For HCP office staff use only. Do not distribute.

Dear Healthcare Professional,

Please note that this sample patient appeal letter on page 3 of this resource includes general guidance related to appealing treatment decisions and fulfilling prior authorizations (PAs). **Please assist your patient in modifying the content in the letter as needed based on your medical judgment and discretion when providing a diagnosis and characterization of his or her medical condition.** For additional guidance, an appeal tips and checklist resource is also included.

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

These enclosures may include OFEV prescribing information, OFEV published clinical studies, patient clinical/diagnostic records and related laboratory reports, and HRCT and lung biopsy results indicating IPF (usual interstitial pneumonia).

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.

Please instruct your patient to remove the title from the appeal letter that states, "Sample Appeal Letter: Patient" before sending it to the health plan.

INDICATION

OFEV is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

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.
- Patients with a 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 IPF studies, diarrhea was the most frequent gastrointestinal event reported in 62% versus 18% 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 11% and discontinuation in 5% of OFEV patients versus 0 and less than 1% 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. 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 IPF studies, arterial thromboembolic events were reported in 2.5% of OFEV and in less than 1% of placebo patients, respectively. Myocardial infarction (MI) was the most common arterial thromboembolic event, occurring in 1.5% of OFEV and less than 1% of placebo 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 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 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

- In IPF studies, adverse reactions reported in greater than or equal to 5% of OFEV patients, and more than placebo, included diarrhea, nausea, abdominal pain, liver enzyme elevation, vomiting, decreased appetite, weight decreased, headache, 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 MI (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.

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 Appeal Letter: Patient]

[Date]
[Attention]
[Name of Health Plan]
[Health Plan Mailing Address]

[Patient Name]
[Patient Date of Birth]
[Patient ID#]

RE: Authorization for OFEV® (nintedanib)

Dear Appeal Reviewer for Idiopathic Pulmonary Fibrosis:

My name is [patient age] . I am a [patient age] -year-old [male/female] who has been diagnosed with idiopathic pulmonary fibrosis, also known as IPF. I am under the care of Dr [physician name] , who has prescribed OFEV® (nintedanib) capsules to treat my IPF. Dr [physician name] specializes in treating patients with respiratory and lung disorders.

I am writing this letter to appeal your recent decision to deny my doctor's request to use OFEV capsules to treat my diagnosed condition of IPF, and ask that you please reconsider and approve the request for treatment. Your denial on [denial date] , has caused me and my family much distress as there are not many clinical options for patients with IPF. OFEV treatment offers me hope.

I have enclosed the product prescribing information that I obtained from my physician, which describes and supports the use of this therapy that was approved by the US Food and Drug Administration (FDA) in 2014 for the indication of IPF. The safety and efficacy profile of OFEV informing the FDA approval for patients with IPF was based on three randomized, double-blind, placebo-controlled, multicenter trials: one phase 2 and two phase 3 trials.

In closing, I have been diagnosed with IPF and my physician has selected an appropriate therapy for the treatment of my disease. The goal of treatment is to reduce disease progression and lung function decline, which OFEV was shown to do in clinical trials. I would appreciate your consideration and approval of this important therapy. Thank you for your time and reconsideration of my request for OFEV treatment.

If you are seeking medical confirmation of my diagnosis, please contact my physician, Dr [physician name] , who can be reached by phone at [physician phone number] .

Sincerely,

[Patient signature]

APPEAL TIPS AND CHECKLIST

Tips for Filing an Appeal of Treatment Denial

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

IDENTIFY THE REASON FOR DENIAL

- Find out in writing why the authorization request has been denied. The reason should be in the denial letter from the patient's health plan or in the explanation of benefits letter. If you did not receive either of these, they can be obtained from the insurer

DETERMINE THE APPEAL GUIDELINES

- Contact the insurer to find out its deadline for appealing, the number of appeals permitted (some plans only allow one), and the mailing address or fax number to which the appeal should be sent. Some insurers have short appeal periods—you may need to respond promptly. Also, inquire whether the appeal should be submitted by the patient or the healthcare provider and proceed accordingly

CONTACT THE REVIEW DEPARTMENT

- Many denial letters include a telephone number for the review department that physicians can call for further clarification. If a reviewer agrees with your rationale and approves treatment for the patient during the call, the appeal process is completed

COMPOSE A WRITTEN APPEAL

- Most insurers require a written appeal from either the member or the healthcare provider. The insurer should tell you what is needed. A written appeal package includes an appeal letter and supporting documents

PROVIDE ADDITIONAL SUPPORTING DOCUMENTATION[a]

- A patient's appeal package should include all relevant medical documentation—including clinical notes and related test results—to support your case for coverage. Any newly available information related to the patient's condition should be supplied as well

CHECK PATIENT'S INSURER

- Do you know the type of insurance your patient has? Is the treatment a covered benefit? Are there state laws that may impact the treatment decision? Ask your patient to check his or her benefit plan to help determine whether the requested treatment is excluded. If it is, provide a written explanation as to why the plan should make an exception for your patient. Depending on the state where your practice is located, seeking an independent external review may be an option

FOLLOW UP AS NEEDED

- Contact the patient's insurer if they have not responded within 30 to 60 days of receipt of the appeal package

MAINTAIN COMPLETE RECORDS

- Retain a duplicate copy of all documentation submitted with the patient's appeal and record all subsequent communications made to the patient's insurer. Include the date and the name of the person contacted

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

APPEAL TIPS AND CHECKLIST (cont'd)

Documents for Filing a Response to Treatment Denial: An Appeal Checklist

If an insurer denies coverage of a prescribed treatment for your patient, the following is a sample checklist of materials you may need for an appeal package. Note that each appeal may need different information depending on the insurer and/or patient. Carefully review each denial and the insurer's requirements to determine what to include in a patient's appeal package.

COMMONLY REQUIRED DOCUMENTS INCLUDE[a]:

- ☐ Statement of medical necessity
- ☐ Patient authorization and notice of release of information
- ☐ Copy of the patient's health plan or prescription card (front and back)
- ☐ Denial information, including the patient's denial letter and/or explanation of benefits
- ☐ Letter of appeal
- ☐ Supporting documentation
  - ☐ OFEV® (nintedanib) capsules prescribing information
  - ☐ OFEV capsules published clinical studies
  - ☐ Patient clinical/diagnostic records and related laboratory reports
  - ☐ HRCT and lung biopsy results indicating IPF (usual interstitial pneumonia)
  - ☐ Radiology report
  - ☐ Pulmonary function tests (eg, FEV_1/FVC, FVC, DL_{CO}, TLC values)

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; TLC=total lung capacity.

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