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Dear Healthcare Professional,

Please note that this resource, *Prior Authorization (PA) Tips and Checklist*, includes general guidance related to appealing treatment decisions and fulfilling prior authorizations. **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.**

INDICATION

OFEV is indicated in adults 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®.

OFEV® (nintedanib) capsules 150mg

Boehringer Ingelheim

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.

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 IPF studies, adverse reactions reported in greater than or equal to 5% of OFEV patients were 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

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 to obtain treatment authorization for OFEV® (nintedanib) capsules. Some plans have specific coverage authorization forms that must be utilized to document this type of letter. Follow the patient's plan requirements when requesting OFEV 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 and lung biopsy results indicating IPF (usual interstitial pneumonia)
    - 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.

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*; TLC=total lung capacity.

[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.