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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Respiratory Agents	**Original Policy Date:**	November 7, 2014
Subject:	Esbriet	**Page:**	1 of 7

Last Review Date: March 8, 2024

Esbriet

Description

Esbriet (pirfenidone)

Pirfenidone

Background
Idiopathic pulmonary fibrosis is a progressive condition in which the lungs develop abnormal tissue changes (fibrosis) over time. As a result, patients with IPF experience shortness of breath, and worsening lung function (1).

Esbriet (pirfenidone) belongs to the chemical class of pyridone which acts on multiple pathways that may be involved in the development of fibrotic lung tissue. Its exact mechanism of action is unknown, however, Esbriet may exert antifibrotic properties by decreasing fibroblast proliferation and the production of fibrosis-associated proteins and cytokines; may decrease the formation and accumulation of extracellular matrix (i.e. collagen) in response to transforming growth factor-beta and platelet derived growth factor. Esbriet is also believed to exert anti-inflammatory properties by decreasing the accumulation of inflammatory cells resulting from a variety of stimuli (2-3).

Regulatory Status
FDA-approved indication: Esbriet is a pyridone indicated for the treatment of idiopathic pulmonary fibrosis (IPF) (2).

Patients eligible for clinical studies were to have percent forced vital capacity (%FVC) greater than or equal to 50% at baseline and a percent predicted diffusing capacity of the lungs for carbon monoxide (%DL_{CO}) greater than or equal to 30%. The primary endpoint was the change in percent predicted forced vital capacity (%FVC) from baseline to study end (2).

Esbriet is metabolized primarily (70 to 80%) via CYP1A2 with minor contributions from other CYP isoenzymes including CYP2C9, 2C19, 2D6 and 2E1. A drug interaction assessment needs to be performed before the start of the medication (2).

Esbriet carries warnings for elevated liver enzymes, drug-induced liver injury, photosensitivity, rash, and gastrointestinal disorders. Cases of drug-induced liver injury have been observed with Esbriet. Liver function tests should be conducted prior to the initiation of therapy with Esbriet. Smoking causes decreased exposure to Esbriet, which may alter the efficacy profile of Esbriet. Patients should be advised to stop smoking prior to treatment with Esbriet and to avoid smoking when using Esbriet (2).

Safety and effectiveness of Esbriet in patients less than 18 years of age have not been established (2).

Related policies
Ofev

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Esbriet may be considered **medically necessary** if the conditions indicated below are met.

Esbriet may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Idiopathic pulmonary fibrosis (IPF)

AND ALL of the following:

1. Idiopathic (i.e., no identifiable cause for pulmonary fibrosis) diagnosis confirmed by **ALL** of the following:
    a. Physical exam
    b. Pulmonary Function Tests
        i. %FVC<82% of predicted
        ii. $\%DL_{CO}$
        iii. %TLC<80% of predicted
    c. CT with classic findings of usual interstitial pneumonitis (UIP)
2. Must be prescribed by a pulmonologist
3. **NO** concurrent therapy with another Prior Authorization (PA) medication for idiopathic pulmonary fibrosis (see Appendix 1)
4. Drug interaction assessment has been performed by the physician
5. **NO** known cause of the interstitial lung disease / fibrosis
6. Patient has had baseline liver function tests performed

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Idiopathic pulmonary fibrosis (IPF)

AND ALL of the following:

1. Assessment by the healthcare professional that the medication is helping the patient by meeting at least **ONE** of the following criteria (while taking this medication):
    a. Slowed the rate of decline of lung function
    b. Improved (or no decline in) symptoms of cough or shortness of breath
    c. Improved sense of well-being
2. **NO** concurrent therapy with another Prior Authorization (PA) medication for idiopathic pulmonary fibrosis (see Appendix 1)

3. Drug interaction assessment has been performed by the physician

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary

Esbriet (pirfenidone) is a pyridone indicated for the treatment of idiopathic pulmonary fibrosis (IPF). Esbriet carries warnings for elevated liver enzymes, drug-induced liver injury, photosensitivity, rash, and gastrointestinal disorders. Safety and effectiveness of Esbriet in pediatric patients have not been established (2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Esbriet while maintaining optimal therapeutic outcomes.

References

1. U.S. National Library of Medicine. (August 2020). Idiopathic pulmonary fibrosis: MedlinePlus Genetics. MedlinePlus. https://medlineplus.gov/genetics/condition/idiopathic-pulmonary-fibrosis/.
2. Esbriet [package insert]. South San Francisco, CA: Genentech USA, Inc.; February 2023.
3. Esbriet. Drug Facts and Comparisons. eFacts [online]. Last updated February 2021. Available from Wolters Kluwer Health, Inc.
4. Pirfenidone [package insert]. Berkeley Heights, NJ: Laurus Generics Inc.; April 2022.

Policy History

Date	Action

November 2014	Addition to PA
December 2014	Annual editorial review and reference update Removal of baseline reading of percent forced vital capacity (%FVC) greater than or equal to 50% per PMPC
March 2015	Annual editorial review and reference update
April 2015	Addition of Idiopathic diagnosis confirmed by the following: CT, Pulmonary Function Test, and Physical exam; no known cause of the interstitial lung disease / fibrosis; also drug interaction assessment has been performed; must be prescribed by a pulmonologist; assessment by the healthcare professional that the medication is helping the patient by meeting at least **ONE** of the following criteria (while taking this medication): slowed the rate of decline of lung function, improved (or no decline in) symptoms of cough or shortness of breath, improved sense of well-being. Removal of predicted diffusing capacity for carbon monoxide (%DL_{CO}) greater than or equal to 30% per SME
June 2015	Annual editorial review and reference update
February 2016	Change of the FVC from 80% to 82%
March 2016	Annual review Policy number changed from 5.13.04 to 5.45.04
September 2016	Annual editorial review and reference update. Addition of the age to renewal requirement
March 2017	Annual editorial review and reference update
March 2018	Annual editorial review and reference update
March 2019	Annual review and reference update
March 2020	Annual editorial review and reference update. Addition of baseline liver function tests requirement
March 2021	Annual review
June 2021	Revised requirement to “no concurrent therapy with another PA medication for IPF” and added Appendix 1
September 2021	Annual review and reference update
March 2022	Annual review and reference update
September 2022	Addition of Pirfenidone (branded generic) to policy
December 2022	Annual review
March 2023	Annual review
December 2023	Annual review and reference update. Per SME, added smoking warning to regulatory status section
March 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.

Appendix 1 - List of PA Medications for IPF

Generic Name	Brand Name
nintedanib	Ofev
pirfenidone	Esbriet