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Interstitial Lung Disease Prior Authorization with Quantity Limit Program Summary

FDA APPROVED INDICATIONS AND DOSAGE[1,2]

Agent(s)	Indication(s)	Dosage
Esbriet® (pirfenidone) Tablet Capsule	Treatment of idiopathic pulmonary fibrosis (IPF)	801 mg three times daily taken with food after 14-day titration
Ofev® (nintedanib) Capsule	Treatment of idiopathic pulmonary fibrosis (IPF)	150 mg twice daily approximately 12 hours apart taken with food
	Slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)	
	Treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype	

CLINICAL RATIONALE

Interstitial Lung Disease

Interstitial lung diseases (ILD) encompass a varied group of more than 200 lung disorders that affect the tissue and space around the alveoli. They are classified together because of similar physiologic, radiographic, clinical, or pathologic manifestations: respiratory symptoms such as shortness of breath and cough, specific chest radiographic abnormalities, typical changes on pulmonary function tests in which lung volume is decreased, and characteristic microscopic patterns of inflammation and fibrosis. Fibrosis is characterized by an increased amount and abnormal structure of the connective tissue, with lung biopsies with a predominance of fibrosis typically indicating advanced disease and poor prognosis.[11]

The underlying causes of ILD can be classified into four categories: diseases associated with a condition that affects other parts of the body (e.g., autoimmune, collagen vascular disease), exposure to agents known to damage the lungs (e.g., medications, occupational exposures [e.g., asbestos, tobacco smoke]), genetic abnormalities (e.g., Hermansky-Pudlak syndrome), or idiopathic etiology (the most common form).[13]

Idiopathic Pulmonary Fibrosis (IPF)

Idiopathic pulmonary fibrosis (IPF) is a form of chronic, progressive fibrosing interstitial pneumonia of unknown origin occurring primarily in older adults and is limited to the lungs.[5,6] IPF is associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia (UIP).[4,6] IPF is characterized by fibroblast foci, featuring vigorous replication of mesenchymal cells and disposition of extracellular matrix. It is thought that repeated episodes of acute lung injury, due to unknown stimulus, leads to wound healing and fibrosis, with loss of lung function.[7] The natural progression can vary with some patients remaining stable for extended periods of time; some having steady, but rapid progression; and some patients experiencing acute exacerbations.[3] Historically, a diagnosis of IPF has been associated with a poor prognosis with many only living for 3-5 years post diagnosis. The estimated prevalence of IPF within the United States has been difficult to establish due to the historical lack of a uniform definition, evolving diagnostic criteria, and difference in case-finding methodologies and study designs. The range is between 14-63 per 100,000 population with an annual incidence of approximately 7-16 per 100,000 population.[4]

Guidelines suggest that IPF be considered in adult patients presenting with unexplained chronic exertional dyspnea, cough, bibasilar inspiratory crackles, and/or finger clubbing.[4,6]
An accurate diagnosis of IPF is a difficult and challenging process. The accuracy of the diagnosis increases with an integrated multidisciplinary approach. This includes dynamic discussion between pulmonologists, radiologists, and pathologists (when appropriate) who are experienced in the diagnosis of ILD.[3] The diagnosis of IPF requires exclusion of other known causes of ILD (e.g., domestic and occupational environmental exposures, connective tissue disease, and drug toxicity), and either the presence of a UIP pattern on HRCT in patients not subjected to surgical lung biopsy (SLB) OR specific combinations of HRCT patterns and histopathological patterns in patients subjected to SLB. Guidelines also recommend serological testing to exclude connective tissues disease.[3,6]

The 2018 guidelines provide a new diagnostic algorithm and schema for correlating histologic and radiologic findings in patients with suspected IPF.[6] Aspects of this algorithm include criteria for four diagnostic categories for patterns of UIP based on HRCT findings (i.e., UIP, probable UIP, indeterminate for UIP, and alternative diagnosis), and four levels of certainty for histopathologic diagnosis (i.e., UIP, probable UIP, indeterminate for UIP, and alternative diagnosis). Below in Table 1 and 2 are the current guidelines on diagnosis of IPF with HRCT and SLB.

Table 1. High Resolution Computed Tomography (HRCT) Scanning Patterns[6]

UIP	Probable UIP	Indeterminate for UIP	Alternative Diagnosis
Subpleural and basal predominant; distribution is often heterogeneous [g] Honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis [h]	Subpleural and basal predominant; distribution is often heterogeneous Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis May have mild ground-glass opacities	Subpleural and basal predominant Subtle reticulation; may have mild ground glass opacities or distortion ("early UIP pattern") CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")	Findings suggestive of another diagnosis include: • CT features: o Cysts o Marked mosaic attenuation o Predominant ground glass opacities o Profuse micronodules o Centrilobular nodules o Nodules o Consolidation • Predominant distribution: o Peribronchovascular o Perilymphatic o Upper or mid-lung • Other: o Pleural plaques (consider asbestosis) o Dilated esophagus (consider connective tissue disease) o Distal clavicular erosions (consider rheumatoid arthritis) o Extensive lymph node enlargement (consider other etiologies) o Pleural effusions, pleural thickening (consider connective tissue disease/drugs)

g – variants of distribution: occasionally diffuse, may be asymmetrical
h – superimposed CT features: mild ground glass opacities, reticular pattern, pulmonary ossification

Table 2. Histopathology Patterns and Features[6]

UIP	Probable UIP	Indeterminate for UIP	Alternative Diagnosis
• Dense fibrosis with architectural distortion (i.e., destructive scarring and/or honeycombing) • Predominant subpleural and/or paraseptal distribution of fibrosis • Patchy involvement of lung parenchyma by fibrosis • Fibroblast foci • Absence of feature to suggest an alternate diagnosis	• Some histologic features from column 1 are present but to an extent that precludes a definite diagnosis of UIP/IPF ***AND*** • Absence of features to suggest an alternative diagnosis **OR** • Honeycombing only	• Fibrosis with or without architectural distortion, with features favoring either a pattern other than UIP or features favoring UIP secondary to another cause [j] • Some histologic features from column 1, but with other features suggesting an alternative diagnosis [k]	• Features of other histologic patterns of IIPs (e.g., absence of fibroblast foci or loose fibrosis) in all biopsies • Histologic findings indicative of other diseases (e.g., hypersensitivity pneumonitis, Langerhans cell histiocytosis, sarcoidosis, LAM)

IIP = idiopathic interstitial pneumonia; LAM = lymphangioleiomyomatosisj – granulomas, hyaline membranes (other than when associated with acute exacerbation of IPF, which may be the presenting manifestation in some patients), prominent airway-centered changes, areas of interstitial inflammation lacking associated fibrosis, marked chronic fibrous pleuritis, organizing pneumonia. Such features may not be overt or easily seen to the untrained eye and often need to be specifically sought.

k – Features that should raise concerns about the likelihood of an alternative diagnosis include a cellular inflammatory infiltrate away from areas of honeycombing, prominent lymphoid hyperplasia including secondary germinal centers, and a distinctly bronchiolocentric distribution that could include extensive peribronchiolar metaplasia.

UIP is characterized on HRCT by the presence of honeycombing, traction bronchiectasis, and traction bronchiolectasis, which may have concurrent fine reticulation and ground-glass opacification. Honeycombing must be present for a definitive HRCT diagnosis of UIP. Honeycombing is manifested on HRCT as clustered cystic airspaces, typically of comparable diameters (3–10 mm but occasionally larger). It is usually subpleural and is characterized by well-defined walls. Traction bronchiectasis/bronchiolectasis is another key feature of IPF and ranges from subtle irregularity and non-tapering to marked airway distortion and varicosity. Ground-glass opacifications superimposed on a fine reticular pattern represents fibrosis and may be seen in patients with IPF. The distribution of UIP on HRCT is characteristically basal and peripheral, though often patchy. The presence of coexistent pleural abnormalities (noted in the alternative diagnosis section in Table 1 above) should lead to consideration of an alternative diagnosis. If HRCT patterns show probable or indeterminate UIP, the 2018 guidelines recommend surgical lung biopsy to make a definitive diagnosis. In patients whose HRCT does not demonstrate a UIP pattern, the surgical lung biopsy may still demonstrate UIP pattern on histopathology.[6] Table 3 below shows the algorithm for diagnosis with the updated guidelines.

Table 3. Idiopathic pulmonary fibrosis diagnosis based upon HRCT and biopsy patterns[6]

IPF Suspected[c]		Histopathology Pattern			
		UIP	**Probable UIP**	**Indeterminate for UIP**	**Alternative Diagnosis**
HRCT Pattern	**UIP**	IPF	IPF	IPF	Non-IPF diagnosis
	Probable UIP	IPF	IPF	IPF (likely)[d]	Non-IPF diagnosis
	Indeterminate	IPF	IPF (likely)[d]	Indeterminate[f]	Non-IPF diagnosis
	Alternative Diagnosis	IPF (likely)[d]/non-IPF diagnosis	Non-IPF diagnosis	Non-IPF diagnosis	Non-IPF diagnosis

c - "Clinically suspected of having IPF" = unexplained symptomatic or asymptomatic patterns of bilateral pulmonary fibrosis on a chest X-ray or chest CT, bibasilar inspiratory crackles, and age greater than 60 years. (Middle aged adults [greater than 40 years and less than 60 years], especially patients with risks for familial pulmonary fibrosis, can rarely present with the otherwise same clinical scenario as the typical patient older than 60 years.)
d - IPF is the likely diagnosis when any of the following features are present:

- Moderate-to-severe traction bronchiectasis/bronchiolectasis (defined as mild traction bronchiectasis/bronchiolectasis in four or more lobes including the lingual as a lobe, or moderate to severe traction bronchiectasis in two or more lobes) in a man over age 50 years or in a woman over age 60 years
- Extensive (greater than 30%) reticulation on HRCT and an age greater than 70 years
- Increased neutrophils and/or absence of lymphocytosis in BAL fluid
- Multidisciplinary discussion reaches a confident diagnosis of IPF

f - Indeterminate

- Without an adequate biopsy is unlikely to be IPF
- With an adequate biopsy may be reclassified to a more specific diagnosis after multidisciplinary discussion and/or additional consultation

Prior to the simultaneous approvals of Esbriet (pirfenidone) and Ofev (nintedanib), there was no FDA approved pharmacologic therapy for idiopathic pulmonary fibrosis. The updated ATS/ERS/JRS/ALAT (American Thoracic Society, European Respiratory Society, Japanese Respiratory Society, and Latin American Thoracic Society) clinical practice guidelines address nintedanib and pirfenidone treatment for IPF. The guidelines suggest that clinicians use nintedanib or pirfenidone in patients with IPF (conditional recommendation, moderate confidence in estimates of effects). As with other interventions, the available evidence focuses on patients with IPF with mild to moderate impairment in pulmonary function tests; it is unknown whether the therapeutic benefits would differ in patients with a more severe impairment in pulmonary function testing or those with other comorbidities. The evidence does not allow suggestions about the optimal duration of therapy, and it is unknown how long the treatment effect endures with ongoing drug therapy.[5]

Currently, there are no head-to-head trials comparing the two agents. A retrospective cohort study assessed the clinical effectiveness of nintedanib and pirfenidone in the treatment of IPF. The primary outcome was all-cause mortality, which was seen reduced in the treated cohort versus the untreated cohort. This mortality benefit was only observed for the first two years of follow-up. No significant differences were noted in all-cause mortality between patients treated with nintedanib versus pirfenidone; however, pirfenidone had a slightly more favorable trend.[14]

The possibility that combined therapy might be of greater benefit is under investigation, with results supporting further research into combination treatment with pirfenidone and nintedanib. An open-label, randomized trial (INJOURNEY) evaluating the safety and tolerability of nintedanib with add-on pirfenidone demonstrated a manageable safety and tolerability profile in patients with IPF, in line with the adverse event profiles of each drug.[15] Another trial, open-label, 24-week, single-arm, phase IV study, assessed safety and tolerability of treatment with pirfenidone and nintedanib in patients with IPF. Combined pirfenidone and nintedanib use for 24 weeks was tolerated by the majority of patients with IPF and associated with a similar pattern of adverse events expected for either treatment alone.[16]

Systemic Sclerosis (Scleroderma)-Associated Interstitial Lung Disease (ILD)
Systemic sclerosis is a connective tissue disease (CTD) that affects numerous organ systems, including skin, blood vessels, heart, lungs, kidneys, gastrointestinal, and musculoskeletal. Pulmonary disease is the leading cause of death in patients with systemic sclerosis, and ILD is a common manifestation that tends to occur early in the course of systemic sclerosis.[8]

The American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) collaborated on classification criteria for the diagnosis of systemic sclerosis, in which they note that systemic sclerosis-associated ILD is diagnosed when there is radiographic evidence of diffuse parenchymal lung disease in patients with systemic sclerosis. The ACR/EULAR criteria

note that ILD is defined as pulmonary fibrosis seen on HRCT or chest radiography, most pronounced in the basilar portions of the lungs.[10]

The American College of Rheumatology (ACR) published a treatment algorithm for systemic sclerosis and related conditions. The ACR recommends the following treatment options for ILD associated with systemic sclerosis:[9]

Induction therapy:
- Mycophenolate mofetil (MMF) as first line therapy
- IV cyclophosphamide as second line therapy
- Rituximab as third line therapy
- Lung transplant or hemopoietic stem cell transplant for select patients as fourth line therapy

Maintenance therapy:
- Mycophenolate mofetil (MMF) as first line therapy
- Azathioprine as second line therapy
- IV or oral cyclophosphamide as third line therapy

Chronic Fibrosing Interstitial Lung Disease with Progressive Phenotype
Patients that have a progressive fibrosing phenotype tend to be characterized by an increasing extent of fibrosis on HRCT, decreasing lung function, worsening of symptoms and quality of life, and early death despite treatment. The progressive phenotype is similar to IPF in clinical behavior and in many of the underlying pathogenic mechanisms, such as repeated chronic epithelial or vascular injuries leading to cell destruction and unregulated repair, that drive a self-sustaining process of pulmonary fibrosis.[12] There are currently no guidelines to define the management of patients with ILD with a progressive phenotype.[11]

Efficacy[2]
The clinical efficacy of Ofev has been studied in patients with chronic fibrosing ILDs with a progressive phenotype in a randomized, double-blind, placebo-controlled phase 3 trial (Study 5 [NCT02999178]). A total of 663 patients were randomized in a 1:1 ratio to receive either Ofev 150 mg twice daily or matching placebo for at least 52 weeks. Randomization was stratified based on high resolution computed tomography (HRCT) fibrotic pattern as assessed by central readers. The primary endpoint was the annual rate of decline in FVC (in mL) over 52 weeks. Other endpoints included time to first acute ILD exacerbation and time to death.

Patients with a clinical diagnosis of a chronic fibrosing ILD were selected if they had relevant fibrosis (greater than 10% fibrotic features) on HRCT and presented with clinical signs of progression (defined as FVC decline greater than or equal to 10%, FVC decline greater than or equal to 5% and less than 10% with worsening symptoms or imaging, or worsening symptoms and worsening imaging all in the 24 months prior to screening). Patients were required to have an FVC greater than or equal to 45% of predicted and a diffusion capacity of the lungs for carbon monoxide (DLCO) 30% to less than 80% of predicted. Patients were required to have progressed despite management deemed appropriate in clinical practice by investigators for the patient's relevant ILD.

Patients with IPF, relevant airways obstruction (i.e., pre-bronchodilator FEV1/FVC less than 0.7), or significant pulmonary hypertension were excluded from the trial. Patients with greater than 1.5 times ULN of ALT, AST, or bilirubin, patients with a known risk or predisposition to bleeding, patients receiving a full dose of anticoagulation treatment, and patients with a recent history of myocardial infarction or stroke were excluded.

The underlying clinical ILD diagnoses in groups represented in the trial were hypersensitivity pneumonitis (26%), autoimmune ILDs (26%), idiopathic nonspecific interstitial pneumonia (19%), unclassifiable idiopathic interstitial pneumonia (17%), and other ILDs (12%).

There was a statistically significant reduction in the annual rate of decline in FVC (in mL) over 52 weeks in patients receiving Ofev compared to patients receiving placebo. The annual rate of decline in FVC (in mL) over 52 weeks was significantly reduced by 107 mL in patients receiving Ofev compared to patients receiving placebo. For the majority of patients, the decline in lung function was less on Ofev than on placebo. The risk of first acute ILD exacerbation did not show a statistically significant difference between the Ofev group compared to placebo (52-week treatment period: HR 0.72, [95% CI: 0.38, 1.37]; whole trial: HR 0.63 [95% CI: 0.37, 1.07]). Survival was evaluated for Ofev compared to placebo in Study 5 to support the primary endpoint (FVC). All-cause mortality was assessed over the study duration and available follow-up period, irrespective of cause of death and whether patients continued treatment. All-cause mortality did not show a statistically significant difference (52-week treatment period: HR 0.94 [95% CI: 0.47, 1.86]; whole trial: HR 0.78 [95% CI: 0.50, 1.21]).

Safety
Neither Esbriet nor Ofev have any FDA labeled contraindications.[1,2]

References

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15. Vancheri C, Kreuter M, Richeldi L, et al. 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.
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Interstitial Lung Disease Prior Authorization with Quantity Limit

TARGET AGENT(S)
Esbriet® (pirfenidone)
Ofev® (nintedanib)

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)
Esbriet (pirfenidone)			
267 mg capsules	45550060000120	M, N, O, or Y	6 capsules
267 mg tablets	45550060000325	M, N, O, or Y	6 tablets
801 mg tablets	45550060000345	M, N, O, or Y	3 tablets
Ofev (nintedanib)			
100 mg capsules	45554050200120	M, N, O, or Y	2 capsules
150 mg capsules	45554050200130	M, N, O, or Y	2 capsules

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of idiopathic pulmonary fibrosis (IPF) AND ALL of the following:
      I. The patient has not had a significant environmental exposure known to cause pulmonary fibrosis (e.g., drugs, asbestos, beryllium, radiation, raising birds/livestock, and metal dusts)
      AND
      II. The patient has no known explanation for interstitial lung disease (e.g., radiation, sarcoidosis, hypersensitivity pneumonitis, bronchiolitis obliterans organizing pneumonia, human immunodeficiency virus (HIV), viral hepatitis, and cancer)
      AND
      III. The patient has undergone serological testing to exclude any connective tissue disease known to cause interstitial lung disease (e.g., scleroderma, polymyositis/dermatomyositis, systemic lupus erythematosus, and rheumatoid arthritis)
      AND
      IV. The patient does not have clinical evidence of active infection (e.g., bronchitis/bronchiolitis, pneumonia, and sinusitis), except in the instance of a diagnosis of IPF pre-dating the infection
      AND
      V. ONE of the following:
         i. ALL of the following:
            a. The patient has usual interstitial pneumonia (UIP) patterns on high-resolution computed tomography (HRCT) scans [containing BOTH of the following features: 1) subpleural, basal predominance 2) honeycombing with or without traction bronchiectasis]
            AND

b. The patient does NOT have the presence of any of the following on HRCT:
    i. CT features (i.e., cysts, marked mosaic attenuation, predominant ground glass opacities, profuse micronodules, centrilobular nodules, nodules, consolidation)
    ii. Predominant distribution (i.e., peribronchovascular, perilymphatic, upper or mid-lung)
    iii. Pleural plaques
    iv. Dilated esophagus
    v. Distal clavicular erosions
    vi. Extensive lymph node enlargement
    vii. Pleural effusions, pleural thickening

AND

c. A pulmonologist and a radiologist, both experienced in the diagnosis of interstitial lung disease, have been consulted with and both determine that the patient has definitive IPF

OR

ii. ALL of the following:
a. The patient has probable UIP patterns on HRCT (i.e., subpleural, basal predominance; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis; may have mild ground-glass opacities)

AND

b. ONE of the following:
    i. The patient has had a surgical lung biopsy that demonstrates UIP pattern on histopathology [containing ALL of the following 4 features: 1) Dense fibrosis with architectural distortion [i.e., destructive scarring and/or honeycombing] 2) predominantly subpleural and/or paraseptal distribution of fibrosis 3) presence of patchy involvement of lung parenchyma by fibrosis 4) presence of fibroblast foci]

    OR

    ii. The patient has had a surgical lung biopsy that demonstrates probable UIP pattern on histopathology [containing ONE of the following features: 1) some of the features listed for UIP patterns on histopathology noted above but to an extent that precludes a definite diagnosis AND absence of features to suggest an alternative diagnosis; OR 2) honeycombing alone].

AND

c. The patient does NOT have the presence of any of the following:
    i. Features of other histologic patterns of idiopathic interstitial pneumonia (e.g., absence of fibroblast foci or loose fibrosis) in all biopsies
    ii. Histological findings indicative of an alternative diagnosis (e.g., hypersensitivity pneumonitis, Langerhans cell histiocytosis, sarcoidosis, lymphangioleiomyomatosis)

AND

d. A pulmonologist, radiologist, and a pathologist all experienced in the diagnosis of interstitial lung disease have been consulted with and determined that the patient has definitive IPF

OR

iii. ALL of the following:

a. The patient has indeterminate UIP patterns on HRCT (i.e., subpleural, basal predominance; subtle reticulation [may have mild ground-glass opacities or distortion]; CT features and/or distribution of lung fibrosis that do not suggest any specific etiology)
AND
b. The patient has had a surgical lung biopsy that demonstrates UIP pattern on histopathology [containing ALL of the following 4 features: 1) Dense fibrosis with architectural distortion [i.e., destructive scarring and/or honeycombing] 2) predominantly subpleural and/or paraseptal distribution of fibrosis 3) presence of patchy involvement of lung parenchyma by fibrosis 4) presence of fibroblast foci]
AND
c. The patient does NOT have the presence of any of the following:
i. Features of other histologic patterns of idiopathic interstitial pneumonia (e.g., absence of fibroblast foci or loose fibrosis) in all biopsies
ii. Histological findings indicative of an alternative diagnosis (e.g., hypersensitivity pneumonitis, Langerhans cell histiocytosis, sarcoidosis, lymphangioleiomyomatosis)
AND
d. A pulmonologist, radiologist, and a pathologist all experienced in the diagnosis of interstitial lung disease have been consulted with and determined that the patient has definitive IPF

OR

B. The patient has a diagnosis of interstitial lung disease (ILD) AND ALL of the following:
I. The requested agent is Ofev
AND
II. The patient's diagnosis has been confirmed on high-resolution computed tomography (HRCT) or chest radiography scans
AND
III. The patient's ILD is associated with systemic sclerosis
AND
IV. ONE of the following:
i. The patient has tried and had an inadequate response to ONE conventional agent (i.e., mycophenolate mofetil, cyclophosphamide, azathioprine)
OR
ii. The patient has an intolerance or hypersensitivity to ONE conventional agent
OR
iii. The patient has an FDA labeled contraindication to ALL conventional agents
AND
V. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pulmonologist, radiologist, pathologist, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

OR

C. The patient has a diagnosis of chronic fibrosing interstitial lung disease (ILD) with a progressive phenotype AND ALL of the following:
I. The requested agent is Ofev
AND
II. The patient has greater than 10% fibrotic features on HRCT
AND

III. The patient presented with clinical signs of progression, defined by at least ONE of the following:
    i. FVC decline greater than or equal to 10%
    OR
    ii. FVC decline greater than or equal to 5% and less than 10% with worsening symptoms or imaging
    OR
    iii. Worsening symptoms and worsening imaging within the past 24 months

AND

IV. The patient has an FVC greater than or equal to 45% of predicted

AND

V. The patient has a diffusion capacity of the lungs for carbon monoxide (DLCO) between 30% to less than 80% of predicted

AND

VI. The patient does NOT meet any of the following:
    i. A diagnosis of IPF
    ii. Relevant airway obstructions (i.e., pre-bronchodilator FEV1/FVC less than 0.7)
    iii. Significant pulmonary hypertension
    iv. Greater than 1.5 times the upper limit of normal for ALT, AST, or bilirubin
    v. Known risk or predisposition to bleeding
    vi. Receiving full dose anticoagulation treatment
    vii. Recent history of MI or stroke

AND

VII. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pulmonologist, radiologist, pathologist, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

OR

D. The patient has another FDA approved indication for the requested agent

AND

2. The patient will NOT be using the requested agent in combination with another agent included in this prior authorization program

AND

3. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

4. ONE of the following:
    A. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    B. ALL of the following:
        I. The requested quantity (dose) is greater than the program quantity limit
        AND
        II. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
        AND
        III. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
    OR
    C. ALL of the following:
        I. The requested quantity (dose) is greater than the program quantity limit
        AND
        II. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication

AND

III. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 12 months

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process
   AND
2. The patient has had clinical benefit with the requested agent
   AND
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pulmonologist, radiologist, pathologist, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
4. The patient will NOT be using the requested agent in combination with another agent included in this prior authorization program
   AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
6. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
   B. ALL of the following:
      I. The requested quantity (dose) is greater than the program quantity limit
         AND
      II. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
         AND
      III. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
      OR
   C. ALL of the following:
      I. The requested quantity (dose) is greater than the program quantity limit
         AND
      II. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
         AND
      III. The prescriber has provided information in support of therapy with a higher dose for the requested indication

Length of Approval: 12 months