

Clinical Pharmacology BLA Review
Office of Clinical Evaluation (OCE)
Office of Therapeutic Products (OTP)

Submission Number: 125743/68

Product Name: Immune Globulin Intravenous (Human), 10% Liquid

Proposed Indication: For the treatment of primary humoral immunodeficiency (PI)

Applicant: Green Cross Corporation

Subject: Addendum to Clinical Pharmacology Review

Date Submitted: Sep 14, 2023 (Resubmission)

RPM: Nancy Skeeter

Reviewer: Million Tegenge, PhD

Clinical Pharmacology Reviewer, OCE, OTP

Through: Tejashri Purohit-Sheth, MD

Director, Division of Clinical Evaluation General Medicine, OCE/OTP

The Applicant (Green Cross Corporation) previously submitted an Original Biologics License Application (BLA) to license its Immune Globulin (human) Intravenous product (GCC 10% IGIV, ALYGLO) for treatment of patients with primary immunodeficiency (PI). Due to CMC concerns, including concerns related to limited access to the manufacturing site for inspection, FDA issued a complete response (CR) letter on February 25, 2022.

The indication originally proposed by the applicant for Alyglo was for the treatment of patients with primary humoral immunodeficiency (PI) in adults (b) (4)

. At the time of the original submission, the clinical and clinical pharmacology team determined that the submitted pharmacokinetic (PK), safety and efficacy data were adequate to support approval of Alyglo for treatment of adult (aged ≥ 17 years) patients

with PI. The original submission did not include sufficient PK data to support approval in
(b) (4)

In the CR letter, FDA asked the applicant to propose a new plan to support approval in
(b) (4)

. The applicant resubmitted this application to STN125743/0/68 on July 14, 2023, with a complete response. After review of this re-submission, the clinical and clinical pharmacology team continued to conclude that adult data from GC5107_P3 support safety and efficacy of Alyglo for the indication of treatment of PI in adults.

In this re-submission, the applicant addressed the CMC deficiencies; however, there are no new clinical pharmacology data in this re-submission. The Applicant proposed to enroll 6 adolescent subjects aged ≥ 12 years to < 17 years in the ongoing pediatric study that previously enrolled only subjects aged ≥ 2 years to < 12 years, and to delay submission of the complete pediatric study report from September 2023 to November 2016. The proposed plan to study PK, safety, and efficacy in the ≥ 12 years to < 17 years age group is acceptable.

This clinical pharmacology memo amends the dose range and pharmacokinetic analysis reflecting only adult patients with PI.

The PK of ALYGLO was assessed in 22 adults (aged ≥ 17 to 70 years; 10 males and 12 females) patients with PI. The administered dose of ALYGLO during the PK assessment ranged from 313 to 821 mg/kg every 3 or 4 weeks. Blood samples for the PK study were collected after the 5th infusion of ALYGLO at 0.5, 2, 24, 48 hours, and Days 4, 8, 15, 22 (for the 3-week schedule) and 29 (for the 4-week schedule) post-infusion. The mean half-life was 29.6 days, and the mean clearance (baseline uncorrected) was 1.7 mL/day/kg for 28-day day dosing regimen.

The IgG trough level was collected in the intention to treat (ITT) population and the proposed target steady state trough IgG was 500 mg/dL. The mean steady state trough total IgG concentrations ranged from 706 to 768 mg/dL for the 28-day dosing regimen.

Overall, the clinical pharmacology data support the approval of the proposed dosing regimen of 300-800 mg/kg every 21 or 28-day infusion as replacement therapy in adults with primary humoral immunodeficiency.

The following clinical pharmacology labeling comments were communicated to the applicant:

Section 2: Dose

- We updated dose range from 300-900 mg/kg to 300-800 mg/kg. The updated dose range reflect the dose range used in the clinical trial for adult subjects.

Section 8.4: Pediatric Use

- Recommended to remove PK, efficacy, and safety information in pediatric subjects due to insufficient information.

Section 12 .3: Pharmacokinetics

- Recommended to remove PK data for adolescent subjects due to insufficient information.