Interstitial Lung Disease Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
04-01-2024	04-01-2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Esbriet® (pirfenidone)* Tablet Capsule	Treatment of idiopathic pulmonary fibrosis (IPF)	*generic available	1
Ofev® (nintedanib) Capsule	Treatment of idiopathic pulmonary fibrosis (IPF) 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		2

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

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).(4,6,17) 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.(3,6,17)

The 2018 and updated 2022 guidelines provide a new diagnostic algorithm and schema for correlating histologic and radiologic findings in patients with suspected IPF. 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).(6,17)

UIP is characterized on HRCT by the presence of peripheral, basilar-predominant opacities associated with honeycombing and traction bronchiectasis-bronchiolectasis. In patients whose HRCT does not demonstrate a UIP pattern, the surgical lung biopsy may demonstrate UIP pattern on histopathology.(6,17) Table 1 below shows the algorithm for diagnosis with the updated guidelines.

Table 1. Idiopathic pulmonary fibrosis diagnosis based upon HRCT and biopsy patterns(6,17)

IPF Suspected*		Histopathology Pattern			
		UIP	**Probable UIP**	**Indeterminate for UIP (or biopsy not performed)**	**Alternative Diagnosis**
HRCT Pattern	**UIP**	IPF	IPF	IPF	Non-IPF diagnosis
	Probable UIP	IPF	IPF	IPF (likely)**	Non-IPF diagnosis
	Indeterminate	IPF	IPF (likely)**	Indeterminate ***	Non-IPF diagnosis

	Alternative Diagnosis	IPF (likely)**	Indeterminate***	Non-IPF diagnosis	Non-IPF diagnosis

* "Clinically suspected of having IPF" = unexplained patterns of bilateral pulmonary fibrosis on a chest radiography or chest CT, bibasilar inspiratory crackles, and age greater than 60 years. (Middle aged adults [greater than 40 years and less than 60 years], can rarely present with otherwise clinical features, especially in patients with features suggesting familial pulmonary fibrosis.)

** IPF is the likely diagnosis when any of the following features are present:

- Moderate-to-severe traction bronchiectasis and/or bronchiolectasis (defined as mild traction bronchiectasis and/or bronchiolectasis in four or more lobes, including the lingula 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

*** Indeterminate for IPF

- Without an adequate biopsy remains indeterminate
- 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.(5,17)

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 (SSc-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 systemic sclerosis (scleroderma)-associated interstitial lung disease (SSc-ILD):(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 - Esbriet	ASCEND was a phase 3, randomized, double-blind, placebo-controlled, 52-week trial comparing pirfenidone 2403 mg/day (n=278) versus placebo (n=277) in patients with IPF. The primary endpoint was the change in FVC or death at week 52. In the pirfenidone group, there was a relative reduction of 47.9% in the proportion of patients who had an absolute decline of 10 percentage points or more in the percent predicted FVC or who died; there was also a relative increase of 132.5% in the proportion of patients with no decline in FVC (p less than 0.001). Pirfenidone reduced the decline in 6-minute walk distance (6MWD; p=0.04) and improved progression-free survival (PFS; p less than 0.001). There were no significant between-group differences in dyspnea scores (p=0.16), or in rates of death from any cause (p=0.10) or from IPF (p=0.23).(1) CAPACITY 004 and CAPACITY 006 were wo concurrent, phase 3, randomized, double-blind, placebo-controlled trials comparing pirfenidone and placebo in patient with IPF. The primary endpoint was the change in percent predicted FVC from baseline to week 72. In CAPACITY 004, patients were randomized 2:1:2 to pirfenidone 2403 mg/day

	(n=174), pirfenidone 1197 mg/day (n=87), or placebo (n=174). In CAPACITY 006, patients were randomized 1:1 to pirfenidone 2403 mg/day (n=171) or placebo (n=173).(1) In CAPACITY 004, pirfenidone reduced decline in FVC (p=0.001), mean FVC change at week 72 was -8.0% (SD 16.5) in the pirfenidone 2403 mg/day group, and −12.4% (18.5) in the placebo group (difference 4.4%, 95% CI 0.7-9.1); 35/174 (20%) vs. 60/174 (35%) patients, respectively, had a decline of at least 10%. A significant treatment effect was noted at all timepoints from week 24 and in an analysis over all study timepoints (p=0.0007). Mean change in percentage FVC in the pirfenidone 1197 mg/day group was intermediate to that in the pirfenidone 2403 mg/day and placebo groups.(1) In CAPACITY 006, the difference between groups in FVC change at week 72 was not significant (p=0.501). Mean change in FVC at week 72 was −9.0% (SD 19.6) in the pirfenidone group and −9.6% (19.1) in the placebo group, and the difference between groups in predicted FVC change at week 72 was not significant (0.6%, −3.5 to 4.7); however, a consistent pirfenidone effect was apparent until week 48 (p=0.005) and in an analysis of all study timepoints (p=0.007).(1)
Efficacy - Ofev	INPULSIS-1 and INPULSIS-2 were two replicate 52-week phase 3 trials that evaluated safety and efficacy of nintedanib twice daily compared to placebo in 1066 patients with IPF. Patients were randomized 3:2 to nintedanib or placebo. The primary endpoint was the annual rate of decline in FVC. In INPULSIS-1, the adjusted annual rate of change in FVC was −114.7 mL with nintedanib vs. −239.9 mL with placebo (difference, 125.3 mL; 95% CI, 77.7-172.8; p less than 0.001). There was no difference between groups in the time to the first acute exacerbation (HR with nintedanib, 1.15; 95% CI, 0.54-2.42; p=0.67). In INPULSIS-2, the adjusted annual rate of change in FVC was -113.6 mL with nintedanib vs. -207.3 mL with placebo (difference, 93.7 mL; 95% CI, 44.8-142.7; p less than 0.001). There was a significant benefit with nintedanib vs. placebo in the time to the first acute exacerbation (HR, 0.38; 95% CI, 0.19-0.77; p=0.005).(2) INBUILD was a randomized, double-blind, placebo-controlled trial evaluated the use of nintedanib in 663 patients with progressive fibrosing ILD. The primary endpoint was the annual rate of decline in FVC over 52 weeks. The two primary populations for analysis of the primary endpoint were the overall population and patients with a UIP-like fibrotic pattern. In the overall population, the adjusted rate of decline in FVC was -80.8 mL/year with nintedanib vs. -187.8 mL/year with placebo (treatment difference: 107.0 mL/year; 95% CI, 65.4-148.5; p less than 0.001). In patients with a UIP-like fibrotic pattern, the adjusted rate of decline in FVC was -82.9 mL/year with nintedanib vs. -211.1 mL/year with placebo (treatment difference: 128.2 mL/year; 95% CI, 70.8-185.6; p less than 0.001).(2) SENSCIS was a randomized, double-blind, placebo-controlled trial evaluated the use of nintedanib in 576 patients with SSc-ILD. The primary endpoint was the annual rate of decline in FVC over 52 weeks; key secondary endpoints were absolute changes from baseline in the modified Rodnan skin score and in the total score on the SGRQ at week 52. The adjusted annual rate of change in FVC was -52.4 mL/year with nintedanib vs. -93.3 mL/year with placebo (treatment difference: 41.0 mL/year; 95% CI, 2.9-79.0; p=0.04). Secondary endpoint measurements did not differ significantly between treatment arms.(2)
Safety	Neither Esbriet nor Ofev have any FDA labeled contraindications.(1,2)

REFERENCES

Number	Reference
1	Esbriet prescribing information. Genentech USA, Inc. February 2023.
2	Ofev prescribing information. Boehringer Ingelheim Pharmaceuticals, Inc. October 2022.

Number	Reference
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4	Nalysnyk L, Cid-Ruzafa J, Rotella P, Esser D. Incidence and Prevalence of Idiopathic Pulmonary Fibrosis: Review of the Literature. Eur Respir Rev. 2012;21(126):355-361.
5	An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis - An Update of the 2011 Clinical Practice Guideline. Am J Resp Crit Care. 2015;192(2):e3-e19.
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9	Fernández-Codina A, Walker KM, Pope JE. Treatment Algorithms for Systemic Sclerosis According to Experts. Arthritis Rheum. 2018 Nov;70(11):1820-1828.
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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.
16	Flaherty KR, Fell CD, Huggins JT, et al. Safety of Nintedanib Added to Pirfenidone Treatment for Idiopathic Pulmonary Fibrosis. Eur Respir J. 2018;52(2):1-10.
17	Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline. 2022;205(9):e18.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Ofev	nintedanib esylate cap	100 MG ; 150 MG	M ; N ; O ; Y	N		
Esbriet	pirfenidone cap	267 MG	M ; N ; O ; Y	O ; Y		
Esbriet	pirfenidone tab	267 MG ; 534 MG ; 801 MG	M ; N ; O ; Y	N ; O ; Y		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
	Pirfenidone Tab 534MG	534 MG	21	Tablets	180	DAYS			
Esbriet	Pirfenidone Cap 267 MG	267 MG	180	Capsules	30	DAYS			
Esbriet	Pirfenidone Tab 267 MG	267 MG	180	Tablets	30	DAYS			
Esbriet	Pirfenidone Tab 801 MG	801 MG	90	Tablets	30	DAYS			
Ofev	Nintedanib Esylate Cap 100 MG (Base Equivalent)	100 MG	60	Capsules	30	DAYS			
Ofev	Nintedanib Esylate Cap 150 MG (Base Equivalent)	150 MG	60	Capsules	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Esbriet	pirfenidone cap	267 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Esbriet	pirfenidone tab	267 MG ; 534 MG ; 801 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ofev	nintedanib esylate cap	100 MG ; 150 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
	Pirfenidone Tab 534MG	534 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Esbriet	Pirfenidone Cap 267 MG	267 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Esbriet	Pirfenidone Tab 267 MG	267 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Esbriet	Pirfenidone Tab 801 MG	801 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ofev	Nintedanib Esylate Cap 100 MG (Base Equivalent)	100 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Ofev	Nintedanib Esylate Cap 150 MG (Base Equivalent)	150 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical 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 BOTH of the following: 1. Other known causes of interstitial lung disease (ILD) have been excluded (e.g., domestic and occupational environmental exposures, connective tissue diseases, drug toxicities, alternative diagnoses, etc) **AND** 2. ONE of the following: A. The patient had a high-resolution computed tomography (HRCT) scan with results showing a pattern for usual interstitial pneumonia (UIP) **OR** B. The patient had a surgical lung biopsy with pathology confirming UIP **OR** C. The patient had a HRCT scan with results showing a pattern for probable UIP AND a surgical lung biopsy with pathology indicating probable UIP **OR** B. The patient has a diagnosis of systemic sclerosis-associated interstitial lung disease (SSc-ILD) AND ALL of the following: 1. The requested agent is Ofev **AND** 2. The patient's diagnosis has been confirmed on high-resolution computed tomography (HRCT) or chest radiography scans **AND** 3. ONE of the following: A. The patient has tried and had an inadequate response to ONE conventional agent (i.e., mycophenolate mofetil, cyclophosphamide, azathioprine) **OR** B. The patient has an intolerance or hypersensitivity to ONE conventional agent **OR** C. The patient has an FDA labeled contraindication to ALL conventional agents **OR** D. The prescriber has provided documentation that ALL conventional agents cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND**

Module	Clinical Criteria for Approval
	2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** C. The patient has a diagnosis of chronic fibrosing interstitial lung disease (ILD) with a progressive phenotype AND ALL of the following: 1. The requested agent is Ofev **AND** 2. The patient has greater than 10% fibrotic features on HRCT **AND** 3. The patient presented with clinical signs of progression, defined by at least ONE of the following: A. FVC decline greater than or equal to 10% **OR** B. FVC decline greater than or equal to 5% and less than 10% with worsening symptoms or imaging **OR** C. Worsening symptoms and worsening imaging within the past 24 months **AND** 4. The patient has an FVC greater than or equal to 45% of predicted **AND** 5. The patient has a diffusion capacity of the lungs for carbon monoxide (DLCO) between 30% to less than 80% of predicted **AND** 6. The patient does NOT meet any of the following: A. A diagnosis of IPF B. Relevant airway obstructions (i.e., pre-bronchodilator FEV1/FVC less than 0.7) C. Significant pulmonary hypertension D. Greater than 1.5 times the upper limit of normal for ALT, AST, or bilirubin E. Known risk or predisposition to bleeding F. Receiving full dose anticoagulation treatment G. Recent history of MI or stroke **AND** 7. The patient has another FDA approved indication for the requested agent **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., pathologist, pulmonologist, radiologist, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient will NOT be using the requested agent in combination with another agent included in this prior authorization program **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **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., pathologist, pulmonologist, radiologist, 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 **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval:** 12 months