Management of Type 2 Diabetes

At diagnosis of type 2 diabetes

1. Start healthy behaviour interventions (nutritional therapy, weight management, physical activity) ± metformin.

2. Consider a second concurrent disease or comorbidity (CHF, hepatic disease), planning pregnancy, 
   or the treatment of T2DM involves a multi-faceted approach to treat and prevent the symptoms of hyperglycaemia, including dehydration and fatigue, as well as to reduce the risk of cardiovascular (CV) and microvascular complications.

Deciding on the next step—the role of oral anti-diabetes (OAD) medications

For most patients, the first-line glucose-lowering medication is metformin, because of its safety, low cost, and possible heart benefits. However, if when metformin and behaviour interventions are not enough, or are not tolerated, to adequately control a person’s blood glucose levels, a second-line glucose-lowering medication should be added.

When selecting a second-line glucose-lowering medication, it is important to remember that not all OADs are created equal.

Not All Oral Anti-Diabetes Medications Are Created Equal

Start treatment with behaviour interventions

Healthybehaviourinterventions,suchasonutritionaltherapy,physicalactivity,andexercise,arerecommendedasthesignaltotreatthepatientforhypoglycaemiaand/ormetabolicdecompensation.

When is it time to consider medication?

In addition to these behaviour interventions, most people will need medication to help keep their blood glucose levels within their target range.

The treatment of T2DM involves a multi-faceted approach to treat and prevent the symptoms of hyperglycaemia, including dehydration and fatigue, as well as to reduce the risk of cardiovascular (CV) and microvascular complications.

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Start healthy behaviour interventions (nutritional therapy, weight management, physical activity) ± metformin

If not at glycemic target within 3 months, increase metformin

If not at glycemic target

Start antihyperglycemic agent with demonstrated CV benefit:

- Invokana® (canagliflozin)
- Jardiance® (empagliflozin)
- Victoza® (liraglutide)
- Invektra® (canagliflozin-felodipine)

If not at glycemic target

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

Clinical Considerations

- Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy
- DPP-4 inhibitor, GLP-1 receptor agonist, or SGLT2 inhibitor

Choice of Agent

- Metformin
- Sulfonylureas (i.e., gliclazide, glimepiride, glyburide)
- Dipeptidyl peptidase-4 inhibitors
- Sodium-glucose cotransporter 2 inhibitors

Other considerations:

- Reduced eGFR and/or albuminuria
- Clinical CVD or CV risk factors, degree of hyperglycemia, other comorbidities (CHF, hepatic disease), planning pregnancy, cost/coverage, patient preference

Look inside to learn about additional factors to consider when selecting an oral anti-diabetes medication

Reference to the 2018 Diabetes Canada Guidelines (http://guidelines.diabetes.ca/cpg/appendices/app8/index) for complete sick-day medication list instructions

Managing Patients Who Are Sick or at Risk of Dehydration

If a patient begins to feel unwell and is unable to maintain adequate fluid intake, or they experience an acute decline in renal function (e.g., due to GI adverse events or dehydration), give them a “sick day” medication list that instructs them to hold medications that will:

1. Increase their risk for a decline in kidney function, such as:
   - Angiotensin-converting enzyme inhibitors
   - Angiotensin receptor blockers
   - Direct renin inhibitors
   - Nonsteroidal anti-inflammatory drugs
   - Diuretics
   - SGLT2 inhibitors

2. Reduce renal clearance and increase the risk of adverse events, such as:
   - Metformin
   - Sulfonylureas (i.e., gliclazide, glimepiride, glyburide)

When your patients living with T2DM are sick or at risk of dehydration, remember:

- S Sulfonylureas
- A ACE inhibitors
- C Dipeptidyl peptidase-4 inhibitors
- R Sodium-glucose cotransporter 2 inhibitors
- M Metformin
- T Nonsteroidal anti-inflammatory drugs
- I Intravenous agents
- D Direct renin inhibitors
- N Nonsteroidal anti-inflammatory drugs
- S SGLT2 inhibitors

It is also important to inform your patients that when they feel unwell their doses of insulin or noninsulin glucose-lowering medications may need to be adjusted and they will need to increase the frequency of blood glucose self-monitoring.

When selecting a second-line glucose-lowering medication, it is important to remember that not all OADs are created equal.

Not All Oral Anti-Diabetes Medications Are Created Equal

Start treatment with behaviour interventions

Healthy behaviour interventions, such as nutritional therapy, physical activity, and weight management, are recommended as some of the initial treatments (depending on diagnostic levels) in the management of type 2 diabetes (T2DM).

The treatment of T2DM involves a multi-faceted approach to treat and prevent the symptoms of hyperglycemia, including dehydration and fatigue, as well as to reduce the risk of cardiovascular (CV) and microvascular complications.

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For most patients, the first-line glucose-lowering medication is metformin, because of its safety, low cost, and possible heart benefits. However, if and when metformin and behaviour interventions are not enough, or are not tolerated, to adequately control a person’s blood glucose levels, a second-line glucose-lowering medication should be added.

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Clinical considerations for oral anti-diabetes medication selections

<table>
<thead>
<tr>
<th>Class</th>
<th>Drug</th>
<th>Dose(s)</th>
<th>AEC lowering (%)</th>
<th>Weight</th>
<th>CV outcomes*</th>
<th>Renal function</th>
<th>Hypoglycemia</th>
<th>Other considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biguanides</td>
<td>Glipizide*</td>
<td>5 mg, 10 mg, 20 mg &amp; 40 mg</td>
<td>12</td>
<td>1.0</td>
<td>Non-reflexive</td>
<td>Slight increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Biguanides should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>GLP-1 receptor agonists</td>
<td>Exenatide*</td>
<td>2 mg inj, 10 mg inj</td>
<td>12</td>
<td>2.5</td>
<td>Non-reflexive</td>
<td>Slight increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Exenatide should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>Sitagliptin*</td>
<td>10 mg, 25 mg, 50 mg</td>
<td>12</td>
<td>4.6</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Sitagliptin should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>SGLT2 inhibitors</td>
<td>Empagliflozin*</td>
<td>10 mg &amp; 25 mg</td>
<td>12</td>
<td>3.0</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Empagliflozin should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Repaglinide*</td>
<td>1.5 mg, 2.5 mg, 3 mg</td>
<td>12</td>
<td>7.9</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Repaglinide should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>DPP-4 inhibitors</td>
<td>Linagliptin*</td>
<td>20 mg, 40 mg</td>
<td>12</td>
<td>9.4</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Linagliptin should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Acarbose*</td>
<td>100 mg, 200 mg</td>
<td>12</td>
<td>7.0</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Acarbose should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>Sulfonylureas</td>
<td>Chlorpropamide*</td>
<td>50 mg &amp; 100 mg</td>
<td>12</td>
<td>0.7</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Chlorpropamide should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Nateglinide*</td>
<td>30 mg, 60 mg</td>
<td>12</td>
<td>4.4</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Nateglinide should be used cautiously in patients with CV disease.</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Rosiglitazone*</td>
<td>4 mg, 8 mg &amp; 16 mg</td>
<td>12</td>
<td>5.5</td>
<td>Non-reflexive</td>
<td>Minimal increase in BUN and Cr</td>
<td>Rare</td>
<td>No increased risk of hypoglycemia. Rosiglitazone should be used cautiously in patients with CV disease.</td>
</tr>
</tbody>
</table>

*CV outcomes: CV death or CV hospitalization in patients with a history of ischemic heart disease.

Note: The above information is a simplified representation and should be used in conjunction with the respective product monographs and guidelines for complete recommendations and approaches to individualize patient care.
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At diagnosis of type 2 diabetes
Start healthy behaviour interventions (nutritional therapy, weight management, physical activity) and metformin

If A1C < 1.5% above target
Start metformin immediately
If not at glycemic target within 3 months, start a second concurrent antihyperglycemic agent

If not at glycemic target
Start metformin immediately
Consider a second concurrent antihyperglycemic agent
Initiate insulin ± metformin

If not at glycemic target
Clinical CVD?

Yes
Add additional antihyperglycemic agent best suited to the individual based on the following:
Clinical Considerations
Avoidance of hypoglycemia and/or weight gain with adequate glycemic efficacy
Other considerations:
Reduction of eGFR and/or albuminuria, clinical CVD or CV risk factors, degree of hyperglycemia, other comorbidities (CHF, hepatic disease), planning pregnancy, cost/coverage, patient preference
Choice of Agent
DPP-4 inhibitor, GLP-1 receptor agonist, or SGLT2 inhibitor

No
If not at glycemic target

When your patients living with T2DM are sick or at risk of dehydration, remember:
S Sulfonylureas
A ACI inhibitors
D Diuretics, direct renin inhibitors
M Metformin
A Angiotensin receptor blockers
N Nonsteroidal anti-inflammatory drugs
S SGLT2 inhibitors

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