For HCP office staff use only. Do not distribute.

Dear Healthcare Professional,

Please note that this sample Medical Exception Letter 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 systemic sclerosis–associated interstitial lung disease (SSc-ILD). **Please modify the content in the letter as needed based on your 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 SSc-ILD 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
- Be sure to populate an appropriate *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) code matching your patient's diagnosis

Use of the information in this document 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 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 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

- 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. Events were primarily mild to moderate in intensity and occurred within the first 3 months. 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 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. Events were primarily of mild to moderate intensity. Nausea and vomiting led to discontinuation of OFEV in 2% and 1% of patients, respectively.

Please see additional Important Safety Information on next page and full Prescribing Information for OFEV®.

Boehringer Ingelheim

OFEV® (nintedanib) capsules 150mg

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Gastrointestinal Disorders (cont'd)

***Nausea and Vomiting* (cont'd)**

- 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 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 myocardial infarction 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 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 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

- Adverse reactions reported in the SSc-ILD study in greater than or equal to 5% of OFEV patients, and more than placebo, included diarrhea, nausea, vomiting, skin ulcer, abdominal pain, liver enzyme elevation, weight decreased, fatigue, decreased appetite, headache, pyrexia, back pain, dizziness and hypertension.
- 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-100048 10.28.2020

Please see additional Important Safety Information on previous page and full Prescribing Information for OFEV®.

OFEV®
(nintedanib)
capsules 150mg

[Sample General Medical Exception Letter Template]

[Date]
[Health Plan Name]
[Health Plan Contact Name]
[Health Plan Mailing Address]
[Patient Name] [Patient Date of Birth]
[Subscriber ID#]
[Subscriber Group #]

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 systemic sclerosis–associated interstitial lung disease (SSc-ILD). It is my professional opinion that OFEV® (nintedanib) capsules are medically appropriate and necessary, and should be covered and reimbursed for this patient.

[Patient name] has been under my care for SSc-ILD since [date] . Included for your consideration is [patient name] medical history and diagnosis[ICD-10-CM code], a statement summarizing my rationale for treating him/her with OFEV, a copy of the Prescribing Information for OFEV, and other pertinent information related to this request.

[Summary of patient history:]
[• Management/previous management]
[• Response to each management/treatment]
[• Other factors that impact my treatment decision]
[• Date(s) and result(s) of last diagnostic test(s) (eg, PFTs, HRCT, biochemical testing)] [• Any relevant comorbidities]

The enclosed Prescribing Information supports the use of this therapy that was approved by the FDA on September 6, 2019. The efficacy and safety of OFEV informing FDA approval was demonstrated in a clinical trial with over 500 patients with SSc-ILD. The SENSCIS® study was a randomized, double-blind, placebo-controlled trial. Of note, SENSCIS® is the largest phase 3 clinical trial in SSc-ILD to date.

Based upon the patient's clinical condition and a review of the supporting documentation, I am confident you will agree that [patient name] should be treated with OFEV. In order for me to provide appropriate care for my patient, it is important that [health plan name] provide adequate coverage for this treatment.

In summary, my patient, [patient name], has a confirmed diagnosis of SSc-ILD—a life-limiting manifestation of systemic sclerosis (SSc). The goal of therapy is to reduce lung function decline, which OFEV was shown to do in the SENSCIS® clinical trial. Please call me at [physician phone number] if I can be of further assistance, or if you require additional information. Thank you in advance for your immediate attention and prompt review of this matter.

Sincerely,

[Physician Signature] [Patient/legal representative name]

[Physician name] [Patient/legal representative name]

[Enclosures include:]
[• OFEV prescribing information]
[• OFEV published clinical study]
[• Patient clinical/diagnostic records and related laboratory reports]
[— ICD-10-CM diagnosis code]
[— HRCT result indicating SSc-ILD]
[— Radiology report]
[— Pulmonary function tests (eg, FEV1/FVC, FVC, DLCO, TLC values)]
[• Patient authorization and notice of release of information]

DL_{CO}=diffusing capacity of the lungs for carbon monoxide; FEV_1=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.