09-J2000-25

Original Effective Date: 12/15/14

Reviewed: 12/12/18

Revised: 01/15/20

Subject: Nintedanib (Ofev®) Oral Capsules

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Idiopathic pulmonary fibrosis is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, occurring primarily in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia (UIP). It is characterized by progressive worsening of dyspnea and lung function and is associated with a poor prognosis.

The American Thoracic Society published guidelines for the diagnosis and management of IPF in 2011, with an update to treatment recommendations in 2015. According to those guidelines, the diagnosis of IPF requires exclusion of other known causes of interstitial lung disease (e.g., domestic and occupational environmental exposures, connective tissue disease, and drug toxicity), the presence of a UIP pattern on high-resolution computed tomography (HRCT) in patients not subjected to surgical lung biopsy, and specific combinations of HRCT and surgical lung biopsy pattern in patients subjected to surgical lung biopsy.

Nintedanib (Ofev®) was approved by the U.S. Food and Drug Administration (FDA) in October 2014 as a breakthrough therapy for the treatment of idiopathic pulmonary fibrosis (IPF). Prior to FDA approval, nintedanib was designated as an orphan drug for this same indication. In 2019, nintedanib was FDA approved for the treatment of systemic sclerosis-associated interstitial lung disease (SSc-ILD). Nintedanib inhibits multiple receptor tyrosine kinases.

INPULSIS-1 (Safety and Efficacy of BIBF 1120 at High Dose in Idiopathic Pulmonary Fibrosis Patients) and INPULSIS-2 (Safety and Efficacy of BIBF 1120 at High Dose in Idiopathic Pulmonary Fibrosis Patients II) were replicate phase 3 RCTs that enrolled a total of 1,066 patients in a 3:2 ratio to receive 150 mg of nintedanib twice daily versus placebo. Patients were required to have a diagnosis of IPF for less than five years and with an FVC greater than or equal to 50%. Nintedanib significantly reduced the annual

rate of FVC decline compared with placebo in the INPULSIS-1 (-114.7 vs -239.9 mL) and the INPULSIS-2 (-113.6 vs -207.3 mL) randomized trials. Nintedanib significantly reduced acute exacerbations (3.6% vs 9.6%), time to first acute exacerbation, and quality of life in INPULSIS-2 but not in INPULSIS-1. Considering these trials as one, there was no significant benefit of nintedanib on mortality (RR, 0.70; 95% CI, 0.44–1.11) or acute exacerbation of IPF (HR, 0.64; 95% CI, 0.39–1.05). However, fewer patients treated with nintedanib had a more than 10% absolute decline in FVC during the study period (RR, 1.16; 95% CI, 1.06–1.27).

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of nintedanib (Ofev) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with idiopathic pulmonary fibrosis (IPF) OR systemic sclerosis-associated interstitial lung disease (SSc-ILD) confirmed by **ONE** of the following:
    a. Presence of a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) – imaging documentation must be provided
    b. Surgical lung biopsy – lung biopsy documentation must be provided
2. Member's forced vital capacity (FVC) is equal to or greater than 40% of the predicted FVC – documentation of assessment within the most recent 6 months must be provided
3. Member does not have moderate (Child Pugh B) or severe (Child Pugh C) hepatic impairment (see table 1)
4. Nintedanib is prescribed by a pulmonologist
5. Use will not be in combination with pirfenidone (Esbriet)
6. Dose does not exceed 150 mg twice daily – dosage will be achieved using the fewest number of capsules per day

Duration of approval: 6 months

Continuation of nintedanib (Ofev) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of IPF or SSc-ILD, **OR** the member has previously met all indication-specific initiation criteria
2. Member is receiving clinical benefit from treatment with nintedanib – documentation from the medical must be provided

3. Use is not in combination with pirfenidone (Esbriet)
4. Dose does not exceed 150 mg twice daily – dosage will be achieved using the fewest number of capsules per day

Duration of approval: 12 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 150 mg twice daily, with food

Dose Adjustments

- Recommended dosage in patients with mild hepatic impairment (Child Pugh A): 100 mg twice daily approximately 12 hours apart taken with food
- Consider temporary dose reduction to 100 mg, treatment interruption, or discontinuation for management of adverse reactions

Drug Availability

- Capsules: 150 mg and 100 mg

PRECAUTIONS:

Boxed Warning

None

Contraindications

None

Precautions/Warnings

- Elevated liver enzymes
- Gastrointestinal disorders, including perforation
- Embryofetal toxicity
- Arterial thromboembolic events
- Bleeding events

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

J84.112	Idiopathic pulmonary fibrosis
M34.81	Systemic sclerosis with lung involvement

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

Table 1. Child-Pugh Classification of Severity of Liver Disease
Using the table below, a total score of 5-6 is considered grade A (well-compensated disease); 7-9 is grade B (significant functional compromise); and 10-15 is grade C (decompensated disease):

Parameter	Points Assigned		
	1	**2**	**3**
Ascites	Absent	Slight	Moderate
Bilirubin, mg/dL	</=2	2-3	>3
Albumin, g/dL	>3.5	2.8-3.5	<2.8
Prothrombin time • Seconds over control • INR	 1-3 <1.8	 4-6 1.8-2.3	 >6 >2.3
Encephalopathy	None	Grade 1-2	Grade 3-4

REFERENCES:

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3. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2018 [cited 11/28/18]. Available from: http://www.clinicalpharmacology.com/.
4. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 11/28/18]. Available from: http://clinicaltrials.gov/.
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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 12/12/18.

GUIDELINE UPDATE INFORMATION:

12/15/14	New Medical Coverage Guideline.
12/15/15	Review and revision to guideline, consisting of updating position statement, decription, references.
04/15/16	Revision to guidelines; consisting of updating position statement.
12/15/16	Review and revision to guideline, consisting of updating position statement, coding, references.
12/15/17	Review and revision to guideline, consisting of updating dosing and references.
01/15/19	Review and revision to guideline, consisting of updating references.
01/15/20	Revison to guideline; consisting of updating position statement, coding.