Prescribing Information (Great Britain)

Ofev® (nintedanib) 100 mg and 150 mg soft capsules

Soft capsules containing 100 mg or 150 mg nintedanib (as esilate). **Indication:** Ofev is indicated in adults for the treatment of idiopathic pulmonary fibrosis (IPF), other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype and systemic sclerosis associated interstitial lung disease (SSc-ILD). **Dose and Administration:** Treatment should be initiated by physicians experienced in the management of diseases for which Ofev 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. Dose adjustments: In addition to symptomatic treatment if applicable, the management of adverse reactions to Ofev could include dose reduction and temporary interruption until the specific adverse reaction has resolved to levels that allow continuation of therapy. Ofev treatment may be resumed at the full dose (150 mg twice daily in adult patients) or a reduced dose (100 mg twice daily in adult patients). If an adult patient does not tolerate 100 mg twice daily, treatment with Ofev should be discontinued. If diarrhoea, nausea and/or vomiting persist despite appropriate supportive care (including anti-emetic therapy), dose reduction or treatment interruption may be required. The treatment may be resumed at a reduced dose (100 mg twice daily in adult patients) or at the full dose (150 mg twice daily in adult patients). In case of persisting severe diarrhoea, nausea and/or vomiting despite symptomatic treatment, therapy with Ofev should be discontinued. In case of interruptions due to aspartate aminotransferase (AST) or alanine aminotransferase (ALT) elevations > 3× upper limit of normal (ULN), once transaminases have returned to baseline values, treatment with Ofev may be reintroduced at a reduced dose (100 mg twice daily in adult patients) which subsequently may be increased to the full dose (150 mg twice daily in adult patients). Elderly patients (≥ 65 years) No overall differences in safety and efficacy were observed for elderly patients. No a-priori dose adjustment is required in elderly patients. Patients ≥ 75 years may be more likely to require dose reduction to manage adverse effects. Renal impairment: Adjustment of the starting dose in patients with mild to moderate renal impairment is not required. The safety, efficacy, and pharmacokinetics of nintedanib have not been studied in patients with severe renal impairment (<30 mL/min creatinine clearance). Hepatic impairment: In adult patients with mild hepatic impairment (Child Pugh A), the recommended dose of Ofev is 100 mg twice daily approximately 12 hours apart. In patients with mild hepatic impairment (Child Pugh A), treatment interruption or discontinuation for management of adverse reactions should be considered. The safety and efficacy of nintedanib have not been investigated in patients with hepatic impairment classified as Child Pugh B and C. Treatment of patients with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment with Ofev is not recommended. Paediatric population: Nintedanib should not be used in children. Method of administration: Ofev 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. **Contraindications:** Pregnancy; Hypersensitivity to nintedanib, to peanut or soya, or to any of the excipients. **Warnings and Precautions:** Gastrointestinal disorders: *Diarrhoea:* Serious cases of diarrhoea leading to dehydration and electrolyte disturbances have been reported in the post-marketing. Patients should be treated at first signs with adequate hydration and anti-diarrhoeal medicinal products, e.g. loperamide, and may require dose reduction or treatment interruption. Ofev treatment may be resumed at a reduced dose or at the full dose (see Dose and Administration – Dose adjustments). In case of persisting severe diarrhoea despite symptomatic treatment, therapy with Ofev should be discontinued. *Nausea and vomiting:* If symptoms persist despite appropriate supportive care (including anti-emetic therapy), dose reduction or treatment interruption may be required. The treatment may be resumed at a reduced dose or at the full dose (see Dose and Administration – Dose adjustments). In case of persisting severe symptoms therapy with Ofev should be discontinued. Hepatic function: Treatment with Ofev is not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Based on increased exposure, the risk for adverse reactions may be increased in patients with mild hepatic impairment (Child Pugh A). Adult patients with mild hepatic impairment (Child Pugh A) should be treated with a reduced dose of Ofev. Cases of drug-induced liver injury have been observed with nintedanib treatment, including severe liver injury with fatal outcome. The majority of hepatic events occur within the first three months of treatment. Therefore, hepatic transaminase and bilirubin levels should be investigated before treatment initiation and during the first month of treatment with Ofev. Patients should then be monitored at regular intervals during the subsequent two months of treatment and periodically thereafter, e.g. at each patient visit or as clinically indicated. Elevations of liver enzymes (ALT, AST, blood alkaline phosphatase (ALKP), gamma-glutamyl-transferase (GGT)) and bilirubin were reversible upon dose reduction or interruption in the majority of cases. If transaminase (AST or ALT) elevations > 3× ULN are measured, dose reduction or interruption of the therapy with Ofev is recommended and the patient should be monitored closely. Once transaminases have returned to baseline values, treatment with Ofev may be resumed at the full dose or reintroduced at a reduced dose which subsequently may be increased to the full dose (see Dose and Administration – Dose adjustments). If any liver test elevations are associated with clinical signs or symptoms of liver injury, e.g. jaundice, treatment with Ofev should be permanently discontinued. Alternative causes of the liver enzyme elevations should be investigated. Adult patients with low body weight (< 65 kg), Asian and female patients have a higher risk of elevations of liver enzymes. Nintedanib exposure increased linearly with patient age, which may also result in a higher risk of developing liver enzyme elevations. Close monitoring is recommended in patients with these risk factors. Renal function: Cases of renal impairment/failure, in some cases with fatal outcome, have been reported with nintedanib use. Patients should be monitored during nintedanib therapy, with particular attention to those patients exhibiting risk factors for renal impairment/failure. In case of renal impairment/failure, therapy adjustment should be considered. Haemorrhage: Vascular endothelial growth factor receptor (VEGFR) inhibition might be associated with an increased risk of bleeding. Non-serious and serious bleeding events, some of which were fatal, have been reported in the post-marketing period (including patients with or without anticoagulant therapy or other medicinal products that could cause bleeding), patients at known risk for bleeding including patients with inherited predisposition to bleeding or patients receiving a full dose of anticoagulative treatment should only be treated with Ofev if the anticipated benefit outweighs the potential risk. Arterial thromboembolic events: Caution should be used when treating patients at higher cardiovascular risk including known coronary artery disease. Treatment interruption should be considered in patients who develop signs or symptoms of acute myocardial ischemia. Aneurysms and artery dissections: The use of VEGF pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating Ofev, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm. Venous thromboembolism: Due to the mechanism of action of nintedanib patients might have an increased risk of thromboembolic events. Gastrointestinal perforations and ischaemic colitis: Due to the mechanism of action of nintedanib patients might have an increased risk of gastrointestinal perforation. Cases of gastrointestinal perforations and cases of ischaemic colitis, some of which were fatal, have been reported in the post-marketing period. Particular caution should be exercised when treating patients with previous abdominal surgery, previous history of peptic ulceration, diverticular disease or receiving concomitant corticosteroids or NSAIDs. Ofev should only be initiated at least 4 weeks after abdominal surgery. Therapy with Ofev should be permanently discontinued in patients who develop gastrointestinal perforation or ischaemic colitis. Exceptionally, Ofev can be reintroduced after complete resolution of ischaemic colitis and careful assessment of patient's condition and other risk factors. Nephrotic range proteinuria and thrombotic microangiopathy: Very few cases of nephrotic range proteinuria with or without renal function impairment have been reported post-marketing. Histological findings in individual cases were consistent with glomerular microangiopathy with or without renal thrombi. Reversal of the symptoms has been observed after Ofev was discontinued, with residual proteinuria in some cases. Treatment interruption should be considered in patients who develop signs or symptoms of nephrotic syndrome. VEGF pathway inhibitors have been associated with thrombotic microangiopathy (TMA), including very few case reports for nintedanib. If laboratory or clinical findings associated with TMA occur in a patient receiving nintedanib, treatment with nintedanib should be discontinued and thorough evaluation for TMA should be completed. Hypertension: Administration of Ofev may increase blood pressure. Systemic blood pressure should be measured periodically and as clinically indicated. Pulmonary hypertension: Data on the use of Ofev in patients with pulmonary hypertension is limited. Ofev should not be used in patients with severe pulmonary hypertension. Close monitoring is recommended in patients with mild to moderate pulmonary hypertension. Wound healing complication: Based on the mechanism of action nintedanib may impair wound healing. Treatment with Ofev should therefore only be initiated or - in case of perioperative interruption - resumed based on clinical judgement of adequate wound healing. Co-administration with pirfenidone: The benefit/risk of the co-administration of nintedanib with pirfenidone has not been established. Effect on QT interval: Caution should be exercised when nintedanib is administered in patients who may develop QTc prolongation. Allergic reaction: Dietary soya products are known to cause allergic reactions including severe anaphylaxis in persons with soya allergy. Patients with known allergy to peanut protein carry an enhanced risk for severe reactions to soya preparations. **Interactions:** P-glycoprotein (P-gp): Nintedanib is a substrate of P-gp. If co-administered with Ofev, potent P-gp inhibitors (e.g. ketoconazole, erythromycin or cyclosporine) may increase exposure to nintedanib. In such cases, patients should be monitored closely for tolerability of nintedanib. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with Ofev. Potent P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin and St. John's Wort) may decrease exposure to nintedanib. Selection of an alternate concomitant medicinal product with no or minimal P-gp induction potential should be considered. Cytochrome (CYP)-enzymes: Likelihood of drug-drug interactions with nintedanib based on CYP metabolism considered to be low. Other medicinal products: Co-administration of nintedanib with oral hormonal contraceptives did not alter the pharmacokinetics of oral hormonal contraceptives to a relevant extent. Co-administration of nintedanib with bosentan did not alter the pharmacokinetics of nintedanib. **Fertility, Pregnancy and Lactation:** Nintedanib may cause foetal harm in humans. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Ofev and to use highly effective contraceptive methods at initiation of, during and at least 3 months after the last dose of Ofev. Nintedanib does not relevantly affect the plasma exposure of ethinylestradiol and levonorgestrel. The efficacy of oral hormonal contraceptives may be compromised by vomiting and/or diarrhoea or other conditions where the absorption may be affected. Women taking oral hormonal contraceptives experiencing these conditions should be advised to use an alternative highly effective contraceptive measure. There is no information on the use of Ofev in pregnant women, but pre-clinical studies in animals have shown reproductive toxicity. As nintedanib may cause foetal harm also in humans, it must not be used during pregnancy and pregnancy testing must be conducted prior to treatment with Ofev and during treatment as appropriate. Female patients should be advised to notify their doctor or pharmacist if they become pregnant during therapy with Ofev. If the patient becomes pregnant while receiving Ofev, treatment must be discontinued and she should be apprised of the potential hazard to the foetus. There is no information on the excretion of nintedanib and its metabolites in human milk. Pre-clinical studies showed that small amounts of nintedanib and its metabolites (≤ 0.5% of the administered dose) were secreted into milk of lactating rats. A risk to the newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with Ofev. Based on preclinical investigations there is no evidence for impairment of male fertility. From subchronic and chronic toxicity studies, there is no evidence that female fertility in rats is impaired at a systemic exposure level comparable with that at the maximum recommended human dose (MRHD) of 150 mg twice daily. **Undesirable effects:** IPF: Very common (≥ 1/10): diarrhoea, nausea, abdominal pain, hepatic enzyme increased. Common (≥ 1/100 < 1/10): weight decreased, decreased appetite, bleeding, vomiting, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, gamma glutamyl transferase (GGT) increased, rash, headache. Uncommon (≥ 1/1000 < 1/100): thrombocytopenia, dehydration, myocardial infarction, hypertension, pancreatitis, colitis, drug induced liver injury, hyperbilirubinaemia, blood alkaline phosphatase (ALKP) increased, pruritus, alopecia, proteinuria. Not known (cannot be estimated from the available data): aneurysms and artery dissections, renal failure. Other chronic fibrosing ILDs with a progressive phenotype: Very common (≥ 1/10): decreased appetite, diarrhoea, nausea, abdominal pain, vomiting, hepatic enzyme increased, ALT increased. Common (≥ 1/100 < 1/10): weight decreased, bleeding, hypertension, drug induced liver injury, AST increased, GGT increased, ALKP increased, rash, headache. Uncommon (≥ 1/1000 < 1/100): thrombocytopenia, dehydration, myocardial infarction, pancreatitis, colitis, hyperbilirubinaemia, pruritus, alopecia, proteinuria. Not known (cannot be estimated from the available data): aneurysms and artery dissections, renal failure. SSc-ILD: Very common (≥ 1/10): diarrhoea, nausea, abdominal pain, vomiting, hepatic enzyme increased. Common (≥ 1/100 < 1/10): weight decreased, decreased appetite, bleeding, hypertension, ALT increased, AST increased, GGT increased, ALKP increased, headache. Uncommon (≥ 1/1000 < 1/100): thrombocytopenia, colitis, drug induced liver injury, rash, pruritus, renal failure. Not known (cannot be estimated from the available data): dehydration, myocardial infarction, aneurysms and artery dissections, pancreatitis, hyperbilirubinaemia, alopecia, proteinuria. Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 100 mg x 60 capsules £2151.10; 150 mg x 60 capsules £2151.10. **Legal category:** POM. **MA numbers:** 100 mg PLGB 14598/0215; 150 mg PLGB 14598/0216. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in August 2023.**

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Boehringer Ingelheim Drug Safety on 0800 328 1627 (freephone).

Prescribing Information (Northern Ireland)

Ofev® (nintedanib) 100 mg and 150 mg soft capsules

Soft capsules containing 100 mg or 150 mg nintedanib (as esilate). **Indication:** Ofev is indicated in adults for the treatment of idiopathic pulmonary fibrosis (IPF), other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype and systemic sclerosis associated interstitial lung disease (SSc-ILD). **Dose and Administration:** Treatment should be initiated by physicians experienced in the management of diseases for which Ofev 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. Dose adjustments: In addition to symptomatic treatment if applicable, the management of adverse reactions to Ofev could include dose reduction and temporary interruption until the specific adverse reaction has resolved to levels that allow continuation of therapy. Ofev treatment may be resumed at the full dose (150 mg twice daily in adult patients) or a reduced dose (100 mg twice daily in adult patients). If an adult patient does not tolerate 100 mg twice daily, treatment with Ofev should be discontinued. If diarrhoea, nausea and/or vomiting persist despite appropriate supportive care (including anti-emetic therapy), dose reduction or treatment interruption may be required. The treatment may be resumed at a reduced dose (100 mg twice daily in adult patients) or at the full dose (150 mg twice daily in adult patients). In case of persisting severe diarrhoea, nausea and/or vomiting despite symptomatic treatment, therapy with Ofev should be discontinued. In case of interruptions due to aspartate aminotransferase (AST) or alanine aminotransferase (ALT) elevations > 3× upper limit of normal (ULN), once transaminases have returned to baseline values, treatment with Ofev may be reintroduced at a reduced dose (100 mg twice daily in adult patients) which subsequently may be increased to the full dose (150 mg twice daily in adult patients). Elderly patients (≥ 65 years) No overall differences in safety and efficacy were observed for elderly patients. No a-priori dose adjustment is required in elderly patients. Patients ≥ 75 years may be more likely to require dose reduction to manage adverse effects. Renal impairment: Adjustment of the starting dose in patients with mild to moderate renal impairment is not required. The safety, efficacy, and pharmacokinetics of nintedanib have not been studied in patients with severe renal impairment (<30 mL/min creatinine clearance). Hepatic impairment: In adult patients with mild hepatic impairment (Child Pugh A), the recommended dose of Ofev is 100 mg twice daily approximately 12 hours apart. In patients with mild hepatic impairment (Child Pugh A), treatment interruption or discontinuation for management of adverse reactions should be considered. The safety and efficacy of nintedanib have not been investigated in patients with hepatic impairment classified as Child Pugh B and C. Treatment of patients with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment with Ofev is not recommended. Paediatric population: Nintedanib should not be used in children. Method of administration: Ofev 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. **Contraindications:** Pregnancy; Hypersensitivity to nintedanib, to peanut or soya, or to any of the excipients. **Warnings and Precautions:** Gastrointestinal disorders: *Diarrhoea:* Serious cases of diarrhoea leading to dehydration and electrolyte disturbances have been reported in the post-marketing. Patients should be treated at first signs with adequate hydration and anti-diarrhoeal medicinal products, e.g. loperamide, and may require dose reduction or treatment interruption. Ofev treatment may be resumed at a reduced dose or at the full dose (see Dose and Administration – Dose adjustments). In case of persisting severe diarrhoea despite symptomatic treatment, therapy with Ofev should be discontinued. *Nausea and vomiting:* If symptoms persist despite appropriate supportive care (including anti-emetic therapy), dose reduction or treatment interruption may be required. The treatment may be resumed at a reduced dose or at the full dose (see Dose and Administration – Dose adjustments). In case of persisting severe symptoms therapy with Ofev should be discontinued. Hepatic function: Treatment with Ofev is not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Based on increased exposure, the risk for adverse reactions may be increased in patients with mild hepatic impairment (Child Pugh A). Adult patients with mild hepatic impairment (Child Pugh A) should be treated with a reduced dose of Ofev. Cases of drug-induced liver injury have been observed with nintedanib treatment, including severe liver injury with fatal outcome. The majority of hepatic events occur within the first three months of treatment. Therefore, hepatic transaminase and bilirubin levels should be investigated before treatment initiation and during the first month of treatment with Ofev. Patients should then be monitored at regular intervals during the subsequent two months of treatment and periodically thereafter, e.g. at each patient visit or as clinically indicated. Elevations of liver enzymes (ALT, AST, blood alkaline phosphatase (ALKP), gamma-glutamyl-transferase (GGT)) and bilirubin were reversible upon dose reduction or interruption in the majority of cases. If transaminase (AST or ALT) elevations > 3× ULN are measured, dose reduction or interruption of the therapy with Ofev is recommended and the patient should be monitored closely. Once transaminases have returned to baseline values, treatment with Ofev may be resumed at the full dose or reintroduced at a reduced dose which subsequently may be increased to the full dose (see Dose and Administration – Dose adjustments). If any liver test elevations are associated with clinical signs or symptoms of liver injury, e.g. jaundice, treatment with Ofev should be permanently discontinued. Alternative causes of the liver enzyme elevations should be investigated. Adult patients with low body weight (< 65 kg), Asian and female patients have a higher risk of elevations of liver enzymes. Nintedanib exposure increased linearly with patient age, which may also result in a higher risk of developing liver enzyme elevations. Close monitoring is recommended in patients with these risk factors. Renal function: Cases of renal impairment/failure, in some cases with fatal outcome, have been reported with nintedanib use. Patients should be monitored during nintedanib therapy, with particular attention to those patients exhibiting risk factors for renal impairment/failure. In case of renal impairment/failure, therapy adjustment should be considered. Haemorrhage: Vascular endothelial growth factor receptor (VEGFR) inhibition might be associated with an increased risk of bleeding. Non-serious and serious bleeding events, some of which were fatal, have been reported in the post-marketing period (including patients with or without anticoagulant therapy or other medicinal products that could cause bleeding), patients at known risk for bleeding including patients with inherited predisposition to bleeding or patients receiving a full dose of anticoagulative treatment should only be treated with Ofev if the anticipated benefit outweighs the potential risk. Arterial thromboembolic events: Caution should be used when treating patients at higher cardiovascular risk including known coronary artery disease. Treatment interruption should be considered in patients who develop signs or symptoms of acute myocardial ischemia. Aneurysms and artery dissections: The use of VEGF pathway inhibitors in patients with or without hypertension may promote the formation of aneurysms and/or artery dissections. Before initiating Ofev, this risk should be carefully considered in patients with risk factors such as hypertension or history of aneurysm. Venous thromboembolism: Due to the mechanism of action of nintedanib patients might have an increased risk of thromboembolic events. Gastrointestinal perforations and ischaemic colitis: Due to the mechanism of action of nintedanib patients might have an increased risk of gastrointestinal perforation. Cases of gastrointestinal perforations and cases of ischaemic colitis, some of which were fatal, have been reported in the post-marketing period. Particular caution should be exercised when treating patients with previous abdominal surgery, previous history of peptic ulceration, diverticular disease or receiving concomitant corticosteroids or NSAIDs. Ofev should only be initiated at least 4 weeks after abdominal surgery. Therapy with Ofev should be permanently discontinued in patients who develop gastrointestinal perforation or ischaemic colitis. Exceptionally, Ofev can be reintroduced after complete resolution of ischaemic colitis and careful assessment of patient's condition and other risk factors. Nephrotic range proteinuria and thrombotic microangiopathy: Very few cases of nephrotic range proteinuria with or without renal function impairment have been reported post-marketing. Histological findings in individual cases were consistent with glomerular microangiopathy with or without renal thrombi. Reversal of the symptoms has been observed after Ofev was discontinued, with residual proteinuria in some cases. Treatment interruption should be considered in patients who develop signs or symptoms of nephrotic syndrome. VEGF pathway inhibitors have been associated with thrombotic microangiopathy (TMA), including very few case reports for nintedanib. If laboratory or clinical findings associated with TMA occur in a patient receiving nintedanib, treatment with nintedanib should be discontinued and thorough evaluation for TMA should be completed. Hypertension: Administration of Ofev may increase blood pressure. Systemic blood pressure should be measured periodically and as clinically indicated. Pulmonary hypertension: Data on the use of Ofev in patients with pulmonary hypertension is limited. Ofev should not be used in patients with severe pulmonary hypertension. Close monitoring is recommended in patients with mild to moderate pulmonary hypertension. Wound healing complication: Based on the mechanism of action nintedanib may impair wound healing. Treatment with Ofev should therefore only be initiated or - in case of perioperative interruption - resumed based on clinical judgement of adequate wound healing. Co-administration with pirfenidone: The benefit/risk of the co-administration of nintedanib with pirfenidone has not been established. Effect on QT interval: Caution should be exercised when nintedanib is administered in patients who may develop QTc prolongation. Allergic reaction: Dietary soya products are known to cause allergic reactions including severe anaphylaxis in persons with soya allergy. Patients with known allergy to peanut protein carry an enhanced risk for severe reactions to soya preparations. **Interactions:** P-glycoprotein (P-gp): Nintedanib is a substrate of P-gp. If co-administered with Ofev, potent P-gp inhibitors (e.g. ketoconazole, erythromycin or cyclosporine) may increase exposure to nintedanib. In such cases, patients should be monitored closely for tolerability of nintedanib. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with Ofev. Potent P-gp inducers (e.g. rifampicin, carbamazepine, phenytoin and St. John's Wort) may decrease exposure to nintedanib. Selection of an alternate concomitant medicinal product with no or minimal P-gp induction potential should be considered. Cytochrome (CYP)-enzymes: Likelihood of drug-drug interactions with nintedanib based on CYP metabolism considered to be low. Other medicinal products: Co-administration of nintedanib with oral hormonal contraceptives did not alter the pharmacokinetics of oral hormonal contraceptives to a relevant extent. Co-administration of nintedanib with bosentan did not alter the pharmacokinetics of nintedanib. **Fertility, Pregnancy and Lactation:** Nintedanib may cause foetal harm in humans. Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with Ofev and to use highly effective contraceptive methods at initiation of, during and at least 3 months after the last dose of Ofev. Nintedanib does not relevantly affect the plasma exposure of ethinylestradiol and levonorgestrel. The efficacy of oral hormonal contraceptives may be compromised by vomiting and/or diarrhoea or other conditions where the absorption may be affected. Women taking oral hormonal contraceptives experiencing these conditions should be advised to use an alternative highly effective contraceptive measure. There is no information on the use of Ofev in pregnant women, but pre-clinical studies in animals have shown reproductive toxicity. As nintedanib may cause foetal harm also in humans, it must not be used during pregnancy and pregnancy testing must be conducted prior to treatment with Ofev and during treatment as appropriate. Female patients should be advised to notify their doctor or pharmacist if they become pregnant during therapy with Ofev. If the patient becomes pregnant while receiving Ofev, treatment must be discontinued and she should be apprised of the potential hazard to the foetus. There is no information on the excretion of nintedanib and its metabolites in human milk. Pre-clinical studies showed that small amounts of nintedanib and its metabolites (≤ 0.5% of the administered dose) were secreted into milk of lactating rats. A risk to the newborns/infants cannot be excluded. Breast-feeding should be discontinued during treatment with Ofev. Based on preclinical investigations there is no evidence for impairment of male fertility. From subchronic and chronic toxicity studies, there is no evidence that female fertility in rats is impaired at a systemic exposure level comparable with that at the maximum recommended human dose (MRHD) of 150 mg twice daily. **Undesirable effects:** IPF: Very common (≥ 1/10): diarrhoea, nausea, abdominal pain, hepatic enzyme increased. Common (≥ 1/100 < 1/10): weight decreased, decreased appetite, bleeding, vomiting, alanine aminotransferase (ALT) increased, aspartate aminotransferase (AST) increased, gamma glutamyl transferase (GGT) increased, rash, headache. Uncommon (≥ 1/1000 < 1/100): thrombocytopenia, dehydration, myocardial infarction, hypertension, pancreatitis, colitis, drug induced liver injury, hyperbilirubinaemia, blood alkaline phosphatase (ALKP) increased, pruritus, alopecia, proteinuria. Not known (cannot be estimated from the available data): aneurysms and artery dissections, renal failure. Other chronic fibrosing ILDs with a progressive phenotype: Very common (≥ 1/10): decreased appetite, diarrhoea, nausea, abdominal pain, vomiting, hepatic enzyme increased, ALT increased. Common (≥ 1/100 < 1/10): weight decreased, bleeding, hypertension, drug induced liver injury, AST increased, GGT increased, ALKP increased, rash, headache. 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Prescribers should consult the Summary of Product Characteristics for further information on side effects. **Pack sizes and NHS price:** 100 mg x 60 capsules £2151.10; 150 mg x 60 capsules £2151.10. **Legal category:** POM. **MA numbers:** 100 mg EU/1/14/979/002; 150 mg EU/1/14/979/004. **Marketing Authorisation Holder:** Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 Ingelheim am Rhein, Germany. Prescribers should consult the Summary of Product Characteristics for full prescribing information. **Prepared in August 2023.**

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