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Pirfenidone

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following pirfenidone products:

- **Esbriet®** (pirfenidone) oral capsules, tablets
- **pirfenidone** oral tablets
- **pirfenidone** oral capsules

Coverage for pirfenidone products (Esbriet and pirfenidone tablets) varies across plans and requires the use of preferred products in addition to the criteria listed below. Refer to the customer's benefit plan document for coverage details.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Pirfenidone products (Esbriet, pirfenidone capsules, and pirfenidone tablets) are considered medically necessary for the treatment of Idiopathic Pulmonary Fibrosis (IPF) when the individual meets ALL of the criteria:

1. 18 years of age or older
2. Forced vital capacity is at least 40% of the predicted value
3. Diagnosis of idiopathic pulmonary fibrosis is confirmed by **ONE** of the following:
   a. Findings on high-resolution computed tomography indicate usual interstitial pneumonia [UIP]
   b. Surgical lung biopsy demonstrates usual interstitial pneumonia [UIP]
   c. The combination of high-resolution computed tomography and biopsy pattern are both indicative of "probable" usual interstitial pneumonia [UIP]
4. Exclusion of other potential causes of interstitial lung disease
5. The medication is prescribed by, or in consultation with, a pulmonologist
6. Preferred products are required, refer to tables below:

Employer Group Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Esbriet (pirfenidone) 267 mg oral capsule	The individual has tried **pirfenidone 267 mg oral capsule** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Esbriet (pirfenidone) 267 mg oral tablet	The individual has tried **pirfenidone 267 mg oral tablet** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Esbriet (pirfenidone) 801 mg oral tablet	The individual has tried **pirfenidone 801 mg oral tablet** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
pirfenidone 534 mg oral tablet	Individual is unable to achieve the desired dose with generic **pirfenidone 267 mg tablets**. [prior authorization is required]

Individual and Family Plan Non-Covered Products and Criteria:

Non-Covered Product	Criteria
Esbriet (pirfenidone) 267 mg oral capsule	The individual has tried **pirfenidone 267 mg oral capsule** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Esbriet (pirfenidone) 267 mg oral tablet	The individual has tried **pirfenidone 267 mg oral tablet** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction
Esbriet (pirfenidone) 801 mg oral tablet	The individual has tried **pirfenidone 801 mg oral tablet** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Non-Covered Product	Criteria
pirfenidone 534 mg oral tablet	Individual is unable to achieve the desired dose with generic **pirfenidone 267 mg tablets**. [prior authorization is required]

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of Pirfenidone products (Esbriet, pirfenidone capsules, and pirfenidone tablets) is considered medically necessary for Idiopathic Pulmonary Fibrosis (IPF) when **BOTH** of the following are met:

1. Pre-treatment clinical condition met the initial criteria
2. There is documentation of beneficial response (for example: a reduction in the anticipated decline in forced vital capacity; six-minute walk distance; and/or a reduction in the number or severity of idiopathic pulmonary fibrosis exacerbations)

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

Concomitant Use with Nintedanib (Ofev®)
Ofev is another medication indicated for the treatment of IPF. The effectiveness and safety of concomitant use of pirfenidone with Ofev have not been established. The 2015 ATS/ERS/JRS, ALAT clinical practice guideline regarding the treatment of idiopathic pulmonary fibrosis (an update of the 2011 clinical practice guidelines) do not recommend taking Ofev and pirfenidone in combination.[10] A small exploratory study was done in which patients with IPF receiving Ofev added on Esbriet.[12] Further research is needed to determine the utility of this combination regimen.

Background

OVERVIEW
Pirfenidone, a pyridone, is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).[1] The safety and effectiveness of pirfenidone in pediatric patients have not been established.

Disease Overview
IPF is a form of chronic interstitial lung pneumonia associated with histologic pattern of usual interstitial pneumonia (UIP).[2] The condition is specific for patients that have clinical features and the histologic pattern of UIP or a classical high-resolution computed tomography scan for IPF. In this lung condition there is cellular proliferation, interstitial inflammation, fibrosis, or the combination of these findings, within the alveolar wall that is not due to infection or cancer.[3] IPF is rather rare and the prevalence in the US ranges from 10 to 60 cases per 100,000. However, in one study, the prevalence was 494 cases per 100,000 in 2011 in adults > 65 years of age, which is higher than previous information. The disease mainly impacts older adults.[2] Symptoms include a progressive dry cough and exertional dyspnea. Patients experience a high disease burden with hospital admissions. The clinical course varies among patients but the mean survival after symptom onset is usually 3 to 5 years. The cause is unknown but environmental and occupational hazards may play a role, as well as a history

of smoking. Medical therapy is only modestly effective and mainly shows the rate of disease progression. Agents FDA-approved for IPF are Ofev® (nintedanib capsules) and pirfenidone. Lung transplantation is a therapeutic option.

Clinical Efficacy
The efficacy of pirfenidone was assessed in patients with IPF in three Phase III, randomized, double-blind, placebo-controlled, multicenter, multinational trials (n = 1,247).[1,4,5] Patients were required to have a percent predicted forced vital capacity (%FVC) ≥ 50% at baseline. Pirfenidone 2,403 mg/day led to a statistically significant change in the %FVC at 52 weeks and 72 weeks, respectively. Also, a reduction in the mean decline in forced vital capacity (in mL) was observed in both studies for patients receiving pirfenidone 2,403 mg/day compared with placebo.[1-3] Some information suggests that patients who have %FVC < 50% may also have some benefits from therapy.[6-9]

Guidelines
In 2015, the clinical practice guideline from the American Thoracic Society (ATS), European Respiratory Society (ERS), the Japanese Respiratory Society (JRS), and Latin American Thoracic Association (ALAT) on the treatment of IPF was updated.[10] Regarding pirfenidone, the guideline suggests use of this medication (conditional recommendation, moderate confidence in estimates of effect). The guideline notes that the data with pirfenidone cannot be generalized to patients with IPF who have more severe impairment of pulmonary function tests or for patients with other significant comorbidities.[10] Updated recommendations by this group in 2022 support use of pirfenidone in patients with IPF.[11]

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