CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209569Orig1s000

Trade Name:	TissueBlue 0.025%
Generic or Proper Name:	Brilliant Blue G Ophthalmic Solution
Sponsor:	D.O.R.C International, b.v.
Approval Date:	December 20, 2019
Indication:	For use as an aid in ophthalmic surgery by selectively staining the internal limiting membrane (ILM).

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209569Orig1s000

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APPLICATION NUMBER:

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APPROVAL LETTER

NDA 209569

NDA APPROVAL

D.O.R.C International, b.v.
Attention: Matthew Carignan
Head of Quality
10 Continental Drive, Building 1
Exeter, NH 03833

Dear Mr. Carignan:

Please refer to your new drug application (NDA) dated and received April 29, 2019, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025%.

This new drug application provides for the use of TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% for use as an aid in ophthalmic surgery by selectively staining the internal limiting membrane (ILM).

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 text submitted and received on December 16, 2019.

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] 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

[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.

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 209569**." Approval of this submission by FDA is not required before the labeling is used.

MARKET PACKAGE

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

Michael Puglisi
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 6162
10903 New Hampshire Avenue
Silver Spring, Maryland
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).*

ADVISORY COMMITTEE

Your application for TissueBlue was not referred to an FDA advisory committee because outside expertise was not necessary. There were no new issues that were likely to have benefited from an Advisory Committee discussion.

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 these requirements are waived or your application is exempt from the requirement. Because this drug product for this indication has an orphan drug designation, you are exempt from this requirement.

POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your post-marketing commitments:

3724-1 Provide 12-month stability update for Batch 14218 and 6-month stability data for Batch 21618.

The timetable you submitted on October 3, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	December 31, 2019
Study Completion:	March 31, 2020
Final Report Submission:	April 30, 2020

3724-2 Any further extension of the expiration date post-approval will need to be submitted for review as a PAS supplement.

The timetable you submitted on October 3, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	May 31, 2020
Study Completion:	April 30, 2021
Final Report Submission:	May 31, 2021

3724-3 A leachable study on at least one stability Batch 14618 should be conducted through its expiration date.

The timetable you submitted on October 3, 2019, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	December 31, 2019
Study Completion:	March 31, 2020
Final Report Submission:	April 30, 2020

3724-4 Develop a consistently readable barcode on the Tyvek blister for the TissueBlue (Brilliant Blue G Ophthalmic Solution) 0.025% product.

The timetable you submitted on December 16, 2019, states that you will conduct this study according to the following schedule:

Final Report Submission: December 31, 2020

A final submitted protocol is one that the FDA has reviewed and commented upon, and you have revised as needed to meet the goal of the study or clinical trial.

Submit chemistry, manufacturing, and controls protocols and post-marketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these post-marketing commitments should be

prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," **or** "**Postmarketing Commitment Correspondence**."

Additionally, the expiration date of 12 months is granted when stored at 15 °C-25 °C.

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 Prescribing Information, Medication Guide, and Patient Package Insert (as applicable) to:

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

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry *Providing Regulatory Submissions in Electronic and Non-Electronic Format—Promotional Labeling and Advertising Materials for Human Prescription Drugs.*[3]

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.[4] Information and Instructions for completing the form can be found at FDA.gov.[5] For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see 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).

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[3] When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.
[4] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf
[5] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf
[6] http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at FDA.gov.[7]

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biological products qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application. If you have any questions, call Michael Puglisi, Regulatory Project Manager, at 301-796-0791.

Sincerely,

{See appended electronic signature page}

Peter Stein, M.D.
Director
Office of New Drugs
Center for Drug Evaluation and Research

ENCLOSURES:
Content of Labeling
Prescribing Information
Carton and Container Labeling

[7] http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm

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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.

/s/

PETER P STEIN
12/20/2019 07:43:13 AM