

Dear Healthcare Professional,

Please note that the sample Medical Exception Letter example on page 3 of this resource includes information that may be required when submitting a request to health plans to make a medical exception and permit access to OFEV® (nintedanib) capsules for your appropriate patients with chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype. **Please modify the content in the letter as needed based on your independent medical judgment and discretion when providing a diagnosis and characterization of the patient's medical condition.**

Some key reminders:

- You may consider using a letter like this if coverage of OFEV for chronic fibrosing ILDs with a progressive phenotype is denied because of a health plan's policy (eg, OFEV is nonformulary, policy has not yet been established)
- Medical exception letters should be signed by both the physician and the patient

Recently, a new ICD-10-CM code was finalized by the Centers for Medicare and Medicaid Services (CMS) to support the diagnosis of chronic fibrosing ILDs with a progressive phenotype. This code is J84.170: Interstitial lung disease with a progressive fibrotic phenotype in diseases classified elsewhere. Additionally, an underlying disease manifestation code (underlying systemic disease) needs to be provided if available (eg, lung diseases due to external agents [J60-J70]).

Use of the information in this document, including the 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, your independent medical judgment.

Before sending the medical exception letter to the health plan, please remove the title that states, "Sample General Medical Exception Letter Template."

INDICATION

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

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 the chronic fibrosing ILDs with a progressive phenotype study, the majority (95%) of patients with ALT and/or AST elevations had elevations less than 5 times ULN and the majority (94%) of patients with bilirubin elevations had elevations less than 2 times ULN.
- 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

- 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. Events were primarily mild to moderate in intensity and occurred within the first 3 months. 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.
- 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 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.

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



Copyright © 2020 Boehringer Ingelheim Pharmaceuticals, Inc.
All rights reserved. (11/20) PC-US-117669



IMPORTANT SAFETY INFORMATION (cont'd)**WARNINGS AND PRECAUTIONS (cont'd)****Gastrointestinal Disorders (cont'd)****Nausea and Vomiting (cont'd)**

- 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 the chronic fibrosing ILDs with a progressive phenotype study, arterial thromboembolic events and myocardial infarction were reported in less than 1% of patients in both treatment arms. 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 the chronic fibrosing ILDs with a progressive phenotype study, bleeding events were reported in 11% of OFEV versus in 13% of placebo patients. In clinical trials, epistaxis was the most frequent bleeding event reported. 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 the chronic fibrosing ILDs with a progressive phenotype study, gastrointestinal perforation was not reported in any treatment arm. 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

- Adverse reactions reported in the chronic fibrosing ILDs with a progressive phenotype study in greater than or equal to 5% of OFEV patients, and more than placebo, were diarrhea, nausea, liver enzyme elevation, vomiting, abdominal pain, decreased appetite, weight decreased, headache, nasopharyngitis, upper respiratory infection, urinary tract infection, fatigue, and back pain.
- 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.

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-100051 10.28.2020

RE: Request for Medical Exception

To whom it may concern:

I am writing to you as a board-certified physician to request a medical exception for the above-mentioned patient who has a confirmed diagnosis of a chronic fibrosing interstitial lung disease (ILD) with a progressive phenotype. It is my professional opinion that OFEV® (nintedanib) capsules is medically appropriate and necessary, and should be covered and reimbursed for this patient.

_____ has been under my care for this chronic fibrosing ILD with a progressive phenotype since _____. Included for your consideration is _____ medical history and diagnosis _____, which summarizes my rationale for treating him/her with OFEV, a copy of the Prescribing Information for OFEV, and other pertinent information related to this request.

The enclosed Prescribing Information supports the use of this therapy that was approved by the FDA on March 9, 2020. The efficacy and safety of OFEV informing FDA approval was demonstrated in INBUILD®, a randomized, double-blind, placebo-controlled phase 3 trial with over 650 patients with chronic fibrosing ILDs with a progressive phenotype. Of note, OFEV is the only FDA-approved therapy for the treatment of chronic fibrosing ILDs with a progressive phenotype. Based upon the patient's clinical condition and a review of the supporting documentation, I am confident you will agree that _____ should be treated with OFEV. To provide appropriate care for my patient, it is important that _____ provide adequate coverage for this treatment.

In summary, my patient, _____, has a confirmed diagnosis of a chronic fibrosing ILD with a progressive phenotype. The goal of therapy is to reduce lung function decline, which OFEV was shown to do in the INBUILD® clinical trial. Please call me at _____ if you require additional information. Thank you in advance for your immediate attention and prompt review of this matter.

Sincerely,

DL_{CO}=diffusing capacity of the lungs for carbon monoxide; FEV₁=forced expiratory volume in 1 second; FVC=forced vital capacity; HRCT=high-resolution computed tomography; ICD-10-CM=*International Classification of Diseases, Tenth Revision, Clinical Modification*; PFTs=pulmonary function tests; TLC=total lung capacity.