GUIDELINES FOR USE

1. Does the patient have a diagnosis of idiopathic pulmonary fibrosis (IPF) and meet ALL of the following criteria?
   - Patient does not have other known causes of interstitial lung disease (e.g., connective tissue disease, drug toxicity, asbestos or beryllium exposure, hypersensitivity pneumonitis, systemic sclerosis, rheumatoid arthritis, radiation, sarcoidosis, bronchiolitis obliterans organizing pneumonia, human immunodeficiency virus (HIV) infection, viral hepatitis, or cancer)
   - Treatment is prescribed by or given in consultation with a pulmonologist
   - Patient has usual interstitial pneumonia (UIP) pattern as evidenced by high-resolution computed tomography (HRCT) alone or via a combination of surgical lung biopsy and HRCT
   - Patient has a predicted forced vital capacity (FVC) of at least 50%
   - Patient has obtained liver function tests prior to starting pirfenidone
   - Patient does not currently smoke cigarettes

   If yes, approve for 12 months by GPID for all dosage strengths with the following quantity limits:
   - 267mg capsule (GPID 34553): #9 capsules (2403mg) per day.
   - 267mg tablet (GPID 42903): #9 tablets (2403mg) per day.
   - 801mg tablet (GPID 42905): #3 tablets (2403mg) per day.

   If no, do not approve.

**DENIAL TEXT:** The guideline named **PIRFENIDONE (Esbriet)** requires a diagnosis of idiopathic pulmonary fibrosis (IPF). IPF is defined by the American Thoracic Society with the following criteria: a) Exclusion of other known causes of interstitial lung disease (ILD) (e.g., connective tissue disease, drug toxicity, asbestos or beryllium exposure, hypersensitivity pneumonitis, systemic sclerosis, rheumatoid arthritis, radiation, sarcoidosis, bronchiolitis obliterans organizing pneumonia, human immunodeficiency virus (HIV) infection, viral hepatitis, or cancer) AND b) The presence of usual interstitial pneumonia (UIP) pattern as evidenced by high-resolution computed tomography (HRCT) alone or via a combination of surgical lung biopsy and HRCT. In addition, the guideline requires:
   - Treatment is prescribed by or given in consultation with a pulmonologist
   - Patient must obtained liver function tests prior to starting pirfenidone
   - Patient has a predicted forced vital capacity (FVC) of at least 50%
   - Patient does not currently smoke cigarettes

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PIRFENIDONE

RATIONALE
Promote appropriate utilization of Esbriet based on FDA approved indication and dosage.

Esbriet (pirfenidone) is one of the first drugs to be approved by the FDA to treat idiopathic pulmonary fibrosis (IPF). Ofev (nintedanib), the other agent for the treatment of IPF, was also approved on the same day. These two drugs were granted Breakthrough Therapy Designation as well as Orphan Drug status since there are no other drugs to date for the treatment of IPF, a disease that affects an estimated 100,000 people (mostly adults over the age of 40) in the United States. IPF is a chronic, progressive disorder of the lower respiratory tract in which lung tissue becomes scarred or fibrotic over time. As a result, patients with IPF experience shortness of breath, cough, and difficulty participating in everyday physical activities.

The American Thoracic Society guidelines state the diagnosis of IPF requires:
a) Exclusion of other known causes of interstitial lung disease (ILD) (e.g., domestic and occupational environmental exposures, connective tissue disease, and drug toxicity)
b) The presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) in patients not subjected to surgical lung biopsy
c) Specific combinations of HRCT and surgical lung biopsy pattern in patients subjected to surgical lung biopsy.

There is no cure for IPF; many people live only about 3 to 5 years, with the most common cause of death related to IPF being respiratory failure. The exact cause of IPF is not known, but the associated risk factors include cigarette smoking, viral infection, environmental pollutants, chronic aspiration, genetic predisposition, and drugs.

Treatment options for IPF have been extremely limited, mainly consisting of supportive care (oxygen therapy, pulmonary rehabilitation) and lung transplantation. The approval of Esbriet provides a new treatment option that may slow disease progression for patients with IPF. It is an orally administered pyridine that exerts anti-inflammatory effects by interfering with the production of Transforming Growth Factor (TGF)-beta, a small protein in the body involved in how cells grow, and Tumor Necrosis Factor (TNF)-alpha, a small protein that is involved in inflammation. In addition, it behaves as an antifibrotic by directly altering the expression, synthesis, and possibly accumulation of collagen.

Esbriet is metabolized primarily (70 to 80%) via CYP1A2 with minor contributions from other CYP isoenzymes including CYP2C9, 2C19, 2D6 and 2E1. The concomitant administration of Esbriet and fluvoxamine or other strong CYP1A2 inhibitors is not recommended because it significantly increases exposure to Esbriet. Concomitant administration of Esbriet and ciprofloxacin moderately increases exposure to Esbriet. Conversely, concomitant use of Esbriet and a CYP1A2 inducer may decrease the exposure of Esbriet and decrease efficacy; this interaction may be particularly important for smokers. Hydrocarbons found in cigarettes are potent CYP1A2 inducers, and for smokers, the AUC and Cmax of Esbriet were 46% and 68% that of non-smokers (respectively). Patients should be instructed to stop smoking prior to and during treatment with Esbriet.

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PIRFENIDONE

RATIONALE (CONTINUED)

Increases in ALT and AST greater than three times the upper limit of normal have been reported, with rare occasions of concomitant elevations in bilirubin. Increases in these liver enzymes were reversible with dose medication or treatment discontinuation. Prior to starting Esbriet, patients should obtain liver function tests.

The most common adverse reactions (≥10%) are nausea, rash, abdominal pain, upper respiratory tract infection, diarrhea, fatigue, headache, dyspepsia, dizziness, vomiting, anorexia, gastro-esophageal reflux disease, sinusitis, insomnia, weight decreased, and arthralgia.

DOSAGE

The recommended daily maintenance dose of Esbriet is 801 mg (three 267 mg capsules, three 267 mg tablets, or one 801 mg tablet) three times a day with food for a total of 2403 mg/day. Doses should be taken at the same time each day.

Upon initiation of treatment, titrate to the full dosage of 2403 mg per day over a 14-day period as follows:

<table>
<thead>
<tr>
<th>TREATMENT DAYS</th>
<th>DOSAGE</th>
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<tbody>
<tr>
<td>Days 1 through 7</td>
<td>267 mg three times a day with food</td>
</tr>
<tr>
<td>Days 8 through 14</td>
<td>534 mg three times a day with food</td>
</tr>
<tr>
<td>Days 15 onward</td>
<td>801 mg three times a day with food</td>
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</tbody>
</table>

Patients who miss 14 or more days of Esbriet should re-initiate treatment by undergoing the initial 2-week titration regimen up to the full maintenance dosage.

Temporary dosage reductions or interruptions of Esbriet may be considered if patients experience significant adverse reactions or elevations in liver enzyme and bilirubin. Modifications in dosage should also be considered when Esbriet is administered concurrently with CYP1A2 inhibitors.

FDA APPROVED INDICATION

Esbriet is a pyridine indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

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REFERENCES


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