CLINICAL PHARMACOLOGY MEMO

NDA	21-773 Serial 0443
Submission Date	January 6, 2021
Brand Name	BYETTA
Generic Name	Exenatide
Reviewer	S.W. Johnny Lau, R.Ph., Ph.D.
Team Leader	Manoj Khurana, Ph.D.
OCP Division	Cardiometabolic and Endocrine Pharmacology
OND Division	Diabetes, Lipid Disorders, and Obesity
Sponsor	AstraZeneca
Formulation; Strength	Solution; 0.25 mg/mL
Submission Type	Post-marketing Requirement (PMR) Study
Indication	Adjunct therapy to diet and exercise to treat Type 2 Diabetes Mellitus (T2DM)

The sponsor submitted the results of pediatric Study H8O-MC-GWBQ (GWBQ) "Safety and Efficacy of Exenatide as Monotherapy and Adjunctive Therapy to Oral Antidiabetic Agents in Adolescents with Type 2 Diabetes" to address the PMR 1559-1. Study H8O-MC-GWBQ was a multicenter, double-blind, placebo-controlled, randomized, parallel, 3-arm study performed in adolescents (males and females aged 10 to 17 years) with T2DM (screening HbA1c 6.5% to 10.5%). Patients subcutaneously received 5 μg, 10 μg, or placebo twice daily for 28 weeks. Patients were naïve to antidiabetic agents, or were receiving oral treatment with metformin, a sulfonylurea, or a combination of metformin and a sulfonylurea at the time of enrollment. The sponsor does not seek pediatric indication for BYETTA because the results of Study H8O-MC-GWBQ was negative for efficacy (see clinical/statistical reviews for details).

Study H8O-MC-GWBQ's report states that:

"*Only 1 patient had at least 1 evaluable post-dose PK concentration assessment available for analysis, and as they were randomized to receive placebo, they were not included in the PK Analysis Set, which had no patients in it. Therefore, no PK analyses were performed*."

However, the sponsor did include the adolescent exenatide pharmacokinetic data from Study 2993-124 "A Randomized, Single-Blind, Dose-Rising, Placebo-Controlled, Crossover Study to Evaluate the Pharmacokinetics, Pharmacodynamics, and Tolerability of Exenatide in Adolescent Subjects With Type 2 Diabetes Mellitus." . The pediatric exenatide C_{max} and $AUC_{0\text{-}inf}$ data are generally consistent with the adult exenatide C_{max} and $AUC_{0\text{-}inf}$ data though Study 2993-124 had a small sample size (See Dr. Manoj Khurana's Clinical Pharmacology review for Study 2993-124 dated July 17, 2008 in DARRTS).

The acceptability of Study H8O-MC-GWBQ data is deferred to the reviews by the Clinical and Statistical reviewers.

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/s/

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