GUARDIANS FOR HEALTH

Diabetes Canada

Recommendations for the prevention of CVD and kidney complications in adults with type 2 diabetes

BLOOD PRESSURE

CHOLESTEROL - LDL-C

GLUCOSE/HbA1c

ASPIRIN THERAPY

Diabetes Canada

This summary is directed at HCPs who treat patients with type 2 diabetes. It contains treatment recommendations from the Diabetes Canada guidelines* that have been thoroughly evaluated and compiled. However, they are provided as a supporting tool for the individual clinical practice of the HCP.

GUARDIANS FOR HEALTH does not take over any guarantee nor makes any warranty with regard to any individual treatment plan decided by the HCP based on these recommendations.

When applying the recommendations, HCPs should also refer to the respective prescribing information applicable in his/her country for a selected medication.

* Guidelines should be used to inform clinical practice but not replace clinical judgment

Not every compound is indicated for the recommendations described in the guidelines. Please check your local label.

Lifestyle management recommendations include smoking cessation, managing body weight, increasing physical activity and following a healthy nutrition plan

Targets for adults with type 2 diabetes

< 130/80 mmHg[1]

Recommended pharmacological treatment for adults with type 2 diabetes: FOR HYPERTENSION

CVD, CKD, end-organ damage, microvascular complications or CV risk factors: an **ACE inhibitor** or an **ARB** is recommended as initial therapy at doses that have demonstrated vascular protection[1]

Combination therapy: addition of **dihydropyridine CCB** is preferred to a thiazide/thiazide-like diuretic when combination therapy with an ACE inhibitor is being considered[1]

Recommended pharmacological treatment for adults with type 2 diabetes: FOR CARDIORENAL PROTECTION AND SPECIAL CONSIDERATIONS

Covered above in treatment for hypertension recommendations

References: 1. Tobe SW *et al. Can J Diabetes*. 2018;42:s186–s189.

Targets for adults with type 2 diabetes

< 2.0 mmol/L or > 50 % reduction from baseline[1]

Recommended pharmacological treatment for adults with type 2 diabetes

Statin therapy should be used to reduce CV risk in patients with any of the following features:[2]

- **Clinical CVD**
- **Aged ≥ 40 years**
- **Aged < 40 years and 1 of the following:**
  - **Diabetes duration > 15 years and aged > 30 years**
  - **Microvascular complications**
  - Warrants therapy based on the presence of other **CV risk factors** according to the *2016 Canadian Cardiovascular Society Guidelines for the Diagnosis and Treatment of Dyslipidemia*

For individuals not at LDL-C goal despite statin therapy, a combination of statin therapy with second-line agents may be used to achieve the goal and the agent used should be selected based upon the size of the existing gap to LDL-C goal[1]

In patients who also have **concomitant clinical CVD, ezetimibe** or **evolocumab** may be used to further reduce MACE, and they should also be considered in those with concomitant familial hypercholesterolemia[1]

References: 1. Mancini GBJ *et al. Can J Diabetes*. 2018;42:s178–s185; 2. Stone JA *et al. Can J Diabetes*. 2018;42:s162–s169.

Targets for adults with type 2 diabetes

Glycemic targets should be individualized[1]

Most patients: an HbA1c of ≤ **7.0 %** should be targeted to reduce the risk of microvascular complications and, if implemented early in the course of disease, CV complications[1]

Patients assessed to be at low risk of hypoglycemia based on class of antihyperglycemic medication(s) utilized and their characteristics: an HbA1c of ≤ 6.5 % may be targeted to reduce the risk of CKD and retinopathy[1]

A higher HbA1c target may be considered in patients with the goals of avoiding hypoglycemia and over-treatment related to antihyperglycemic therapy, in any of the following:[1]

- Functionally dependent: **7.1 %-8.0 %**
- History of recurrent severe hypoglycemia, especially if accompanied by hypoglycemia unawareness: **7.1 %-8.5 %**
- Limited life expectancy: **7.1 %-8.5 %**
- Frail elderly and/or with dementia: **7.1 %-8.5 %**
- End of life: HbA1c measurement not recommended; avoid symptomatic hyperglycemia and any hypoglycemia

Recommended pharmacological treatment for adults with type 2 diabetes: FOR CARDIORENAL PROTECTION

In patients with **ASCVD**:
- **A GLP-1 RA** or **SGLT2 inhibitor**† with CV or renal benefit should be used to reduce the risk of:[2]
  - MACE (liraglutide, dulaglutide, subcutaneous semaglutide, empagliflozin, canagliflozin)
  - HHF (empagliflozin, canagliflozin, dapagliflozin)
  - Progression of nephropathy (empagliflozin, canagliflozin dapagliflozin)

In patients with a **history of HF (reduced ejection fraction ≤40%)**:[2]
- An **SGLT2 inhibitor**† should be used to reduce the risk of:
  - HHF or CV death, if the eGFR is >30 mL/min/1.73 m^2 (dapagliflozin, empagliflozin and canagliflozin)
  - TZD and saxagliptin should be avoided due to their higher risk of HF

In patients with **CKD and an eGFR of >30 mL/min/1.73 m^2**:[2]
- An **SGLT2 inhibitor**† should be used to reduce the risk of:
  - Progression of nephropathy (canagliflozin, empagliflozin, dapagliflozin)
  - HHF (canagliflozin, dapagliflozin, empagliflozin)
  - MACE (canagliflozin, empagliflozin)
- A **GLP-1 RA** may be considered to reduce the risk of MACE (liraglutide, semaglutide)

In patients **aged ≥60 years with at least 2 CV risk factors**††, inclusion of the following classes in glycemic management should be considered:[2]
- A **GLP-1 RA** with proven CV outcome benefit to reduce the risk of MACE (dulaglutide, liraglutide, subcutaneous semaglutide)

OR
- An **SGLT2 inhibitor**† with proven cardiorenal outcome benefit if eGFR is >30 mL/min/1.73 m^2, to reduce the risk of:
  - HHF (dapagliflozin, canagliflozin)
  - Progression of nephropathy (canagliflozin, dapagliflozin)

Recommended pharmacological treatment for adults with type 2 diabetes: FOR GLUCOSE-LOWERING

If glycemic targets are not achieved within 3 months using healthy behavior interventions alone, antihyperglycemic therapy should be added to reduce the risk of microvascular complications – metformin[|] should usually be selected before other agents due to its low risk of hypoglycemia and weight gain and long-term experience with this agent[2]

Other appropriate agents for reviewing, adjusting or advancing therapy include: alpha-glucosidase inhibitors, DPP-4 inhibitors, GLP-1 RAs, meglitinides, SGLT2 inhibitors[†], SUs, TZDs and insulin[2]

In treatment adjustment or advancement, the choice of anti-hyperglycemic medication should be individualized according to clinical priorities[2]

If reducing risk of hypoglycemia is a priority: incretin agents (DPP-4 inhibitor or GLP-1 RA), SGLT2 inhibitors[†], acarbose and/or pioglitazone should be considered as add-on medication to improve glycemic control with a lower risk of hypoglycemia than other agents[2]

If weight loss is a priority: a GLP-1 RA and/or SGLT2 inhibitor[†] should be considered as add-on medication to improve glycemic control with increased weight loss compared with other agents[2]

In people not achieving glycemic targets on existing non-insulin antihyperglycemic medication(s): the addition of a basal insulin regimen should be considered over premixed insulin or bolus-only regimens if lower risk of hypoglycemia and/or preventing weight gain are priorities[2]

[†] SGLT2 inhibitor labeling varies by region and individual agent with regard to indicated level of eGFR for initiation and continued use – please refer to Prescribing Information.
[††] CV risk factors are defined as any of the following: smoking (tobacco use); hypertension (untreated BP ≥ 140/95 mmHg or current antihypertensive therapy); dyslipidemia (untreated LDL-C > 3.4 mmol/L, or HDL-C < 1.0 mmol/L for men, or HDL-C < 1.3 mmol/L for women, or triglyceride > 2.3 mmol/L, or current lipid-lowering therapy); central obesity.[2]

References: 1. Imran SA *et al. Can J Diabetes*. 2018;42:s42–s46; 2. Lipscombe L et al. *Can J Diabetes*. 2020;44:575–591.

Recommended pharmacological treatment for adults with type 2 diabetes: FOR CV PROTECTION

Primary prevention

Aspirin should not be used routinely for the primary prevention of CVD events; aspirin may be used in the presence of additional CV risk factors[1]

Secondary prevention

Low-dose aspirin therapy (81-162 mg) should be used to prevent CV events in patients with established CVD[1]

References: 1. Stone JA *et al. Can J Diabetes.* 2018;42:s162–s169.

ASPIRIN THERAPY

Abbreviations

ACE:	angiotensin-converting enzyme
ARB:	angiotensin receptor blocker
ASCVD:	atherosclerotic cardiovascular disease
BP:	blood pressure
CCB:	calcium channel blocker
CKD:	chronic kidney disease
CV:	cardiovascular
CVD:	cardiovascular disease
DPP-4:	dipeptidyl peptidase-4
eGFR:	estimated glomerular filtration rate
GLP-1 RA:	glucagon-like peptide-1 receptor agonist
HF:	heart failure
HHF:	hospitalization for heart failure
LDL-C:	low-density lipoprotein cholesterol
MACE:	major adverse cardiovascular events
SGLT2:	sodium-glucose co-transporter-2
SU:	sulfonylurea
TZD:	thiazolidinedione

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