Guideline Summary NGC-9997

Guideline Title

Optimal use recommendations for second- and third-line therapy for patients with type 2 diabetes.

Bibliographic Source(s)

Canadian Agency for Drugs and Technologies in Health (CADTH). Optimal use recommendations for second and third-line therapy for patients with type 2 diabetes. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Jul. 19 p. [13 references]

Guideline Status

This is the current release of the guideline.

Scope

Disease/Condition(s)

Type 2 diabetes mellitus

Guideline Category

Assessment of Therapeutic Effectiveness

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Pharmacology

Intended Users

Advanced Practice Nurses

Health Care Providers

Health Plans

Hospitals

Managed Care Organizations

Nurses

Pharmacists

Physician Assistants

Physicians

Public Health Departments

Utilization Management

Guideline Objective(s)

- To provide recommendations for the optimal prescribing and use of second-line pharmacotherapy for patients with diabetes inadequately controlled on metformin
- To provide recommendations for the optimal prescribing and use of third-line therapy for patients with diabetes inadequately controlled on metformin and a sulfonylurea

- To provide recommendations for the optimal prescribing and use of alternative medication for patients unable to use insulin

Target Population

- Patients with type 2 diabetes inadequately controlled with metformin monotherapy
- Patients with type 2 diabetes inadequately controlled with metformin and sulfonylurea combination therapy

Note: Inadequate control was defined as glycated hemoglobin (A1C) >6.5% or fasting plasma glucose >7 mmol/L or two-hour post-prandial glucose >10 mmol/L.

Interventions and Practices Considered

1. Addition of a sulfonylurea to metformin therapy
2. Addition of insulin neutral protamine Hagedorn (NPH) to metformin and sulfonylurea therapy
3. Addition of a dipeptidyl peptidase-4 (DPP-4) inhibitor to metformin and sulfonylurea therapy
4. Thiazolidinediones (TZDs)
5. Glucagon-like peptide-1 (GLP-1) analogues
6. Basal insulin
7. Alpha-glucosidase inhibitors
8. Meglitinides
9. Biphasic insulin

Major Outcomes Considered

- Glycated hemoglobin (A1C) levels
- Changes in body weight
- Hypoglycemia
- Diabetes-related complications
- Serious adverse events
- Mortality
- Cost-effectiveness/cost-utility

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

The evidence for developing recommendations was derived from the following Canadian Agency for Drugs and Technologies in Health (CADTH) reports (see the "Availability of Companion Documents" field):

- Second-Line Pharmacotherapy for Type 2 Diabetes — Update
- Third-Line Pharmacotherapy for Type 2 Diabetes — Update

Policy Questions

Evidence-informed recommendations were developed by the Canadian Drug Expert Committee (CDEC) to address the following policy questions:

1. What is the optimal second-line therapy for patients with type 2 diabetes experiencing inadequate glycemic control with metformin monotherapy?
2. What is the optimal third-line therapy for patients with type 2 diabetes experiencing inadequate glycemic control with metformin and a sulfonylurea?
3. If insulin is the recommended third-line therapy for most patients, what alternative(s) are recommended for patients unable to use insulin?

Research Questions

The following research questions were composed, given the previously listed policy questions:

Second-Line Pharmacotherapy

1. What is the comparative efficacy and safety of second-line antihyperglycemic drugs in adults with type 2 diabetes experiencing inadequate glycemic control on metformin monotherapy?

2. What is the cost-effectiveness of second-line antihyperglycemic drugs in adults with type 2 diabetes experiencing inadequate glycemic control on metformin monotherapy?

Third-Line Pharmacotherapy

1. What is the comparative efficacy and safety of third-line antihyperglycemic drugs in adults with type 2 diabetes experiencing inadequate glycemic control on metformin and a sulfonylurea?

2. What is the cost-effectiveness of third-line antihyperglycemic drugs in adults with type 2 diabetes experiencing inadequate glycemic control on metformin and a sulfonylurea?

Literature Review

Published literature was identified by searching the following bibliographic databases: MEDLINE with In-Process records and daily updates via Ovid; EMBASE via Ovid; The Cochrane Library via Ovid; and PubMed.

Grey literature (literature that is not commercially published) was identified by searching keys sections of the Grey Matters checklist (http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters), which includes the websites of regulatory agencies, health technology assessment agencies, and professional associations. Google and other Internet search engines were used to search for additional web-based materials. These searches were supplemented by reviewing the bibliographies of key papers, and through contacts with appropriate experts and industry.

For second-line therapy and third line therapy, the search identified documents published between January 1, 2009 and May 7, 2012. Regular alerts were established to update these searches until the publication of the final reports.

Full literature search strategies, including specific search terms used, can be found in the second-line therapy and third-line therapy reports (see the "Availability of Companion Documents" field).

Inclusion/Exclusion Criteria

Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), and economic studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009, and May 7, 2012 for second- and third-line therapy. Conference abstracts were excluded from the search results.

Second-Line Therapy

Inclusion Criteria

Study Design: RCTs

Population: Patients inadequately controlled with metformin monotherapy. Inadequate control was defined as glycated hemoglobin (A1C) >6.5% or fasting plasma glucose >7 mmol/L or two-hour post-prandial glucose >10 mmol/L.

Interventions/comparators: Metformin plus any one of the following: placebo/no treatment, sulfonylurea, glucagon-like peptide-1 (GLP-1) analogue, dipeptidyl peptidase-4 (DPP-4) inhibitor, meglitinide, thiazolidinediones (TZDs), alpha-glucosidase inhibitor, insulin (basal, bolus, biphasic). Agents within each drug class were included in the review only if they were approved for marketing in one or more of Canada, the United States, or the European Union.

Outcomes: Mortality, diabetes-related complications, A1C, body weight, hypoglycemia, serious adverse events

Exclusion Criteria

- More than 15% of the patients used a drug other than metformin monotherapy at baseline, and no results were reported for the subgroup of metformin users.
- Initial therapy consisted of a combination of metformin with another antidiabetes drug.
- Second-line antidiabetes drugs added to metformin monotherapy were compared with switching to second-line therapy (i.e., discontinuation of metformin monotherapy).
- Switch from metformin to another antidiabetes drug(s) was compared with switch to placebo or no therapy (i.e., no active comparator).
- Treatment duration was less than four weeks.

Third-line Therapy

Inclusion Criteria

Study Design: RCTs

Population: Patients inadequately controlled with metformin and sulfonylurea combination therapy. Inadequate control was defined as A1C >6.5% or fasting plasma glucose >7 mmol/L or two-hour post-prandial glucose >10 mmol/L.

Interventions/comparators: Metformin and a sulfonylurea plus any one of the following: placebo/no treatment, GLP-1 analogue, DPP-4 inhibitor, meglitinide, TZDs, alpha-glucosidase inhibitor, insulin (basal, bolus, biphasic). Agents within each drug class were included in the review only if they were approved for marketing in one or more of the following countries: Canada, the United States, or the European Union.

Outcomes: Mortality, diabetes-related complications, A1C, body weight, hypoglycemia, serious adverse events

Exclusion Criteria

- More than 15% of the sample used drugs other than metformin and sulfonylurea without a subgroup analysis for patients inadequately controlled on combination therapy with metformin and sulfonylureas.
- Studies evaluating the switch from combination therapy to another antidiabetes drug(s) in which the comparator was placebo or no antidiabetes therapy (i.e., no active comparator)
- Studies with a duration of less than four weeks
- Non-English publications

Number of Source Documents

Second-line pharmacotherapy: a total of 60 unique randomized controlled trials (RCTs) were included

- Second-line pharmacotherapy: a total of 69 unique randomized controlled trials (RCTs) were included.
- Third-line pharmacotherapy: a total of 40 unique RCTs were included.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus (Committee)

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis of Randomized Controlled Trials

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

The evidence for developing recommendations was derived from the following Canadian Agency for Drugs and Technologies in Health (CADTH) reports (see the "Availability of Companion Documents" field):

- Second-Line Pharmacotherapy for Type 2 Diabetes — Update
- Third-Line Pharmacotherapy for Type 2 Diabetes — Update

Second- and Third-Line Pharmacotherapies

Outcomes of Interest

Compared with the original CADTH analysis, this update focused on outcomes that were primary considerations of CADTH's Therapeutic Review Panel in developing the original recommendations. These include mortality, diabetes-related complications, glycated hemoglobin (A1C), bodyweight, hypoglycemia, and serious adverse events (SAEs). Evidence for diabetes-related complications was only reviewed from randomized controlled trials (RCTs) that were designed and powered to compare the effect of two or more treatments on such end points.

Data Extraction and Critical Appraisal

Data extraction and risk of bias assessment were performed by one reviewer, and verified by a second reviewer. Disagreements at any of these stages were resolved through consensus or by a third reviewer if consensus could not be reached. Risk of bias for the included RCTs was assessed using the Scottish Intercollegiate Guidelines Network questionnaire (SIGN-50).

Statistical Analysis

The original network meta-analyses (NMAs) for second- and third-line therapy were updated with data from the newly identified trials. The methodology employed was the same as that used in the original CADTH analysis. WinBUGS (MRC Biostatistics Unit, Cambridge, UK) was used for the network meta-analyses according to the routine developed at the Universities of Bristol and Leicester. Metformin monotherapy was the reference group for all network meta-analyses analyses. Posterior densities for unknown parameters were estimated using Markov Chain Monte Carlo methods. Basic parameters were assigned non-informative or vague prior distributions. Point estimates and 95% credible intervals (CrIs) were used to summarize all findings. The probability of a drug class being optimal was estimated for each outcome based on the proportion of Markov Chain Monte Carlo simulations in which its relative measure of effect was best. We also calculated the mean rank for each drug class. Model diagnostics including trace plots and the Brooks-Gelman-Rubin statistic were assessed to ensure model convergence. Two chains were fit into WinBUGS for each analysis, each employing ≥20,000 iterations, with a burn-in of ≥20,000 iterations.

Frequentist pairwise meta-analysis was performed using R — a language and software environment for statistical computing. A random effects model was used for the reference case in all pairwise and NMAs. The robustness of the reference case for A1C was assessed using alternative modelling, sensitivity analyses, and meta-regressions.

Pharmacoeconomic Review Process

The following research questions were addressed in the updated pharmacoeconomic review of second- and third-line diabetes pharmacotherapy:

1. What is the cost-effectiveness of second-line antidiabetes drugs in adults with type 2 diabetes inadequately controlled on metformin monotherapy?
2. What is the cost-effectiveness of third-line antidiabetes drugs in adults with type 2 diabetes inadequately controlled on metformin and a sulfonylurea?

The cost-utility analysis was conducted using a new version of the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model previously used in the original CADTH reviews. The newer UKPDS Outcomes Model was updated to reflect the most current clinical evidence, drug prices, and management costs. The key feature of this update was the incorporation of GLP-1 analogues.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Process for Updating the Optimal Therapy Recommendations

The evidence from the updated clinical and pharmacoeconomic reviews was discussed by the Canadian Drug Expert Committee (CDEC), which developed updated Optimal Therapy Recommendations for second- and third-line diabetes

pharmacotherapy. CDEC is an advisory body to the Canadian Agency for Drugs and Technologies in Health (CADTH), composed of individuals with expertise in drug therapy, drug evaluation, and drug utilization; and including public members to bring a lay perspective.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Second-Line Pharmacotherapy

The Committee considered the results of a class-level cost-effectiveness analysis that compared alternative second-line therapies in adults with type 2 diabetes inadequately controlled with metformin monotherapy. The analysis compared nine treatment classes added to metformin as second-line therapy (alpha-glucosidase inhibitors, sulfonylureas, meglitinides, thiazolidinediones [TZDs], basal insulin, biphasic insulin, dipeptidyl peptidase-4 [DPP-4] inhibitors, glucagon-like peptide-1 [GLP-1] analogues, and placebo). The lowest cost alternative for each class of drugs was used in the primary economic analysis. The average daily costs of treatments were estimated with and without the additional cost of blood glucose test strips (see Table 2 in the original guideline document).

Average test strip use, by type of pharmacotherapy, was obtained from an analysis of the Ontario Public Drug Programs. A cost of $0.729 per test strip plus a pharmacy fee of $7.00 per 100 test strips was applied. The United Kingdom Prospective Diabetes Study Outcomes Model was used to forecast the cumulative incidence of diabetes-related complications during a 40-year time horizon, as well as associated costs. For each treatment strategy, inputs for predictive risk factors in the model — such as hemoglobin A1C, body mass index, and body weight — were informed by the results of the systematic review and network meta-analysis. Overall hypoglycemia, severe hypoglycemia, and congestive heart failure (regarding TZDs) were also considered in the model.

In the reference-case analysis, the addition of a sulfonylurea to metformin monotherapy was associated with the most favourable cost-effectiveness estimate compared with metformin monotherapy, with an incremental cost per quality-adjusted life year (QALY) gained of $8,445 relative to metformin alone (see Table 3 in the original guideline document). Other active treatments were more costly and associated with a range of QALYs gained compared with sulfonylureas, although absolute differences in QALYs across classes were small. Cost-effectiveness results were robust to variation in model inputs and assumptions. Cost-effectiveness acceptability curves showed that sulfonylureas had the highest probability of being the most cost-effective second-line treatment option for willingness-to-pay thresholds above ~$22,000 per QALY gained.

A limitation of the economic analysis was the lack of adequate clinical data to inform key model inputs, especially the impact of insulin use and hypoglycemia on quality of life, and the incidence of hypoglycemia across various treatments.

Third-Line Pharmacotherapy

The Committee considered the results of a class-level cost-effectiveness analysis that compared alternative third-line therapies in adults with type 2 diabetes inadequately controlled with metformin and a sulfonylurea. The analysis compared five classes added to metformin and a sulfonylurea as third-line therapy (basal insulin, biphasic insulin, DPP-4 inhibitors, GLP-1 analogues, and placebo). The lowest cost alternative for each class of drugs was used in the primary economic analysis. TZDs were not included in the reference-case analysis, as they are not indicated for third-line treatment of type 2 diabetes in Canada, but they were included in a sensitivity analysis. The average daily costs of treatments were estimated with and without the additional cost of blood glucose test strips (see Table 4 in the original guideline document). Average test strip use, by type of pharmacotherapy, was obtained from an analysis of the Ontario Public Drug Programs. A cost of $0.729 per test strip, plus a pharmacy fee of $7.00 per 100 test strips, was applied. The United Kingdom Prospective Diabetes Study Outcomes Model was used to forecast the cumulative incidence of diabetes-related complications during a 40-year time horizon, as well as associated costs. For each treatment strategy, inputs for predictive risk factors in the model — such as hemoglobin A1C, body mass index, and body weight — were informed by the results of the systematic review and network meta-analysis. Overall hypoglycemia, severe hypoglycemia, and congestive heart failure (regarding TZDs) were also considered in the model.

In the reference-case analysis, the addition of insulin neutral protamine Hagedorn (NPH) (representing the basal insulin class) to metformin plus a sulfonylurea was associated with the most favourable cost-effectiveness estimates among active treatments, with an incremental cost per QALY gained of $68,442 relative to metformin plus a sulfonylurea alone (see Table 5 of the original guideline document). Other active treatments were more costly and less effective in QALYs gained compared with insulin NPH, with the exception of GLP-1 agonists, which were associated with QALY gains of 8.2957 versus 8.2923 for insulin NPH. Differences between treatments in QALYs were small, hence cost-effectiveness results were driven primarily by lifetime costs. Cost-effectiveness results were sensitive to variation in model inputs and assumptions. In some circumstances, DPP-4 inhibitors became the most cost-effective therapeutic option in circumstances such as if insulin was considered undesirable by patients (i.e., high disutility was applied for insulin injections), if higher rates of hypoglycemia were assumed among patients using insulin than in the reference case analysis, or if a higher disutility was assigned to cases of mild to moderate hypoglycemia. Cost-effectiveness acceptability curves showed that the addition of insulin NPH had the highest probability of being the most cost-effective third-line treatment option for willingness-to-pay thresholds above ~$69,000 per QALY gained.

To assess the cost-effectiveness of third-line therapies for patients unable to use insulin, a sensitivity analysis was performed in which insulins were removed as treatment options. In this scenario, the addition of a DPP-4 inhibitor to metformin and a sulfonylurea represented the most cost-effective option, with an incremental cost utility ratio (ICUR) of $113,254 per QALY gained compared with the combination of metformin and a sulfonylurea.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Recommendations

Major Recommendations

Recommendation 1: The Canadian Drug Expert Committee (CDEC) recommends that a sulfonylurea be added to metformin for most adults with type 2 diabetes inadequately controlled on metformin alone.

Reasons for Recommendation

1. All of the drug classes demonstrated similar improvements in glycated hemoglobin (A1C). Sulfonylureas were the most cost-effective treatment option, with an incremental cost-utility ratio (ICUR) of $8,445 per quality-adjusted life-year (QALY) gained compared with metformin alone.
2. There are considerably more long-term safety data for sulfonylureas compared to drugs from the newer classes of antihyperglycemic agents.

Of Note

Although there were 69 randomized controlled trials (RCTs) included in the systematic review, the evidence was limited by the lack of adequate data for clinically important outcomes such as diabetes-related complications and severe hypoglycemia.

The Committee identified the values of safety, efficacy, and cost-effectiveness as being of particular importance in making this recommendation.

Recommendation 2: The CDEC recommends that insulin neutral protamine Hagedorn (NPH) be added for most adults with type 2 diabetes inadequately controlled on metformin and a sulfonylurea.

Reasons for Recommendation

1. Based on the results of a network meta-analysis of 24 RCTs in patients with type 2 diabetes mellitus and inadequate glycemic control on metformin and a sulfonylurea, statistically significant reductions in hemoglobin A1C of similar magnitude were found for all classes of antihyperglycemic drugs added to existing therapy, with the exception of alpha-glucosidase inhibitors and meglitinides. The addition of insulin NPH to metformin plus a sulfonylurea was associated with the most favourable cost-effectiveness estimate.
2. There are considerably more long-term safety data for the use of insulin NPH compared with drugs from the newer classes of antihyperglycemic agents.

Of Note

1. The evidence provided in the 40 RCTs that were included in the Canadian Agency for Drugs and Technologies in Health (CADTH) systematic review was limited by the lack of data for clinically important outcomes such as diabetes-related complications and severe hypoglycemia.
2. Long-acting insulin analogues at prices similar to insulin NPH would also be an option for patients inadequately controlled on metformin and a sulfonylurea.
3. Although there is more clinical experience with dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like peptide-1 (GLP-1) analogues since the original CADTH recommendations were published, the Committee concluded that there remains uncertainty regarding the long-term safety of these drug classes. The Committee noted that additional long-term follow-up data — including the results of ongoing trials designed to investigate the effects of DPP-4 inhibitors and GLP-1 analogues on cardiovascular end points — may help address this uncertainty in the future.

The Committee identified the values of safety, efficacy, and cost-effectiveness as being of particular importance in making this recommendation.

Recommendation 3: In circumstances where patients are unable to use insulin as a third-line option, the CDEC recommends that a DPP-4 inhibitor may be added to metformin and sulfonylurea therapy.

Reason for Recommendation

DPP-4 inhibitors were the most cost-effective option when insulins were excluded from the cost-effectiveness analysis.

Of Note

1. The Committee noted that there are few instances where patients with type 2 diabetes are unable to use insulin after adequate education and training. However, the Committee recognized that an alternative to insulin should be available to facilitate optimal glycemic control for such patients.
2. The Committee noted that although DPP-4 inhibitors were the most cost-effective option when insulin is not an option, the addition of agents from this drug class to metformin and a sulfonylurea was associated with a relatively high incremental cost per QALY gained relative to metformin and a sulfonylurea alone ($113,254).

The Committee identified the values of efficacy and cost-effectiveness as of particular importance in making this recommendation.

Clinical Algorithm(s)

None provided

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The recommendations are based on clinical (systematic reviews of randomized controlled trials, network meta-analysis, and individual randomized controlled trials) and cost-effectiveness evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Optimal second- and third-line therapy for type-2 diabetes that results in improved health outcomes and is cost-effective

Potential Harms

Harms of Second-Line Therapy

- Harms associated with various second-line antidiabetes drugs were evaluated using the following end points: hypoglycemic events (overall and severe), changes in body weight, and adverse events. Network meta-analyses were conducted for change from baseline in body weight and overall hypoglycemia. Events of severe hypoglycemia and severe adverse events were too rare (e.g., the majority of trials reported zero events) in the included randomized controlled trials (RCTs) to perform meaningful comparisons across drug classes.
- Thirty-five RCTs were included in a network meta-analysis for changes from baseline in body weight (N = 20,178). Treatment with sulfonylureas, meglitinides, thiazolidinediones (TZDs), basal insulin, biphasic insulin, and rapid-acting insulin analogue resulted in significantly greater increases in body weight than metformin monotherapy (range 1.7 kg to 3.1 kg), with no significant differences between these classes. Dipeptidyl peptidase-4 (DPP-4) inhibitors and alpha-glucosidase inhibitors did not significantly affect body weight. The only drug class associated with a significant reduction in body weight versus metformin monotherapy was glucagon-like peptide-1 (GLP-1) analogues (−1.8 kg, 95% credible interval [CrI], −3.0 to −0.5).
- Forty-eight RCTs were included in the updated network meta-analysis for overall hypoglycemia (N = 24,284). Relative to metformin monotherapy, the risk of hypoglycemia was significantly elevated with insulins, sulfonylureas, and meglitinides (odds ratios were 4.1 to 7.0 for insulins, 7.5 for sulfonylureas, and 8.3 for meglitinides). TZDs, alpha-glucosidase inhibitors, DPP-4 inhibitors, and GLP-1 analogues were not associated with a significant increase in the risk of hypoglycemia.

Harms of Third-Line Therapy

- Harms associated with various third-line antihyperglycemic drugs were evaluated using the following end points: hypoglycemic events (overall and severe), changes in body weight, and adverse events. A network meta-analysis was conducted for change from baseline in body weight; however, results for overall and severe hypoglycemia could not be pooled in this manner. Events of severe hypoglycemia and severe adverse events were too rare (e.g., the majority of trials reported zero events) in the included RCTs to perform meaningful comparisons across drug classes.
- Eighteen RCTs were included in the updated network meta-analysis for body weight (N = 7,907). When added to metformin and a sulfonylurea, basal insulin, biphasic insulin, rapid-acting insulin analogue, and TZD were associated with significantly greater increases in body weight than occurred with metformin and sulfonylurea alone (range 1.9 kg to 5.0 kg). DPP-4 inhibitors and alpha-glucosidase inhibitors were weight-neutral, whereas GLP-1 analogues were associated with statistically significant weight loss (−1.6 kg, 95% CrI, −2.8 to −0.4). Meglitinides were associated with a non-significant trend toward increased body weight.
- Basal insulin, TZDs, DPP-4 inhibitors, and GLP-1 analogues were associated with a significantly greater risk of overall hypoglycemia than placebo when given in combination with metformin and a sulfonylurea. The various insulin-containing strategies were typically associated with a greater risk of overall hypoglycemia relative to other active comparators. Biphasic and bolus insulins were associated with a significantly greater risk of overall hypoglycemia than basal insulin. Events of severe hypoglycemia were relatively rare for all drug classes, limiting the ability to make meaningful comparisons between drug classes.

Qualifying Statements

Qualifying Statements

- The information in this report is intended to help health care decision-makers, patients, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. The information in this report should not be used as a substitute for the application of clinical judgment in respect to the care of a particular patient or other professional judgment in any decision-making process, nor is it intended to replace professional medical advice. While the Canadian Agency for Drugs and Technologies in Health (CADTH) has taken care in the preparation of this report to ensure that its contents are accurate, complete, and up-to-date, CADTH does not make any guarantee to that effect. CADTH is not responsible for any errors or omissions or injury, loss, or damage arising from or as a result of the use (or misuse) of any information contained in or implied by the information in this report.
- CADTH takes sole responsibility for the final form and content of this report. The statements, conclusions, and views expressed herein do not necessarily represent the view of Health Canada or any provincial or territorial government.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Pocket Guide/Reference Cards

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Canadian Agency for Drugs and Technologies in Health (CADTH). Optimal use recommendations for second and third-line therapy for patients with type 2 diabetes. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Jul. 19 p. [13 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Jul

Guideline Developer(s)

Canadian Agency for Drugs and Technologies in Health - Nonprofit Organization

Source(s) of Funding

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Guideline Committee

Canadian Drug Expert Committee (CDEC)

Composition of Group That Authored the Guideline

Members of the Canadian Drug Expert Committee: Dr. Robert Peterson (*Chair*), Dr. Lindsay Nicolle (*Vice-Chair*), Dr. Ahmed Bayoumi, Dr. Bruce Carleton, Ms. Cate Dobhran, Mr. Frank Gavin, Dr. John Hawboldt, Dr. Peter Jamieson, Dr. Julia Lowe, Dr. Kerry Mansell, Dr. Irvin Mayers, Dr. James Silvius, and Dr. Adil Virani

Financial Disclosures/Conflicts of Interest

None

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Canadian Agency for Drugs and Technologies in Health (CADTH) Web site.

Availability of Companion Documents

The following are available:

- Second-line pharmacotherapy for type 2 diabetes — update. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Jul. 94 p. Electronic copies: Available in Portable Document Format (PDF) from the Canadian Agency for Drugs and Technologies in Health (CADTH) Web site.
- Third-line pharmacotherapy for type 2 diabetes — update. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Jul. 85 p. Electronic copies: Available in PDF from the CADTH Web site.
- Second- and third-line pharmacotherapy for type 2 diabetes — update of CADTH 2010 reviews. Project protocol. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2012 Nov. 17 p. Electronic copies: Available in PDF from the CADTH Web site.
- Type 2 diabetes—second- and third-line therapies. CADTH optimal therapy newsletter. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Aug. Electronic copies: Available in PDF from the CADTH Web site.
- Optimal second- and third-line therapy in type 2 diabetes. Project in brief. Ottawa (ON): Canadian Agency for Drugs

and Technologies in Health (CADTH); 2013 Sep. 1 p. Electronic copies: Available in PDF from the CADTH Web site.

- Prescribing aid. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2013 Jul. 2 p. Electronic copies: Available in PDF from the CADTH Web site.
- McIntosh B, Cameron C, Singh S, Yu C, Ahuja T, Welton N, Dahl M. Second-line therapy in patients with type-2 diabetes inadequately controlled with metformin monotherapy: a systematic review and mixed treatment comparisons meta-analysis. 2011 Mar. Wiki version available at the Open Medicine Web site.
- Guideline for starting and adjusting insulin for type 2 diabetes. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2010 Mar. 5 p. Electronic copies: Available in PDF from the CADTH Web site.

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on October 7, 2013. The information was verified by the guideline developer on November 14, 2013.

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