

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209511Orig1s000

Trade Name: XARACOLL

Generic or Proper Name: Bupivacaine hydrochloride

Sponsor: Innocoll Pharmaceuticals Ltd.

Approval Date: August 28, 2020

Indication: Indicated in adults for placement into the surgical site to produce postsurgical analgesia for up to 24 hours following open inguinal hernia repair

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APPROVAL LETTER

NDA 209511

NDA APPROVAL

Innocoll Pharmaceuticals Ltd.
c/o Innocoll Inc., an affiliate of Innocoll Pharmaceuticals Limited
3803 West Chester Pike
Suite 190
Newtown Square, PA 19073

Attention: Laura Grablutz
Head of Regulatory Affairs

Dear Ms. Grablutz:

Please refer to your new drug application (NDA) dated and received October 31, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Xaracoll (bupivacaine HCl) implant.

We acknowledge receipt of your amendment dated February 26, 2020, which constituted a complete response to our November 30, 2018, action letter.

This new drug application provides for the use of Xaracoll in adults for placement into the surgical site to produce postsurgical analgesia for up to 24 hours following open inguinal hernia repair.

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 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 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 209511.**” Approval of this submission by FDA is not required before the labeling is used.

DATING PERIOD

The dating period for Xaracoll shall be 24 months from the date of manufacture when stored at 20 °C to 25 °C (68 °F to 77°F); excursions permitted between 15 °C and 30 °C (59 °F and 86 °F) [See USP Controlled Room Temperature]

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 deferring submission of the following pediatric studies according to the timetables listed below because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the 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)(4)(C) of the FDCA. These required studies are listed below.

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

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>.

- 3928-1 Conduct a randomized, controlled study to evaluate the safety, tolerability, pharmacokinetics, and analgesic effect of the bupivacaine HCl collagen implant in children 2 to less than 17 years of age following open inguinal hernia repair.

Final Protocol Submission: 02/2016 (complete)
Study Completion: 01/2024
Final Report Submission: 05/2024

- 3928-2 Conduct a randomized, controlled study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of the bupivacaine HCl collagen implant in children from birth to less than 2 years of age following open inguinal hernia repair.

Draft Protocol Submission: 04/2021
Final Protocol Submission: 07/2021
Study Completion: 03/2023
Final Report Submission: 08/2023

Your deferred pediatric studies required under section 505B(a) of the 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)(4)(C) of the FDCA.

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 protocol for 3928-2 to your IND 077127, with a cross-reference letter to this NDA. 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-*

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>.

*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

METHODS VALIDATION

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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 Allison Meyer, Regulatory Project Manager, at 301-796-1258.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, MD

Acting Director

Division of Anesthesiology, Addiction Medicine
and Pain Medicine

Office of Neuroscience

Center for Drug Evaluation and Research

ENCLOSURES:

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

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>

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
08/28/2020 08:13:04 PM