CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209471Orig1s000

Trade Name:	Combogesic
Generic or Proper Name:	Acetaminophen and ibuprofen tablets
Sponsor:	AFT Pharmaceuticals, Inc
Approval Date:	March 1st, 2023
Indication:	Short-term management of mild to moderate acute pain.

CENTER FOR DRUG EVALUATION AND RESEARCH

209471Orig1s000

CONTENTS

Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	**X**
Labeling	**X**
REMS	
Summary Review	**X**
Officer/Employee List	**X**
Office Director Memo	
Cross Discipline Team Leader Review	
Clinical Review(s)	**X**
Product Quality Review(s)	**X**
Non-Clinical Review(s)	**X**
Statistical Review(s)	**X**
Clinical Microbiology / Virology Review(s)	
Clinical Pharmacology Review(s)	**X**
Other Reviews	**X**
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	**X**
Administrative/Correspondence Document(s)	**X**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

209471Orig1s000

APPROVAL LETTER

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.[1] Content of labeling must be identical to the enclosed labeling (text for the

[1] 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.*[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 *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

[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.

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.

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.[3]

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

[3] 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.*[4]

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.[5] Information and Instructions for completing the form can be found at FDA.gov.[6]

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

[4] For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/media/128163/download.
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[6] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf

ENCLOSURES:

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

U.S. Food and Drug Administration
Silver Spring, MD 20993
www.fda.gov

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/

RIGOBERTO A ROCA
03/01/2023 11:33:45 AM