<div align="center">

Division of Pulmonology, Allergy, and Critical Care

REGULATORY PROJECT MANAGER LABELING REVIEW

</div>

Application: NDA 205832/S-027

Name of Drug: Ofev (nintedanib) capsules

Applicant: Boehringer Ingelheim Pharmaceuticals, Inc. (BI)

<div align="center">

Labeling Reviewed

</div>

Submission Date: January 25, April 19, and 26, 2024
Receipt Date: January 25, April 19, and 26, 2024
Labeling Comments/IR: April 10, 2024 ; April 23, 2024

Background and Summary Description:

Ofev (nintedanib) is an oral tablet approved on October 15, 2014, for the treatment of idiopathic pulmonary fibrosis (IPF) in adults. Since then, two additional indications were approved, for treatment of interstitial lung disease (ILD) and for systemic sclerosis-associated interstitial lung disease (SSc-ILD) in adults in in 2019 and 2020 respectively.

On May 19, 2023, BI submitted pediatric efficacy supplement ____ (b) (4) that proposes the indication of fibrosing interstitial lung (ILDs) in children 6 – 17 years of age and to add Animal Toxicity Data subsection under Section 8.4 Pediatric Use in the USPI. The Division issued Compete Response to supplement ____ (b) (4) ____. The Division also found it appropriate to add the findings identified in juvenile animal studies in the current approved label. Accordingly, the division issued a Prior supplement request on November 28, 2024.

On January 25, 2024, BI submitted prior approval labeling supplement sNDA 205832/S-027 in response to PAS request that the division issued on November 28, 2023. PAS request was to add information from pediatric study 1199.337 and animal toxicity data statement consistent with findings from repeat-dose toxicity studies of nintedanib in rodents and non-rodents to the USPI subsection 8.4, Pediatric Use.

On April 10, 2024, the division responded to BI with a labeling IR conveying that the proposed statement stating that treatment-related bone changes are ____ (b) (4) does not accurately reflect findings in animal studies and requested to submit a revised label that complies with the November 28, 2023, PAS. Subsequently, BI responded on April 19, 2024, stating ____ (b) (4) ____

1

(b) (4)

On April 24, 2024, the division responded to BI acknowledging the rationale for the additional evaluation of the reversibility from the toxicology data and further proposed to revise the language under Animal Toxicity Data under 8.4. from (b) (4) to (b) (4)

On April 26, 2024, BI responded with the counter proposal stating "…These changes were *fully or at least partially reversible*…" by reasoning that the revised statement is an accurate representation of the results of bone changes observed in trials conducted by nonclinical evaluation of nintedanib in both rats and monkeys, as described in BI's April 19, 2024, response.

Review

On May 1, 2024, non-clinical team determined that the proposal language submitted on April 26, 2024, is acceptable.

Labeling review was completed by Non-Clinical team Luqi Pei, Ph.D and Team leader Carol Galvis, Ph.D. Clinical team Khalid Puthawala, M.D. senior clinical reviewer and Robert Lim, M.D. Deputy Director for Safety concurred acceptability of the sponsor's proposal language in a review a dated June 13, 2024.

The label submitted on April 26, 2024, was compared to the last approved labeling dated January 13, 2022. There were no additional revisions to the labeling other than those proposed by the applicant on April 26, 2024, and the edits suggested by the division.

Recommendations

The recommendation is to approve the labeling supplement.

Julianne Lee	6.13.24
Regulatory Project Manager	Date
Ladan Jafari	6.14.24
Chief, Project Management Staff	Date

2

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

JULIANNE Y LEE
06/18/2024 03:55:17 PM