CLINICAL PHARMACOLOGY REVIEW
MEMORANDUM
(Addendum to the original review dated December 10, 2020)

NDA	214231
Submission Date	March 27, 2020
Brand Name	ZEGALOGUE
Generic Name	Dasiglucagon
Reviewer	S.W. Johnny Lau, R.Ph., Ph.D.
Team Leader	Manoj Khurana, Ph.D.
Division Director	Shirley K. Seo, Ph.D.
OCP Division	Division of Cardiometabolic and Endocrine Pharmacology
OND Division	Division of Diabetes, Lipid Disorders, and Obesity
Sponsor	Zealand Pharma A/S
Dosage form; Strength	Solution: 0.6 mg/0.6 mL
Associated IND	127866
Proposed indication	Treatment of severe hypoglycemia in patients with diabetes aged 6 years and above

Background
Refer to Clinical Pharmacology review dated December 10, 2020 in DARRTS Reference ID: 4715185 for the Clinical Pharmacology information of dasiglucagon. The purpose of this addendum is to revise the recommendation of a statement appeared on Page 3/39 in Section 1.1 Recommendations for the approval of the proposed indication for dasiglucagon.

Recommendation
The second sentence for the Section 1.1 Recommendations should read "The application is approvable from a clinical pharmacology perspective for patients with **diabetes** aged 6 years and above." instead of "The application is approvable from a clinical pharmacology perspective for patients with T1DM aged 6 years and above."

Rationale
The sponsor conducted all Phase 3 clinical studies in patients with type 1 diabetes mellitus (T1DM) for dasiglucagon. The sponsor did not include patients with type 2 diabetes mellitus (T2DM) in the development program of dasiglucagon due to the potential confounding effect of endogenous insulin production on endpoint assessment as indicated in the end of Phase 2 meeting minutes in DARRTS on July 28, 2017 Reference ID: 4131786. Upon discussions with the clinical review team and that the mechanism of action of dasiglucagon is through the stimulation of hepatic breakdown of glycogen to release glucose, the efficacy outcome of the dasiglucagon development program should be applicable to both patients with T1DM and patients with T2DM. Furthermore, clinical guidelines for treatment of severe hypoglycemia do not distinguish between treatment of patients with T1DM and treatment of patients with T2DM. Thus, the second sentence for the Section 1.1 Recommendations should read "The application is approvable from a clinical pharmacology perspective for patients with **diabetes** aged 6 years and above."

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/s/

SZE W LAU
02/26/2021 11:33:12 AM

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03/01/2021 11:10:57 AM

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03/04/2021 02:42:07 PM