FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
May 25, 2016

DRAFT QUESTIONS

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1. **DISCUSSION:** Discuss any issues related to the efficacy or safety of lixisenatide for the treatment of patients with type 2 diabetes mellitus. Please comment on whether any of these issues preclude approval of lixisenatide.

2. **DISCUSSION:** Discuss the benefit(s) of starting the fixed-combination drug product containing lixisenatide and insulin glargine in patients with type 2 diabetes mellitus not treated with either a basal insulin or a GLP-1 agonist (i.e., starting two new drugs at once). In your discussion, identify the patient population in whom this use would be particularly useful, and address why you would select the fixed-combination over use of an available GLP-1 agonist or basal insulin in these patients. Explain your rationale using data from the briefing materials, presentations, or your own clinical experience.

3. **DISCUSSION:** Discuss the benefit(s) of using the fixed-combination drug product containing lixisenatide and insulin glargine in patients with type 2 diabetes previously treated with either a basal insulin or a GLP-1 agonist (i.e., adding a single new drug to an existing regimen). In your answer, identify the patient population in whom use of the fixed-combination drug product in this manner would be particularly useful. Explain your rationale using data from the briefing materials, presentations, or your own clinical experience.

4. **DISCUSSION:** Discuss clinical concerns related to the use of the fixed-combination product which combines a drug that, when used alone, has a wide effective dose range and is titrated to effect on a continuous scale (i.e., insulin glargine) with a drug that, when used alone, has one or two recommended effective dose(s) (i.e., lixisenatide).

   Specifically discuss:

   a. Issues related to loss of dosing flexibility including but not limited to: Use of potentially ineffective doses of one agent in populations with low insulin requirements, inability to dose the two drugs independently with the device presentation proposed, inability to increase the insulin dose beyond 60 units.

   b. Issues related specifically to product presentation/devices including but not limited to: use errors that may occur in the care setting related to a lack of clarity on the amount of each product delivered with each given dose, insufficient understanding that, unlike insulin products, the maximum dose for the combination is capped, inadequate understanding of the role of the two devices.

DRAFT QUESTIONS (cont.)

5. **VOTE:** Based on data in the briefing materials and presentations at today's meeting do you recommend approval of the lixisenetide/glargine fixed-combination drug delivered using the proposed pen devices for the treatment of adult patients with type-2 diabetes mellitus?

   a. If you voted yes, explain your rationale and discuss whether use of the combination should be approved for patients not treated with a basal insulin or a GLP-1, for patients who are inadequately controlled on either a basal insulin or a GLP-1 analog or for both populations. Recommend additional post-approval studies if you think these are needed.

   b. If you voted no, explain your rationale and recommend additional pre-approval studies if you think these are needed.