EU Risk Management Plan
for
Nintedanib Accord
(nintedanib)

RMP version to be assessed as part of this application:

RMP Version number	3.1
Data lock point for this RMP	29-Jul-2025
Date of final sign off	13-Aug-2025

Rationale for submitting an updated RMP: This RMP has been updated as per the request for supplementary information (RfSI) for Nintedanib Accord (EMEA/H/C/006179) dated 29-Jul-2025.

Summary of significant changes in this RMP: Significant changes have been updated in following sections of this RMP: Part I, Part VI, and Part VII (Annex 7 and Annex 8).

Other RMP versions under evaluation: Not Applicable

Details of the currently approved RMP:

Version	Approved with procedure	Date of approval
2.0	EMEA/H/C/006179/0000	19-Jun-2024

QPPV name: Arletta Werynska

QPPV signature: 

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Part I: Product(s) Overview

Table 1: Product Overview

Active substance(s) (INN or common name)	nintedanib
Pharmacotherapeutic group(s) (ATC Code)	**Pharmacotherapeutic group(s):** Antineoplastic agents, protein kinase inhibitors ATC code: L01EX09
Marketing Authorisation Applicant	Accord Healthcare S.L.U., Spain
Medicinal products to which this RMP refers	01
Invented name(s) in the European Economic Area (EEA)	Nintedanib Accord
Marketing authorisation procedure	Centralised Procedure (EMEA/H/C/006179)
Brief description of the product	Chemical class: Nintedanib is a member of the class of oxindoles that is a kinase inhibitor. It is an aromatic ester, a methyl ester, a member of oxindoles, an enamine, an aromatic amine, an aromatic amide and a N-alkylpiperazine. It is a conjugate base of a nintedanib (1+).
	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: Nintedanib Accord 100 mg soft capsule Each soft capsule contains nintedanib esylate equivalent to 100 mg nintedanib *Excipient with known effect* Each 100 mg soft capsule contains 1.2 mg of soya lecithin. Nintedanib Accord 150 mg soft capsule Each soft capsule contains nintedanib esylate equivalent to 150 mg nintedanib *Excipient with known effect* Each 150 mg soft capsule contains 1.8 mg of soya lecithin.
Hyperlink to the Product Information	Refer Module 1.3.1 for Product Information
Indication(s) in the EEA	*Current* Nintedanib Accord is indicated in adults for the treatment of idiopathic pulmonary fibrosis (IPF). Nintedanib Accord is also indicated in adults for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype.

	Nintedanib Accord is indicated in adults for the treatment of systemic sclerosis associated interstitial lung disease (SSc-ILD).
	Proposed: Nintedanib Accord 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 Accord is indicated in 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* **Posology:** **For indications relating to IPF, ILDs and SSc-ILD:** Adults: Treatment should be initiated by physicians experienced in the management of diseases for which nintedanib is approved. *Adults* The recommended dose is 150 mg nintedanib 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. **Method of administration:** Nintedanib is for oral use. The capsules should be taken with food, swallowed whole with water, and should not be chewed. The capsule should not be opened or crushed. Nintedanib Accord capsules may be taken with a small amount (one teaspoonful) of cold or room temperature soft food, such as apple sauce or chocolate pudding, and

	must be swallowed unchewed immediately, to ensure the capsule stays intact.
	Proposed: **For indications relating to ILDs and SSc-ILD:** Paediatric patients: Treatment should be initiated only after involvement of a multidisciplinary team (physicians, radiologists, pathologists) experienced in the diagnosis and treatment of fibrosing interstitial lung diseases (ILDs). *Children and adolescents from 6 to 17 years old* The recommended dose of Nintedanib Accord 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 (see SmPC section 4.2 for more detailed information).
Pharmaceutical form(s) and strengths	*Current* **Pharmaceutical form(s):** Soft Capsules **Strengths**:100 mg and 150 mg
Is the product subject to additional monitoring in the EU?	No

Part II: Safety specification

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

Not applicable

Module SII - Non-clinical part of the safety specification

Not applicable

Module SIII - Clinical trial exposure

Not applicable

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

Module SV - Post-authorisation experience

SV.1 Post-authorisation exposure

Not applicable

Module SVI - Additional EU requirements for the safety specification

Potential for misuse for illegal purposes

Not applicable - there is no potential for misuse for illegal purposes.

Module SVII - Identified and potential risks

There is a European Public Assessment Report (Summary of the RMP) available for the reference product Ofev (nintedanib), (Version 12.3, dated 10-Sep-2024) published on the EMA website on 10-Mar-2025. The safety concerns mentioned in Module SVIII, are in-line with summary of safety concerns for the reference product.

Hence, this section remains “Not applicable”.

SVII.1 Identification of safety concerns in the initial RMP submission

SVII.1.1. Risks not considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.1.2. Risks considered important for inclusion in the list of safety concerns in the RMP

Not applicable

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

Not applicable

SVII.3 Details of important identified risks, important potential risks, and missing information

SVII.3.1. Presentation of important identified risks and important potential risks

Not applicable

SVII.3.2 Presentation of the missing information

Not Applicable

Module SVIII - Summary of the safety concerns

Table 2: Summary of safety concerns

Important identified risks	• Drug-induced liver injury (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 tooth development disorders in paediatric population
Missing information	• Treatment of SSc-ILD patients with pulmonary hypertension

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 following risks concerning use of Nintedanib Accord are appended in Annex 4 of this RMP.

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

Purpose: For collection and reporting of safety information while use of Nintedanib Accord.

III.2 Additional pharmacovigilance activities

None proposed

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable

Part IV: Plans for post-authorisation efficacy studies

Not applicable

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

Risk Minimisation Plan

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

None proposed

V.3 Summary of risk minimisation measures

Not Applicable

Part VI: Summary of the risk management plan

Summary of risk management plan for Nintedanib Accord (nintedanib)

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

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

This summary of the RMP for Nintedanib Accord 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 Nintedanib Accord's RMP.

I. The medicine and what it is used for

Nintedanib Accord is authorised in adults for the treatment of idiopathic pulmonary fibrosis (IPF), and for the treatment of other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype. In addition, Nintedanib Accord is authorised in adults, adolescents and children aged 6 years and older for the treatment of systemic sclerosis associated interstitial lung diseases (SSc-ILDs), as well as for the treatment of clinically significant, progressive fibrosing interstitial lung diseases (ILDs) in children and adolescents from 6 to 17 years old (see SmPC for the full indication).

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

Further information about the evaluation of Nintedanib Accord's benefits can be found in Nintedanib Accord's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage https://www.ema.europa.eu/en/medicines/human/EPAR/nintedanib-accord.

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

Important risks of Nintedanib Accord, together with measures to minimise such risks and the proposed studies for learning more about Nintedanib Accord's 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, 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 Accord is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Nintedanib Accord 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 Nintedanib Accord. 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):

Important identified risks	• Drug-induced liver injury (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 tooth 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 Accord.

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

There are no studies required for Nintedanib Accord.

Annex 4 - Specific adverse drug reaction follow-up forms

MAH has developed follow-up questionnaires for the following safety concerns:

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

Targeted Follow-up Questionnaire for Drug-Induced Liver Injury and Hepatic Failure

***PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.**

PATIENT DETAILS:

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

SUSPECTED DRUG(S):

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNES OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness: ☐ Patient Died	☐ Life Threatening	☐ Congenital Abnormality
☐ Involved/Prolonged Hospitalisation	☐ Disability/Incapacity	☐ Medically Significant

Reported Cause(s) of Death#:		
Death date & time:	Autopsy done: ☐Yes ☐No	
Autopsy findings:		

In case of death reported

ACTION TAKEN WITH SUSPECTED DRUGS:

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

1. When did the first signs or symptoms of the reported hepatic event occur?
   - ☐ Before start of treatment with Nintedanib Accord, please specify _____days/weeks
   - ☐ After start of treatment with Nintedanib Accord, please specify _____days/weeks;
   - ☐ Unknown

2. Did the patient had a past and/or current history of:

   If applicable; Specify diagnosis or signs and symptoms; Date]
   - ☐ Jaundice (personal or family history)
   - ☐ Hereditary metabolic diseases (e.g. M. Wilson, haemochromatosis)
   - ☐ Metabolic-induced liver disease (NASH)
   - ☐ Alcohol-induced liver disease
   - ☐ History of drug allergy/hypersensitivity reaction
   - ☐ Infectious diseases (e.g. HIV, EBV, CMV, Cocksackle, malaria)
   - ☐ Blood transfusions
   - ☐ Recent administration of drugs with known hepatic toxicity
   - ☐ Environmental exposure to liver toxins (CCl4, death cap, vinyl chloride)
   - ☐ Substance abuse/Intoxications -Autoimmune disorders (e.g. PBC, PSC)
   - ☐ Treatment of hepatitis B/C

3. Had the patient any malignancy or other manifestation (Past and Current History):

   ☐Yes ☐ No ☐Unknown

   Yes, if applicable; Specify diagnosis or signs and symptoms; Date
   - ☐Extrahepatic manifestations (e.g. gallstones, infestations, pancreatitis)
   - ☐Hepatic malignancy
   - ☐Extrahepatic malignancy

4. Laboratory Parameter (Include: exact value or ↑, ↓, ←→; Unit; Date; Baseline-Prior to event, Maximum or minimum, after event subsided)

AST _____

CHE _____

ALT _____

Albumin _____

ANA _____

Bili total _____

PT(INR) _____

AFP _____

y-GT _____

Bili direct _____

Bili indirect _____

ASM _____

CEA _____

AMA _____

AP _____

7. Hepatitis-Serology (exact viral load or positive/negative) (Hepatitis A Parameter; Value; Unit)

☐Anti-lgM; +/-; _

☐Anti-lgG; +/-; _

☐HAV-RNA; _; Copies/ml

8. Hepatitis-Serology {exact viral load or positive/negative) (Hepatitis B Parameter; value; Unit]

HBsAg; +/-; _	Anti-Hbe; +/-; _
Anti-HBs; +/-; _	Anti-HBc; +/-; _
HbeAg; +/-; _	Anti-HBc-lgM; +/-; _
HBV-DNA; _; Copies/ml	

9. Hepatitis-Serology (exact viral load or positive/negative) (Hepatitis C Parameter; Value; Unit]

Antl-HCV; +/-; _ HCV-RNA; _; Copies/ml

10. Evidence for viral relapse under current regimen?

☐Yes ☐No ☐Unknown

If "Yes" please specify:

11. Evidence for viral co-Infections?

HBV/HDV ☐Yes ☐No ☐Unknown

HCV/HIV ☐Yes ☐No ☐Unknown

HBV/HIV ☐Yes ☐No ☐Unknown

Others, please specify._____

12. Liver biopsy results available? (Please provide details)

☐Yes ☐No ☐Unknown

13. Findings of Liver biopsy:

_____

_____

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

☐Yes ☐No ☐Unknown

15. Findings on imaging:

_____

_____

16. Please enter all drugs where a dechallenge or challenge was performed:

_____(Tradename/Generic), for which a discontinuation was deemed necessary

☐Discontinued due to AE- ☐Yes ☐No ☐Not related

☐Dechallenge- ☐Positive ☐Negative ☐Not related;

☐Rechallenge- ☐Positive ☐Negative ☐Not related

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address: Postcode:	Email:	Tel No.

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**

Targeted Follow-up Questionnaire for Myocardial infarction and Arterial Thromboembolism (ATE)

***PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.**

PATIENT DETAILS:

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

SUSPECTED DRUG(S):

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNESS OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness: ☐ Patient Died ☐ Involved/Prolonged Hospitalisation	☐ Life Threatening ☐ Disability/Incapacity	☐ Congenital Abnormality ☐ Medically Significant

Reported Cause(s) of Death#:		
Death date & time:	Autopsy done: ☐Yes ☐No	
Autopsy findings:		

In case of death reported

ACTION TAKEN WITH SUSPECTED DRUGS:

[redacted]

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

1. When did the first signs or symptoms of the reported event occur?
   - ☐ Before start of treatment with Nintedanib Accord, please specify: _____days/weeks/months.
   - ☐ After start of treatment with Nintedanib Accord, please specify:_____days/weeks/months.

2. What was the location/nature of the event?
   - ☐ Ischaemic stroke
   - ☐ Pulmonary embolism
   - ☐ Myocardial infarction
   - ☐ Acute extremity ischaemia
   - ☐ Other event; please specify._____

3. Did the patient have a past or recent medical history of an ATE event?
   ☐ Yes, ☐ No, ☐ Unknown

4. Did the patient have any past or recent medical history of an underlying vascular disorder or are current vascular risk factors known?
   ☐ Yes, ☐ No, ☐ Unknown
   If "Yes" please specify:

   _____

   _____

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

   - ☐ Venous thrombosis
   - ☐ Coagulopathy
   - ☐ Atrial fibrillation
   - ☐ Arterial hypertension
   - ☐ Diabetes mellitus
   - ☐ Hypercholesterolaemia
   - ☐ Other, please specify._____
   - ☐ Smoking
   - ☐ Coronary artery disease
   - ☐ Peripheral arterial occlusive disease
   - ☐ Coronary stent placement
   - ☐ PTCA
   - ☐ ACBG

6. Are relevant laboratory parameters available?
   ☐ Yes, ☐ No, ☐ Unknown

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]

☐ Yes, ☐ No, ☐ Unknown

☐ AST_____	☐ CKMB_____	☐ INR_____	☐ CK_____
☐ ALT_____	☐ Troponin_____	☐ aPTT_____	☐ Platelet count_____
☐ LDH_____	☐ Hb_____		

8. Are relevant ECG findings available?

☐Yes ☐ No ☐ Unknown

If yes, please specify findings

_____

_____

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

☐Yes ☐ No, ☐ Unknown

If yes, please specify findings

_____

_____

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

☐ No treatment

☐ Surgical procedure

☐ Percutaneous intervention

☐ Thrombolytic drug treatment

☐ Other drug treatment

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

☐Yes, ☐ No, ☐ Unknown

If yes, please specify._____

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address:	Email:	Tel No.
Postcode:		

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**

Targeted Follow-up Questionnaire for Bleeding

***PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.**

PATIENT DETAILS:

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

SUSPECTED DRUG(S):

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNESS OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness: ☐ Patient Died ☐ Involved/Prolonged Hospitalisation	☐ Life Threatening ☐ Disability/Incapacity	☐ Congenital Abnormality ☐ Medically Significant
Reported Cause(s) of Death#:		
Death date & time:	Autopsy done: ☐ Yes ☐ No	
Autopsy findings:		

In case of death reported

ACTION TAKEN WITH SUSPECTED DRUGS:

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

1. What was the gastrointestinal/respiratory location of the bleeding?
   - ☐ Haemoptysis: coughing up blood
   - ☐ Epistaxis: nose bleed
   - ☐ Gastrointestinal haemorrhage
   - ☐ Haematemesis: red blood or coffee grounds material
   - ☐ Melena: black, tarry, foul-smelling stool
   - ☐ Haematochezia: bright red or maroon blood from rectum
   - ☐ Occult GI bleeding: blood in stool in the absence of overt

2. Did the patient have the following locations of bleeding?
   - ☐ Intracranial haemorrhage (including haemorrhagic stroke)
   - ☐ Skin bleeding (including haematoma and contusion)
   - ☐ Blood in urine
   - ☐ Genital haemorrhage
   - ☐ Wound haemorrhage /procedural site haemorrhage
   - ☐ Other site (specify)_____

3. When did the first signs or symptoms of the reported bleeding event occur?
   - ☐ Before start of treatment with Nintedanib Accord, please specify:_____days/weeks/months
   - ☐ After start of treatment with Nintedanib Accord, please specify:_____days/weeks/months.

4. Did the patient have any past medical history of bleeding?
   ☐ Yes, ☐ No, ☐ Unknown
   If "Yes" please specify:_____

5. Was the patient on anticoagulation or anti-platelet or thrombolytic therapy?
   ☐ Yes, ☐ No, ☐ Unknown
   If "Yes" please specify (including dose):_____

6. Was there an alternative explanation, other than Nintedanib Accord, for the bleeding event?
   ☐ Yes ☐ No ☐ Unknown
   If "Yes" please specify:_____

7. Did the patient suffer from liver diseases that might have influenced the bleeding event?
   ☐Yes ☐ No ☐ Unknown
   If "Yes" please specify:_____

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

☐Yes ☐ No ☐ Unknown If "Yes" please specify:_____
9. Which of the following treatments were provided for the bleeding event? ☐ No treatment ☐ Surgical procedure, please specify: _____ ☐ Blood transfusion (units) ☐ Other drugs, please specify: _____

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address: Postcode:	Email:	Tel No.

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**

Targeted Follow-up Questionnaire for Perforation

*PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.

PATIENT DETAILS:

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

SUSPECTED DRUG(S):

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNESS OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness: ☐ Patient Died	☐ Life Threatening	☐ Congenital Abnormality
	☐ Disability/Incapacity	☐ Medically Significant
☐ Involved/Prolonged Hospitalisation		

Reported Cause(s) of Death#:	
Death date & time:	Autopsy done: ☐ Yes ☐ No
Autopsy findings:	

In case of death reported

ACTION TAKEN WITH SUSPECTED DRUGS:

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

[redacted]

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

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

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

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

☐ Before start of treatment with Nintedanib Accord, please specify:_____ days/weeks/months
☐ After start of treatment with Nintedanib Accord, please specify:_____ days/weeks/months
☐ Unknown

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

☐Yes, ☐ No, ☐ Unknown

If "Yes" please specify: _____

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

☐Yes, ☐ No, ☐ Unknown

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

_____

_____

(Kind of surgery; Date of surgery; Indication for surgery; Outcome/Complications)

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

Date	Reason for diagnostic test	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/Completed
☐Diverticular disease			

☐ Crohn's disease			
☐ Ulcerative colitis			
☐ Peptic ulcer disease			
☐ Other past or concomitant disorder relevant to the reported event			

8. Concomitant medications ☐ Yes ☐ No

☐ Corticosteroid ☐ NSAID

Indication_____

Start date_____

Stop date / ongoing_____

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

☐Yes, ☐ No, ☐ Unknown

If "Yes" please specify:_____

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

☐ Surgical treatment, please specify:_____

☐ Drug treatment, please specify:_____

☐ Other treatment, please specify:_____

☐ No treatment

☐ Unknown

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address:	Email:	Tel No.
Postcode:		

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**

Targeted Follow-up Questionnaire - Effect on bone development and growth in paediatric population

***PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.**

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNESS OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness:		
☐ Patient Died	☐ Life Threatening	☐ Congenital Abnormality
☐ Involved/Prolonged Hospitalisation	☐ Disability/Incapacity	☐ Medically Significant

Reported Cause(s) of Death#:	
Death date & time:	Autopsy done: ☐ Yes ☐ No
Autopsy findings:	

ACTION TAKEN WITH SUSPECTED DRUGS:

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

1. 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_____

2. What was patient's height before Nintedanib Accord administration? If available, please provide historical height measurements (Inch/Cm/Foot) and the corresponding patient's age. _____

3. What is the current patient's age and height? Age (Years):_____Height (Inch/Cm/Foot):_____

4. What is the patient's Tanner stage? _____

5. For female patients: Did the patient have menarche? ☐ Yes ☐ No ☐ Unknown

If yes, at which age? Age:_____Years

6. Did the patient undergo bone imaging(s)? ☐ Yes ☐ No ☐ Unknown

If yes, please provide the date(s) and description of the findings.

Date:_____Description_____

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

8. 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):_____

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

10. Was treatment with Nintedanib Accord interrupted/discontinued following the event? ☐ Yes ☐ No

If yes, please provide the date when treatment with Nintedanib Accord was interrupted/discontinued.

Date: _____

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

Date:_____

_____

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address:	Email:	Tel No.
Postcode:		

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**

Targeted Follow-up Questionnaire - Effect on tooth development disorders in paediatric population

***PLEASE DO NOT LEAVE ANY FIELD BLANK. STRIKE IT OUT IF INFORMATION IS 'NOT AVAILABLE' OR 'NOT APPLICABLE'.**

Initials	Age/Age group*	Gender:	Weight (kg)	Height (cm)	Date of Birth	Hospital Ref.

Drug/Brand Name	Manufacturer & Batch No.	Route of Administration	Daily Dosage	Indication	Date Started	Date Stopped
1.						
2.						
3.						
4.						

DETAILS OF SUSPECTED ADVERSE REACTION(S):

Date reaction started: 1) 2)	Date reaction stopped: 1) 2)

Please describe the reaction and details of any treatment given or investigation performed.	Outcome: ☐ Recovered ☐ Not Recovered ☐ Recovered with Sequel ☐ Recovering ☐ Fatal ☐ Unknown

SERIOUSNESS OF ADVERSE REACTION(S):

Do you consider the reaction to be serious?	☐ **Yes**	☐ **No**
If Yes, Reason for Seriousness: ☐ Patient Died ☐ Involved/Prolonged Hospitalisation	☐ Life Threatening ☐ Disability/Incapacity	☐ Congenital Abnormality ☐ Medically Significant
Reported Cause(s) of Death#:		
Death date & time:	Autopsy done: ☐ Yes ☐ No	
Autopsy findings:		

ACTION TAKEN WITH SUSPECTED DRUGS:

☐ Dose Decreased	☐ Dose Increased	☐ Drug withdrawn	☐ Dose not changed	☐ Unknown

[redacted]

CONCOMITANT MEDICATION (incl. herbal or self-medication):

Drug/Brand Name	Route of Admin	Daily Dosage	Indication	Date Started	Date Stopped
1.					
2.					
3.					

ADDITIONAL INFORMATION:

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

2. Does the patient wear dental braces? _____

3. Did the patient undergo orthodontic treatment in the past or recently? ☐ Yes ☐ No

If yes, please specify (including the date) _____

Date:_____

4. Did the patient have any dental trauma? ☐ Yes ☐ No

If yes, please specify (including the date) _____

Date:_____

5. Does the patient have a good oral hygiene? ☐ Yes ☐ No

6. Did the patient receive treatment with antineoplastic drugs in the past or recently? ☐ Yes ☐ No

If yes, please specify (including dosage, date when started and date when last administered)

Dosage:_____ Start Date:_____ End Date:_____

7. Did the patient undergo oral dental examination? ☐Yes ☐ No

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

_____

_____

Date:_____

8. Did the patient undergo dental imaging(s)? ☐ Yes ☐ No

If yes, please provide description of the findings (including the date when dental imaging was performed)

_____

_____

Date:_____
9. Please provide the FDI (Fédération Dentaire Internationale) tooth/teeth number(s) for the affected teeth. _____
10. Was treatment with Nintedanib Accord interrupted/discontinued following the event? ☐Yes ☐ No If yes, please provide the date when treatment with Nintedanib Accord was interrupted/discontinued. Date:_____
11. Did the patient receive treatment for the event? ☐Yes ☐ No If yes, please specify_____

REPORTER DETAILS*:

Title, Name & Surname	Occupation	Signature	Date

Postal Address: Postcode:	Email:	Tel No.

*** Only information which is required for follow-up shall be filled. Preferred mode of communication should be asked from enquirer and accordingly above details should be filled.**