

Pharmacy Policy Bulletin

Title: Pulmonary Fibrosis agents

Policy #: Rx.01.164

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

▸ Intent:

The intent of this policy is to communicate the medical necessity criteria for **pirfenidone (Esbriet®)** and **nintedanib (Ofev®)** as provided under the member's prescription drug benefit.

▸ Description:

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive, incurable fibrotic disorder of the lower respiratory tract that typically affects adults over the age of 40. IPF is characterized by varying degrees of fibrosis, collagen deposits, and distortion of the pulmonary architecture. Although the specific initiating factor(s) leading to IPF are unknown, lung injury progresses due to the interaction of growth factors, cytokines, and other mediators, leading to fibroblast proliferation and excessive extracellular matrix deposition in the lungs. Pharmacologic treatments are limited. Prior to the FDA approval of pirfenidone (Esbriet®) and nintedanib (Ofev®) in October 2014, no medications were approved for the treatment of IPF. Traditional approaches have included various anti-inflammatory and immunosuppressive agents; however, these approaches do not seem to be effective and are no longer considered part of routine maintenance care. Early trials of agents with antifibrotic properties were disappointing. Thus, treatment has predominantly been limited to supportive care, including oxygen therapy and pulmonary rehabilitation. Lung transplantation is also an option for selected patients. Five year survival is approximately 20-30%.

Nintedanib (Ofev®) inhibits multiple receptor tyrosine kinases and nonreceptor tyrosine kinases, including platelet-derived growth factor (PDGFR alpha and PDGFR beta), fibroblast growth factor receptor (FGFR1, FGFR2, FGFR3), vascular endothelial growth factor (VEGFR1, VEGFR2, and VEGFR3), and Fms-like tyrosine kinase-3 (FLT3). Nintedanib binds competitively to the adenosine triphosphate (ATP) binding pocket of these receptors and blocks the intracellular signaling which is crucial for the proliferation, migration, and transformation of fibroblasts. Nintedanib (Ofev®) is indicated for the treatment of idiopathic pulmonary fibrosis.

The precise mechanisms of action for pirfenidone (Esbriet®) have not been fully elucidated; however, pirfenidone 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. Pirfenidone is also believed to exert anti-inflammatory properties by decreasing the accumulation of inflammatory cells resulting from a variety of stimuli. Pirfenidone (Esbriet®) is indicated for the treatment of idiopathic pulmonary fibrosis.

Nintedanib and pirfenidone appear to slow disease progression. Neither medication is a cure for IPF.

▸ **Policy:**

INITIAL CRITERIA

Pirfenidone (Esbriet®) or Nintedanib (Ofev®) is approved when ALL of the following inclusion criteria are met:

1. Diagnosis of Idiopathic Pulmonary Fibrosis (IPF) confirmed by BOTH of the following;
 - a. High resolution CT scan or biopsy; and
 - b. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis
2. Prescribed by a pulmonologist or lung transplant specialist; and
3. Liver function tests have been performed prior to therapy start; and
4. The member is a non-smoker or has not smoked for a minimum of 6 weeks

REAUTHORIZATION CRITERIA

Pirfenidone (Esbriet®) or Nintedanib (Ofev®) is re-approved when ALL of the following inclusion criteria are met:

1. Member has experienced stabilization from baseline or a less than 10% decline in forced vital capacity (FVC); AND
2. Has not experienced AST or ALT elevations greater than 5 times the upper limit of normal (ULN) or greater than 3 times ULN with signs or symptoms of severe liver damage; and
3. The member is a non-smoker

Authorization duration: Initial and reauthorization approvals will be granted for 12 months

▸ **Black Box Warning:**

None

▸ **Guidelines:**

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Esbriet® (pirfenidone) [prescribing information]. South San Francisco, CA. Genentech, Inc. October 2017. Available at: https://www.gene.com/download/pdf/esbriet_prescribing.pdf . Accessed February 19, 2019.

King TE. Treatment of idiopathic pulmonary fibrosis. UpToDate. November 2018 Available at: https://www.uptodate.com/contents/treatment-of-idiopathic-pulmonary-fibrosis?source=see_link§ionName=MEDICAL%20THERAPIES&anchor=H13191574#H13191574 . Accessed February 18, 2019.

Ofev® (nintedanib) [prescribing information]. Ridgefield, CT. Boehringer Ingelheim. November 2018. Available at: <https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Ofev/ofev.pdf> . Accessed February 18, 2019.

Raghu G, et al. An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis: An Update of the 2011 Clinical Practice Guideline. Am J Respir Crit Care Med. 2015 Jul;192:e3-e19. DOI: 10.1164/rccm.201506-1063ST

Applicable Drugs:

 Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

| Brand name | Generic name |
|------------|--------------|
| Ofev® | nintedanib |
| Esbriet® | pirfenidone |

Cross References:

N/A

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|-----------------------------------|------------------|
| Policy Version Number: | 7.00 |
| P&T Approval Date: | January 10, 2019 |
| Policy Effective Date: | April 01, 2019 |
| Next Required Review Date: | January 10, 2020 |

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.