PRIOR AUTHORIZATION POLICY

POLICY: Idiopathic Pulmonary Fibrosis and Related Lung Disease – Ofev Prior Authorization Policy

- Ofev® (nintedanib capsules – Boehringer Ingelheim)

REVIEW DATE: 07/10/2024

OVERVIEW

Ofev, a kinase inhibitor, is indicated for the following uses:[1]

- **Idiopathic pulmonary fibrosis** (IPF), treatment.
- **Interstitial lung diseases, chronic fibrosing with a progressive phenotype**, treatment.
- **Interstitial lung disease associated with systemic sclerosis**, to slow the rate of decline in pulmonary function.

The safety and effectiveness of Ofev in pediatric patients have not been established.[1]

Disease Overview

IPF is a form of chronic interstitial lung pneumonia associated with histologic pattern of usual interstitial pneumonia (UIP).[2] The condition is specific for patients that have clinical features and the histologic pattern of UIP or a classical high-resolution computed tomography (HRCT) scan for IPF. In this lung condition there is cellular proliferation, interstitial inflammation, fibrosis, or the combination of these findings, within the alveolar wall that is not due to infection or cancer.[3] IPF is rather rare and the prevalence in the US ranges from 10 to 60 cases per 100,000. However, in one study, the prevalence was 494 cases per 100,000 in 2011 in adults > 65 years of age, which is higher than previous information. The disease mainly impacts older adults.[2] Symptoms include a progressive dry cough and exertional dyspnea. Patients experience a high disease burden with hospital admissions. The clinical course varies among patients but the mean survival after symptom onset is usually 3 to 5 years. The cause is unknown but environmental and occupational hazards may play a role, as well as a of smoking. Medical therapy is only modestly effective and mainly shows the rate of disease progression. Agents FDA-approved for IPF are Ofev and Esbriet® (pirfenidone capsules and film-coated tablets). Lung transplantation is a therapeutic option.

Interstitial lung disease is a common manifestation of systemic sclerosis and is a leading cause of death.[4-6] Among patients who have systemic sclerosis, up to one-half of patients may have interstitial lung disease.[7] The estimate prevalence and annual incidence of systemic sclerosis-associated interstitial lung disease is 1.7 to 4.2 and 0.1 to 0.4 per 100,000 individuals, respectively.[7] However, it is notable that systemic sclerosis is a connective disease that it not limited to the lungs but impacts the skin, blood vessels, heart, kidneys, gastrointestinal tract, and musculoskeletal system. The condition displays great heterogeneity and can be challenging to treat.[4] When the disease affects the internal organs, significant morbidity and mortality may result. Mycophenolate, cyclophosphamide, and azathioprine are immunosuppressants that are utilized in the treatment of interstitial lung disease associated with systemic sclerosis. Corticosteroids are also used. Besides Ofev, Actemra® (tocilizumab subcutaneous injection) is also indicated for use in patients with systemic sclerosis-associated interstitial lung disease.

Clinical Efficacy

Idiopathic Pulmonary Fibrosis (IPF)

The clinical efficacy of Ofev if patients with IPF was established in one Phase II study and two Phase III studies that were identical in design (n = 1,231).[1,8,9] The trials were randomized, double-blind, placebo-controlled studies comparing treatment with Ofev 150 mg twice daily with placebo for 52 weeks. In the two Phase III studies, patients were ≥ 40 years of age and had a forced vital capacity (FVC) ≥ 50% of the predicted value. The diagnosis was confirmed by HRCT and, if available, surgical lung biopsy specimens were assessed. For all three studies, a statistically significant reduction in the annual rate of decline of FVC was observed in patients receiving Ofev compared with patients receiving placebo. Also, data shows that the proportion of patients that demonstrated categorical declines in lung function was lower for patients given Ofev compared with placebo. Acute IPF exacerbations were also reduced.[1,8,9] Some information suggests that patients who have FVC < 50% of predicted may also have some benefits from therapy.[10-13]

Interstitial Lung Diseases, Chronic Fibrosing with a Progressive Phenotype

The efficacy of Ofev was assessed in patients ≥ 18 years of age with chronic fibrosis interstitial lung diseases with a progressive phenotype in a Phase III, double-blind, placebo-controlled trial (INBUILD) [n = 663].[1,14,15] Patients received Ofev 150 mg BID or placebo for at least 52 weeks and the main endpoint was the annual rate in decline in FVC over 52 weeks. Patients who had a clinical diagnosis of chronic fibrosing interstitial lung disease were involved in the trial if they had relevant fibrosis (greater than 10% fibrotic features) and had clinical signs of progression (e.g., FVC decline ≥ 10%, recent FVC decline ≥ 5% but < 10% with worsening symptoms or imaging, or worsening symptoms and worsening imaging). Patients were required to have an FVC ≥ 45% of predicted and a diffusing capacity of the lung for carbon monoxide of at least 30% and < 80% of predicted.

Interstitial Lung Disease Associated with Systemic Sclerosis

The efficacy of Ofev was established in SENSCIS, a randomized, double-blind, placebo-controlled Phase III trial in patients ≥ 18 years of age with systemic sclerosis-related interstitial lung disease (n = 576).[1,5] Patients were randomized to Ofev or placebo for at least 52 weeks and up to 100 weeks. Patients had ≥ 10% fibrosis on a chest HRCT scan conducted within the previous 12 months and had an FVC ≥ 40% of predicted. The primary efficacy endpoint was the annual rate of decline in FVC over 52 weeks. The annual rate of decline of FVC over 52 weeks was significantly reduced by 41 mL in patients receiving Ofev vs. placebo (-52 mL for Ofev vs. -93 mL with placebo).

Guidelines

In 2015, the clinical practice guideline from the American Thoracic Society (ATS), European Respiratory Society (ERS), the Japanese Respiratory Society (JRS), and Latin American Thoracic Association (ALAT) on the treatment of IPF were updated.[16] Regarding Ofev, the guideline suggests use of this medication (conditional recommendation, moderate confidence in estimates of effect). The guideline notes that the data with Ofev focuses on patients with IPF who have mild to moderate impairment in pulmonary function tests. It is not known if the benefits would differ among patients with more severe impairment in pulmonary function testing or in patients who have other comorbidities.[16] Updated recommendations by this group in 2022 support use of Ofev in patients with IPF.[17] Regarding the treatment of progressive pulmonary fibrosis, Ofev is a suggested treatment in patients who have failed standard management for fibrotic interstitial lung disease (e.g., immunosuppressive treatment) other than IPF.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Ofev. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of

patients treated with Ofev, approval requires Ofev to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ofev is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Idiopathic Pulmonary Fibrosis**. Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Forced vital capacity is ≥ 40% of the predicted value; AND
     - **iii.** The diagnosis is confirmed by ONE of the following (a or b):
       - **a)** Findings on high-resolution computed tomography indicate usual interstitial pneumonia; OR
       - **b)** A surgical lung biopsy demonstrates usual interstitial pneumonia; AND
     - **iv.** Medication is prescribed by or in consultation with a pulmonologist; OR
   - **B)** Patient is Currently Receiving Ofev. Approve if the patient meets ALL of the following (i, ii and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has experienced a beneficial response to therapy over the last year while receiving Ofev; AND
       Note: For a patient who has received less than 1 year of therapy, response is from baseline prior to initiating Ofev. Examples of a beneficial response include a reduction in the anticipated decline in forced vital capacity, six-minute walk distance, and/or in the number or severity of idiopathic pulmonary fibrosis exacerbations.
     - **iii.** Medication is prescribed by or in consultation with a pulmonologist.

2. **Interstitial Lung Diseases, Chronic Fibrosing with a Progressive Phenotype.** Approve for 1 year if the patient meets ONE of the following (A or B):
   Note: Examples of conditions include hypersensitivity pneumonitis; idiopathic non-specific interstitial pneumonitis; idiopathic non-specific interstitial pneumonia; unclassifiable idiopathic interstitial pneumonia; autoimmune interstitial lung disease (e.g., rheumatoid arthritis interstitial lung disease); exposure-related interstitial lung disease; and mixed connective tissue disease interstitial lung disease. This is not associated with idiopathic pulmonary fibrosis (see indication above).
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Forced vital capacity is ≥ 40% of the predicted value; AND
     - **iii.** According to the prescriber, the patient has fibrosing lung disease impacting more than 10% of lung volume on high-resolution computed tomography; AND
     - **iv.** According to the prescriber, the patient has clinical signs of progression; AND
       Note: Examples of clinical signs of progression include a forced vital capacity decline ≥ 10% of the predicted value or forced vital capacity decline ≥ 5% to < 10% with worsening symptoms and/or worsening imaging.
     - **v.** Medication is prescribed by or in consultation with a pulmonologist; OR

B) Patient is Currently Receiving Ofev. Approve if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient has experienced a beneficial response to therapy over the last year while receiving Ofev; AND

  Note: For a patient who has received less than 1 year of therapy, response is from baseline prior to initiating Ofev. Examples of a beneficial response include a reduction in the anticipated decline in forced vital capacity, six-minute walk distance, and/or in the number or severity of interstitial lung disease-related exacerbations.
- **iii.** Medication is prescribed by or in consultation with a pulmonologist.

3. Interstitial Lung Disease Associated with Systemic Sclerosis. Approve for 1 year if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Forced vital capacity is ≥ 40% of the predicted value; AND
- **iii.** Diagnosis is confirmed by high-resolution computed tomography; AND
- **iv.** Medication is prescribed by or in consultation with a pulmonologist or a rheumatologist; OR

B) Patient is Currently Receiving Ofev. Approve if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient has experienced a beneficial response to therapy over the last year while receiving Ofev; AND

  Note: For a patient who has received less than 1 year of therapy, response is from baseline prior to initiating Ofev. Examples of a beneficial response include a reduction in the anticipated decline in forced vital capacity, six-minute walk distance, and/or in the number or severity of disease-related exacerbations.
- **iii.** Medication is prescribed by or in consultation with a pulmonologist or a rheumatologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Ofev is not recommended in the following situations:

1. Ofev is Being Used Concomitantly with Esbriet (pirfenidone capsules). Esbriet is another medication indicated for IPF. The effectiveness and safety of concomitant use of Ofev with Esbriet have not been established. The 2015 ATS/ERS/JRS/ALAT clinical practice guideline regarding the treatment of idiopathic pulmonary fibrosis (an update of the 2011 clinical practice guideline) does not recommend taking Ofev and Esbriet in combination.[16] A small exploratory study was done in which patients with IPF receiving Ofev added on to Esbriet.[18] Further research is needed to determine the utility of this combination regimen.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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