transmitted disease? (Gonorrhea, Chlamydia, Trichomoniasis, Herpes, other)

    ☐ Yes: Specify: _____Date_____

    ☐ No

    ☐ Don't know

11. Does the patient have (or have history of) the following?

    ☐ HIV Date: _____

    ☐ Cancer Type: _____

☐ Don't know

☐ Autoimmune disease Type: _____

7. How many pregnancies has the patient had? _____

How many live births: _____

How many miscarriages: _____

How many elective abortions: _____

8. Age of patient at first pregnancy? _____

12. Has the patient taken immunosuppressant medications?

☐ Yes: Specify: ___Date_____

☐ No

☐ Don't know

13. How many sexual partners in patient's lifetime? _____

14. Age when patient became sexually active? _____

Ischemic heart disease/myocardial infarction checklist

In addition to collecting routine information for this adverse event, please ensure the following additional information is provided and/or confirmed.

Event Description:

Did the patient present with any of the following signs or symptoms? **Check all that apply.**

☐ Angina pectoris (chest pain on exertion or stress) ☐ Nausea/Vomiting

☐ Choking pain ☐ Oedema in extremities

☐ Tightness or squeezing in the chest ☐ Restlessness

☐ Pain in left arm ☐ Fatigue

☐ Cold, clammy or pale skin ☐ Sweating

☐ Pain in jaw ☐ Pallor

☐ Decreased urine output ☐ Fever

☐ Shortness of breath ☐ Palpitation

☐ Loss of consciousness ☐ Musculoskeletal pain

☐ Dizziness ☐ None of the above

When did the symptoms begin?

☐ During exercise ☐ At rest ☐ During sleep ☐ Other *(please specify)*

What was the duration of the symptoms?

Were any of the following diagnostic tests performed? Check all that apply and please specify which test(s), dates and results.

☐ ECG ☐ Echocardiogram ☐ Stress test ☐ Chest x-ray

☐ Blood test (e.g. cholesterol levels, thyroid function tests, blood glucose, CPK levels, troponin)

☐ Coronary angiography/Cardiac catheterization ☐ None of the above

Patient History:

Does the patient have a history of any of the following prior to the start of the suspect drug? **Check all that apply.**

☐ Diabetes ☐ Hypertension ☐ Hyperlipidemia ☐ Hyperthyroidism

☐ Obesity ☐ Hypothyroidism ☐ Alcohol abuse ☐ Sleep apnea

☐ Smoker ☐ Myocardial infarction ☐ Bradycardia ☐ Syncope

☐ Drugs of abuse (e.g. cocaine) ☐ Transient ischemic attack/Stroke

☐ Prolonged QT interval ☐ Obliterating arteriopathy of the lower limb

☐ Limited physical activity *(please specify)*

☐ Family history of myocardial infarction *(please specify)*

☐ None of the above

Was the patient taking any of the following drugs? **Check all that apply.**

☐ Antihypertensives ☐ Ergotamines and derivatives

☐ Beta-Blockers ☐ Antiarrhythmic agents

☐ Antipsychotics (e.g. haloperidol, pimozide) ☐ Oral contraceptives

☐ Calcium channel blockers (please specify dihydropyridine or non-dihydropyridine)

☐ Antibiotics (e.g. erythromycin, clarithromycin) ☐ None of the above