RISK MANAGEMENT PLAN
For
Nintedanib
Version 0.3

RMP Version to be Assessed as Part of this Application:

RMP Version Number	0.3
Data Lock Point for this RMP	27-May-2024
Date of Final Sign Off	15-May-2025
Rationale for Submitting an Updated RMP	RMP amended in line with Day 180 assessment report dated 25-Apr-2025 for nintedanib procedure number EMEA/H/C/006486.
Summary of Significant Changes in this RMP	The following significant changes were made in line with Day 94 assessment report and Day 120 list of question: • RMP amended in line with Day 94 assessment report dated 21-Oct-2024 and Day 120 list of question dated 14-Nov-2024 for nintedanib procedure number EMEA/H/C/006486. • Aligning Part II Module SVII and Part V according to the Guideline on GVP Module V – Risk management systems (Rev 2) and Guidance on the format of the RMP in the EU in integrated format for generic applications. • Specific adverse drug reaction follow-up forms added in annex 4. RMP amended in line with Day 180 assessment report comments dated on 25-Apr-2025 and the reference medicinal product Ofev RMP v12.3: • Addition of paediatric indication • addition of IIR Weight decreased in paediatric population, • re-wording of IPRs “Effect on bone development and growth if used off-label in paediatric patients <18 years-of-age” and “Effect on teeth development if used off-label in paediatric patients <18 years-of-age” to “Effect on bone development and growth in paediatric population” and respectively “Effect on teeth development disorders in paediatric population” • addition of TFU questionnaires for IPRs Effect on bone development and growth in paediatric population and

	Effect on tooth development disorders in paediatric population

Other RMP Versions Under Evaluation:

RMP Version Number	0.2
Submitted On	21-Feb-2025
Procedure Number	EMEA/H/C/006486

Details of the Current RMP:

Version Number	Not applicable
Approved with Procedure	Not applicable
Date of Approval (Opinion Date)	Not applicable

Approver	Dr Eiko Soehlke, MD MPH, EEA QPPV
Signature	QPPV oversight declaration: The content of this RMP has been reviewed and approved by the marketing authorisation applicant's QPPV. The electronic signature is available on file.
E-mail address of contact person	PV.RMP@Viatris.com

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LIST OF TABLES

LIST OF ABBREVIATIONS

Abbreviation	Definition
ADR	Adverse Drug Reaction
ATC	Anatomical Therapeutic Chemical Classification System
CHMP	Committee for Medicinal Products for Human Use
CMDh	Coordination Group for Mutual Recognition and Decentralised Procedures – Human
DCP	Decentralised Procedure
DDD	Daily Defined Dose
DILI	Drug-induced liver injury
DHPC	Direct Healthcare Professional Communication
EEA	European Economic Area
EPAR	European Public Assessment Report
EU	European Union
EURD	European Union Reference Date
GVP	Good pharmacovigilance practices
HCP	Healthcare Professional
ICSR	Individual Case Safety Report
MAA	Marketing Authorization Applicant
MAH	Marketing Authorization Holder
MRP	Mutual Recognition Procedure
PAC	Patient Alert Card
PL	Package Leaflet
PPP	Pregnancy Prevention Programme
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PTC	Patient Treatment Course
PTD	Patient Treatment Days
PTM	Patient Treatment Months
PTY	Patient Treatment Years
PVA	Pharmacovigilance Agreement
QPPV	Qualified Person for Pharmacovigilance
MedDRA	Medical Dictionary for Regulatory Activities
DLP	Data Lock Point
SmPC	Summary of Product Characteristics
SSc-ILD	Systemic sclerosis associated interstitial lung disease
WHO	World Health Organization

PART I: PRODUCT(S) OVERVIEW

Table 1: Part 1.1-Product Overview

Active Substance(s) (INN or Common Name)	Nintedanib
Pharmacotherapeutic Group(s) (ATC Code)	Antineoplastic agent, protein kinase inhibitor L01EX09
Marketing Authorisation <Holder> <Applicant>	Viatris Limited, Ireland
Medicinal Products to Which this RMP Refers	1
Invented Name(s) in the European Economic Area (EEA)/UK	Nintedanib Viatris
Marketing Authorisation Procedure	Centralized EMEA/H/C/006486
Brief Description of the Product	Chemical class Nintedanib is an antineoplastic agent belonging to the class of protein kinase inhibitors. Summary of mode of action Nintedanib is a small molecule tyrosine kinase inhibitor including the receptors platelet-derived growth factor receptor (PDGFR) α and β, fibroblast growth factor receptor (FGFR) 1-3, and VEGFR 1-3. In addition, nintedanib inhibits Lck (lymphocyte-specific tyrosine-protein kinase), Lyn (tyrosine-protein kinase lyn), Src (proto-oncogene tyrosine-protein kinase src), and CSF1R (colony stimulating factor 1 receptor) kinases. Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these kinases and blocks the intracellular signalling cascades, which have been demonstrated to be involved in the pathogenesis of fibrotic tissue remodelling in interstitial lung diseases. Important information about its composition Not applicable
Hyperlink to the Product Information:	PI available in section 1.3.1 of the dossier
Indication(s) in the EEA/UK	Current: Nintedanib Viatris is indicated in adults for the treatment of idiopathic pulmonary fibrosis (IPF).

	Nintedanib Viatris is also indicated in adults for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype. Nintedanib Viatris is indicated in children and adolescents from 6 to 17 years old for the treatment of clinically significant, progressive fibrosing interstitial lung diseases (ILDs). Nintedanib Viatris is indicated in adults, adolescents and children aged 6 years and older for the treatment of systemic sclerosis associated interstitial lung disease (SSc-ILD).
Dosage in the EEA	Current: The recommended dose is 150 mg twice daily administered approximately 12 hours apart. The 100 mg twice daily dose is only recommended to be used in patients who do not tolerate the 150 mg twice daily dose. If a dose is missed, administration should resume at the next scheduled time at the recommended dose. If a dose is missed the patient should not take an additional dose. The recommended maximum daily dose of 300 mg should not be exceeded. The recommended dose of Nintedanib Viatris for paediatric patients aged 6 to 17 years of age is based on the patient's weight and is administered twice daily, approximately 12 hours apart. The dose should be adjusted according to weight as treatment progresses.
Pharmaceutical Form(s) and Strength	Current: 100 mg and 150 mg soft capsules
Is/Will the Product Be Subject to Additional Monitoring in the EU/UK?	No

PART II: SAFETY SPECIFICATION

Part II: Module SI - Epidemiology of the Indication(s) and Target Population(s)

Not applicable.

Part II: Module SII - Non-clinical Part of the Safety Specification

Not applicable.

Part II: Module SIII - Clinical Trial Exposure

Not applicable.

Part II: Module SIV - Populations Not Studied in Clinical Trials

SIV.1 Exclusion Criteria in Pivotal Clinical Studies Within the Development Programme

Not applicable.

SIV.2 Limitations to Detect Adverse Reactions in Clinical Trial Development Programmes

Not applicable.

SIV.3 Limitations in Respect to Populations Typically Under-represented in Clinical Trial Development Programmes

Not applicable.

Part II: Module SV - Post-authorisation Experience

Not applicable.

Part II: Module SVI - Additional EU/UK Requirements for the Safety Specification

Not applicable.

Part II: Module SVII - Identified and Potential Risks

Not applicable.

Part II: Module SVIII - Summary of the Safety Concerns

Table 2: SVIII- Summary of safety concerns

Important Identified Risks	DILI Bleeding Myocardial infarction Weight decreased in paediatric population
Important Potential Risks	Venous thromboembolism Arterial thromboembolism excluding myocardial infarction Perforation Hepatic failure Effect on bone development and growth in paediatric population Effect on teeth development disorders in paediatric population
Missing Information	Treatment of SSc-ILD patients with pulmonary hypertension

PART III: PHARMACOVIGILANCE PLAN (INCLUDING POST-AUTHORISATION SAFETY STUDIES)

The Pharmacovigilance System Master File contains details of the system and processes that the applicant has in place to identify and/or characterize the risks recognised in the safety specification.

III.1 Routine Pharmacovigilance Activities

Routine pharmacovigilance activities beyond ADRs reporting and signal detection:

Specific adverse reaction follow-up questionnaires for

Important identified risks

- DILI (restricted to serious events of liver enzyme increases, DILI, and hepatic failure)
- Myocardial infarction (note: one follow up questionnaire for all arterial thromboembolism events)
- Bleeding (defined as serious according to GVP, assessed as serious by reporter, listed in IME list or initial case without enough information for assessment of seriousness).

Important potential risks

- Arterial thromboembolism excluding myocardial infarction (note: one follow up questionnaire for all arterial thromboembolism events)
- Perforation
- Hepatic failure
- Effect on bone development and growth in paediatric population
- Effect on tooth development disorders in paediatric population

The forms are provided in Annex 4 - Specific Adverse Drug Reaction Follow-up Forms of this RMP.

III.2 Additional Pharmacovigilance Activities

As current routine pharmacovigilance activities are sufficient, no additional pharmacovigilance activities are recommended.

PART IV: PLANS FOR POST-AUTHORISATION EFFICACY STUDIES

Not applicable.

PART V: RISK MINIMISATION MEASURES

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product. Ofev® (MAH: Boehringer Ingelheim International GmbH).

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for Nintedanib Viatris (Nintedanib)

This is a summary of the risk management plan (RMP) for Nintedanib Viatris. The RMP details important risks of nintedanib, how these risks can be minimised, and how more information will be obtained about nintedanib's risks and uncertainties (missing information).

Nintedanib Viatris's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how it should be used.

This summary of the RMP for Nintedanib Viatris should be read in the context of all the 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 Nintedanib Viatris 's RMP.

I. The Medicine and What it is Used For

Nintedanib Viatris is authorised in adults for the treatment of idiopathic pulmonary fibrosis (IPF). Nintedanib Viatris is also indicated in adults for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype. Nintedanib Viatris is indicated in children and adolescents from 6 to 17 years old for the treatment of clinically significant, progressive fibrosing interstitial lung diseases (ILDs).
Nintedanib Viatris is indicated in adults, adolescents and children aged 6 years and older for the treatment of systemic sclerosis associated interstitial lung disease (SSc-ILD).

It contains nintedanib as the active substance and is administered by oral route.

Further information about the evaluation of Nintedanib Viatris's benefits can be found in Nintedanib Viatris's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Nintedanib Viatris, together with measures to minimise such 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 public (e.g. with or without prescription) can help to minimises its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse events is collected continuously and regularly analysed 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 Nintedanib Viatris is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Nintedanib Viatris are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken by patients. 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 Nintedanib Viatris. 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/use in special patient populations etc.);

Table 3: Part VI.1- Summary of safety concerns

Important Identified Risks	DILI Bleeding Myocardial infarction Weight decreased in paediatric population
Important Potential Risks	Venous thromboembolism Arterial thromboembolism excluding myocardial infarction Perforation Hepatic failure Effect on bone development and growth in paediatric population Effect on teeth development disorders in paediatric population
Missing Information	Treatment of SSc-ILD patients with pulmonary hypertension

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 Nintedanib Viatris.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Nintedanib Viatris.

PARTS VII: ANNEXES

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 – Tabulated Summary of Planned, On-going and Completed Pharmacovigilance Study Programme

Not applicable.

Annex 3 - Protocols for Proposed, On-going and Completed Studies in the Pharmacovigilance Plan

Not applicable.

Annex 4 - Specific Adverse Drug Reaction Follow-up Forms

Table of content:

Sr. No	Specific Adverse Drug Reaction Follow up forms
1	Bleeding Questionnaire
2	ATE Questionnaire
3	Hepatic Questionnaire
4	Perforation Questionnaire
5	Tooth development disorder Questionnaire
6	Bone development and growth Questionaire

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Bleeding for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

A. Bleeding Questionnaire

(Please select one or multiple appropriate answers)

1. What was the gastrointestinal/respiratory location of the bleeding?

   a) Haemoptysis: coughing up blood
   b) Epistaxis: nose bleed
   c) Gastrointestinal haemorrhage
   d) Haematemesis: red blood or coffee grounds material
   e) Melena: black, tarry, foul-smelling stool
   f) Haematochezia: bright red or maroon blood from rectum
   g) Occult GI bleeding: blood in stool in the absence of overt

2. Did the patient had the following locations of bleeding?

   a) Intracranial haemorrhage (including haemorrhagic stroke)
   b) Skin bleeding (including haematoma and contusion)
   c) Blood in urine
   d) Genital haemorrhage
   e) Wound haemorrhage /procedural site haemorrhage other site (please specify)

3. When did the first signs or symptoms of the reported bleeding event occur?

   a) Before start of treatment with Nintedanib Viatris, please specify: days/weeks/months;

      _____

   b) After start of treatment with Nintedanib Viatris, please specify: days/weeks/months;

      _____

4. Did the patient have any past medical history of bleeding?

   a) Yes, No, Unknown:
   b) If ”Yes” please specify:_____

5. Was the patient on anticoagulation or anti-platelet or thrombolytic therapy?

   a) If ”Yes” please specify (including dose):

      _____

6. Was there an alternative explanation, other than Nintedanib Viatris for the bleeding event?

a) If "Yes" please specify:
_____

7. Did the patient suffer from liver diseases that might have influenced the bleeding event?

a) If "Yes" please specify:

_____

8. Did the patient suffer from an injury (e.g. fall, trauma, accident) that might have influenced the bleeding event?

a) If "Yes" please specify:
_____

9. Which of the following treatments were provided for the bleeding event?

a) No treatment
b) Surgical procedure, please specify:_____
c) Blood transfusion [units]
d) Other drugs, please specify:_____

D. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates. This box can also be used to add extra information if you have run out of space in the other fields)

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

Please be aware that information provided to Viatris relating to you, may be used to comply with applicable laws and regulations. Viatris processes your personal or sensitive data in accordance with applicable data protection laws and the Viatris Privacy Statement, available to you either on https://www.viatris.com/en/viatris-privacy-notice or upon request.

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Arterial thromboembolism for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

B. ATE (Arterial thromboembolism) Questionnaire

(Please select one or multiple appropriate answers)

1. When did the first signs or symptoms of the reported event occur?

a) Before start of treatment with Nintedanib Viatris, please specify: days/weeks/months.
b) After start of treatment with Nintedanib Viatris, please specify: days/weeks/months.

2. What was the location / nature of the event?

a) Ischaemic stroke
b) Pulmonary embolism
c) Myocardial infarction
d) Acute extremity ischaemia
e) Other event; please specify. _____

3. Did the patient have a past or recent medical history of an ATE event?

_____

4. Did the patient have any past or recent medical history of an underlying vascular disorder or are current vascular risk factors known?

_____

5. Is there a known history or a known risk factor of

a) Venous thrombosis
b) Coagulopathy
c) Atrial fibrillation
d) Arterial hypertension
e) Diabetes mellitus
f) Hypercholesterolaemia
g) Smoking
h) Coronary artery disease
i) Peripheral arterial occlusive disease
j) Coronary stent placement
k) PTCA
l) ACBG

m) Other, please specify._____

6. Are relevant laboratory parameters available?

_____

7. If relevant laboratory parameters are available, please specify. [Unit; Baseline (Prior to event); Date of Baseline; Maximum or minimum; Date of maximum or minimum]

a) AST
b) ALT
c) LDH
d) CK
e) CKMB
f) Troponin
g) Hb
h) Platelet count
i) INR
j) aPTT

8. Are relevant ECG findings available?

a) If yes, please specify._____

9. Was any relevant imaging (CT, MRI) performed?

a) If yes, please specify findings._____

10. Which of the following treatments were provided for the ATE event? Please specify.

a) No treatment;
b) surgical procedure;
c) percutaneous intervention;
d) thrombolytic drug treatment;
e) other drug treatment

11. Was there an alternative explanation, other than Nintedanib Viatris, for the current ATE event?

a) If yes, please specify._____

D. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates.

This box can also be used to add extra information if you have run out of space in the other fields)

5. Outcome of event:

☐ Recovered/resolved ☐ Not recovered/ Not resolved

☐ Resolved with sequelae ☐ Fatal

☐ Unknown ☐ Other

If 'Other', please specify:

_____

_____

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

Please be aware that information provided to Viatris relating to you, may be used to comply with applicable laws and regulations. Viatris processes your personal or sensitive data in accordance with applicable data protection laws and the Viatris Privacy Statement, available to you either on https://www.viatris.com/en/viatris-privacy-notice or upon request.

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Hepatic events for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

(Please select one or multiple appropriate answers)

Hepatic Questionnaire

1. When did the first signs or symptoms of the reported hepatic event occur?

a) Before start of treatment with Nintedanib Viatris, please specify days/weeks;
_____
b) After start of treatment with Nintedanib Viatris, please specify days/weeks;
_____
c) Unknown

2. Did the patient had a Past and Current History of: [Yes, if applicable; Specify diagnosis or signs and symptoms; Date]

a) Jaundice (personal or family history)
b) Hereditary metabolic diseases (e.g. M. Wilson, haemochromatosis)
c) Metabolic-induced liver disease (NASH)
d) Alcohol-induced liver disease

3. Did the patient had a Past and Current History of: [Yes, if applicable; Specify diagnosis or signs and symptoms; Date]

a) History of drug allergy/hypersensitivity reaction
b) Infectious diseases (e.g. HIV, EBV, CMV, Cocksackie, malaria)
c) Blood transfusions

4. Did the patient experienced in the Past and Current History: [Yes, if applicable; Specify diagnosis or signs and symptoms; Date]

a) Recent administration of drugs with known hepatic toxicity
b) Environmental exposure to liver toxins (CCl4, death cap, vinyl chloride)
c) Substance abuse/Intoxications - Autoimmune disorders (e.g. PBC, PSC)
d) Treatment of hepatitis B/C

5. Had the patient any malignancy or other manifestation (Past and Current History): [Yes, if applicable; Specify diagnosis or signs and symptoms; Date]

a) Extrahepatic manifestations (e.g. gallstones, infestations, pancreatitis)
b) Hepatic malignancy
c) Extrahepatic malignancy

6. Laboratory Parameter (include: exact value or ↑↓↔; Unit; Date; Baseline (Prior to event, Maximum or minimum, after event subsided]

a) AST
b) ALT
c) γ-GT
d) AP
e) CHE
f) Bili total
g) Bili direct
h) Bili indirect
i) Albumin
j) PT (INR)
k) ASM
l) AMA
m) ANA
n) AFP
o) CEA

7. Hepatitis-Serology (exact viral load or pos/neg) [Hepatitis A Parameter; Value; Unit]

a) Anti-IgM; +/-; ___
b) Anti-IgG; +/-; ___
c) HAV-RNA; ___ ; Copies/ml

8. Hepatitis-Serology (exact viral load or pos/neg) [Hepatitis B Parameter; Value; Unit]

a) HBsAg; +/-; ___
b) Ati-HBs; +/-; ___
c) HbeAg; +/-; ___
d) Anti-Hbe; +/-; ___
e) Anti-HBc; +/-; ___
f) Anti-HBc-IgM; +/-; ___
g) HBV-DNA; ___ ; Copies/ml

9. Hepatitis-Serology (exact viral load or pos/neg) [Hepatitis C Parameter; Value; Unit]

a) Anti-HCV; +/-; ___
b) HCV-RNA; ___; Copies/ml

10. Evidence for viral relapse under current regimen?

_____

11. Evidence for viral co-infections?

a) HBV/HDV [YES ; NO; UNKNOWN]
b) HBV/HIV [YES ; NO; UNKNOWN]
c) HCV/HIV [YES ; NO; UNKNOWN]
d) Others, please specify.

12. Liver biopsy results available? (Please attach)

13. Findings of Liver biopsy:

_____

14. Was any imaging performed (CT, MRI, ultrasound, etc.)?

_____

15. Findings on imaging:

_____

16. Please enter all drugs where a dechallenge or rechallenge was performed:
(Tradename/Generic, for which a discontinuation was deemed necessary)

a) Discontinued due to AE- Y/N/NR;
b) Dechallenge- Pos/neg/NR;
c) Rechallenge- Pos/neg/NR; Results

D. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates. This box can also be used to add extra information if you have run out of space in the other fields)

5. Outcome of event:

☐ Recovered/resolved ☐ Not recovered/ Not resolved

☐ Resolved with sequelae ☐ Fatal

☐ Unknown ☐ Other

If 'Other', please specify:

_____

_____

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

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TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Perforation for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

Perforation Questionnaire:

(Please select one or multiple appropriate answers)

1. What was the location/ nature of the perforation?

a) Gastric ulcer
b) Duodenal ulcer
c) Small-intestine diverticulum
d) Colon diverticulum / diverticulitis
e) Gastrointestinal tumour perforation
f) Peritonitis as sequel of chronic inflammatory bowel disease
g) Peritonitis as sequel of acute appendicitis
h) Procedural complication (e g endoscopy)
i) Other, please specify:_____

2. When did the first signs or symptoms of the reported perforation occur?

a) Before start of treatment with Nintedanib Viatris, please specify: days/weeks/months;
_____
b) After start of treatment with Nintedanib Viatris, please specify: days/weeks/months; unknown
_____

3. Did the patient have any past medical history of gastrointestinal perforation?

a) If ”Yes” please specify:
_____

4. Did the patient have any prior abdominal surgery (including endoscopic surgery)?

_____

5. If patient had prior abdominal surgery please give details:

a) Kind of surgery;
b) Date of surgery;
c) Indication for surgery;
d) Outcome/Complications

6. Please provide recent diagnostic tests (e.g. imaging, endoscopy, histology, microbiology) relevant in the context for the reported perforation event.

a) Date;
b) Reason for diagnostic test;

c) Result

7. Past or concomitant disorders relevant for the reported gastrointestinal perforation event

[Yes; No; Location/final diagnosis; Date/time of onset; Treatment (kind of treatment, ongoing or completed)]

a) Diverticular disease
b) Crohn's disease
c) Ulcerative colitis
d) Peptic ulcer disease
e) Other past or concomitant disorder relevant to the reported event

8. Concomitant medications (Yes; No; Indication; Start date; Stop date / ongoing)

a) Corticosteroid
b) NSAID

9. Was there an alternative explanation, other than Nintedanib Viatris, for the perforation?

a) If "Yes" please specify:

_____

10. Which of the following treatments were administered for the perforation?

a) Surgical treatment, please specify:_____
b) Drug treatment, please specify: _____
c) Other treatment, please specify: _____
d) No treatment
e) Unknown

D. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates. This box can also be used to add extra information if you have run out of space in the other fields)

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

Please be aware that information provided to Viatris relating to you, may be used to comply with applicable laws and regulations. Viatris processes your personal or sensitive data in accordance with applicable data protection laws and the Viatris Privacy Statement, available to you either on https://www.viatris.com/en/viatris-privacy-notice or upon request.

TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Tooth development disorder for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

Please provide patient's dental medical history (including dental caries, impacted teeth).

Does the patient wear dental braces?

Did the patient undergo orthodontic treatment in the past or recently? If yes, please specify (including the date).

Did the patient have any dental trauma? If yes, please specify (including the date).

Does the patient have a good oral hygiene?

Did the patient receive treatment with antineoplastic drugs in the past or recently? If yes, please specify (including dosage, date when started and date when last administered).

Did the patient undergo oral dental examination? If yes, please provide description of the findings (including the date when dental examination(s) was (were) performed).

Did the patient undergo dental imaging(s)? If yes, please provide description of the findings (including the date when dental imaging was performed).

Please provide the FDI (Fédération Dentaire Internationale) tooth/teeth number(s) for the affected teeth.

Was treatment with Nintedanib Viatris interrupted/discontinued following the event? If yes, please provide the date when treatment with Nintedanib Viatris was interrupted/discontinued.

Did the patient receive treatment for the event? If yes, please specify.

4. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates. This box can also be used to add extra information if you have run out of space in the other fields)

5. Outcome of event:

☐ Recovered/resolved ☐ Resolved with sequelae

☐ Unknown ☐ Fatal

☐ Not recovered/ Not resolved ☐ Other

If 'Other', please specify:

_____

_____

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

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TARGETED FOLLOW UP FORM	Template v3.0, Effective date: 23-Dec-2024
Viatris Case No.:	

You have reported an adverse reaction(s) of Bone development and growth for Nintedanib Viatris. This questionnaire is being sent to you for obtaining valuable additional information about the reported case to thoroughly evaluate the relation to Nintedanib Viatris exposure. The Questionnaire is already prefilled with all the available information collected at the time of the initial report, only additional information should be filled in. By providing as detailed information as possible, you can make a useful contribution to the safety of Nintedanib Viatris.

1. Patients Details:

Patient's Initials	
Age/Date of birth	years/months (DD-MMM-YYYY)
Gender	☐ Male ☐ Female
Is the patient pregnant?	☐ Yes If yes, how many weeks: Date of LMP (Last Menstrual Period): (DD-MMM-YYYY) ☐ No
Weight	lbs/kg
Height	ins/cms

2. Drug information at the time of event:

Product(s) suspected to have caused the Adverse Event (Check box to indicate confirmed Viatris products)	**Batch No. / Expiry Date**	**Route** (oral, etc.)	**Daily Dose** (e.g. 20 mg tablet 3 times a day)		**Treatment Dates**		**Indication** (what drug is being taken for)
			Dose/ Unit	**Frequency**	**Start Date**	**Stop Date**	
☐							
☐							
Concomitant Product(s) *(additional products taken within the 30 days period prior to the adverse event(s) occurring)*							

3. Adverse Event details:

Was the patient diagnosed with any growth disorder such as growth hormone deficiency or any genetic disorder that is associated with short stature (e.g. Turner Syndrome)? If yes, please specify.

What was patient's height before nintedanib administration? If available, please provide historical height measurements and the corresponding patient's age.

What is the current patient's age and height?

What is the patient's Tanner stage?

For female patients: Did the patient have menarche? If yes, at which age?

Did the patient undergo bone imaging(s)? If yes, please provide the date(s) and description of the findings.

What is the status of epiphyseal closure (i.e., open/partially closed physis/ closed physis)?

Did patient receive treatment with medications that are known to have impact on growth (e.g. corticosteroids)? If yes, please specify (including dose and treatment duration).

Did patient experience other medical conditions that might explain the growth impairment (e.g., chronic diarrhea, infections)? If yes, please specify.

Was treatment with Nintedanib Viatris interrupted/discontinued following the event? If yes, please provide the date when treatment with Nintedanib Viatris was interrupted/discontinued.

What was the clinical evolution following Nintedanib Viatris interruption (e.g. findings on follow-up bone imaging, height measurements)? If applicable, please provide the date(s) when follow-up was performed.

4. Additional/supporting information:

(Please give additional details on the adverse events, sequence of events, including hospitalisation details, treatment, and/or laboratory tests. This includes start and stop dates. This box can also be used to add extra information if you have run out of space in the other fields)

5. Outcome of event:

☐ Recovered/resolved ☐ Not recovered/ Not resolved

☐ Resolved with sequelae ☐ Fatal

☐ Unknown ☐ Other

If 'Other', please specify:

_____

6. Reporter's Details:

I certify that this Questionnaire is accurate and truthful to the best of my knowledge and does not contain any false, fictitious, or fraudulent statements.

Name/Initials:

Occupation:

☐ Physician ☐ Pharmacist ☐ Nurse ☐ Other Healthcare Professional

☐ Patient/Consumer

Signature and Date:

Annex 5 - Protocols for Proposed and On-going Studies in RMP Part IV

Not applicable.

Annex 6 - Details of Proposed Additional Risk Minimisation Activities (If Applicable)

Not applicable.

Annex 7 - Other Supporting Data (Including Referenced Material)

Not applicable.

Annex 8 – Summary of Changes to the Risk Management Plan Over Time

Table 4: Annex 8 - Summary of Changes to Risk Management Plan Over Time

Version	Approval Date	Procedure	Change
0.1	Not applicable	EMEA/H/C/006486	Not applicable
0.2	Not applicable	EMEA/H/C/006486	• RMP amended in line with Day 94 assessment report dated 21-Oct-2024 and Day 120 list of question dated 14-Nov-2024 for nintedanib procedure number EMEA/H/C/006486. • Aligning Part II Module SVII and Part V according to the Guideline on GVP Module V – Risk management systems (Rev 2) and Guidance on the format of the RMP in the EU in integrated format for generic applications. • Specific adverse drug reaction follow-up forms added in annex 4.
0.3	Not applicable	EMEA/H/C/006486	RMP amended in line with Day 180 assessment report comments dated on 25-Apr-2025 and the reference medicinal product Ofev RMP v12.3: • Addition of paediatric indication • addition of IIR Weight decreased in paediatric population, • re-wording of IPRs “Effect on bone development and growth if used off-label in paediatric patients <18 years-of-age” and “Effect on teeth development if used off-label in paediatric patients <18 years-of-age” to “Effect on bone development and growth in paediatric population” and respectively “Effect on teeth development disorders in paediatric population” • addition of TFU questionnaires for IPRs Effect on bone development and growth in paediatric population and Effect on tooth development disorders in paediatric population