CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

214324Orig1s000

Trade Name:	Tyvaso DPI inhalation powder
Generic or Proper Name:	*Treprostinil*
Sponsor:	United Therapeutics Corp.
Approval Date:	May 23, 2022
Indication:	Tyvaso DPI is a prostacyclin mimetic indicated for the treatment of: • Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies with Tyvaso establishing effectiveness predominately included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%). • Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. The study with Tyvaso establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%).

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APPROVAL LETTER

NDA 214324

NDA APPROVAL

United Therapeutics Corp.
Attention: Sarah Gemberling, PhD, RAC
Manager, Regulatory Affairs
55 TW Alexander Drive, PO Box 14186
Research Triangle Park, NC 27709

Dear Dr. Gemberling:

Please refer to your new drug application (NDA) dated April 16, 2021, received April 16, 2021, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tyvaso DPI (treprostinil) inhalation powder.

We acknowledge receipt of your amendment dated December 23, 2021, which constituted a complete response to our October 15, 2021, action letter.

We acknowledge receipt of your major amendment dated February 18, 2022, which extended the goal date by three months.

This NDA provides for the use of Tyvaso DPI (treprostinil) inhalation powder for the treatment of pulmonary arterial hypertension (PAH; WHO Group I) and pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3), to improve exercise ability.

APPROVAL & LABELING

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at FDA.gov.[1] Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, and Instructions for Use) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST

[1] http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm

may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As.*[2]

The SPL will be accessible via publicly available labeling repositories.

CARTON AND CONTAINER LABELING

Submit final printed carton and container labeling that are identical to the enclosed carton and container labeling , as soon as they are available, but no more than 30 days after they are printed. Please submit these labeling electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labeling for approved NDA 214324**." Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

Based on the stability data submitted to date, the expiry dating period for Tyvaso DPI (treprostinil) inhalation powder shall be 18 months from the date of manufacture when stored at 2°C to 8°C (36°F to 46°F).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because this drug product has an orphan drug designation for the treatment of PAH, you are exempt from this requirement for the PAH indication only.

We are waiving the pediatric study requirement for the treatment of PH-ILD because necessary studies are impossible or highly impracticable considering the number of pediatric patients with PH-ILD is extremely rare.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. For information about submitting promotional materials, see the final guidance for industry *Providing Regulatory Submissions in Electronic and Non-*

[2] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

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