Pharmacy Policy Bulletin

Title: Interstitial Lung Disease 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:

Interstitial lung diseases (ILDs) are a heterogenous group of disorders that are characterized by the inflammation and scarring of the lungs. Some ILDs have known causes and some are idiopathic. The treatment choices and prognosis vary among the different causes and types of ILDs.

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%

Systemic Sclerosis is a rare and heterogenous autoimmune disease characterized by immune dysregulation, microvascular damage, and organ fibrosis. Interstitial lung disease (ILD) is a common manifestation of systemic sclerosis that tends to occur early in the course of disease.

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 and systemic sclerosis associated with Interstitial Lung Disease (SSc-ILD).

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:

Idiopathic Pulmonary Fibrosis (IPF)

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

A. Diagnosis of Idiopathic Pulmonary Fibrosis (IPF); and
B. Diagnosis was confirmed by BOTH of the following:
    1. High resolution CT scan or biopsy; and
    2. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis; AND
C. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD)

INITIAL CRITERIA: Nitedanib (Ofev®) is approved when ALL of the following inclusion criteria are met:

A. Diagnosis of Systemic Sclerosis Associated Interstitial Lung Disease (SSc-ILD); and
B. Diagnosis was confirmed by BOTH of the following:
    1. High resolution CT scan or biopsy; and
    2. Member does not have evidence or suspicion of an alternative interstitial lung disease diagnosis; and
C. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Chronic Fibrosing Interstitial Lung Disease (ILDs) with a progressive phenotype

INITIAL CRITERIA: Nitedanib (Ofev®) is approved when ALL of the following inclusion criteria are met:

A. Diagnosis of Chronic Fibrosing Interstitial Lung Disease (ILDs) with a progressive phenotype; and
B. Disease has a progressive phenotype as observed by one of the following:
    a. Decline of forced vital capacity (FVC); or
    b. Worsening of respiratory symptoms; or
    c. Increased extent of fibrosis seen on imagine; and
C. Diagnosis was 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; and
D. Prescribed by or in consultation with a pulmonologist or lung transplant specialist

Initial authorization: 12 months

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

A. Documentation of positive clinical response to therapy (e.g. member has experienced stabilization from baseline or a less than 10% decline in forced vital capacity (FVC)); and
B. Member 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
C. The member is not actively smoking

Reauthorization: 12 months

Black Box Warning as shown in the drug Prescribing Information:

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. July 2019. Available at: https://www.gene.com/download/pdf/esbriet_prescribing.pdf . Accessed March 25, 2021.

King TE. Treatment of idiopathic pulmonary fibrosis. UpToDate. August 2019. Available at: https://www.uptodate.com/contents/treatment-of-idiopathic-pulmonary-fibrosis?source=see_link&sectionName=MEDICAL%20THERAPIES&anchor=H13191574#H13191574. Accessed March 25, 2021

Ofev® (nintedanib) [prescribing information]. Ridgefield, CT. Boehringer Ingelheim. October 2020. Available at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Ofev/ofev.pdf . Accessed March 25, 2021.

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:

Off-Label Use Rx.01.33

Policy Version Number:	10.00
P&T Approval Date:	March 18. 2021
Policy Effective Date:	July 01, 2021
Next Required Review Date:	March 18, 2022