March 7, 2016

Canadian Agency for Drugs and Technologies in Health (CADTH)
865 Carling Avenue, Suite 600
Ottawa, Ontario
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Subject: Canadian Diabetes Association Feedback on New Drugs for Type 2 Diabetes: A Therapeutic Review Update

Thank you for the opportunity to provide feedback on the proposed scope for the CADTH initiative, New Drugs for Type 2 Diabetes: A Therapeutic Review Update. The Canadian Diabetes Association leads the fight against diabetes by helping those affected by diabetes live healthy lives, preventing the onset and consequences of diabetes, and discovering a cure. We advocate on behalf of people with diabetes for equitable and timely access to the drugs and supports needed to optimally manage their disease. People with diabetes have a large stake in how medications are reviewed and potentially approved for reimbursement by public drug plans in Canada. We believe that drug review processes must incorporate the best available evidence, be reviewed with scientific rigour, be clinically relevant but also transparent, consistent and fair.

Based on the CADTH's Proposed Project Scope, we submit the following comments for consideration:

1. In the evaluation of the efficacy and comparative efficacy of drugs to treat type 2 diabetes, randomized controlled trials are the most appropriate study design to confidently report results. However, in the evaluation of harms and comparative harms, the use of observational studies should also be included. For practice support question 1, observational studies should be included to identify adverse effects and describe the characteristics of patients who are intolerant sulfonylurea or insulin therapy.

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2. When considering the efficacy and comparative efficacy of treatments, reviewers should keep in mind that people with type 2 diabetes are not a homogeneous population.
   - Several sub-populations within the type 2 diabetes population may experience additional benefits/harms from a therapy, for example people with cardiovascular disease, at high risk of cardiovascular disease, the frail elderly, people at differing weights and the duration of diabetes diagnosis. The data should be stratified and reported separately for these subgroups. The potential differential impact is very important to clinicians as they manage patients with co-morbidities and risk factors with the goal to optimize health outcomes.
   - Extreme care must be taken when combining data across studies in a meta-analysis and network meta-analysis to ensure that only data from similar populations are aggregated. Results become hard to interpret if data from dissimilar populations are combined.

3. Throughout the CADTH review, both the class effect and the potential individual effect of drug therapies should be considered.

4. The following should be noted for the therapies listed in Table 2.
   - Exenatide weekly (Bydureon) should be listed in the table, and evaluated separately from exenatide daily dosing.
   - Data for once daily and once weekly GLP-1 analogue products should be evaluated separately as they behave differently with respect to both efficacy and side effects.
   - Albiglutide was approved by Health Canada as a GLP-1 analogue and should be included in the review.
   - Insulin glargine should be evaluated as glargine 100 units/mL and glargine 300 units/mL given the differences observed in head-to-head studies.
   - The insulin lispro product (Humalog 200 units/mL) should be included in Table 2.

5. Hypoglycemia is a significant adverse effect of managing diabetes and should be evaluate as a clinical outcome, and in terms of direct and indirect costs.

6. Early results from the LEADER trial have described cardiovascular benefit with liraglutide for patients with type 2 diabetes and at high cardiovascular risk. Although timelines for the CADTH therapeutic review have not been posted, I suggest that your review and recommendations consider these full results which are to be released in June 2016 to allow for up-to-date recommendations.

7. The proposed policy questions to investigate third line therapy have assumed a sulfonylurea or insulin as second-line therapy. However, the proposed scope has indicated that second-line therapy is also being evaluated as part of the review, including an evaluation of metformin + DPP-4 inhibitor, metformin + GLP-1R agonist, and metformin + SGLt2 inhibitor. Thus a sulfonylurea or insulin should not be pre-determined to be the default second-line treatment for evaluating add-on therapy. Add-on therapy should be evaluated for metformin + DPP-4 inhibitor, metformin + GLP-1R agonist, and metformin + SGLt2 inhibitor. Furthermore, consideration should be given to the differential impact on the sub-populations.

I appreciate the opportunity to provide input into this important initiative. Please feel free to contact me with any questions or comments.

Yours sincerely,

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