Pharmacy Policy

Idiopathic Pulmonary Fibrosis Agents

Policy Number: 9.057
Version Number: 2.0
Version Effective Date: 11/14/2016

Product Applicability  □ All Plan* Products

Well Sense Health Plan
☒ New Hampshire Medicaid
☒ NH Health Protection Program

Boston Medical Center HealthNet Plan
☒ MassHealth
☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct
□ Senior Care Options

Note: Disclaimer and audit information is located at the end of this document.

Policy Summary

The Plan may authorize coverage of idiopathic pulmonary fibrosis agents when appropriate criteria are met.

Description of Item or Service

Idiopathic pulmonary fibrosis (IPF) is a specific type of chronic, progressive fibrosing interstitial pneumonia of unknown cause, affecting mostly older adults. The clinical symptoms of IPF are non-specific and typically present with a gradual onset, usually over six months. Based on the limited prevalence data available, the prevalence of IPF ranges from 27.9 cases to 63 cases per 100,000 persons in the United States per the results of a cohort study conducted in 2005. Idiopathic pulmonary fibrosis has a poor prognosis with death rates increasing with increasing age, and is consistently higher in men than women. IPF is thought to be the leading indication for lung transplantation.

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The optimal medical management of IPF has not yet been identified. Treatment strategies for idiopathic pulmonary fibrosis include the assessment and management of comorbid conditions according to current practice guidelines, including chronic obstructive pulmonary disease, obstructive sleep apnea, gastroesophageal reflux disease, and coronary artery disease. Other strategies include tobacco cessation, oxygen therapy in select patients, lung transplantation, vaccination against influenza and pneumococcal infection, and use of pharmacotherapy agents. Several agents have been evaluated for the treatment of IPF: systemic corticosteroids (prednisone), immunosuppressants (azathioprine, cyclophosphamide), tyrosine kinase inhibitors (nintedanib), and antifibrotic agents (pirfenidone). Of these, nintedanib and pirfenidone are the only two with FDA approved indication. Systemic corticosteroids (prednisone) and immunosuppressants (azathioprine, cyclophosphamide) are not recommended for use in IPF.

Nintedanib (Ofev®) is a tyrosine kinase inhibitor indicated for the treatment of idiopathic pulmonary fibrosis. Nintedanib targets growth factor receptors involved in the pulmonary fibrosis disease process. It inhibits the platelet-derived growth factor receptor (PDGFR), fibroblast growth factor receptor (FGFR) and vascular endothelial growth factor receptor (VEGFR). Nintedanib was studied in three randomized, double-blind, placebo-controlled, 52-week trials. A total of 723 patients with IPF received Nintedanib 150 mg twice daily and 508 patients received placebo. The median duration of exposure was 10 months for patients treated with nintedanib and 11 months for patients treated with placebo. Nintedanib showed attenuated reduction in pulmonary function over 52 weeks but did not show significant reductions in exacerbation rates or mortality. Nintedanib is available as oral capsules and dosed 150mg twice daily with food. Dose adjustment may be necessary if adverse event occurs, including elevated liver enzymes and in patients with mild hepatic impairment (Child Pugh A). The most commonly reported adverse events associated with nintedanib are diarrhea, nausea, abdominal pain and liver enzyme elevation.

Pirfenidone (Esbriet®) is another agent indicated for the treatment of idiopathic pulmonary fibrosis. It is a synthetic nonpeptide anti-inflammatory, antioxidant and antifibrotic agent; its mechanism of action in IPF is unknown. Pirfenidone was studied in three randomized, double-blind, placebo-controlled trials in which a total of 623 patients received 2403 mg/day of pirfenidone and 624 patients received placebo. The mean duration of exposure to pirfenidone was 62 weeks in these 3 trials. In two of the three trials, pirfenidone resulted in a statistically significant reduction in lung function decline from baseline compared to placebo.

The CAPACITY trial combined the results of two large-scale randomized controlled trials to assess pirfenidone in reducing the decline in FVC in patients with idiopathic pulmonary fibrosis compared to placebo for 72 weeks. In study 004, 435 patients were randomized to one of three treatment groups (high-dose pirfenidone [2,403 mg/d], low-dose pirfenidone [1,197 mg/d], and placebo). This study found that pirfenidone treatment had a reduction in decline of FVC during the 72 treatment period. In study 006, 3444 patients were randomized to only two treatment groups (high dose pirfenidone [2,403 mg/d] and placebo). This study found that pirfenidone had no benefit in reducing decline in FVC during the same period. Analysis of the combined studies showed a pirfenidone treatment effect on reducing decline in FVC. Fewer overall death and fewer deaths related to idiopathic pulmonary fibrosis occurred in the high dose pirfenidone groups than in the placebo group.

The ASCEND trial randomized 555 patients to either high-dose pirfenidone or placebo for 52 weeks. Study results found pirfenidone significantly reduced the proportion of patients who had a more than 10% decline in
their FCV and death. Additionally, as secondary endpoints, pirenidone significantly reduced the rate of decline in the six-minute walk distance and improved progression-free survival when compared with placebo, but did not reduce dyspnea or death from any cause.

The recommended maintenance dose of pirenidone is 3 capsules (801mg) 3 times daily with food; a 2 week dose titration period is required. Dose adjustments may be necessary for adverse events, and when co-administered with other medications, specifically strong CYP1A2 inhibitors. Use of pirenidone with strong CYP1A2 inducers is not recommended. The most commonly reported adverse event associated with pirenidone are nausea, rash, dizziness, vomiting, gastroesophageal reflux disease, sinusitis, insomnia, weight decrease and arthralgia. Liver function tests should be monitored at baseline and while on treatment with pirenidone.

The 2015 update of the 2011 ATS/ERS/JRS/ALAT clinical practice guideline for treatment of idiopathic pulmonary fibrosis recognizes Ofev® and Esbriet® as treatment options for patients with idiopathic pulmonary fibrosis. To date, there are no comparison studies evaluating the efficacy between Ofev® and Esbriet®. There is no available information to support the concurrent use of Ofev® and Esbriet®.

Policy

The Plan may approve coverage of idiopathic pulmonary fibrosis agents for members meeting the following criteria:

**Prior Authorization**

A prior authorization request will be required for all prescriptions for Esbriet®, Ofev®. These requests will be approved when the following criteria are met:

**Esbriet®, Ofev®**

**Initial therapy (Duration of Approval – Maximum of 1 year)**

1. A diagnosis of idiopathic pulmonary fibrosis; **AND**
2. Medication is prescribed by or in collaboration with a pulmonologist

**Re-authorization of Therapy (Duration of Approval – Maximum of 1 year)**

Prior Authorization is required for all prescriptions for continued treatment beyond the initial approval duration. These requests will be approved when the following criteria are met:

1. Initial criteria were previously met; **AND**
2. There is a decrease in pulmonary function deterioration and no significant adverse events.

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Idiopathic Pulmonary Fibrosis Agents

Quantity Limitations Apply - see appendix 1

Limitations

The Plan will not approve coverage of idiopathic pulmonary fibrosis agents in the following instances:

1. When the criteria above has not been met.
2. Concurrent use of Ofev® and Esbriet®.

Clinical Background Information and References


Appendix 1: Quantity Limitations

<table>
<thead>
<tr>
<th>Medication Name</th>
<th>Quantity Limitation</th>
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<tbody>
<tr>
<td>Esbriet</td>
<td>270 capsules per 30 days</td>
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<tr>
<td>Ofev</td>
<td>60 capsules per 30 days</td>
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<table>
<thead>
<tr>
<th>Original Approval Date</th>
<th>Original Effective Date</th>
<th>Policy Owner</th>
<th>Approved by</th>
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<tr>
<td>07/09/2015</td>
<td>11/04/2015</td>
<td>Pharmacy Services</td>
<td>Pharmacy &amp; Therapeutics (P&amp;T) Committee</td>
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**Policy Revisions History**

<table>
<thead>
<tr>
<th>Review Date</th>
<th>Summary of Revisions</th>
<th>Revision Effective Date</th>
<th>Approved by</th>
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<tr>
<td>07/14/2016</td>
<td>P&amp;T annual review, no changes required.</td>
<td>11/14/2016</td>
<td>P&amp;T Committee</td>
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**Next Review Date**

07/13/2017

**Other Applicable Policies**

9.002 Mandatory Generic Substitution Policy
9.015 Quantity Limitation Policy
OCA 3.14 Medically Necessary Policy

**Reference to Applicable Laws and Regulations, If Any**

**Disclaimer Information**

Medical Policies are the Plan’s guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member’s benefit document, and when appropriate, coordinates with the Member’s health care Providers to consider the individual Member’s health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan’s service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member’s benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with

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applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.