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
October 24 – 25, 2018

QUESTIONS

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1. **DISCUSSION:** Discuss the impact of the recommendations in the 2008 Guidance for Industry: Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes on the assessment of cardiovascular risk for drugs indicated to improve glycemic control in patients with type 2 diabetes mellitus.

2. **DISCUSSION:** For each recommendation described in the 2008 guidance, discuss its value in the evaluation of the safety of new antidiabetic drugs. The recommendations we would like you to consider are:

    a. Establishment of an independent cardiovascular endpoints committee for prospective adjudication.

    b. Inclusion of patients at higher risk for cardiovascular events in phase 2 and phase 3 trials to obtain sufficient endpoints to allow for a meaningful estimate of risk.

    c. Exclusion of 1.8 from the upper bound of the two-sided 95% confidence interval for the estimated risk ratio prior to approval.

    d. Exclusion of 1.3 from the upper bound of the two-sided 95% confidence interval for the estimated risk ratio to conclude that there is no unacceptable increase in cardiovascular risk.

3. **DISCUSSION**: Discuss how cardiovascular safety findings from members of a drug class should or should not be applied to all members of the drug class.

4. **VOTE:** The 2008 Guidance for Industry: Diabetes Mellitus – Evaluating Cardiovascular Risk in New Antidiabetic Therapies to Treat Type 2 Diabetes provided recommendations on excluding an unacceptable increase in cardiovascular risk for all new therapies to improve glycemic control in patients with type 2 diabetes regardless of the presence or absence of a signal for cardiovascular risk in the development program.

    Should an unacceptable increase in cardiovascular risk be excluded for all new drugs to improve glycemic control in patients with type 2 diabetes, regardless of the presence or absence of a signal for cardiovascular risk in the development program?

    a. If ‘Yes’, provide your rationale. Include in your discussion what changes, if any, you would recommend to the 2008 guidance and why, and what kind of assessment would be appropriate and when it should be conducted.

    b. If ‘No’, provide your rationale. Include in your discussion what might constitute a signal of cardiovascular risk that would warrant conduct of a cardiovascular outcome trial or other form of cardiovascular risk assessment.