Clinical Policy: Nintedanib (Ofev)

Reference Number: CP.PCH.54
Effective Date: 03.01.25
Last Review Date: 02.25
Line of Business: Commercial, HIM

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 in adults:

- 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, cellular analysis of bronchoalveolar lavage fluid, or transbronchial lung cryobiopsy 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 both of the following (a and b):
   a. 300 mg per day;
   b. 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 both of the following (a and b):
   a. 300 mg per day;
   b. 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 both of the following (a and b):
    a. 300 mg per day;
    b. 2 capsules per day.

Approval duration: 6 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
    a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
    b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
    a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
    b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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 both of the following (a and b):
    a. 300 mg per day;
    b. 2 capsules per day.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.33 for health insurance marketplace; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and HIM.PA.103 for health insurance marketplace; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and HIM.PA.154 for health insurance marketplace.

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 and HIM.PA.154 for health insurance marketplace, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACR: American College of Rheumatology
ATS: American Thoractic Society
CTD: connective tissue disease
DLCO: carbon monoxide diffusing capacity
FDA: Food and Drug Administration
FVC: forced vital capacity
HRCT: high resolution computed tomography
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) 2022 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, transbronchial lung cryobiopsy, or cellular analysis of bronchoalveolar lavage fluid is recommended to confirm the diagnosis of IPF. Patients with a probable UIP pattern can receive a diagnosis of IPF without confirmation by lung biopsy after multidisciplinary discussion in the appropriate clinical setting (e.g., 60 years old, male, smoker).

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.
Examples of SSc skin/internal organ manifestations and associated laboratory tests:
- 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.; October 2022. Available at: http://www.ofev.com. Accessed December 4, 2024.
2. Raghu G, Remy-Jardin M, Richeldi L, et al. Idiopathic pulmonary fibrosis (an update) and progressive pulmonary fibrosis in adults: An official ATS/ERS/JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 2022; 205(9): e18-47.
3. 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. September 1, 2018; 198(5):e44-e68.
4. 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.
5. Flaherty KR, Wells AU, Cottin V, et al. Nintedanib in progressive fibrosing interstitial lung diseases. N Engl J Med 2019;381:1718-27.
6. 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.
7. 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.
8. 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.
9. Roofeh D, Jaafar S, Vummidi D, Khanna D. Management of systemic sclerosis-associated interstitial lung disease. Curr Opin Rheumatol. 2019; 31(3): 241–249.
10. Rahaghi FF, Hsu VM, Kaner RJ, et al. Expert consensus on the management of systemic sclerosis-associated interstitial lung disease. Respiratory Research. 2023; 24: 6.
11. Ganesh R, Montesi SB, Silver RM, et al. Treatment of systemic sclerosis–associated interstitial lung disease: Evidence-based recommendations. An official American Thoracic Society clinical practice guideline. Am J Respir Crit Care Med. January 15, 2024; 209(2): 137-152.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per December SDC and prior clinical guidance (adapted from CP.PHAR.285).	12.02.24	02.25

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.