Esbriet (pirfenidone) & Ofev (nintedanib)

**Benefit Application**

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

**Policy**

**Required Documentation**

1. The following information is necessary to initiate the prior authorization review:
   a. For idiopathic pulmonary fibrosis initial review, submit reports documenting the result of a chest high-resolution computed tomography (HRCT) study. If a surgical lung biopsy is conducted, submit the associated pathology report.
   b. For idiopathic pulmonary fibrosis review for continuation, submit liver function tests (LFTs) that contain ALT, AST, and bilirubin levels.

**Criteria for Approval**

Authorization of up to 6 months may be granted for patients prescribed Esbriet or Ofev for the treatment of idiopathic pulmonary fibrosis who meet ALL of the following criteria:

1. The patient has undergone a diagnostic work-up consistent with the American Thoracic Society guidelines which includes the following:
   a. The patient does not have a known etiology for interstitial lung disease such as sarcoidosis, scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, bronchiolitis obliterans organizing pneumonia, or drug toxicity AND
      i. The patient has completed an HRCT study of the chest which reveals a result consistent with the usual interstitial pneumonia (IUP) pattern, OR
      ii. The patient has completed an HRCT study of the chest which reveals a result consistent with the possible UIP pattern and the diagnosis is supported by surgical lung biopsy (SLB). If SLB has not been previously conducted, the diagnosis is supported by a multidisciplinary discussion between a radiologist and pulmonologist who are experienced in IPF
2. Esbriet & Ofev will not be used in combination
3. The prescriber will collect liver function tests on the schedule recommended in the package insert
4. The medication must be prescribed by, or in conjunction with, a pulmonologist

**Continuation of Therapy**

All patients (including new patients) requesting authorization for continuation of therapy may be granted an authorization for 12 months provided the following criteria is met:

1. The patient’s ALT and AST is not greater than 5x the upper limit of normal (ULN) OR the ALT or AST is not greater than 3x and less than or equal to 5x the ULN with symptoms or hyperbilirubinemia
2. The patient has experienced a reduction in disease progression
3. Esbriet & Ofev will not be used in combination

Prior approval is required. Submit a prior approval/treatment request now.

Quantity limits apply:

- Esbriet = 2403 mg/day
- Ofev = 300 mg/day

Clinical Rationale

Ofev and Esbriet both received fast track, priority review, and orphan status with breakthrough designation from the FDA given the rarity and fatal nature of Idiopathic Pulmonary Fibrosis (IPF), a fibrotic lung disease of unknown etiology. IPF is chronic and progressive, resulting in scarring of the lungs. Patients become oxygen dependent, wheelchair- and house-bound. It’s rare, with an estimated prevalence of 100,000 persons in the United States, and associated with a poor prognosis (median survival of 2 to 3 years). There are no other FDA approved nor evidenced based therapies. Per the 2011 ATS/ERS/JRS/ALAT international guidelines, there is no proven drug therapy for IPF and therefore the guidelines do not specifically recommend the use of any pharmacologic agents. Systemic corticosteroids and immunosuppressants have been used as part of standard care, albeit limited and inconsistent evidence of benefit. Patients primarily rely on oxygen therapy and pulmonary rehabilitation. Lung transplant is associated with a 5-year survival rate of 40% to 50% for appropriate candidates.

Ofev and Esbriet offer different mechanisms of action for the treatment of IPF. Both produced modest improvements for their primary efficacy outcome (change in FVC from baseline) in trials, and inconsistent effects across secondary efficacy measures (e.g. progression free survival, acute exacerbations of IPF, 6MWD). While the majority of trials demonstrated the rate of decline in FVC was reduced with Ofev and Esbriet, it was modest with absolute treatment differences of 4.4% to 4.6% in Esbriet trials and 3.1% to 3.2% in Ofev trials, when compared to placebo. The clinical significance of this measure remains questionable, particularly as prevention of FVC decline did not consistently translate to improved quality of life or dyspnea scores nor reductions in acute exacerbations of IPF or progression free survival across trials. Additionally, FVC is not considered an established surrogate for mortality, nor is the clinical meaningfulness of the FVC effect size established. While pooled analyses of Esbriet trials demonstrated improved mortality with Esbriet at one year, none of the three individual trials found a significant mortality difference in favor of the agent. Similarly, Ofev trials failed to produce a significant difference in mortality. Ultimately, there is no current understanding of how FVC, nor how these agents, impact mortality, the ideal efficacy outcome measure in a disease with a median survival of 2 to 3 years.

Overall, there is no clear advantage to either product from an efficacy or safety standpoint. Both have significant tolerability issues and potential safety concerns, which may direct treatment selection for individual patients. From a practical perspective, patients may prefer Ofev, which has considerably less pill burden, 2 capsules per day compared to Esbriet, which requires 9.

Based on what’s known to date, both drugs have demonstrated ability to slow the rate of deterioration as measured by FVC, though patients won’t note improvement in symptoms and there is no clear demonstrable evidence either will delay mortality. Regardless, they are currently the only FDA approved therapies for this rare, progressive, and fatal disease.

References


**POLICY HISTORY**

Policy #: 05.01.85  
**Policy Creation:** September 2015  
Reviewed:  
Revised:  
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