Clinical Policy: Nintedanib (Ofev)

Reference Number: CP.PHAR.285
Effective Date: 11.01.16
Last Review Date: 08.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Nintedanib (Ofev®) is a kinase inhibitor.

FDA Approved Indication(s)

Ofev is indicated:

- For the treatment of idiopathic pulmonary fibrosis (IPF);
- For the treatment of chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype;
- To slow the rate of decline in pulmonary function in patients with systemic sclerosis associated interstitial lung disease (SSc-ILD).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Ofev is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Idiopathic Pulmonary Fibrosis (must meet all)**:**

1. Diagnosis of IPF;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. Member meets (a and b):
   a. Pulmonary fibrosis on high resolution computed tomography (HRCT) with one of the following (i or ii):
      i. Usual interstitial pneumonia (UIP) pattern;
      ii. Probable or indeterminate UIP pattern, and surgical lung biopsy or cellular analysis of bronchoalveolar lavage fluid confirms the diagnosis of IPF;
   b. Known causes of pulmonary fibrosis have been ruled out *(see Appendix D);*
5. Baseline forced vital capacity (FVC) ≥ 50% of predicted;
6. Baseline carbon monoxide diffusing capacity (DLCO) ≥ 30% of predicted;
7. Ofev is not prescribed concurrently with Esbriet®;
8. Member is not an active smoker as evidenced by recent (within the last 30 days) negative nicotine metabolite (i.e., cotinine) test;
9. Dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 6 months

B. Chronic Fibrosing Interstitial Lung Disease (must meet all):
1. Diagnosis of one of the following chronic fibrosing ILD subtypes (a-g):
   a. Chronic fibrosing hypersensitivity pneumonitis;
   b. Autoimmune ILD (e.g., rheumatoid arthritis-related ILD);
   c. Mixed connective tissue disease-associated ILD;
   d. Idiopathic non-specific interstitial pneumonia;
   e. Unclassifiable idiopathic interstitial pneumonia;
   f. Environmental/occupational exposure-related ILD;
   g. Sarcoidosis;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. For new starts only: member meets both of the following within the past 24 months (a and b):
   a. Pulmonary fibrosis affecting > 10% of lung volume on HRCT;
   b. Documentation of one of the following (i or ii):
      i. A relative decline in the FVC of ≥ 10% of the predicted value;
      ii. A relative decline in the FVC of 5% to < 10% of the predicted value plus either worsening of respiratory symptoms or an increased extent of fibrosis on HRCT;
5. Baseline FVC ≥ 45% of predicted;
6. Baseline DLCO ≥ 30% of predicted;
7. Ofev is not prescribed concurrently with Esbriet;
8. Member is not an active smoker as evidenced by recent (within the last 30 days) negative nicotine metabolite (i.e., cotinine) test;
9. Dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 6 months

C. Systemic Sclerosis Associated Interstitial Lung Disease (must meet all)**:**
1. Diagnosis of SSc-ILD;
2. Prescribed by or in consultation with a pulmonologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets (a and b):
   a. Pulmonary fibrosis affecting ≥ 10% of lung volume on HRCT;
   b. Additional signs of SSc are identified *(see Appendix E);*
5. Failure of a ≥ 3 consecutive month trial of cyclophosphamide or mycophenolate mofetil at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Baseline FVC ≥ 40% of predicted;
7. Baseline DLCO ≥ 30% of predicted;
8. Ofev is not prescribed concurrently with Esbriet;
9. Member is not an active smoker as evidenced by recent (within the last 30 days) negative nicotine metabolite (i.e., cotinine) test;
10. Dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Ofev is not prescribed concurrently with Esbriet;
4. If request is for a dose increase, new dose does not exceed 300 mg (2 capsules) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACR: American College of Rheumatology
ATS: American Thoracic Society
CTD: connective tissue disease
DLCO: carbon monoxide diffusing capacity
FDA: Food and Drug Administration
FVC: forced vital capacity
IPF: idiopathic pulmonary fibrosis
ILD: interstitial lung disease
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
SSc-ILD: systemic sclerosis associated interstitial lung disease
UIP: usual interstitial pneumonia

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cyclophosphamide (Cytoxan®, Neosar®)	**SSc-ILD*** PO: 1 – 2 mg/kg/day IV: 600 mg/m^2/month	PO: 2 mg/kg/day IV: 600 mg/m^2/month
mycophenolate mofetil (CellCept®)	**SSc-ILD*** PO: 1 – 3 g/day	3 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: American Thoracic Society (ATS) 2018 IPF Guidelines
- ATS diagnostic criteria for IPF are built around pulmonary fibrosis findings on HRCT and exclusion of known causes of ILD (e.g., domestic and occupational environmental exposures, CTD, drug toxicity).
- UIP is the hallmark radiologic pattern of IPF. Honeycombing is a distinguishing feature of UIP and must be present for a definite HRCT diagnosis of UIP to be made.
- In patients with a probable or indeterminate UIP pattern, surgical lung biopsy or cellular analysis of bronchoalveolar lavage fluid is recommended to confirm the diagnosis of IPF.

Appendix E: American College of Rheumatology (ACR) 2013 SSc Classification Criteria
While the majority of patients with SSc experience skin thickening and variable involvement of internal organs, there is no one confirmatory test for SSc. Similar to the IPF guidelines above, ACR lists HRCT as a diagnostic method for determining pulmonary fibrosis in SSc-ILD. The other diagnostic parameters below are drawn from ACR's scoring system purposed for clinical trials. While informative, ACR cautions that the scoring system parameters are not all inclusive of the myriad of SSc manifestations that may occur across musculoskeletal, cardiovascular, renal, neuromuscular and genitourinary systems.
<u>Examples of SSc skin/internal organ manifestations and associated laboratory tests:</u>
- Skin thickening of the fingers
- Fingertip lesions
- Telangiectasia
- Abnormal nailfold capillaries
- Raynaud's phenomenon
- SSc-ILD
- Pulmonary arterial hypertension
- SSc-related autoantibodies
  - Anticentromere
  - Anti–topoisomerase I [anti–Scl-70]
  - Anti–RNA polymerase III

Appendix F: General Information

- Smoking was associated with decreased exposure to Ofev, which may alter the efficacy profile of Ofev.
- The Ofev pivotal studies included only patients with mild to moderate lung impairment per FVC and DLCO.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
IPF, SSc-ILD, chronic fibrosing ILD with a progressive phenotype	150 mg PO BID approximately 12 hours apart (100 mg BID for patients with mild hepatic impairment or management of adverse reactions)	300 mg/day

VI. Product Availability

Capsules: 100 mg, 150 mg

VII. References

1. Ofev Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2022. Available at: https://docs.boehringer-ingelheim.com/Prescribing%20Information/PIs/Ofev/ofev.pdf. Accessed March 30, 2022.
2. Raghu G, Remy-Jardin M, Myers JL. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. American Thoracic Society. Am J Respir Crit Care Med. Stepember 1, 2018; 198(5):e44-e68.
3. van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: an American College of Rheumatology/European League against Rheumatism Collaborative Initiative. Ann Rheum Dis. 2013; 72:1747-1755.
4. Flaherty KR, Wells AU, Cottin V, et al. Nintedanib in progressive fibrosing interstitial lung diseases. N Engl J Med 2019;381:1718-27.
5. Richeldi L, Varone F, Bergna M, et al. Pharmacological management of progressive-fibrosing interstitial lung diseases: a review of the current evidence. Eur Respir Rev 2018;27:180074.
6. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: Idiopathic pulmonary fibrosis: Evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011; 183: 788-824.
7. Raghu G, Rochwerg B, Zhang Y, et al. An official ATS/ERS/JRS/ALAT clinical practice guideline: Treatment of idiopathic pulmonary fibrosis: An update of the 2011 clinical practice guideline. Am J Respir Crit Care Med. July 15, 2015; 192(2): e3–e19.
8. Roofeh D, Jaafar S, Vummidi D, Khanna D. Management of systemic sclerosis-associated interstitial lung disease. Curr Opin Rheumatol. 2019; 31(3): 241–249.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: policies combined for Centene Medicaid and Commercial lines of business; no significant changes from previously approved corporate policy; Medicaid: removed requirement for high-	05.10.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
resolution computed tomography or surgical lung biopsy findings confirming diagnosis; Commercial: added age requirement, approval durations modified from length of benefit to 6/12 months; references reviewed and updated.		
Added HIM line of business due to addition of agent(s) to the HIM formulary with PA	03.15.19	
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.21.19	08.19
Criteria added for new FDA indication: SSc-ILD; diagnostic criteria added for IPF; references reviewed and updated.	10.22.19	02.20
3Q 2020 annual review: criteria added for new FDA indication: chronic fibrosing ILD with a progressive phenotype; references reviewed and updated.	04.21.20	08.20
3Q 2021 annual review: for IPF, added requirements for HRCT UIP pattern and surgical biopsy/bronchoalveolar lavage per ATS guidelines; for SSc-ILD, added rheumatologist prescriber option per specialist feedback, clarified the fibrosis should affect at least 10% of lung volume on HRCT per pivotal trial inclusion criteria, and added redirection to cyclophosphamide or mycophenolate mofetil; for all indications, added baseline FVC/DLCO requirements per pivotal trial inclusion criteria, requirement against concurrent use with Esbriet, and requirement that member is not an active smoker; modified HIM.PHAR.21 to HIM.PA.154; added legacy WellCare initial 12 month approval duration; retire WCG.CP.PHAR.285; references reviewed and updated.	06.24.21	08.21
3Q 2022 annual review: no significant changes; for legacy WellCare, modified initial approval duration from 12 months to 6 months to align with other lines of business; references reviewed and updated.	03.30.22	08.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.