



AVAILABLE OCT 1, 2020!

Newly Approved ICD-10-CM Code for Patients With Chronic Fibrosing Interstitial Lung Diseases (ILDs) With a Progressive Phenotype^{1,2}

»» Selecting the new ICD-10-CM code

The Centers for Medicare and Medicaid Services (CMS) approved an ICD-10-CM manifestation code to use for patients with chronic fibrosing ILDs with a progressive phenotype^{1,2}:

J84.170

Interstitial lung disease with a progressive fibrotic phenotype in diseases classified elsewhere



A chronic fibrosing ILD with a progressive phenotype is considered a manifestation of an underlying condition (ie, “in diseases classified elsewhere”) and may be coded with J84.170¹



Effective October 1, 2020, J84.170 will be available as an option to identify patients with chronic fibrosing ILDs with a progressive phenotype on the OFEV® (nintedanib) capsules Prescription Form, which can be submitted to health plans when prescribing OFEV for these patients. An underlying disease ICD-10-CM code should also be provided¹

Use of the information in this document, including the suggested ICD-10-CM code, does not guarantee that the health plan will provide reimbursement for OFEV, and it is not intended to be a substitute for, or an influence on, independent medical judgment.



Contact your Boehringer Ingelheim Reimbursement and Access Associate Director (RAAD) with questions or for more information

INDICATIONS

OFEV is indicated for the treatment of idiopathic pulmonary fibrosis (IPF). OFEV is indicated for the treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype.

OFEV is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD).

IMPORTANT SAFETY INFORMATION

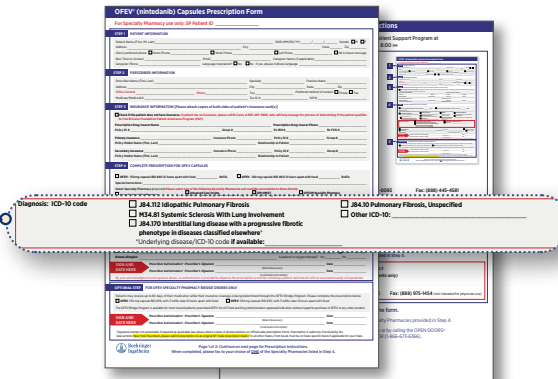
WARNINGS AND PRECAUTIONS

Hepatic Impairment: OFEV is not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Patients with mild hepatic impairment (Child Pugh A) can be treated with a reduced dosage (100 mg twice daily). Consider treatment interruption or discontinuation for management of adverse reactions.

Elevated Liver Enzymes and Drug-Induced Liver Injury

- Cases of drug-induced liver injury (DILI) have been observed with OFEV treatment. In the clinical trials and post-marketing period, non-serious and serious cases of DILI were reported. Cases of severe liver injury with fatal outcome have been reported in the post-marketing period. The majority of hepatic events occur within the first three months of treatment. OFEV was associated with elevations of liver enzymes (ALT, AST, ALKP, and GGT) and bilirubin. Liver enzyme and bilirubin increases were reversible with dose modification or interruption in the majority of cases.
- In IPF studies, the majority (94%) of patients with ALT and/or AST elevations had elevations less than 5 times ULN and the majority (95%) of patients with bilirubin elevations had elevations less than 2 times ULN.
- In the chronic fibrosing ILDs with a progressive phenotype study, the majority (95%) of patients with ALT and/or AST elevations had

»» Completing the OFEV prescription form



When prescribing OFEV for chronic fibrosing ILDs with a progressive phenotype:

- The OFEV prescription form has the option to select the new ICD-10-CM code, J84.170
 - Include the underlying disease ICD-10-CM code, if known

elevations less than 5 times ULN and the majority (94%) of patients with bilirubin elevations had elevations less than 2 times ULN.

- In the SSc-ILD study, a maximum ALT and/or AST greater than or equal to 3 times ULN was observed in 4.9% of patients treated with OFEV.
- Patients with low body weight (less than 65 kg), patients who are Asian, and female patients may have a higher risk of elevations in liver enzymes. Nintedanib exposure increased with patient age, which may result in increased liver enzymes.
- Conduct liver function tests prior to initiation of treatment, at regular intervals during the first three months of treatment, and periodically thereafter or as clinically indicated. Measure liver function tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Dosage modifications, interruption, or discontinuation may be necessary for liver enzyme elevations.

Gastrointestinal Disorders

Diarrhea

- Events were primarily mild to moderate in intensity and occurred within the first 3 months.
- In IPF studies, diarrhea was the most frequent gastrointestinal event reported in 62% versus 18% of patients treated with OFEV and placebo, respectively. Diarrhea led to permanent dose reduction in 11% and discontinuation in 5% of OFEV patients versus 0 and less than 1% in placebo patients, respectively.
- In the chronic fibrosing ILDs with a progressive phenotype study, diarrhea was reported in 67% versus 24% of patients treated with OFEV and placebo, respectively. Diarrhea led to permanent dose reduction in 16% and discontinuation in 6% of OFEV patients, compared to less than 1% of placebo-treated patients, respectively.

ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.

Please see additional Important Safety Information on next page and [click here](#) for full Prescribing Information, including Patient Information, for OFEV®.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Gastrointestinal Disorders (cont'd)

Diarrhea (cont'd)

- In the SSc-ILD study, diarrhea was the most frequent gastrointestinal event reported in 76% versus 32% of patients treated with OFEV and placebo, respectively. Diarrhea led to permanent dose reduction in 22% and discontinuation in 7% of OFEV patients versus 1% and 0.3% in placebo patients, respectively.
- Dosage modifications or treatment interruptions may be necessary in patients with diarrhea. Treat diarrhea at first signs with adequate hydration and antidiarrheal medication (e.g., loperamide), and consider dose reduction or treatment interruption if diarrhea continues. OFEV treatment may be resumed at the full dosage (150 mg twice daily), or at the reduced dosage (100 mg twice daily), which subsequently may be increased to the full dosage. If severe diarrhea persists, discontinue treatment.

Nausea and Vomiting

- In IPF studies, nausea was reported in 24% versus 7% and vomiting was reported in 12% versus 3% of patients treated with OFEV and placebo, respectively. Nausea and vomiting led to discontinuation of OFEV in 2% and 1% of patients, respectively.
- In the chronic fibrosing ILDs with a progressive phenotype study, nausea was reported in 29% versus 9% and vomiting was reported in 18% versus 5% of patients treated with OFEV and placebo, respectively. Nausea led to discontinuation of OFEV in less than 1% of patients, and vomiting led to discontinuation of OFEV in 1% of the patients.
- In the SSc-ILD study, nausea was reported in 32% versus 14% and vomiting was reported in 25% versus 10% of patients treated with OFEV and placebo, respectively. Nausea and vomiting led to discontinuation of OFEV in 2% and 1% of patients, respectively.
- In most patients, events were primarily of mild to moderate intensity. If nausea or vomiting persists despite appropriate supportive care including anti-emetic therapy, consider dose reduction or treatment interruption. OFEV treatment may be resumed at full dosage or at reduced dosage, which subsequently may be increased to full dosage. If severe nausea or vomiting does not resolve, discontinue treatment.

Embryo-Fetal Toxicity: OFEV can cause fetal harm when administered to a pregnant woman and patients should be advised of the potential risk to a fetus. Women should be advised to avoid becoming pregnant while receiving OFEV and to use highly effective contraception at initiation of treatment, during treatment, and at least 3 months after the last dose of OFEV. Nintedanib does not change the exposure to oral contraceptives containing ethinylestradiol and levonorgestrel in patients with SSc-ILD. However, the efficacy of oral hormonal contraceptives may be compromised by vomiting and/or diarrhea or other conditions where drug absorption may be reduced. Advise women taking oral hormonal contraceptives experiencing these conditions to use alternative highly effective contraception. Verify pregnancy status prior to starting OFEV and during treatment as appropriate.

Arterial Thromboembolic Events

- In IPF studies, arterial thromboembolic events were reported in 2.5% of OFEV and less than 1% of placebo patients, respectively. Myocardial infarction (MI) was the most common arterial thromboembolic event, occurring in 1.5% of OFEV and in less than 1% of placebo patients.
- In the chronic fibrosing ILDs with a progressive phenotype study, arterial thromboembolic events and MI were reported in less than 1% of patients in both treatment arms.
- In the SSc-ILD study, arterial thromboembolic events were reported in 0.7% of patients in both the OFEV-treated and placebo-treated patients. There were 0 cases of MI in OFEV-treated patients compared to 0.7% of placebo-treated patients.
- Use caution when treating patients at higher cardiovascular risk, including known coronary artery disease. Consider treatment interruption in patients who develop signs or symptoms of acute myocardial ischemia.

Risk of Bleeding

- OFEV may increase the risk of bleeding.
- In IPF studies, bleeding events were reported in 10% of OFEV versus 7% of placebo patients.
- In the chronic fibrosing ILDs with a progressive phenotype study, bleeding events were reported in 11% of OFEV versus 13% of placebo patients.

- In the SSc-ILD study, bleeding events were reported in 11% of OFEV versus 8% of placebo patients.
- In clinical trials, epistaxis was the most frequent bleeding event. There have been post-marketing reports of non-serious and serious bleeding events, some of which were fatal. Use OFEV in patients with known risk of bleeding only if the anticipated benefit outweighs the potential risk.

Gastrointestinal Perforation

- OFEV may increase the risk of gastrointestinal perforation.
- In IPF studies, gastrointestinal perforation was reported in less than 1% of OFEV versus in 0% of placebo patients.
- In the chronic fibrosing ILDs with a progressive phenotype study, gastrointestinal perforation was not reported in any treatment arm.
- In the SSc-ILD study, no cases of gastrointestinal perforation were reported in either OFEV or placebo-treated patients.
- In the post-marketing period, cases of gastrointestinal perforations have been reported, some of which were fatal. Use caution when treating patients who have had recent abdominal surgery, have a previous history of diverticular disease, or who are receiving concomitant corticosteroids or NSAIDs. Discontinue therapy with OFEV in patients who develop gastrointestinal perforation. Only use OFEV in patients with known risk of gastrointestinal perforation if the anticipated benefit outweighs the potential risk.

ADVERSE REACTIONS

- Most common adverse reactions reported (greater than or equal to 5%) are diarrhea, nausea, abdominal pain, vomiting, liver enzyme elevation, decreased appetite, headache, weight decreased and hypertension.
- In IPF studies, the most frequent serious adverse reactions reported in patients treated with OFEV, more than placebo, were bronchitis (1.2% vs. 0.8%) and MI (1.5% vs. 0.4%). The most common adverse events leading to death in OFEV patients versus placebo were pneumonia (0.7% vs. 0.6%), lung neoplasm malignant (0.3% vs. 0%), and myocardial infarction (0.3% vs. 0.2%). In the predefined category of major adverse cardiovascular events (MACE) including MI, fatal events were reported in 0.6% of OFEV versus 1.8% in placebo patients.
- In the chronic fibrosing ILDs with a progressive phenotype study, the most frequent serious adverse event reported in patients treated with OFEV, more than placebo, was pneumonia (4% vs. 3%). Adverse events leading to death were reported in 3% of OFEV patients and in 5% of placebo patients. No pattern was identified in the adverse events leading to death.
- In the SSc-ILD study, the most frequent serious adverse events reported in patients treated with OFEV, more than placebo, were interstitial lung disease (2.4% vs. 1.7%) and pneumonia (2.8% vs. 0.3%). Within 52 weeks, 5 patients treated with OFEV (1.7%) and 4 patients treated with placebo (1.4%) died. There was no pattern among adverse events leading to death in either treatment arm.

DRUG INTERACTIONS

- **P-glycoprotein (P-gp) and CYP3A4 Inhibitors and Inducers:** Coadministration with oral doses of a P-gp and CYP3A4 inhibitor, ketoconazole, increased exposure to nintedanib by 60%. Concomitant use of potent P-gp and CYP3A4 inhibitors (e.g., erythromycin) with OFEV may increase exposure to nintedanib. In such cases, patients should be monitored closely for tolerability of OFEV. Management of adverse reactions may require interruption, dose reduction, or discontinuation of therapy with OFEV. Coadministration with oral doses of a P-gp and CYP3A4 inducer, rifampicin, decreased exposure to nintedanib by 50%. Concomitant use of P-gp and CYP3A4 inducers (e.g., carbamazepine, phenytoin, and St. John's wort) with OFEV should be avoided as these drugs may decrease exposure to nintedanib.
- **Anticoagulants:** Nintedanib may increase the risk of bleeding. Monitor patients on full anticoagulation therapy closely for bleeding and adjust anticoagulation treatment as necessary.

USE IN SPECIFIC POPULATIONS

- **Nursing Mothers:** Because of the potential for serious adverse reactions in nursing infants from OFEV, advise women that breastfeeding is not recommended during treatment.
- **Reproductive Potential:** OFEV may reduce fertility in females of reproductive potential.
- **Smokers:** Smoking was associated with decreased exposure to OFEV, which may affect the efficacy of OFEV. Encourage patients to stop smoking prior to and during treatment.

CL-OF-100050 10.28.2020

References: 1. Centers for Medicare and Medicaid Services. 2021 ICD-10-CM. <https://www.cms.gov/medicare/icd-10/2021-icd-10-cm>. Accessed September 2, 2020. 2. Centers for Disease Control and Prevention. ICD-10-CM. <https://icd10cmtool.cdc.gov/?fy=FY2020>. Accessed September 9, 2020.

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