Diabetes Canada
Clinical Practice Guidelines
2018 Update

Dr Monique Bergenwall  RPh, PharmD, ACPR
Clinical Pharmacist - Grandview Medical Centre Family Health Team
Presenter Disclosure

- I have no current or past relationships with commercial entities.
- I have received no speaker’s fee for this learning activity.
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Learning Objective

To identify major changes within the 2018 Diabetes Canada Clinical Practice Guidelines\(^1\) pertinent to pharmacists working with adult patients with type 2 diabetes mellitus (T2DM).

Presentation Outline

- Targets for Glycemic Control
  - A1c & Plasma Glucose Targets
  - Monitoring of Glycemic Control

- Antihyperglycemic Therapy

- Pharmacotherapy for Cardiovascular Protection

- Additional Topics
  - Weight Management
  - Sick Day Management
  - Hyperglycemic Emergencies in Adults
  - Pre-Diabetes
  - Complementary & Alternative Medicine
  - Diabetes & Driving

- Online Tools for Practitioners
Topics Not Covered

- Chapter 10: Physical Activity & Diabetes
- Chapter 11: Nutrition Therapy
- Chapter 12: Glycemic Management of Type 1
- Chapter 16: In-Hospital Management
- Chapter 18: Diabetes & Mental Health
- Chapter 19: Influenza & Other Vaccinations
- Chapter 20: Diabetes & Transplantation
- Chapter 24: Screening for the Presence of CVD
- Chapter 27: Management of Acute Coronary Syndromes
- Chapter 28: Treatment of Diabetes in People with Heart Failure
- Chapter 30: Retinopathy
- Chapter 31: Neuropathy
- Chapter 32: Foot Care
- Chapter 33: Sexual Dysfunction & Hypogonadism
- Chapter 34: Type 1 in Children & Adolescents
- Chapter 35: Type 2 in Children & Adolescents
- Chapter 36: Pregnancy
- Chapter 38: Type 2 Diabetes in Indigenous People

Targets for Glycemic Control
A1c & Plasma Glucose (PG)
## Targets for Glycemic Control

<table>
<thead>
<tr>
<th>A1c Target</th>
<th>Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 6.5 %</td>
<td>Adults with type 2 diabetes (T2DM) at low risk of hypoglycemia, to reduce the risk of chronic kidney disease (CKD) and retinopathy</td>
</tr>
<tr>
<td>≤ 7.0 %</td>
<td>Most adults with T2DM</td>
</tr>
</tbody>
</table>
| 7.1 → 8.5% | **7.1 - 8.0%**  
Functionally dependent patients  

7.1 - 8.5%  
At-risk patients with:  
• Recurrent severe hypoglycemia and/or hypoglycemia unawareness  
• Limited life expectancy  
• Frail elderly and/or with dementia  

[Grade D, Consensus]  

**End of life:** A1C measurement not recommended. Avoid symptomatic hyperglycemia and any hypoglycemia. [Grade D, Consensus]

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## Targets for Glycemic Control

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>A1c (%)</th>
<th>Preprandial PG (mmol/L)</th>
<th>2h Postprandial PG (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most patients</td>
<td>≤ 7.0</td>
<td>4.0 - 7.0</td>
<td>5.0 - 10.0</td>
</tr>
<tr>
<td>If A1c ≤ 7.0 % is not achieved despite achieving above targets</td>
<td>4.0 - 5.5</td>
<td>[Grade D, Level 4]</td>
<td>5.0 - 8.0</td>
</tr>
</tbody>
</table>

Monitoring of Glycemic Control

- **Continuous Glucose Monitoring (CGM) Systems**
  - **2013 Guidelines:** CGM is recommended for patients with T1DM to improve A1c and reduce episodes of hypoglycemia

- **Flash Glucose Monitoring (FGM)**
  - Freestyle Libre®
    - Only flash glucose monitor available in Canada
  - **New recommendation:** FGM may be offered to people with diabetes to decrease time spent in hypoglycemia.\(^4,5\)
    - [Grade B, Level 2 for type 1 diabetes; Grade B, Level 2 for T2DM]
Pharmacotherapy for T2DM

Antihyperglycemic Agents
Initiation of Antihyperglycemic Agents

Chapter 13 - Pharmacologic Glycemic Management of Type 2 Diabetes in Adults

Figure 1. Management of hyperglycemia in type 2 diabetes

Initiation of Antihyperglycemic Agents

Irrespective of A1c
This includes patients with:
• Dehydration
• Unintentional weight loss
• DKA
• HHS

Insulin may be tapered or discontinued once stability is achieved.

Initiation of Antihyperglycemic Agents

Prioritize use of antihyperglycemic agents with demonstrated CV benefit in patients with established CVD\(^7,8,9\)

This includes:
- MI
- Established CAD on angiography
- Unstable angina
- Stroke
- PAD

Canagliflozin

- Review conducted by an independent committee found the evidence for CV benefit to be weaker for canagliflozin
  - Interim analysis of CANVAS study data in 2012 → unblinding of study data
    - Unblinding of data = Potential threat to internal validity
  - Decision was made to combine CANVAS with CANVAS-R data
    - Increased power for CV outcomes
    - Revision of study protocol = Potential threat to internal validity

- No significant benefit for individual outcomes
- Increased risk of fractures and amputations with canagliflozin

SGLT2is & Special Populations

- **Chronic Kidney Disease & Heart Failure (HF)**
  - **New recommendation:** In adults with T2DM and clinical CVD in whom glycemic targets are not achieved with existing antihyperglycemic medication(s) and with an eGFR >30 mL/min/1.73m², an SGLT2i may be added to:
    - Reduce the risk of progression of nephropathy.\(^8\,9\)
      - [Grade B, Level 2 for empagliflozin; Grade C, Level 3 for canagliflozin]
    - Reduce the risk of heart failure hospitalization.\(^7\,8\)
      - [Grade B, Level 2 for empagliflozin; Grade C, Level 2 for canagliflozin].

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Initiation of Antihyperglycemic Agents

**Clinical CVD?**

- YES
  - Start antihyperglycemic agent with demonstrated CV benefit: emagliflozin (Grade A, Level 1A), liraglutide (Grade A, Level 1A), canagliflozin†† (Grade C, Level 2)
  - If not at glycemic target

- NO

**Add additional antihyperglycemic agent best suited to the individual based on the following:**

<table>
<thead>
<tr>
<th>Clinical Considerations</th>
<th>Choice of Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy</td>
<td>DPP-4 inhibitor, GLP-1 receptor agonist or SGLT2 inhibitor</td>
</tr>
<tr>
<td>Other considerations: Reduced eGFR and/or albuminuria</td>
<td>See Appendix 7.</td>
</tr>
<tr>
<td>Clinical CVD or CV risk factors</td>
<td>See Table below.</td>
</tr>
<tr>
<td>Degree of hyperglycemia</td>
<td></td>
</tr>
<tr>
<td>Other comorbidities (CHF, hepatic disease†)</td>
<td></td>
</tr>
<tr>
<td>Planning pregnancy‡</td>
<td></td>
</tr>
<tr>
<td>Cost/coverage</td>
<td></td>
</tr>
<tr>
<td>Patient preference</td>
<td></td>
</tr>
</tbody>
</table>

Initiation of Antihyperglycemic Agents

Figure 1. Management of hyperglycemia in type 2 diabetes (continued)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>↑</th>
<th>↓↓</th>
<th>but usually requires 3 to 4 times daily dosing</th>
<th>Gastrointestinal side effects</th>
<th>Requires 3 times daily dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylurea</td>
<td></td>
<td></td>
<td></td>
<td>Gliclazide and glimepiride associated with less hypoglycemia than glyburide</td>
<td>Poor durability</td>
<td></td>
</tr>
<tr>
<td>Weight loss agent (orlistat)</td>
<td>None</td>
<td>↓</td>
<td>↓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*alo, alogliptin; cana, canagliflozin; empa, empagliflozin; glar, glargine; lira, liraglutide; exenatide long-acting release; lixi, lixisenatide; saxa, saxagliptin; sita, sitagliptin.*

If not at glycemic targets

Add another antihyperglycemic agent from a different class and/or add/intensify insulin regimen

Make timely adjustments to attain target A1C within 3-6 months

Renal Function

* May be considered when indicated for CV and renal protection with eGFR <60 but >30 ml/min/1.73m²

Figure 2. Antihyperglycemic medications and renal function

Insulin Recommendations

New Recommendations

▶ In adults with T2DM treated with basal insulin therapy, consider the following options if reducing the risk of hypoglycemia is a priority:

▶ **Insulin degludec** may be considered over insulin glargine U-100
  ▶ Decreased risk of overall and nocturnal hypoglycemia\(^{10, 11}\)
    ▶ [Grade B, Level 2 for patients with ≥1 risk factor for hypoglycemia; Grade C, Level 3 for others]
  ▶ Decreased risk of severe hypoglycemia in patients at high CV risk\(^{12}\)
    ▶ [Grade C, Level 3]

▶ **Insulin glargine U-300** may be considered over insulin glargine U-100
  ▶ Decreased risk of overall and nocturnal hypoglycemia\(^{13}\)
    ▶ [Grade C, Level 3]

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Insulin & AHAs

New Recommendations

- **GLP-1 Receptor Agonists**
  - Consider as *add-on therapy*, before initiating bolus insulin or intensifying insulin
    - Weight loss and lower risk of hypoglycemia as compared to single or multiple boluses
      - [Grade A, Level 1A]

- **SGLT2 Inhibitors**
  - Consider as *add-on therapy* to insulin
    - Weight loss and lower risk of hypoglycemia as compared to additional insulin
      - [Grade A, Level 1A]

- **DPP-4 Inhibitors**
  - *May be* considered as *add-on therapy* to insulin
    - No weight gain and lower risk of hypoglycemia as compared to additional insulin
      - [Grade A, Level 1A]

Diabetes in Older People

- **New Recommendation**: DPP-4 inhibitors should be used over sulfonylureas as second line therapy to metformin, because of a lower risk of hypoglycemia\textsuperscript{21}
  - [Grade B, Level 2]

- **Updated Recommendation**: Insulin detemir, glargine U-100, glargine U-300 and degludec may be used instead of NPH or human 30/70 insulin to lower the frequency of hypoglycemic events\textsuperscript{22,23}
  - [Grade D, Consensus for degludec and glargine U-300]

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Pharmacotherapy for T2DM

Medications for CV Risk Reduction
Hypertension

Diagnosis of Diabetes

With CKD or CVD

ACEi or ARB

Without CKD or CVD

1. ACEi or ARB
2. DHP-CCB
3. Thiazide/thiazide-like diuretic

If addition of a second antihypertensive is required, ACEi + CCB is preferable to ACEi + thiazide.

Recommendations fully harmonized with Hypertension Canada Guidelines.

Dyslipidemia

- Treatment targets fully harmonized with Canadian Cardiovascular Society dyslipidemia guidelines.

- **New Recommendation:** Fasting or non-fasting lipid profiles are both appropriate.
  - If triglycerides > 4.5 mmol/L, recommend fasting lipid profile.
    - [Grade D, Consensus]

- **New Recommendation:** In patients with clinical CVD, ezetimibe or evolocumab may be used to further reduce CV events.²³,²⁴
  - [Grade A, Level 1 for ezetimibe; Grade A, Level 1 for evolocumab]

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Cardiovascular Protection

**New Recommendation:** ACE inhibitor or ARB, at doses that have demonstrated vascular protection, should be used to reduce CV risk in adults with diabetes with any of the following:

- **Clinical CVD** 26,27
  - [Grade A, Level 1]
- **Age ≥55 years with an additional CV risk factor** (Total cholesterol >5.2 mmol/L, HDL-C <0.9 mmol/L, hypertension, albuminuria, smoking) or **end organ damage** (albuminuria, retinopathy, left ventricular hypertrophy) 26,27
  - [Grade A, Level 1]
- **Microvascular complications**
  - [Grade D, Consensus]

**Doses that have demonstrated vascular protection include:**

- Perindopril 8 mg once daily 28
- Ramipril 10 mg once daily 26
- Telmisartan 80 mg once daily 27

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Additional Topics
Weight Management

**New Recommendation:** Weight management medication may be considered in people with diabetes who are overweight or obese to promote weight loss and improve glycemic control.

- **Liraglutide**[^30]
  - [Grade A, Level 1A]
- **Orlistat**[^31]
  - [Grade A, Level 1A]


![Table 5: Medications approved for the treatment of obesity in type 2 diabetes](image-url)
Sick Day Management

- Previous sick day management recommendations have been updated to include SGLT2is.

- **Updated Recommendation**: Metformin, insulin secretagogues and SGLT2is should be temporarily withheld during acute illnesses associated with reduced oral intake or dehydration.
  
  - [Grade D, Consensus]

- **New Recommendation**: SGLT2is should be temporarily withheld prior to major surgical procedures, and during acute infections and serious illness to reduce the risk of ketoacidosis.
  
  - [Grade D, Consensus]
Hyperglycemic Emergencies in Adults

- **Diabetic Ketoacidosis & SGLT2 Inhibitors**
  - SGLT2is can precipitate **euglycemic DKA**
  - **New recommendation**: Individuals treated with SGLT2is with symptoms of DKA should be assessed for this condition even if BG is not elevated.
    - [Grade D, Consensus]

- **Precipitating factors:**
  - *Insulin dose reduction or omission*
    - *May occur at time of introduction of SGLT2i*
  - *Surgery or infection*
  - *Exercise*
  - *Low carbohydrate or reduced food intake*

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Other Topics

► **Pre-Diabetes**

► No new recommendations regarding the use of pharmacotherapy to help reduce the risk of T2DM in patients with pre-diabetes.

► Emerging evidence to support the use of liraglutide

► **Complimentary and Alternative Medicine**

► No new recommendations regarding the use of CAM in patients with diabetes

► Insufficient evidence to support the use of any natural health products (NHPs)

► Updated list of NHPs that have been evaluated

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Diabetes & Driving

- New Chapter
- Reviews recommendations for reporting of unfit drivers

- Hypoglycemia Monitoring
  - Drivers with diabetes treated with insulin secretagogues and/or insulin:
    - Measure BG level immediately before and at least every 4 hours while driving
    - Should not drive when BG level is < 4.0 mmol/L
    - If BG level is < 4.0 mml/L, they should not drive until at least 40 minutes after their BG level has risen to > 5.0 mmol/L
    - Refrain from driving immediately if they experience severe hypoglycemia while driving, and notify their HCP

Online Tools for Practitioners

- Diabetes Canada Clinical Practice Guidelines Website: http://guidelines.diabetes.ca/

Clinical Decision Support Tools

- Screening for GDM
- Physical Activity Decision Tool
- Screening for and Diagnosing Diabetes
- Self-Monitoring Blood Glucose
- Reducing Vascular Risk
- Pharmacotherapy for Type 2 Diabetes
- Individualizing Your Patient's A1c Target
- Insulin Order Sets
Questions?
References


References


