CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

216264Orig1s000

Trade Name:	BLUDIGO
Generic or Proper Name:	indigotindisulfonate sodium injection
Sponsor:	Provepharm SAS
Approval Date:	July 8, 2022
Indication:	For use as a visualization aid in the cystoscopic assessment of the integrity of the ureters in adults following urological and gynecological open, robotic, or endoscopic surgical procedures.

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APPROVAL LETTER

NDA 216264

NDA APPROVAL

Provepharm SAS
C/o Provepharm Inc.
Attention: Arvind Pathak, PhD
US Agent for Provepharm SAS
100 Springhouse Drive
Suite 105
Collegeville, PA 19426

Dear Dr. Pathak:

Please refer to your new drug application (NDA) dated September 9, 2021, received September 9, 2021, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bludigo (indigotindisulfonate sodium) injection.

This NDA provides for the use of Bludigo (indigotindisulfonate sodium) injection as a visualization aid in the cystoscopic assessment of the integrity of the ureters in adults following urological and gynecological open, robotic, or endoscopic surgical procedures.

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) 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]

[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.

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 216264**." 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 Bludigo (indigotindisulfonate sodium) injection shall be 18 months from the date of manufacture when stored at 25°C.

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 birth to less than 2 years because necessary studies are impossible or highly impracticable. This is because in the case of IV use in bladder repair surgery after trauma, cases are rare (0.05% to 0.2% of all injuries) and unpredictable in timing, in contrast to elective surgery for urogynecological conditions.

We are deferring submission of your pediatric study for ages 2 years to less than 18 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act/FDCA is a required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(4)(C) of the Federal Food, Drug, and Cosmetic Act/FDCA. This required study is listed below.

4300-1 Deferred pediatric study under PREA -An open-label, multicenter study to evaluate the safety, pharmacokinetics, and conspicuity of Indigo Carmine Injection 0.8% solution when used as an aid in the determination of ureteral patency in pediatric patients from 2 years to less than 18 years of age.

Final Protocol Submission: 01/2023
Study Completion: 01/2025
Final Report Submission: 07/2025

For purposes of the protocol, 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 to your IND 137856, with a cross-reference letter to this NDA.

Reports of this required pediatric postmarketing study 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 this study. 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.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments:

4300-2 Conduct an Open-Label, Randomized, Multicenter Trial to Evaluate the Efficacy and Safety of Two Different Doses of Bludigo™ (Indigotindisulfonate Sodium Injection, USP) 0.8% When Used as an Aid in the Determination of Ureteral Patency.

[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.

The timetable you submitted on June 30, 2022, states that you will conduct this study according to the following schedule:

Draft Protocol Submsision: 09/2022
Final Protocol Submission: 01/2023
Trial Completion: 12/2024
Final Report Submission: 06/2025

4300-3 Conduct an Open-label, Parallel group, Single-Dose Trial to Investigate the Influence of Renal Impairment on the Efficacy and Safety of Two Doses of Bludigo™ (Indigotindisulfonate Sodium Injection, USP) 0.8% When Used as an Aid in the Determination of Ureteral Patency.

The timetable you submitted on June 30, 2022, states that you will conduct this study according to the following schedule:

Draft Protocol Submission: 09/2022
Final Protocol Submission: 01/2023
Trial Completion: 06/2025
Final Report Submission: 12/2025

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]

[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

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 Alberta Davis-Warren, Regulatory Project Manager, at 301-796-3908.

Sincerely,

{See appended electronic signature page}

Libero Marzella, MD, PhD
Director
Division of Imaging and Radiation Medicine
Office of Specialty Medicine
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURE(S):

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

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/

LIBERO L MARZELLA
07/08/2022 04:18:14 PM