Clinical Policy Title:	nintedanib
Policy Number:	RxA.440
Drug(s) Applied:	Ofev®
Original Policy Date:	03/06/2020
Last Review Date:	07/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Nintedanib (Ofev®) is a kinase inhibitor.

Ofev® is indicated for:

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
nintedanib (Ofev®)	IPF, ILDs, SSc-ILD	150 mg orally twice daily approximately 12 hours apart. Not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment. Recommended dosage in patients with mild hepatic impairment (Child Pugh A): 100 mg twice daily approximately 12 hours apart taken with food.	300 mg/day

Dosage Forms

- Capsules: 100 mg, 150 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Attestation that liver function tests in all patients and pregnancy tests in females of reproductive potential are conducted prior to initiating treatment;
5. Member meets at least one of the following (a or b):
   a. Pulmonary fibrosis on high resolution computed tomography (HRCT);
   b. Known causes of pulmonary fibrosis have been ruled out (e.g., domestic and occupational environmental exposures, CTD, drug toxicity);
6. Dose does not exceed 300 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Systemic Sclerosis Associated Interstitial Lung Disease (must meet all)**:**

1. Diagnosis of SSc-ILD;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. Attestation that liver function tests in all patients and pregnancy tests in females of reproductive potential are conducted prior to initiating treatment;
5. Member meets (a and b):
   a. Pulmonary fibrosis on HRCT;
   b. Additional signs of SSC are identified;
6. Dose does not exceed 300 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Chronic Fibrosing Interstitial Lung Disease (must meet all)**:**

1. Diagnosis of chronic fibrosing interstitial lung diseases with a progressive phenotype;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. Attestation that liver function tests in all patients and pregnancy tests in females of reproductive potential are conducted prior to initiating treatment;
5. Member meets both of the following (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 forced vital capacity (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;
6. Dose does not exceed 300 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 300 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
IPF: idiopathic pulmonary fibrosis
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer
HRCT: high resolution computed tomography
SSc-ILD: systemic sclerosis associated interstitial lung disease
FVC: forced vital capacity

APPENDIX B: Therapeutic Alternatives
Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Existing data for the use of Ofev® for non-small cell lung cancer (NSCLC) as a second- line agent show statistically significant improvement in progression free survival, but the clinical significance of the improvement (0.7 months) is questionable. Additionally, there is no significant difference in overall survival in patients treated with Ofev®. The National Comprehensive Cancer Network (NCCN) guidelines do not currently mention Ofev® as a treatment alternative for NSCLC.
- The following are potential risks in taking this medication: elevated liver enzymes and drug-induced liver injury, gastrointestinal disorders, embryo-fetal toxicity, arterial thromboembolic events, bleeding and gastrointestinal performation.
- Examples of Chronic Fibrosing Interstitial Lung Disease includes:
  - Chronic fibrosing hypersensitivity pneumonitis;
  - Autoimmune ILD (e.g., rheumatoid arthritis-related ILD);
  - Mixed connective tissue disease-associated ILD;
  - Idiopathic non-specific interstitial pneumonia;
  - Unclassifiable idiopathic interstitial pneumonia;
  - Environmental/occupational exposure-related ILD;
  - Sarcoidosis;

References

1. Ofev® Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; January 2022.

Available at: www.ofev.com. Accessed March 28, 2022.
2. Raghu G, Rochwerg B, Yuang Z, 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. 2015; 192(2): e3-e19. Available at: https://www.atsjournals.org/doi/10.1164/rccm.201506-1063ST. Accessed March 28, 2022.
3. Keating GM. Nintedanib: a review of its use in patients with idiopathic pulmonary fibrosis. Drugs. 2015;75:1131-1140. Available at: https://pubmed.ncbi.nlm.nih.gov/26063212/. Accessed March 28, 2022.
4. 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. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5450933/. Accessed March 28, 2022.
5. Distler O, Highland KB, Gahlemann M, et al. Nintedanib for Systemic Sclerosis Associated Interstitial Lung Disease. N Engl J Med. 2019 Jun 27;380(26):2518-2528. Available at: https://www.nejm.org/doi/10.1056/NEJMoa1903076. Accessed March 28, 2022.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title was updated. 2. Indications were updated. 3. Dosing information updated. 4. Initial Approval criteria updated. 5. Continued Therapy Approval criteria II.A.1 was rephrased. 6. Appendices updated. 7. References were updated.	07/27/2020	09/14/2020
Policy was reviewed: 1. Dosing Information dosing regimen was updated to include “Not recommended in patients with moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment….” 2. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 3. Initial Approval Criteria I.C.7 was updated to include “Dose does not exceed 300 mg per day…”. 4. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 5. Continued Therapy Approval Criteria II.A.1 was rephrased to “Member is currently receiving medication that has been authorized by RxAdvance…” 6. References were reviewed and updated.	06/30/2021	09/14/2021
Policy was reviewed:	03/28/2022	07/18/2022

1. Initial Approval Criteria, I.A.5.b: Updated diagnostic criteria from Known causes of pulmonary fibrosis have been ruled out to Known causes of pulmonary fibrosis have been ruled out (e.g., domestic and occupational environmental exposures, CTD, drug toxicity). 2. Initial Approval Criteria, I.C.5: Updated to remove prior smoking criteria "Member is a non-smoker or has been abstinent for at least 6 weeks". 3. Initial Approval Criteria, I.C.5: Updated to remove prior diagnostic criteria "Documented pulmonary function test within the past 60 days reflecting Forced vital Capacity (FVC)≥45% of predicted". 4. Initial Approval Criteria, I.C.5: Updated to include new diagnostic criteria Member meets both of the following (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 forced vital capacity (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. Appendix A: Updated to remove abbreviation FDA. 6. Appendix A: Updated to include abbreviations FVC and SSc-ILD. 7. Appendix D: Updated to add examples of Chronic Fibrosing Interstitial Lung Disease. 8. References were reviewed and updated.		