



Our STN: BL 125668/o

BLA APPROVAL
December 12, 2018

Octapharma Pharmazeutika Produktionsges.m.b.H.
Attention: Mr. Stanley Ammons
Octapharma USA Inc.
121 River Street, Suite 1201
Hoboken, NJ 07030

Dear Mr. Ammons:

Please refer to your Biologics License Application (BLA) for Immune Globulin Subcutaneous (Human)-hipp dated December 28, 2017, received December 29, 2017, submitted under section 351(a) of the Public Health Service Act (PHS Act).

LICENSING

We have approved your BLA for Immune Globulin Subcutaneous (Human)-hipp effective this date. You are hereby authorized to introduce or deliver for introduction into interstate commerce, Immune Globulin Subcutaneous (Human)-hipp under your existing Department of Health and Human Services U.S. License No.1646. Immune Globulin Subcutaneous (Human)-hipp is indicated for treatment of primary humoral immunodeficiency (PI) in adults.

The review of this product was associated with the following National Clinical Trial (NCT) numbers: 01888484 and 02627300.

MANUFACTURING LOCATIONS

Under this license, you are approved to manufacture Immune Globulin Subcutaneous (Human)-hipp drug substance at Octapharma Pharmazeutika Produktionsges.m.b.H. in Vienna, Austria. The final formulated product will be manufactured, filled, labeled, and packaged at OCTAPHARMA Pharmazeutika Produktionsges.m.b.H., Oberlaaer Strasse 235, Vienna, Austria. The final product container can also be inspected, labeled, and packaged at Octapharma Dessau GmbH facility in Germany.

You may label your product with the proprietary name CUTAQUIG and market it in 1 g, 1.65 g, 2 g, 3.3 g, 4 g, and 8 g single-use vials.

We did not refer your application to the Blood Products Advisory Committee because our review of information submitted in your BLA, including the clinical study design and trial results, did not raise concerns or controversial issues that would have benefited from an advisory committee discussion.

DATING PERIOD

The dating period for Immune Globulin Subcutaneous (Human)-hipp shall be 24 months from the date of manufacture when stored at 5 ± 3 °C with 6 months at $25^{(b) (4)}$ °C during the shelf-life. The date of manufacture shall be defined as the date of final sterile filtration of the formulated drug product.

FDA LOT RELEASE

Please submit final container samples of the product in final containers together with protocols showing results of all applicable tests. You may not distribute any lots of product until you receive a notification of release from the Director, Center for Biologics Evaluation and Research (CBER).

BIOLOGICAL PRODUCT DEVIATIONS

You must submit reports of biological product deviations under 21 CFR 600.14. You should identify and investigate all manufacturing deviations promptly, including those associated with processing, testing, packaging, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA 3486 to the Director, Office of Compliance and Biologics Quality, at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

MANUFACTURING CHANGES

You must submit information to your BLA for our review and written approval under 21 CFR 601.12 for any changes in, including but not limited to, the manufacturing, testing, packaging or labeling of Immune Globulin Subcutaneous (Human)-hipp, or in the manufacturing facilities.

LABELING

Under 21 CFR 201.57(c)(18), patient labeling must be referenced in section 17 PATIENT COUNSELING INFORMATION. Patient labeling must be available and may either be reprinted immediately following the full prescribing information of the package insert or accompany the prescription product labeling.

We hereby approve the draft package insert labeling submitted under amendment 45, dated December 11, 2018 and the draft carton and container labeling submitted under amendment 45, dated December 11, 2018.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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* at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible via publicly available labeling repositories.

PACKAGE AND CONTAINER LABELS

Please electronically submit final printed package and container labels that are identical to the approved package and container labels, according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications* at <https://www.fda.gov/downloads/drugs/guidancecompliance/regulatoryinformation/guidances/ucm333969.pdf>.

All final labeling should be submitted as Product Correspondence to BLA 125668/o at the time of use (prior to marketing) and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71-G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

ADVERSE EVENT REPORTING

You must submit adverse experience reports in accordance with the adverse experience reporting requirements for licensed biological products (21 CFR 600.80) and you must submit distribution reports as described in 21 CFR 600.81. For information on adverse experience reporting, please refer to the guidance for industry *Providing Submissions in Electronic Format – Postmarketing Safety Reports* at <https://www.fda.gov/downloads/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm458559.pdf> and FDA's Adverse Event reporting System website at <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm115894.htm>. For information on distribution reporting, please refer to the guidance for industry *Electronic Submission of Lot Distribution Reports* at <http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Post-MarketActivities/LotReleases/ucm061966.htm>.

In addition, you must submit adverse event reports for any infectious disease transmission within 15 days after learning of the event. Infectious disease transmission refers to an adverse event that involves suspected or confirmed transmission of an infectious agent, whether the recipient develops the infectious disease or only has serologic or other evidence. If an infectious disease transmission event is serious and unexpected, you must submit a 15-day "alert report," as required under 21 CFR 600.80(c)(1)(i). Infectious disease transmission events that do not meet criteria for expedited submission require periodic reports and must be submitted as individual safety case reports within 15 days, as authorized under 21 CFR 600.80(c)(2)(i). You should submit reports for all other non-expedited adverse events under the periodic reporting requirements specified in 21 CFR 600.80(c)(2).

PEDIATRIC REQUIREMENTS

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages zero to two years because the necessary studies are impossible or highly impracticable. This is because primary humoral immune deficiency is rarely diagnosed before two years of age, making recruitment of sufficient subjects for a clinical trial of pediatric patients in this age range highly impracticable.

We are deferring submission of your pediatric study for ages two to less than 17 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 under 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 according to 21 CFR 601.28 and section 505B(a)(3)(B) of the FDCA. In addition, section 506B of the FDCA and 21 CFR 601.70 require you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

Label your annual report as an “**Annual Status Report of Postmarketing Study Requirement/Commitments**” and submit it to the FDA each year within 60 calendar days of the anniversary date of this letter until all Requirements and Commitments subject to the reporting requirements under section 506B of the FDCA are released or fulfilled. This required study is listed below:

1. Deferred pediatric study (protocol SCGAM-01) under PREA for the treatment of primary humoral immunodeficiency in pediatric patients ages two to < 17 years of age. The study will provide pharmacokinetic data for at least two subjects ages two to < 6 years, at least six subjects ages six to < 12 years, and at least four subjects ages 12 to < 17 years of age, as well as safety and efficacy data for at least four subjects ages two to < 6 years, at least 10 subjects ages six to < 12 years, and at least six subjects ages 12 to < 17 years of age. The final report will compare efficacy and safety between pediatric age cohorts and between pediatric and adult subjects included in the study.

Final Protocol Submission: January 31, 2019

Study Completion Date: August 31, 2020

Final Report Submission: December 31, 2020

Submit the to-be-amended protocol to your IND 15617, with a cross-reference letter to this BLA, STN BL 125668/o explaining that this protocol was submitted to the IND.

Submit final study reports to this BLA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated as:

- **Required Pediatric Assessment**

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

We acknowledge your written commitment as described in your letter of November 26, 2018 as outlined below:

2. Octapharma commits to setting a final (b) (4) specification following a year of release testing for CUTAQUIG. The final (b) (4) specification and justification will be submitted as a Prior Approval Supplement by January 1, 2020.

Final Report Submission: January 1, 2020

We request that you submit information concerning nonclinical and chemistry, manufacturing, and control postmarketing commitments and final reports to your BLA, STN BL 125668/o. Please refer to the sequential number for each commitment.

Please use the following designators to prominently label all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- **Postmarketing Commitment – Status Update**
- **Postmarketing Commitment – Final Study Report**
- **Supplement contains Postmarketing Commitment – Final Study Report**

For each postmarketing commitment not subject to the reporting requirements of 21 CFR 601.70, you may report the status to FDA as a **Postmarketing Commitment – Status Update**. The status report for each commitment should include:

- the sequential number for each study as shown in this letter;
- the submission number associated with this letter;
- describe what has been accomplished to fulfill the non-section 506B PMC; and,
- summarize any data collected or issues with fulfilling the non-section 506B PMC.

When you have fulfilled your commitment, submit your final report as **Postmarketing Commitment – Final Study Report** or **Supplement contains Postmarketing Commitment – Final Study Report**.

Sincerely,

Wilson W. Bryan, MD
Director
Office of Tissues and Advanced Therapies
Center for Biologics Evaluation and Research