

**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  
June 20, 2017

**QUESTIONS**

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1. **DISCUSSION:** The Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (LEADER) trial assessed several non-CV safety outcomes including medullary thyroid carcinoma, pancreatic neoplasm, and pancreatitis. Please discuss whether the data presented today inform the potential for a causal relationship between liraglutide use and these non-CV safety outcomes. Please also discuss whether additional studies should be conducted to further evaluate these.
  
2. **DISCUSSION:** Please comment on the design, conduct, and results of LEADER and whether LEADER...
  - a. Adequately addresses the post-approval CV risk assessment as recommended in the 2008 FDA Guidance titled *Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes*.
  
  - b. Provides substantial evidence establishing that liraglutide reduces the risk of major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with type 2 diabetes mellitus and high cardiovascular risk.

In your discussion, consider the patient population enrolled (e.g., baseline cardiovascular disease history), reliability of the results (e.g., impact of missing data), the clinical meaningfulness of the results, and the consistency of the results across the components of the MACE endpoint and subgroups.

3. **VOTE:** Do the results of LEADER establish that use of liraglutide in patients with Type 2 Diabetes Mellitus (T2DM) is not associated with unacceptably high cardiovascular risk? **Provide the rationale for your vote.**
  
4. **VOTE:** Does the LEADER trial provide the substantial evidence needed to establish that liraglutide 1.8 mg daily reduces cardiovascular risk in patients with T2DM? **Provide the rationale for your vote.**
  - a. If yes, discuss the population for whom you believe this benefit applies.
  
  - b. If no, comment on what additional data would be needed.