For HCP office staff use only. Do not distribute.

Dear Healthcare Professional,

Please note that this sample physician letter of medical necessity on page 3 of this resource includes general guidance related to appealing treatment decisions and fulfilling prior authorizations (PAs). **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.** For additional guidance, a PA tips and checklist resource is also included.

Please be aware that PA requirements may vary according to health plan. For instance, the plan may require that only the patient submit a letter. In this case, it is the responsibility of the HCP to provide appropriate supporting documentation under separate cover.

Use of the information in this document does not guarantee that the health plan will provide reimbursement for OFEV® (nintedanib) capsules, and it is not intended to be a substitute for, or an influence on, your independent medical judgment.

Before sending the letter of medical necessity to the health plan, please remove the title that states, "Sample Letter of Medical Necessity: Physician."

INDICATION

OFEV is indicated in adults 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.
- 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.

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)

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.

Nephrotic Range Proteinuria: Cases of proteinuria within the nephrotic range have been reported in the postmarketing period. Histological findings, when available, were consistent with glomerular microangiopathy with or without renal thrombi. Improvement in proteinuria has been observed after OFEV was discontinued; however, in some cases, residual proteinuria persisted. Consider treatment interruption in patients who develop new or worsening proteinuria.

ADVERSE REACTIONS

- In the SSc-ILD study, adverse reactions reported in greater than or equal to 5% of OFEV patients were 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.

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

OFEV® (nintedanib) capsules 150mg

[Sample Letter of Medical Necessity: Physician]

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

RE: Authorization for OFEV® (nintedanib)

Dear Sir or Madam:

I am writing on behalf of the above-mentioned patient, [patient name] , to document the medical necessity and request authorization for OFEV® (nintedanib) capsules, to slow the rate of decline in pulmonary function for this patient with systemic sclerosis–associated interstitial lung disease (SSc-ILD).

On September 6, 2019, the US Food and Drug Administration (FDA) approved an indication for OFEV to slow the rate of decline in pulmonary function in patients with SSc-ILD. My patient, [patient name] , has a confirmed diagnosis of SSc-ILD, a life-limiting manifestation of systemic sclerosis. It is my professional opinion that OFEV is medically appropriate and necessary for the treatment of this disease in my patient. The goal of therapy is to slow the rate of decline in pulmonary function, which OFEV was shown to do in the SENSCIS® clinical trial.

I have attached the Prescribing Information that supports the use of this therapy. The efficacy and safety of OFEV informing FDA approval was demonstrated in a clinical trial of over 500 patients with SSc-ILD. The SENSCIS® trial was a randomized, double-blind, placebo-controlled trial. Of note, SENSCIS® is the largest phase 3 clinical trial in SSc-ILD to date, and currently, OFEV is the only oral therapy approved by the FDA to slow the rate of decline in pulmonary function in patients with SSc-ILD.

In light of this clinical information and my patient's condition, I am also enclosing the most recent copy of the patient's medical history and diagnosis [(ICD-10-CM code)] for your review and consideration for prior authorization approval.

In summary, OFEV offers therapy that can slow the rate of decline in pulmonary function in patients with SSc-ILD, so it is my professional opinion that OFEV is the appropriate choice for this patient.

[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]

Based upon the patient's clinical condition and a review of the supporting documentation, I am confident you will agree that this is the appropriate course of therapy.

Please feel free to contact me directly at [physician phone number] if you require additional information to make a determination.

Thank you in advance for your immediate attention and prompt review of this matter.

Sincerely,

[Physician signature] [Physician 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]
  - [— PFTs (eg, FEV_1/FVC, FVC, DL_{CO}, 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*; ILD=interstitial lung disease; PFTs=pulmonary function tests; TLC=total lung capacity.

PA TIPS AND CHECKLIST

Tips for Handling PA Requirements From Health Plans

This document provides a checklist and relevant tips that may be useful when creating a letter of medical necessity. Some plans have specific coverage authorization forms that must be utilized to document a letter of medical necessity. Follow the patient's plan requirements when requesting OFEV® (nintedanib) capsules to avoid treatment delays. Please contact third-party payers directly for specific information on their current coverage policies.

UNDERSTAND HEALTH PLAN REQUIREMENTS

- Be sure to fulfill any plan-specific guidelines and/or requirements for authorizing treatment

PROVIDE CORRECT IDENTIFICATION (ID) NUMBERS

- Indicate the individual provider ID number versus the group practice/facility provider ID number on the prescription form
- Obtain the patient ID number from his or her insurance card
- Provide correct ICD-10-CM diagnosis code(s) for the condition/diagnosis

INCLUDE SUPPORTING DOCUMENTS[a]

- Whenever possible, submit all required supporting documents with the PA request. For example, a health plan may need documentation showing the results from any laboratory testing
- Include a photocopy of the patient's health plan prescription card (front and back)

CHECK FOR THE STATEMENT OF MEDICAL NECESSITY

- The statement of medical necessity may need to be updated and/or resubmitted. This form is usually valid for 12 months from the original dated signature

BE AWARE OF DEADLINES

- Prepare in advance and collect any required documents to meet all deadlines for PA submission

FOLLOW UP

- If you do not receive a decision within 5 to 7 days, be sure to follow up via phone or email

MAINTAIN COMPLETE RECORDS

- Keep a copy of everything you submit for the PA. Keep a log of every phone call you make to the patient's health plan, including the date and the name of the person with whom you spoke

[a]Please be aware that PA requirements may vary according to health plan. For instance, the plan may require that only the patient submit a letter. In this case, it is the responsibility of the HCP to provide appropriate supporting documentation under separate cover.

PA TIPS AND CHECKLIST (CONT'D)

PA Submission Checklist

Prior authorization criteria may vary by plan. Please be sure to consult the website for the patient's insurer to confirm PA criteria, if available. Here is a checklist of the forms and documents you may need to submit to a health plan to obtain PA. (Be sure to fill out all requested information.)

- ☐ Sender and recipient contact information (eg, fax number, email address)
- ☐ Completed prescription form
- ☐ Copy of the patient's health insurance card and/or prescription card (include front and back), including all relevant membership numbers
- ☐ Supporting documentation (as required)[a]
  - ☐ PA form specific to health plan
  - ☐ Patient history and physical findings/diagnosis
  - ☐ Complete test and lab results, including:
    - HRCT indicating ILD
    - Radiology report
    - Pulmonary function tests (eg, FEV_1/FVC, FVC, DL_{CO}, TLC values)
  - ☐ Chart notes from healthcare provider or clinician
  - ☐ Hospital admission or emergency department notes, if applicable or relevant
  - ☐ Patient authorization and notice of release of information

Confirm receipt of documentation for all PA submissions and query for additional information if criteria are unclear.

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