SUMMARY OF RISK MANAGEMENT PLAN FOR VARGATEF (NINTEDANIB)

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

Vargatef's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Vargatef should be used.

This summary of the RMP for Vargatef 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 Vargatef's RMP.

I. THE MEDICINE AND WHAT IT IS USED FOR

Vargatef is authorised in combination with docetaxel for the treatment of adult patients with locally advanced, metastatic or locally recurrent NSCLC of adenocarcinoma tumour histology after first line chemotherapy (see SmPC for the full indication). It contains nintedanib as the active substance and it is given orally.

Further information about the evaluation of Vargatef's benefits can be found in Vargatef'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/vargatef.

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of Vargatef, together with measures to minimise such risks and the proposed studies for learning more about Vargatef'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.

If important information that may affect the safe use of Vargatef is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Vargatef are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. 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 Vargatef. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

List of important risks and missing information

Table 1 Important risks and missing information

Important identified risks	Diarrhoea
	Liver enzyme elevations and hyperbilirubinaemia including DILI
	Neutropenia
	Sepsis
	VTE
	Perforation (GI and non-GI)
	Bleeding
	Hypertension
	Myocardial infarction
Important potential risks	ATE excluding myocardial infarction
	Treatment in pregnant women and teratogenicity
	Hepatic failure
	Cardiac failure
	QT prolongation
Missing information	Treatment in breastfeeding women
	Treatment of patients with moderate and severe hepatic impairment (Child Pugh B/C)
	Treatment of patients with renal impairment
	Treatment of patients with healing wounds
	Treatment of subpopulations with co-morbid CNS conditions such as dementia, depression, brain metastasis, or with co-morbid conditions such as arthritis and osteoporosis
	Treatment of patients weighing <50 kg

II.B Summary of important risks

Diarrhoea	
Evidence for linking the risk to the medicine	In the main (pivotal) clinical trial of Vargatef (trial 1199.13), diarrhoea was more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. In the post-marketing setting, diarrhoea is among the most frequently reported events. Diarrhoea was non-serious in more than 85% of the reported cases. Serious cases of diarrhoea leading to dehydration and electrolyte disturbances have been reported with nintedanib. Cases of renal impairment / failure, in some cases with fatal outcome, have been reported with nintedanib use.
Risk factors and risk groups	Possible causes and risk factors for diarrhoea in cancer patients include the type and location of the cancer, surgery, chemotherapy, effects of other drugs, radiotherapy, diet, infection, and comorbidities. Diarrhoea is a known adverse effect of docetaxel.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Liver enzyme elevations and hyperbilirubinaemia including DILI	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), elevations of liver enzymes and total bilirubin were more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. Furthermore, liver enzyme elevations are among the most frequently reported events in the post-marketing setting. Cases of DILI have been observed with nintedanib treatment. In the post-marketing period, severe liver injury with fatal outcome has been reported in a patient with IPF after treatment with Ofev (nintedanib approved in the indication of IPF).
Risk factors and risk groups	Population pharmacokinetics analyses in patients with NSCLC and IPF revealed that female and Asian patients have a higher risk of elevations in liver enzymes upon nintedanib treatment. Nintedanib exposure increased linearly with patients' age and was inversely correlated to weight. The increased nintedanib exposure may result in a higher risk of developing liver enzyme elevations.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, 4.8, and 4.9. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Neutropenia	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), neutropenia AEs of CTC AE grade ≥3 (moderate to severe intensity) and decreased neutrophil count grade ≥3 measured as laboratory value were slightly more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone.
Risk factors and risk groups	Docetaxel (which is used in combination with nintedanib for treatment of NSCLC) has myelosuppressive effects, and is associated with neutropenia, febrile neutropenia, and infection. In a review of cancer patients, commonly identified risk factors for neutropenia or febrile neutropenia, other than the chemotherapy type, generally included advanced age, low performance status (decreased general condition), high serum lactate dehydrogenase level, low pre-treatment leukocyte count, low serum albumin, and severe neutropenia or decreased haemoglobin level during a previous chemotherapy cycle (in the absence of subsequent chemotherapy dose reduction or use of myeloid growth factors to mitigate the risk). All grade and severe grade neutropenia due to docetaxel is increased in Asian patients compared to white/Caucasian patients.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Sepsis	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), sepsis was more frequent in patients treated with nintedanib in combination with docetaxel compared to patients treated with docetaxel alone. Cases of sepsis have also been reported in the post-marketing setting.
Risk factors and risk groups	Factors that can predispose lung cancer patients to infection include neutropenia, chronic obstructive pulmonary disease, obstructive lesions, advanced age, and altered immune function. Because neutropenia is a common adverse drug reaction for many chemotherapeutic agents and neutropenia is a major risk factor for sepsis, the chemotherapy regimen administered (specific drugs, doses, and schedule) is an important determinant of sepsis risk among patients with cancer. Older age and male gender have also been reported as risk factors for sepsis among lung cancer patients.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

VTE	
Evidence for linking the risk to the medicine	The medical concept of VTE includes venous thrombotic events and pulmonary embolism. In the pivotal clinical trial of Vargatef (trial 1199.13), venous thromboembolic events were more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. Venous thromboembolic events have also been reported in the post-marketing setting.
Risk factors and risk groups	Reasons leading to the development of VTE in cancer patients are frequently categorised as cancer-related (with rates highest in lung cancer patients, patients with any cancer of the adenocarcinoma subtype, and patients with advanced stage disease), treatment-related (with higher rates seen with the use of chemotherapy, antiangiogenic medications, and erythropoiesis-stimulating agents), and patient-related (with high rates among the obese, those with prolonged immobility, and those with a history of VTE). The risk of VTE varies over time after a diagnosis of cancer. The risk is highest early after diagnosis, and there is a strong correlation between metastatic-stage cancer and risk of VTE. Hospitalised patients, patients undergoing surgery, and patients receiving chemotherapy are at particularly high risk for VTE.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Perforation (GI and non-GI)	
Evidence for linking the risk to the medicine	Perforation is a rare event. In the pivotal clinical trial of Vargatef (trial 1199.13), the frequency of GI perforation events was balanced between the treatment arms. Cases of GI perforation, some of which were fatal, have been reported infrequently in the pivotal clinical trial of Vargatef and in the post-marketing setting. The medical concept of non-GI perforation includes perforations, fistulae, and abscesses outside the GI tract. In the pivotal clinical trial of Vargatef (trial 1199.13), AEs in the medical concept of 'non-GI perforation' were more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. The majority of AEs were abscesses with a preferred location in the lung or the chest, and mainly of CTC AE grade 1 and 2 (mild intensity).
Risk factors and risk groups	Risk factors for perforation include cancer-related conditions (e.g. abdominal carcinomatosis), other underlying diseases (peptic ulcer disease, diverticulitis, bowel obstruction), chemotherapy-induced colitis, abdominal irradiation, history of bowel surgery, and drugs (steroids, non-steroidal anti-inflammatory drugs).
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Bleeding	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), bleeding was slightly more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. The imbalance in the overall population was driven by patients with squamous NSCLC. In patients with adenocarcinoma, the frequency of bleeding in both treatment arms was comparable. Serious and non-serious bleeding events, some of which were fatal, have been reported in the pivotal clinical trial of Vargatef and in the post-marketing setting. Post-marketing bleeding events include, but are not limited to, GI, respiratory and central nervous system organs, with the most frequent being respiratory.
Risk factors and risk groups	Common risk factors for bleeding include inherited predisposition to bleeding, advanced age, hypertension, invasive procedures, injuries, and use of anticoagulants. The risk of bleeding in advanced NSCLC patients appears to depend on the tumour histology; studies in advanced NSCLC have suggested that patients with squamous cell carcinoma and large cell carcinoma have a higher risk of bleeding than patients with adenocarcinoma or non-squamous cell carcinoma. Epidemiological studies suggest that patients with tumour cavitation, prophylactic anticoagulation therapy, and age >65 years with CNS metastases may also be at increased risk of bleeding events.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Hypertension	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), hypertension was more frequent in patients treated with nintedanib in combination with docetaxel as compared to patients treated with docetaxel alone. Hypertension has been reported in the post-marketing setting. In the vast majority of cases, the reported events of hypertension are non-serious.
Risk factors and risk groups	Common risk factors for hypertension are smoking (history of), overweight/obesity, not being physically active, stress, metabolic disorders (dyslipidaemia, diabetes mellitus), advanced age, male gender, and race (Black).
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC sections 4.2 and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Myocardial infarction	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), AEs reflecting MI were infrequently reported and slightly less frequent in the Vargatef arm compared to the placebo arm. In the post-marketing setting, cases of MI have been infrequently reported, some of the cases being in patients with risk factors.
Risk factors and risk groups	Patients who have experienced ATE, including MI, are at an increased risk to experience further thromboembolic events. Chemotherapy itself is considered to be one of the most important risk factors for venous and arterial thromboembolic events in the cancer setting. Cancer patients on chemotherapy presenting predisposing factors in their medical history (such as smoking history, obesity, diabetes, and previous cardiovascular disease) are at a higher risk to experience ATE, including MI.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2, 4.4, and 4.8. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Arterial thromboembolism excluding myocardial infarction	
Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), in NSCLC the frequency of ATE was comparable between the 2 treatment arms. However, in the pivotal clinical trials in IPF, an increased frequency of ATE was observed in patients treated with nintedanib monotherapy as compared to patients treated with placebo. Different medical history and risk factors of the IPF patient population need to be taken into consideration. In the post-marketing setting in NSCLC, a low number of ATE cases has been reported, mainly in patients with risk factors.
Risk factors and risk groups	Patients who have experienced ATE (including MI and coronary artery disease) are at an increased risk of experiencing further thromboembolic events. Chemotherapy itself is considered to be one of the most important risk factors for venous and arterial thromboembolic events in the cancer setting. Cancer patients on chemotherapy presenting predisposing factors (such as smoking history, obesity, diabetes, and previous cardiovascular disease) in their medical history are at higher risk of experiencing ATE.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Treatment in pregnant women and teratogenicity	
Evidence for linking the risk to the medicine	Angiogenesis is critical to foetal development. Following administration of nintedanib to rats, the inhibition of angiogenesis resulted in absorption of foetuses and increased incidence of malformations. These effects occurred at dose levels resulting in plasma drug concentrations comparable to, or lower than, those reached in humans during treatment with Vargatef.
Risk factors and risk groups	Women of childbearing potential are at risk to become pregnant, if they do not use effective contraception or failure of contraception occurs.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.6. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Hepatic failure	
Evidence for linking the risk to the medicine	'Liver enzyme elevations and hyperbilirubinaemia including DILI' is an important identified risk of Vargatef. DILI can be severe and can lead to hepatic failure. In the pivotal clinical trial of Vargatef (trial 1199.13), the majority of the AEs included in the medical concept of 'hepatic failure' (including precursors and symptoms), were liver enzyme elevations which were reversible in the majority of cases. In the post-marketing setting, reported events comprised liver enzyme elevations and/or hepatic events as a consequence of the underlying malignancy. None of the reported events met the medical definition of hepatic failure.
Risk factors and risk groups	Not known in patients with NSCLC.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2 and 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Cardiac failure	
Evidence for linking the risk to the medicine	Some approved VEGF inhibitors (bevacizumab, sorafenib, sunitinib, and pazopanib) are associated with undesirable effects such as cardiac failure, congestive cardiac failure, or decrease in left ventricular ejection fraction. The range of kinases inhibited by TKIs is variable. It is currently not possible to define a specific class of typical TKIs that may be considered to have a higher risk of inducing cardiovascular events.
Risk factors and risk groups	Main risk factors for cardiac failure are increasing age, family history, hypertension, and coronary artery disease, including a history of MI. Other risk factors are diabetes mellitus, obesity, metabolic syndrome, and other cardiac disorders (e.g. arrhythmia, cardiac valve disorder). Additional risk factors in cancer patients are previous cardiotoxic anticancer therapies.
Risk minimisation measures	Routine risk minimisation measures: Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

QT prolongation	
Evidence for linking the risk to the medicine	QT prolongation and/or torsades de pointes have been reported with some VEGF inhibitors (e.g. sunitinib, vandetanib, sorafenib, and pazopanib). Nintedanib did neither show inhibition of the hERG channel nor unequivocally drug-related effects on heart rate, QT interval, or any other ECG parameter *in vivo* at relevant human therapeutic plasma concentrations. In a dedicated clinical trial of nintedanib monotherapy in patients with renal cell carcinoma, single oral doses, as well as multiple oral doses, of 200 mg nintedanib administered twice daily for 15 days did not prolong the QTcF interval. In the pivotal clinical trial of Vargatef (trial 1199.13) and in the post-marketing setting, no AEs indicating QT prolongation have been reported.
Risk factors and risk groups	Risk factors for QT prolongation are female gender, low serum potassium, low serum magnesium, bradycardia, left ventricular hypertrophy, congestive heart failure, recent conversion from atrial fibrillation, a family history of long QT syndrome, and use of QT prolonging drugs.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Treatment in breastfeeding women	
Evidence for linking the risk to the medicine	There is no information on the excretion of Vargatef and its metabolites in human breast milk. Data from non-clinical studies showed that only small amounts (<0.5% of the administered dose of the mother substance and its metabolites) were secreted into the milk of lactating rats. No administration of Vargatef during breastfeeding has been reported.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.6. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None
Treatment of patients with moderate and severe hepatic impairment (Child Pugh B/C)	
Evidence for linking the risk to the medicine	In patients with moderate hepatic impairment classified as Child Pugh B, limited safety data are available; the efficacy of Vargatef has not been investigated. In patients with severe hepatic impairment classified as Child Pugh C, the safety and efficacy of Vargatef have not been investigated. No patients with moderate or severe hepatic impairment have been identified among the reported post-marketing cases.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Sections 4.2 and 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

Treatment of patients with renal impairment	
Evidence for linking the risk to the medicine	The safety, efficacy, and pharmacokinetics of Vargatef have not been studied in patients with compromised renal function. Less than 1% of a single dose of Vargatef is excreted via the kidney. Thus, renal function is not thought to have an impact on elimination and/or Vargatef plasma levels. The reported events from post-marketing in patients with renal impairment are consistent with the known safety profile of nintedanib administered in combination with docetaxel and the advanced tumour disease, with no information to suggest any new safety concern.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.2. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None
Treatment of patients with healing wounds	
Evidence for linking the risk to the medicine	Due to its mechanism of action, Vargatef may impair wound healing. Consequently, patients with major injuries and/or surgery within 10 days prior to trial randomisation, or with incomplete wound healing, were excluded from trial 1199.13. No formal studies investigating the effect of Vargatef on wound healing have been performed. The available information about the safety of Vargatef in patients with healing wounds from post-marketing is very limited.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None
Treatment of subpopulations with co-morbid CNS conditions such as dementia, depression, brain metastasis, or with co-morbid conditions such as arthritis and	

osteoporosis	
Evidence for linking the risk to the medicine	Patients with active brain metastases were excluded from trial 1199.13 because of a potential risk of intracranial bleeding and a potential for progression of neurological symptoms. In trial 1199.13, a limited number of patients in both treatment arms had stable brain metastases. No intracranial haemorrhage has been reported in trial 1199.13. In cases from post-marketing, it is not possible to identify whether a patient had active or stable brain metastases. The reported events in patients with brain metastases reflect the advanced tumour disease or consequences of the brain metastases. Otherwise, the reported events are consistent with the known safety profile of nintedanib administered in combination with docetaxel. In trial 1199.13, there were no patients with dementia at baseline. The available information about the safety of Vargatef in patients with dementia from post-marketing is very limited. In trial 1199.13, the number of patients with depression, arthritis, and osteoporosis was too small to allow for a meaningful analysis. The events reported from post-marketing in patients with depression and in patients with osteoporosis are consistent with the known safety profile of Vargatef and the advanced tumour disease. The events reported in patients with arthritis are consistent with the known safety profile of Vargatef, the advanced tumour disease, and pre-existing disorders/concomitant medications in these patients.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.4. (only concerning patients with brain metastases) Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None
Treatment of patients weighing <50 kg	

Evidence for linking the risk to the medicine	In the pivotal clinical trial of Vargatef (trial 1199.13), only a small number of patients weighed less than 50 kg, both in the overall population (Vargatef: 32 patients; placebo: 34 patients) and in the adenocarcinoma population (Vargatef: 17 patients; placebo: 20 patients). Population PK analyses showed an inverse correlation between body weight and exposure to nintedanib. In the post-marketing setting, many patients with a weight lower than 50 kg are experiencing tumour progression or consequences of tumour progression. The remaining events are consistent with the known safety profile of Vargatef, and docetaxel or events that are related to the underlying NSCLC.
Risk minimisation measures	Routine risk minimisation measures: Labelling in SmPC Section 4.4. Prescription only medicine. Treatment with Vargatef should be initiated and supervised by a physician experienced in the use of anticancer therapies. Additional risk minimisation measures: None

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 Vargatef.

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

There are no studies required for Vargatef.

ABBREVIATIONS

ATE	Arterial thromboembolism
CNS	Central nervous system
CTC AE	Common Terminology Criteria for Adverse Event
DILI	Drug-induced liver injury
EMA	European Medicines Agency
EPAR	European Public Assessment Report
GI	Gastro-intestinal
IPF	Idiopathic pulmonary fibrosis
MI	Myocardial infarction
NSCLC	Non-small cell lung cancer
RMP	Risk Management Plan
SmPC	Summary of Product Characteristics
TKI	Tyrosine kinase inhibitor
VTE	Venous thromboembolism