CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

209963Orig1s000

Trade Name:	GOPRELTO nasal solution, 4%
Generic or Proper Name:	cocaine hydrochloride
Sponsor:	Genus Lifesciences, Inc.
Approval Date:	December 14, 2017
Indication:	GOPRELTO (cocaine hydrochloride nasal solution, 4%), for the induction of local anesthesia of the mucous membranes when performing diagnostic procedures and surgeries on or through the nasal cavities in adults.

CENTER FOR DRUG EVALUATION AND RESEARCH

209963Orig1s000

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APPLICATION NUMBER:

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 209963

NDA APPROVAL

Genus Lifesciences, Inc.
514 North 12th Street
Allentown, PA 18102

Attention: William Reightler
Vice President of Regulatory Affairs

Dear Mr. Reightler:

Please refer to your New Drug Application (NDA) dated and received November 23, 2016, and your amendments, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA), for GOPRELTO (cocaine hydrochloride nasal solution, 4%).

We acknowledge receipt of your major amendment dated July 31, 2017, which extended the goal date by three months.

This new drug application provides for the use of GOPRELTO (cocaine hydrochloride nasal solution, 4%), for the induction of local anesthesia of the mucous membranes when performing diagnostic procedures and surgeries on or through the nasal cavities 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. 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 titled *Providing Regulatory Submissions in Electronic Format — Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (May 2015, Revision 3)*. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 209963**." Approval of this submission by FDA is not required before the labeling is used.

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 deferring submission of your 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 under 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)(C) of the Federal Food, Drug, and Cosmetic Act/FDCA. These required studies are listed below.

3241-1 Conduct a juvenile animal study to characterize the impact of cocaine on brain development and male reproductive tissue and development to support pediatric dosing in children under 3 years of age.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	12/2017
Final Protocol Submission:	06/2018
Study Completion:	11/2018
Final Report Submission:	02/2019

3241-2 Conduct a juvenile animal study to characterize the impact of cocaine on brain development and male reproductive tissue and development to support pediatric dosing in children 3 years of age to less than 17 years of age.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	12/2017
Final Protocol Submission:	06/2018
Study Completion:	11/2018
Final Report Submission:	02/2019

3241-3 Conduct a multicenter, sequential age-group trial to evaluate the pharmacokinetic and safety profiles of a single topical administration of GOPRELTO for the induction of local anesthesia of the mucous membranes when performing diagnostic procedures and surgeries on or through the nasal cavities in pediatric subjects two years of age to less than 17 years of age.

The timetable you submitted on December 1, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	02/2018
Final Protocol Submission:	11/2018
Trial Completion:	12/2020
Final Report Submission:	06/2021

3241-4 Conduct a multicenter trial to evaluate the pharmacokinetic profile, efficacy, and safety of a single topical administration of GOPRELTO for the induction of local anesthesia of the mucous membranes when performing diagnostic procedures and surgeries on or through the nasal cavities in pediatric patients from birth to less than two years of age.

The timetable you submitted on December 1, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	10/2020
Final Protocol Submission:	04/2021
Trial Completion:	12/2023
Final Report Submission:	06/2024

Submit the protocols to your IND 118527, with a cross-reference letter to this NDA.

Reports of 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.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient identify an unexpected serious risk of fertility, embryo-fetal developmental, and/or pre-/post-natal developmental adverse events.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

3241-5 Conduct a female fertility and early embryonic development study in the rat model to adequately characterize the effect of cocaine on female fertility and early embryonic development.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	01/2018
Final Protocol Submission:	04/2018
Study Completion:	10/2018
Final Report Submission:	03/2019

3241-6 Conduct an embryo-fetal development study in the rat model to characterize the teratogenic potential of cocaine.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	12/2017
Final Protocol Submission:	03/2018
Study Completion:	05/2018
Final Report Submission:	10/2018

3241-7 Conduct an embryo-fetal development study in the rabbit model to characterize the teratogenic potential of cocaine.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	12/2017
Final Protocol Submission:	03/2018
Study Completion:	06/2018
Final Report Submission:	11/2018

3241-8 Conduct a pre- and post-natal development study in the rat model to characterize the impact of cocaine on development, including exposure during lactation to weaning, growth and development, functional assessments, and reproductive capacity of the offspring.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Draft Protocol Submission:	03/2018
Final Protocol Submission:	06/2018
Study Completion:	02/2019
Final Report Submission:	08/2019

3241-9 Submit a complete histopathological assessment from the 14-day rat intranasal toxicology study testing (b) (4) (Study Number 256501 or 558503) and revise the final study report accordingly.

The timetable you submitted on November 20, 2017, states that you will conduct this study according to the following schedule:

Study Completion:	12/2017
Final Report Submission:	01/2018

Submit protocols to your IND 118527 with a cross-reference letter to this NDA. Submit nonclinical and chemistry, manufacturing, and controls protocols and all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **Required Postmarketing Protocol Under 505(o), Required Postmarketing Final Report Under 505(o), Required Postmarketing Correspondence Under 505(o).**

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

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, Medication Guide, and patient PI (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 (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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.

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 Diana L. Walker, PhD, Regulatory Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Rigoberto Roca, MD
Deputy Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
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/

RIGOBERTO A ROCA
12/14/2017