VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Idiopathic Pulmonary Fibrosis and Related Lung Disease – Ofev® (nintedanib capsules – Boehringer Ingelheim)

DATE REVIEWED: 10/02/2019; selected revision 03/25/2020

OVERVIEW

Ofev, a kinase inhibitor, is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).[1] Also, Ofev is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease. Ofev is additionally indicated for the treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype.

Disease Overview

IPF is a form of chronic interstitial lung pneumonia associated with histologic pattern of usual interstitial pneumonia (UIP).[8] The condition is specific for patients that have clinical features and the histologic pattern of IUP 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.[9] 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.[8] 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 history 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.[11,12] Among patients who have systemic sclerosis, up to one-half of patients may have interstitial lung disease.[17] 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.[17] 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.[11] 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. Ofev is the first medication specifically indicated for this use.[1]

Clinical Efficacy

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).[1-3] The trials were randomized, double-blind, placebo-controlled studies comparing treatment with Ofev 150 mg BID 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 high-resolution computed tomography

(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 forced vital capacity (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.[1-3] Some information suggests that patients who have FVC < 50% of predicted may also have some benefits from therapy.[14-16]

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 ILD (n = 576).[1,12] Patients were randomized to Ofev or placebo for at least 52 weeks and up to 100 weeks. Patients had ≥ 10% fibrosis on a chest high resolution computed tomography (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 forced vital capacity (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).

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].[1,18,19] Patients receiving 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.

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.[4] 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.[4] The 2011 guideline for the diagnosis and management of IPF from ATS/ERS/JRS/ALAT notes that the accuracy of the diagnosis of IPF increases with multidisciplinary interactions between pulmonologists, radiologists, and pathologists experienced in the diagnosis of interstitial lung disease (ILD).[5] The guidelines also state that the diagnosis of IPF requires exclusion of other known causes of ILD; the presence of a usual interstitial pneumonia pattern on HRCT in patients not subjected to surgical lung biopsy; and specific combinations of HRCT and surgical lung biopsy pattern in patients subjected to surgical lung biopsy.[5]

In 2017, The European League Against Rheumatism updated the recommendations for the treatment of systemic sclerosis.[13] Ofev is not addressed. Regarding patients with lung involvement, cyclophosphamide should be considered for the treatment for interstitial lung disease due to systemic sclerosis, especially for patients with progressive interstitial lung disease.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Ofev. 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. All approvals are provided for 3 years in duration unless otherwise noted below.

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 3 years if the patient meets the following criteria (A, B, C, and D).
   - **A)** The patient is ≥ 40 years of age; AND
   - **B)** The agent is prescribed by or in consultation with a pulmonologist; AND
   - **C)** The forced vital capacity (FVC) is ≥ 40% of the predicted value; AND
   - **D)** The diagnosis is confirmed by one of the following (i or ii):
     - **i.** Findings on high-resolution computed tomography indicates usual interstitial pneumonia (UIP); OR
     - **ii.** A surgical lung biopsy demonstrates usual interstitial pneumonia.

2. **Interstitial Lung Disease Associated with Systemic Sclerosis.** Approve for 3 years if the patient meets the following criteria (A, B, C, and D).
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The agent is prescribed by or in consultation with a pulmonologist or a rheumatologist; AND
   - **C)** The forced vital capacity (FVC) is ≥ 40% of the predicted value; AND
   - **D)** The diagnosis is confirmed by high-resolution computed tomography.

3. **Chronic Fibrosing Interstitial Lung Disease.** Approve for 3 years if the patient meets the following criteria (A, B, C and D):
   - **A)** The patient is ≥ 18 years of age; AND
   - **B)** The forced vital capacity is ≥ 45% of the predicted value; AND
   - **C)** According to the prescriber the patient has fibrosing lung disease impacting more than 10% of lung volume on high-resolution computed tomography; AND
   - **D)** According to the prescriber the patient has clinical signs of progression.

   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).

   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 (ILD) [e.g., rheumatoid arthritis ILD]; exposure-related IDL; and mixed connective tissue disease ILD.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Ofev has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Ofev is Being Used Concomitantly with Esbriet® (pirfenidone capsules)**. Esbriet is another medication indicated for IPF.[6] 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 guidelines) do not recommend taking Ofev and Esbriet in combination.[4] A small exploratory study was done in which patients with IPF receiving Ofev added-on Esbriet.[7] Further research is needed to determine the utility of this combination regimen. Ofev and Esbriet have not been used concomitantly in the management of systemic sclerosis-associated interstitial lung disease.

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

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HISTORY

Type of Revision	Summary of Changes	Date Reviewed
Annual revision	No criteria changes	12/12/2018
Early annual revision	The Policy header was changed to add the description "and Related Lung Disease" to the Idiopathic Pulmonary Fibrosis title. Also, the following criteria changes were made: **1. Idiopathic Pulmonary Fibrosis:** The forced vital capacity threshold was changed from ≥ 50% to ≥ 40%. Previously, only the baseline (before initiation of therapy) values were accepted but now the timing of the assessment is not specified. **2. Interstitial Lung Disease Associated with Systemic Sclerosis:** New criteria were developed based on this new FDA-approved use.	10/02/2019
Selected revision.	Criteria were changed as follows: **1.Chronic Fibrosing Interstitial Lung Disease:** Criteria were added to address the new indication of use. Criteria are to approve for 3 years of the patient meets all of the following: 1) The patient is ≥ 18 years of age; and 2); the forced vital capacity is ≥ 45% of the predicted value; and 3) according to the prescriber the patient has fibrosing lung disease impacting more than 10% of lung volume on high-resolution computed tomography; and 4) according to the prescriber the patient has clinical signs of progression. Notes were added that detailed clinical signs of progression and examples of conditions.	03/25/2020

FDA – Food and Drug Administration.