



# Louisiana

## Pharmacotherapy for Idiopathic Pulmonary Fibrosis

**Policy #** 00467

**Original Effective Date:** 01/21/2015

**Current Effective Date:** 01/17/2018

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

### **When Services May Be Eligible for Coverage**

*Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:*

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider nintedanib (Ofev<sup>®</sup>)<sup>†</sup> or pirfenidone (Esbriet<sup>®</sup>)<sup>†</sup> for the treatment of idiopathic pulmonary fibrosis (IPF) to be **eligible for coverage**.

### Patient Selection Criteria

Coverage eligibility for nintedanib (Ofev) or pirfenidone (Esbriet) will be considered when all of the following criteria are met:

- Ofev and Esbriet are NOT used as combination therapy; AND
- Patient has a confirmed diagnosis of IPF by:
  - Exclusion of other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, drug toxicity); AND
    - The presence of usual interstitial pneumonia pattern on high-resolution computed tomography (HRCT) in patients not subjected to surgical lung biopsy; OR
    - A combination of HRCT and surgical lung biopsy pattern that is indicative of a diagnosis of IPF in patients subjected to surgical lung biopsy.

### **When Services Are Considered Investigational**

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of nintedanib (Ofev) or pirfenidone (Esbriet) when patient selection criteria are NOT met to be **investigational**.\*

### **Background/Overview**

There are currently only two drugs that are FDA approved for the treatment of IPF, Ofev and Esbriet. Ofev is a small molecule that inhibits multiple receptor tyrosine kinase and non-receptor tyrosine kinases. It is believed that Ofev mainly works by vascular endothelial growth factor (VEGFR) inhibition. Ofev is dosed at 150mg twice daily. There is also consideration for dose reductions as the drug is also supplied in a 100mg capsule dosage form. Esbriet's mechanism of action is unknown, however it does belong to the chemical class of pyridone drugs. Esbriet is dosed at 801mg (three 267mg capsules) three times a day. Dose modifications are also recommended for this drug.

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### **Idiopathic Pulmonary Fibrosis**

Idiopathic pulmonary fibrosis is a rare, chronic, fatal disease characterized by a progressive and irreversible loss of lung function (decline in forced vital capacity [FVC]). Idiopathic pulmonary fibrosis usually occurs in middle aged to elderly adults, and is more common in males. Survival rates are poor in patients with IPF.

### **FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

Both Esbriet and Ofev were approved in October of 2014 for the treatment of IPF. These two agents are the first drugs that are FDA approved for this indication.

### **Rationale/Source**

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The clinical efficacy of Ofev was established in 3 pivotal trials (Studies 1, 2, and 3). These were randomized, double-blind, placebo-controlled studies comparing treatment with Ofev 150 mg twice daily to placebo for 52 weeks. Studies 2 and 3 were identical in design. Study 1 was very similar in design. Patients were randomized in a 3:2 ratio (1:1 for Study 1) to either Ofev 150 mg or placebo twice daily for 52 weeks. Study 1 also included other treatment arms (50 mg daily, 50 mg twice daily, and 100 mg twice daily) that are not further discussed. The primary endpoint was the annual rate of decline in FVC. Time to first acute IPF exacerbation was a key secondary endpoint in Studies 2 and 3 and a secondary endpoint in Study 1. Change from baseline in FVC percent predicted and survival were additional secondary endpoints in all studies. A statistically significant reduction in the annual rate of decline of FVC (in mL) was demonstrated in patients receiving Ofev compared to patients receiving placebo based on the random coefficient regression model, adjusted for gender, height, and age. The rate of decline for Ofev in the 3 studies ranged from -60mL to -115mL vs. a rate of decline ranging from -191mL to -240mL in the placebo group. The treatment effect on FVC was consistent in all 3 studies.

The efficacy of Esbriet was evaluated in patients with IPF in three phase 3, randomized, double-blind, placebo-controlled, multicenter trials (Studies 1, 2, and 3). Study 1 was a 52 week trial comparing Esbriet 2403mg/day vs. placebo in patients with IPF. Studies 2 and 3 were nearly identical, however Study 2 had an intermediate dose treatment arm. The study drug was administered three times daily. The primary endpoint was the change in percent predicted FVC from baseline to study end. The first two studies showed a statistically significant change in the percent FVC from baseline. The third study showed no statistically significant difference for the change in percent FVC from baseline.

### **References**

1. Ofev [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, Connecticut.
2. Esbriet [package insert]. Intermune, Inc. Brisbane, California.

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3. Ofev. Express Scripts Drug Evaluation. Updated October 2014.
4. Esbriet Express Scripts Drug Evaluation. Updated October 2014.
5. An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management. Am J Respir Crit Care Med, Vol.183, No. 6, (2011), pp 788-824.

### **Policy History**

Original Effective Date: 01/21/2015

Current Effective Date: 01/17/2018

01/08/2015 Medical Policy Committee review  
 01/21/2015 Medical Policy Implementation Committee approval. New policy.  
 01/07/2016 Medical Policy Committee review  
 01/22/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.  
 01/05/2017 Medical Policy Committee review  
 01/18/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.  
 01/04/2018 Medical Policy Committee review  
 01/17/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.  
 Next Scheduled Review Date: 01/2019

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  3. Reference to federal regulations.

\*\*Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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