



NDA 209471

**NDA APPROVAL**

AFT Pharmaceuticals, Inc.  
c/o Chesapeake Regulatory Group, Inc.  
6574 River Clyde Drive  
Highland, MD 20777

Attention: David Zuchero, MS, JD  
U.S. Agent

Dear Mr. Zuchero:

Please refer to your new drug application (NDA) dated and received March 1, 2017, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Combogesic (acetaminophen and ibuprofen) tablets.

We acknowledge receipt of your amendment dated July 27, 2021, which constituted a complete response to our November 6, 2020, action letter.

This NDA provides for the use of Combogesic (acetaminophen and ibuprofen) tablets for the short-term management of mild to moderate acute pain.

### **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.

### **WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS**

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

### **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.<sup>1</sup> Content of labeling must be identical to the enclosed labeling (text for the

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<sup>1</sup> <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Prescribing Information and Medication Guide) as well as annual reportable changes not included in the enclosed labeling. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.<sup>2</sup>

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 *SPL Standard for Content of Labeling Technical Qs & As*. For administrative purposes, designate this submission “**Final Printed Carton and Container Labeling for approved NDA 209471.**” 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 Combogesic (acetaminophen and ibuprofen) tablets shall be 36 months from the date of manufacture when stored at 20°C–25°C (68°F–77°F) with excursions permitted within USP controlled room temperature to of 15°– 30°C (59°F – 86°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.

We are waiving the pediatric study requirement for ages from birth to less than 6 months because necessary studies are impossible or highly impracticable. This is because it is challenging to study efficacy of the analgesic effect of this combination product in this pediatric age group.

We are deferring submission of your pediatric studies for ages 6 months to 2 years, 2 years to less than 12 years, and 12 years to less than 17 years for this application

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<sup>2</sup> 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>.

because this product is ready for approval for use in adults and the pediatric studies in these age groups have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required as postmarketing studies. The statuses of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

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|--------|--|
| 4401-1 | Conduct a study of the efficacy, safety, and pharmacokinetics of Combogesic in patients aged 12 to less than 17 years of age with mild to moderate acute pain.                     |
|        | Draft Protocol Submission: 09/2023   |
|        | Final Protocol Submission: 12/2023   |
|        | Study Completion: 03/2025  |
|        | Final Report Submission: 08/2025   |
| 4401-2 | Conduct a study of the efficacy, safety, and pharmacokinetics of Combogesic Oral Suspension in patients aged 2 to less than 12 years of age with mild to moderate acute pain.      |
|        | Draft Protocol Submission: 01/2026   |
|        | Final Protocol Submission: 04/2026   |
|        | Study Completion: 07/2027  |
|        | Final Report Submission: 12/2027   |
| 4401-3 | Conduct a study of the efficacy, safety, and pharmacokinetics of Combogesic Oral Suspension in infants from 6 months to less than 2 years of age with mild to moderate acute pain. |
|        | Draft Protocol Submission: 05/2028   |
|        | Final Protocol Submission: 08/2028   |
|        | Study Completion: 11/2029  |
|        | Final Report Submission: 04/2030   |

FDA considers the term *final* to mean that the applicant has submitted a protocol, the FDA review team has sent comments to the applicant, and the protocol has been revised as needed to meet the goal of the study or clinical trial.<sup>3</sup>

Submit the protocols to your IND 107435 with a cross-reference letter to this NDA.

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<sup>3</sup> See the guidance for Industry *Postmarketing Studies and Clinical Trials—Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (October 2019)*.  
<https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

Reports of these required pediatric postmarketing studies must be submitted as an NDA or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

### **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-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs*.<sup>4</sup>

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the Prescribing Information, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at FDA.gov.<sup>5</sup> Information and Instructions for completing the form can be found at FDA.gov.<sup>6</sup>

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Sandy Truong, Senior Regulatory Project Manager, at 301-796-5719.

Sincerely,

*{See appended electronic signature page}*

Rigoberto Roca, MD  
Director  
Division of Anesthesiology, Addiction Medicine,  
and Pain Medicine  
Office of Neuroscience  
Center for Drug Evaluation and Research

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<sup>4</sup> For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/media/128163/download>.

<sup>5</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>

<sup>6</sup> <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>

ENCLOSURES:

- Content of Labeling
  - Prescribing Information
  - Medication Guide
- Carton and Container Labeling

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**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.**  
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/s/  
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