Application Type	BLA
STN	125683/0
CBER Received Date	July 9, 2018
PDUFA Goal Date	July 9, 2019
Division / Office	DCEPT/OTAT
Committee Chair	Jennifer Reed, Ph.D.
Clinical Reviewer(s)	Deborah Belsky, M.D.
Project Manager	Patrick Riggins, Ph.D. & Candido Alicea, Ph.D.
Priority Review	No
Reviewer Name(s)	Jiang Hu, Ph.D.
Review Completion Date / Stamped Date	
Supervisory Concurrence	Renée C. Rees, Ph.D., Team Leader, Therapeutics Evaluation Branch
	Boguang Zhen, Ph.D., Branch Chief, Therapeutics Evaluation Branch
Applicant	Grifols Therapeutics LLC
Established Name	Immune Globulin Subcutaneous (Human), 20% (IGSC 20%)
(Proposed) Trade Name	(b) (4)
Pharmacologic Class	Immunoglobulins
Formulation(s), including Adjuvants, etc	Immune Globulin Subcutaneous (Human), 20%
Dosage Form(s) and Route(s) of Administration	Liquid solution for subcutaneous infusion
Dosing Regimen	0.2 g/mL, from daily up to biweekly
Indication(s) and Intended Population(s)	For the treatment of primary humoral immunodeficiency (PI) for subjects 2 years of age and older

EXECUTIVE SUMMARY

This original Biologics License Application (BLA) submission is for Immune Globulin Subcutaneous (Human), 20% (IGSC 20%; (b) (4)) for the treatment of primary humoral immunodeficiency (PI). The new IGSC 20% manufacturing process is based on the currently licensed process used for Immune Globulin Injection (Human), IGIV 10%, Caprylate/Chromatography Purified (Gamunex-C) but includes an additional (b) (4) step to increase the protein concentration to 20%. The (b) (4) for IGSC 20% includes the addition of polysorbate 80 for enhanced stability of the final drug product over shelf-life.

The applicant did not submit clinical efficacy studies in support of this BLA. The clinical support is provided by the Clinical Study Report (CSR) of GTI1502, a prospective, multi-center, open-label, cross-over, 6-month pharmacokinetic (PK), safety and tolerability study of IGSC 20% compared with Immune Globulin Injection 10% (IGIV 10%) in subjects with PI.

Study GTI1502 includes a 4 or 5 week IV phase (used as a reference stage) in which IGIV 10% was administered, and a 24 week SC phase in which IGSC 20% was administered. Both primary and secondary study endpoints in GTI1502 are PK variables. There were 61 subjects screened from 20 study centers in US and Canada and 53 subjects were enrolled, including 38 adult subjects and 15 pediatric subjects (age 2 to 16 years). A total of 50 subjects in the IV phase and 41 subjects in the SC phase had sufficient serum concentration of IgG versus time profiles for assessment of steady state PK parameters. PK analysis was performed using all available and valid total IgG concentration data from these subjects. I defer to the PK reviewer to verify the PK analysis results submitted by the applicant for GTI1502. The overall safety profile of IGSC 20% is similar to that of IGIV 10%. No major safety concerns were observed in this study.