Drug Coverage Policy

Effective Date……10/15/2024
Coverage Policy Number……IP0311
Policy Title…… Pirfenidone

Idiopathic Pulmonary Fibrosis and Related Lung Disease – Pirfenidone

- Esbriet® (pirfenidone capsules and film-coated tablets - Genentech, generic)

INSTRUCTIONS FOR USE
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Cigna Healthcare Coverage Policy

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]

Medical Necessity Criteria

Pirfenidone is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Idiopathic Pulmonary Fibrosis.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Forced vital capacity is ≥ 40% of the predicted value; AND
     - **iii.** Diagnosis of idiopathic pulmonary fibrosis is confirmed by ONE of the following (a or b):
       - **a)** Findings on high-resolution computed tomography indicate usual interstitial pneumonia; OR
       - **b)** A surgical lung biopsy demonstrates usual interstitial pneumonia; AND
     - **iv.** Medication is prescribed by or in consultation with a pulmonologist; AND
     - **v.** Preferred product criteria is met for the product(s) as listed in the below tables; OR
   - **B)** Patient is Currently Receiving Pirfenidone. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND

ii. Patient has experienced a beneficial response to therapy over the last year while receiving pirfenidone; AND
Note: For a patient who has received less than 1 year of therapy, response is from baseline prior to initiating pirfenidone. Examples of a beneficial response include 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.

iii. Medication is prescribed by or in consultation with a pulmonologist.

Employer Plans:

Product	Criteria
Esbriet capsules (pirfenidone 267 mg capsules)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried generic pirfenidone; AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.
Esbriet tablets (pirfenidone 267 and 801 mg tablets)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried generic pirfenidone; AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.
pirfenidone 534 mg tablet (branded generic)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried generic pirfenidone (pirfenidone 267 mg tablets or capsules); AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.

Individual and Family Plans:

Product	Criteria
Esbriet capsules (pirfenidone 267 mg capsules)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried generic pirfenidone [may require prior authorization]; AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.
Esbriet tablets (pirfenidone 267 and 801 mg tablets)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii):

Product	Criteria
	i. Patient has tried generic pirfenidone [may require prior authorization]; AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.
pirfenidone 534 mg tablet (branded generic)	Approve for 1 year if the patient meets BOTH of the following (A and B): **A)** Patient meets the above medical necessity criteria; AND **B)** Patient meets BOTH of the following (i and ii): **i.** Patient has tried generic pirfenidone (pirfenidone 267 mg tablets or capsules) [may require prior authorization]; AND **ii.** Patient has experienced inadequate efficacy or significant intolerance, according to the prescriber.

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Pirfenidone is Being Used Concomitantly with Ofev (nintedanib capsules)**. 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 guideline) does not recommend taking Ofev and pirfenidone in combination.[10] A small exploratory study was done in which patients with IPF receiving Ofev added on pirfenidone.[12] Further research is needed to determine the utility of this combination regimen.

References

1. Esbriet® capsules and film coated tablets [prescribing information]. South San Francisco, CA: Genentech; February 2023.
2. Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. *N Engl J Med*. 2018;378(19):1811-1823.
3. Lynch JP, Huynh RH, Fishbein MC, et al. Idiopathic pulmonary fibrosis: epidemiology, clinical features, prognosis, and management. *Semin Respir Crit Care Med*. 2016;37:331-357.
4. King TE, Bradford WZ, Castro-Bernardini S, et al, for the ASCEND Study Group. A phase 3 trial of pirfenidone in patients with idiopathic pulmonary fibrosis. *N Engl J Med*. 2014;370(22):2083-2092.
5. Noble PW, Albera C, Bradford WZ, et al, for the CAPACITY Study Group. Pirfenidone in patients with idiopathic pulmonary fibrosis (CAPACITY): two randomized trials. *Lancet*. 2011;377:1760-1769.

6. King CS, Nathan SD. POINT: Should all patients with idiopathic pulmonary fibrosis, even those with more than moderate impairment, be treated with nintedanib or pirfenidone? Yes. *Chest*. 2016;150(2):273-275.
7. Nathan SD, Costabel U, Albera C, et al. Pirfenidone in patients with idiopathic pulmonary fibrosis and more advanced lung function impairment. *Respir Med*. 2019;153:44-51.
8. Costabel U, Albera C, Glassberg MK, et al. Effect of pirfenidone in patients with more advanced idiopathic pulmonary fibrosis. *Respir Research*. 2019;20:55.
9. Richeldi L, Crestani B, Azuma A, et al. Outcomes following decline in forced vital capacity in patients with idiopathic pulmonary fibrosis: results from the INPULSIS and INPULSIS-ON trials of nintedanib. *Respir Med*. 2019;156:20-25.
10. Raghu G, Rochwerg B, Zhang Y, et al, on behalf of the ATS, ERS, JRS, and ALAT. An official ATS/ERS/JRS/ALAT clinical practice guideline: treatment of idiopathic pulmonary fibrosis. Executive summary. An update of the 2011 clinical practice guideline. *Am J Respir Crit Care Med*. 2015;192(2):238-248.
11. Raghu G, Remy-Jardin M, Richeldi L, et al, on behalf of the ATS, ERS, JRS, and ALAT. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults. An official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med*. 2022;205(9):e18-e47.
12. Vancheri C, Kreuter M, Richeldi L, et al, INJOURNEY trial investigators. Nintedanib with add-on pirfenidone in idiopathic pulmonary fibrosis: results of the INJOURNEY trial. *Am J Respir Crit Care Med*. 2018;197(3):356-363.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Updated** policy name from "Pirfenidone" to "Idiopathic Pulmonary Fibrosis and Related Lung Disease – Pirfenidone." **Idiopathic Pulmonary Fibrosis – Initial Therapy. Removed** the requirement for both high-resolution computed tomography and biopsy pattern to indicate "probable" usual interstitial pneumonia. **Removed** the criterion to exclude other potential causes of interstitial lung disease. **Idiopathic Pulmonary Fibrosis – Patient is Currently Receiving Pirfenidone. Added** a note stating that for patients who have received less than 1 year of therapy, the beneficial response is from baseline prior to initiating pirfenidone.	10/15/2024

The policy effective date is in force until updated or retired.