DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204768

**NDA APPROVAL**

Iroko Pharmaceuticals, LLC
One Kew Place
150 Rouse Boulevard
Philadelphia, PA 19112

Attention: Steve Jensen
Sr. Vice President, Regulatory Affairs & Quality

Dear Mr. Jensen:

Please refer to your New Drug Application (NDA) dated April 30, 2013, received April 30, 2013, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tivorbex (indomethacin) capsules, 20 mg and 40 mg.

We acknowledge receipt of your amendments dated June 4, and 28 (2), July 25, August 15 and 30, September 4, October 3, 18, and 28, November 12, 19, 22, and 26, and December 6, 12, and 19, 2013, and January 13 and 15, and February 4, and 20, 2014.

This new drug application provides for the use of Tivorbex (indomethacin) capsules for the treatment of mild to moderate acute pain in adults.

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 text.

## 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 http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide). 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*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 204768**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

## MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Kimberly Compton
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 3168
10903 New Hampshire Avenue
Silver Spring, MD
*Use zip code* **20903** *if shipping via United States Postal Service (USPS).*
*Use zip code* **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

## REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for birth to less than one year because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

We are deferring submission of your pediatric study for ages 1 year to less than 17 years for this application because this product is ready for approval for use in adults and the pediatric study have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act (FDCA)are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This required studies are listed below.

2128-1 An open-label pharmacokinetic and safety study or studies of an age appropriate formulation of indomethacin in pediatric patients 6 through 17 years of age

| | |
|---|---|
| Final Protocol Submission: | April 1, 2015 |
| Study/Trial Completion: | February 1, 2017 |
| Final Report Submission: | October 2, 2017 |

2128-2 An open-label pharmacokinetic and safety study or studies of an age appropriate formulation of indomethacin in pediatric patients 2 through 6 years of age

| | |
|---|---|
| Final Protocol Submission: | November 2, 2015 |
| Study/Trial Completion: | October 2, 2017 |
| Final Report Submission: | June 1, 2018 |

2128-3 A pharmacokinetic, safety, and efficacy study or studies of an age appropriate formulation of indomethacin in pediatric patients 1 through 2 years of age

| | |
|---|---|
| Final Protocol Submission: | June 1, 2018 |
| Study/Trial Completion: | April 30, 2021 |
| Final Report Submission: | December 31, 2021 |

Submit the protocols to your IND 101940, with a cross-reference letter to this NDA.

Reports of this/these required pediatric postmarketing studies must be submitted as a new drug application (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. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

**EXPIRY DATING PERIOD**

A 24-month expiry dating period is granted for Tivorbex, both dosage strengths in all presentations, when stored at 25°C (77°F) with excursions permitted from 15° to 30°C (59° to 86°F).

**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 Kimberly Compton, RPh, Sr. Regulatory Project Manager at 301-796-1191.

Sincerely,

*{See appended electronic signature page}*

Sharon H. Hertz, MD
Deputy Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure(s):
Content of Labeling
Carton and Container Labeling

---

**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**

---

/s/

---

SHARON H HERTZ
02/24/2014