

# IN BRIEF A Summary of the Therapeutic Review Project

## Second-Line Therapy for Type 2 Diabetes

### Key Messages

- For adults with type 2 diabetes **without established cardiovascular disease**, add a sulfonylurea drug to metformin once metformin, diet, and exercise are not enough to control blood glucose levels.
- For adults with type 2 diabetes **with established cardiovascular disease**, refer to the CADTH Common Drug Review (CDR) recommendations on individual drugs<sup>a</sup> that have been reviewed for this indication.

<sup>a</sup> As of May 2017, the only drug reviewed by CDR for this indication is empagliflozin (Jardiance). The recommendation is to reimburse empagliflozin for patients with type 2 diabetes as a second-line therapy after metformin if these patients have established cardiovascular disease as defined in the EMPA-REG OUTCOME trial:

Presence of one or more of the following –

- MI >2 months prior
- Multi-vessel CAD
- Single vessel CAD, with positive stress test or with hospitalization for UA in prior year
- UA >2 months prior and evidence of CAD
- Stroke >2 months prior
- Occlusive PAD.

MI = myocardial infarction; CAD = coronary artery disease; UA = unstable angina; PAD = peripheral artery disease.

### Context

Type 2 diabetes is a chronic disease that occurs when the pancreas does not produce enough insulin or the body does not properly use the insulin that it makes. It causes high blood glucose, which can be measured by glycated hemoglobin (A1C), and other complications such as cardiovascular disease and kidney failure. Type 2 diabetes is a growing concern in Canada, placing a significant burden on patients and the health care system. Effective strategies for preventing and managing diabetes are critical – this has been an area of focus for CADTH.

Drug treatments for type 2 diabetes were initially reviewed by CADTH in 2010, and again in 2013. This project is an update to these two large projects.

### Technology

The treatment of type 2 diabetes usually begins with lifestyle modifications (diet and exercise), followed by treatment with oral or injectable drugs. Metformin is typically used as the first-line treatment. Once metformin is not enough, the most commonly prescribed second-line treatments are drugs in the classes of sulfonylureas, insulins, dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) analogues, and sodium-glucose cotransporter-2 (SGLT-2) inhibitors.

### Issue

New drugs have become available for the treatment of type 2 diabetes in the last couple of years, some with promising clinical trial data on cardiovascular outcomes. An updated review of these drug treatments, and updated recommendations, were needed.

### Methods

CADTH conducted a systematic review and network meta-analysis of the clinical evidence and performed a cost-effectiveness analysis. Data available up to June 2016 were examined. Based on the results, and considering input from stakeholder groups, an expert committee updated the CADTH 2013 recommendations.

### Results

All the drugs reviewed worked well for treating diabetes in that they all similarly reduced A1C when added to metformin. No one drug class showed any clear superiority in efficacy or safety outcomes. The drugs that provide the best value for money for second-line treatment are the sulfonylureas, which cost considerably less than the new drugs on the market.

There are some new clinical trial data showing that certain drugs may help protect patients with type 2 diabetes and established cardiovascular disease. At this time, there is not enough evidence to make a general recommendation for a whole drug class, but the expert committee remains supportive of the individual drug recommendation for empagliflozin to reduce the incidence of cardiovascular death. This was a CDR recommendation made prior to this therapeutic review. CADTH will continue to review and provide recommendations for drugs with this indication as they become available.

## Read more about CADTH and its review of this topic:



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CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

May 2017