CADTH

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CADTH Optimal Use Project in Brief

Optimal Second- and Third-Line Therapy in Type 2 Diabetes

Condition

Type 2 diabetes is a chronic disease that results when the pancreas does not produce enough insulin, or the body does not properly use the insulin that it makes.

Drugs

The treatment of patients with type 2 diabetes usually begins with lifestyle modifications, followed by treatment with oral antidiabetes drugs. Metformin is typically used as the first-line oral drug in most patients. Other medication classes currently available for the treatment of type 2 diabetes include: sulfonylureas, meglitinides, alpha-glucosidase inhibitors, thiazolidinediones (TZDs), dipeptidyl peptidase-4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) analogues, and insulins.

Issues

Given that type 2 diabetes is a progressive disease, most patients will eventually require additional antidiabetes drugs. However, current guidelines do not provide specific guidance on the optimal treatment algorithm when metformin is no longer adequate to achieve glycemic control. Also, there is considerable variability in the costs of diabetes treatments, and expenditures in Canada are rising.

In 2010, CADTH issued recommendations for the optimal choice of second- and third-line drugs after metformin for patients with type 2 diabetes. Since then, new antidiabetes treatments have been approved for use in Canada.

Methods

CADTH updated its earlier systematic reviews of clinical evidence and performed an updated cost-effectiveness analysis. Based on the results, an expert panel updated CADTH's 2010 recommendations.

Key Messages

For most adult patients with type 2 diabetes, when proper diet and exercise are not enough to control hyperglycemia:

- Start oral therapy with metformin.
- Add a sulfonylurea to metformin when metformin alone is not enough to adequately control hyperglycemia.
- Add neutral protamine Hagedorn (NPH) insulin when metformin and a sulfonylurea are not enough to adequately control hyperglycemia.*
  OR
  Add a DPP-4 inhibitor to metformin and a sulfonylurea in the rare instances when insulin is not an option.

Optimize the dose of the drug at each stage of therapy before moving to the next. Proper diet and exercise should be encouraged at every stage.

*Patients experiencing significant hypoglycemia during efforts to reach target glycated hemoglobin (A1C) with NPH insulin may benefit from a switch to a long-acting insulin analogue (i.e., insulin glargine or insulin detemir).

Research Results

The results of the updated clinical and economic evaluations remained similar to those of the original analyses: glycemic control was similar across most drug classes, there were some differences in the risk of weight gain and hypoglycemia, and sulfonylureas and insulin NPH were the most cost-effective options for second- and third-line therapy, respectively.

For the full reports and tools, visit www.cadth.ca/t2dm.