


## Type 2 diabetes management toolbox: from lifestyle to insulin

The management of type 2 diabetes is multi-faceted, including patient education on management of their condition, lifestyle interventions and pharmacological treatments. Managing HbA<sub>1c</sub> levels can reduce a patient's risk of microvascular complications associated with diabetes, but treatment regimens and target HbA<sub>1c</sub> levels need to be tailored to the individual. Lowering HbA<sub>1c</sub> levels is only one aspect of managing type 2 diabetes; other essential components are managing cardiovascular and renal risk factors and helping patients prioritise dietary and physical interventions.

### KEY PRACTICE POINTS:

- Lifestyle interventions are crucial at all stages of management for patients with type 2 diabetes, reducing the need for pharmacological treatment and inducing remission in some people; help patients by providing regular advice, encouragement and referral to appropriate support programmes
- The overall aim of pharmacological treatment with glucose-lowering medicines is to help reduce HbA<sub>1c</sub> levels and the risk of complications
- HbA<sub>1c</sub> targets and the choice of pharmacological treatment should be individualised taking into account overall health status, co-morbidities and risks associated with hypoglycaemia; targets and management may need to change over time
- Check HbA<sub>1c</sub> levels at least annually, but three- to six-monthly if required
- A recommended approach to initiating glucose-lowering medicines is:
  - Initiate metformin at diagnosis; if HbA<sub>1c</sub> levels are > 64 mmol/mol, more intensive treatment may be required
  - If treatment with metformin alone does not reduce HbA<sub>1c</sub> levels to the desired target, add empagliflozin,\* dulaglutide,\* vildagliptin, a sulfonylurea (glipizide or gliclazide) or pioglitazone
  - If further intensification is required, initiate insulin. Alternatively, combine three oral glucose-lowering medicines or two oral medicines and dulaglutide.
  - Prior to intensifying any pharmacological regimen, check the patient's adherence to their existing medicine regimen and diet and physical activity approaches
- If insulin is required, a basal insulin regimen is the preferred option in most clinical situations. Funded options are isophane insulin (usual first choice) and insulin glargine.

\* Special Authority criteria apply. N.B. Dulaglutide funded from 1 September, 2021.

 This article covers the management of patients with type 2 diabetes. Guidance on the management of patients with type 1 diabetes is available from: <https://bpac.org.nz/2019/diabetes-insulin.aspx>


This is a revision of a previously published article.  
What's new for this update:

- Based on guidance from the NZSSD type 2 diabetes management guideline 2021
- Updated type 2 diabetes management algorithm including the new diabetes medicines, empagliflozin and dulaglutide
- Inclusion of a weight-based approach to determine the initial dose for patients initiating basal insulin

## Diabetes management essentials

Type 2 diabetes continues to be a significant health issue in New Zealand. Overall, 5% of the adult population has been diagnosed with type 2 diabetes, with the highest rates among people of Māori, Pacific and South-Asian ethnicity, people who are socioeconomically disadvantaged and older people (aged > 65 years).<sup>1, 2</sup> The prevalence is also increasing in younger people.

Optimal management, including lifestyle approaches (i.e. a healthy diet and exercise), diabetes education and support, and pharmacological treatments, are key to reducing the risk of long-term diabetes complications and help people with type 2 diabetes to live well.

 For further information on diabetes in young people, see: "A rising tide of type 2 diabetes in younger people: what can primary care do?", Page 50

### Management begins with lifestyle


A healthy lifestyle is the foundation of treatment for all people with type 2 diabetes. Cardiovascular disease (CVD) is the greatest cause of early mortality and morbidity in people with type 2 diabetes, and appropriate nutrition and physical activity interventions simultaneously address cardiovascular risk factors and levels of glycaemia.<sup>3</sup>

The first step following diagnosis of type 2 diabetes should be to try to induce remission through lifestyle interventions to achieve weight loss (see below) and metformin treatment (see: "Pharmacological treatment to reduce HbA<sub>1c</sub> levels").<sup>3, 4</sup> Additional pharmacological treatments may be required to reduce HbA<sub>1c</sub> levels, but these may be able to be de-escalated or discontinued in some patients who make significant changes to their lifestyle.<sup>4</sup> Weight loss should be encouraged at any stage of type 2 diabetes to induce remission, slow progression, step down treatment intensity or delay the need to escalate treatment.

**Key lifestyle goals** for patients to aim for include:<sup>3</sup>

- At least 150 minutes per week of moderate intensity exercise – this may not be immediately achievable, but patients should have a plan to increase their level of physical activity to reach this goal
- Weight loss (5 – 10% of total body weight) in those who are overweight\* – various dietary approaches are available; consider patient preference, tolerance, nutritional requirements, co-morbidities, cultural suitability and cost
- Eating foods with a high fibre content, such as fruits, vegetables and whole grains, and avoiding sugar-sweetened beverages or foods with added sugars

\* BMI > 30 kg/m<sup>2</sup> or BMI > 25 kg/m<sup>2</sup> with waist circumference > 88 cm in females or > 102 cm in males<sup>3</sup>

 For further information on weight loss in type 2 diabetes management, see: "Weight loss for the prevention and treatment of type 2 diabetes", Page 15

**Diabetes education and support is a critical aspect of lifestyle management.** The goal is to enable the patient to take an active role in their care without making them feel judged or to blame for having diabetes. Providing patients with an explanation of what goes wrong at a biological level with an increasing duration of type 2 diabetes can help them understand the need for making changes to their lifestyle and the role of medicines in diabetes management.

*For example, explain to patients that their body is not responding to insulin as well as someone without diabetes, and that in turn the pancreas increases insulin levels in order to decrease blood glucose levels. However, this cannot be maintained long-term and for many people additional oral medicines or injecting dulaglutide or insulin becomes necessary as time goes on. Losing weight, exercising and eating well can improve the body's sensitivity to insulin and therefore this is something that the patient can do to reduce their need for medicines. In some patients, significant sustained lifestyle changes can normalise HbA<sub>1c</sub> levels and medicines may no longer be required.*

**Connect patients to services that can assist with lifestyle changes and provide support.** This could include referring patients to a dietitian, providing them with a Green Prescription to connect with a Green Prescription support person, or making patients aware of programmes offered by a local PHO, DHB (e.g. DESMOND) or Māori health provider. Diabetes New Zealand has branches throughout the country that provide a variety of services. For further information, see: [www.diabetes.org.nz](http://www.diabetes.org.nz)

## Pharmacological treatment to reduce HbA<sub>1c</sub> levels


Prescribing medicines to reduce HbA<sub>1c</sub> levels in patients with type 2 diabetes is a balancing act, which aims to reduce HbA<sub>1c</sub> levels as far as possible without causing harm.<sup>5</sup> Hypoglycaemia is the main limiting adverse effect associated with reducing HbA<sub>1c</sub> levels, and it can carry substantial risks, particularly in patients who are frail. Hypoglycaemia is associated with an increased risk of falls and cognitive impairment, and may increase the risk of mortality.<sup>5</sup>

### Choosing a target: the first step

A HbA<sub>1c</sub> target should be individualised and determined by factors such as the patient's co-morbidities, potential duration of the patient's exposure to hyperglycaemia, history of hypoglycaemia and overall health status (Table 1).<sup>3,6</sup>

Reaching and maintaining target HbA<sub>1c</sub> levels can reduce a patient's risk of microvascular complications, e.g. retinopathy, nephropathy, and neuropathy.<sup>3,6</sup> Reducing HbA<sub>1c</sub> in patients with particularly high levels, e.g. > 80 mmol/mol, to a more moderate level, e.g. < 65 mmol/mol, is thought to offer the greatest reductions in risk of microvascular complications.<sup>6</sup> Aiming for a very low target is not always best if the risks associated with reducing HbA<sub>1c</sub> levels, e.g. hypoglycaemia, outweigh the benefits.<sup>3,6</sup> Reducing HbA<sub>1c</sub> is also part of

the multi-factorial risk reduction strategy, which includes increasing physical activity, smoking cessation and managing hypertension and dyslipidaemia, to reduce macrovascular complications of diabetes.<sup>7</sup>

 For further discussion on adjusting HbA<sub>1c</sub> treatment targets, see: [bpac.org.nz/2019/diabetes-elderly.aspx](http://bpac.org.nz/2019/diabetes-elderly.aspx)

## Prescribing glucose-lowering medicines: choosing the right tools for the job

The pharmacological management of type 2 diabetes typically follows a stepwise progression with lifestyle interventions, i.e. diet and exercise to induce weight loss, reinforced at each intensification step (Figure 1). The intensity of pharmacological treatments required to reduce and maintain HbA<sub>1c</sub> at target levels varies greatly between patients and also depends on the extent of lifestyle changes, the length of time they have had diabetes and their particular circumstances and preferences.<sup>5</sup> For patients with high HbA<sub>1c</sub> levels (> 64 mmol/mol) at diagnosis, initiating two medicines is recommended (e.g. metformin and vildagliptin).<sup>3</sup> For patients with very high HbA<sub>1c</sub> levels, e.g. > 80 – 90 mmol/mol, or significant symptoms of hyperglycaemia at diagnosis, initiation of insulin (in addition to metformin) is recommended.<sup>3</sup> It is often possible to reduce insulin or remove it from the regimen once HbA<sub>1c</sub> stabilises.<sup>8</sup>

**Table 1:** Patient characteristics to consider when selecting a HbA<sub>1c</sub> target<sup>3,5,6</sup>

Target	< 48 mmol/mol	< 53 mmol/mol	54 – 70 mmol/mol
Reasons for choosing target	Greatest reduction in risk of microvascular complications. Appropriate if can be achieved without adverse effects.	Reasonable balance between reduction in risk of microvascular complications with risks of treatment	Appropriate if benefits from treating to lower levels are outweighed by risk of hypoglycaemia
Characteristics of patients who may benefit from this target	<ul style="list-style-type: none"> <li>■ Young, e.g. aged &lt; 40 years</li> <li>■ Are at low risk of hypoglycaemia (i.e. not on insulin or a sulfonylurea)</li> <li>■ Considering pregnancy or are pregnant</li> <li>■ Have microvascular complications (particularly retinopathy and nephropathy)</li> </ul>	<ul style="list-style-type: none"> <li>■ Most patients</li> </ul>	<ul style="list-style-type: none"> <li>■ Older patients at risk of falls and fractures</li> <li>■ Frailty</li> <li>■ Cognitive impairment</li> <li>■ Functionally dependent</li> <li>■ Hypoglycaemia experienced at lower targets</li> <li>■ Live alone and are at risk of severe hypoglycaemia</li> <li>■ Short life expectancy</li> <li>■ Already have advanced microvascular or macrovascular diabetes complications</li> <li>■ Require multiple medicines to achieve lower HbA<sub>1c</sub> targets and have complications caused by polypharmacy</li> </ul>

## STEP 1

### Metformin

- **Initiate metformin at or soon after diagnosis** for all patients with type 2 diabetes ( $\text{HbA}_{1c} \geq 50$  mmol/mol)
  - If patients have contraindications to using metformin, initiate an alternative glucose-lowering medicine
  - If patients have high  $\text{HbA}_{1c}$  levels at diagnosis, e.g.  $> 64$  mmol/mol, consider initiating metformin + another non-insulin medicine; if levels are very high  $> 80 - 90$  mmol/mol, insulin initiation is recommended
- **Consider initiating metformin** in combination with lifestyle advice for patients with “pre-diabetes” ( $\text{HbA}_{1c}$  41 – 49 mmol/mol)



## STEP 2

### Add a second non-insulin glucose-lowering medicine

See Figure 1 in “New diabetes medicines funded: empagliflozin and dulaglutide” for further guidance on selecting an option.

Initiate any one of the following medicines in combination with metformin:

- Empagliflozin<sup>\*\*</sup>
- Dulaglutide<sup>†</sup>
- Vildagliptin<sup>\*</sup>
- Pioglitazone
- A sulfonylurea: either gliclazide or glipazide
- Acarbose<sup>\*\*</sup>

### Add a third non-insulin glucose-lowering medicine

An alternative to initiating insulin; the options are:

- Three oral glucose-lowering medicines
- Two oral glucose-lowering medicines + an injectable GLP-1 receptor agonist (i.e. dulaglutide<sup>†</sup>)



## STEP 3

### Add insulin

- Once daily long-acting insulin is typically used when first initiating insulin; isophane insulin is appropriate for most patients

\* Combination formulations with metformin available

† Special Authority criteria apply. For further information see: “New diabetes medicines funded: empagliflozin and dulaglutide”

\*\* May be useful for some patients, however, when added to metformin treatment it is less effective at lowering  $\text{HbA}_{1c}$  levels than other oral medicines

‡ Dual treatment with dulaglutide and empagliflozin is not currently funded

### Review management at each step

- Measure  $\text{HbA}_{1c}$  levels at three to six month intervals
- Discuss diet and physical activity approaches
- Discuss medicine use and adverse effects
- Ask about hypoglycaemia
- Review management of cardiovascular and renal risk factors

### Determine whether changes in treatment are necessary and an appropriate interval for the next review.

Options could include:

- Continuing with the same plan for treatment
- Increasing dietary or physical activity approaches
- Increasing doses of, or adding, glucose-lowering medicines
- Switching medicines due to adverse effects
- De-escalating treatment

**Figure 1:** Optimising the management of  $\text{HbA}_{1c}$  levels with glucose-lowering medicines in patients with type 2 diabetes<sup>3,5</sup>

## Step 1: Metformin is the initial choice of oral medicine for most patients

Metformin is recommended as the initial pharmacological approach for patients with type 2 diabetes, as it reduces HbA<sub>1c</sub> levels, decreases cardiovascular disease risk independent of glycaemic control, may assist with weight loss and has a low risk of hypoglycaemia (Figure 1 and Table 2).<sup>3</sup> Initiate metformin at a low dose, e.g. 500 mg once daily, and gradually increase the dose over the following weeks to a maximum of 1.5 – 2 g daily, in divided doses, as tolerated.<sup>9</sup> A higher maximum dose of 3 g, daily may be prescribed for patients with creatinine clearance > 120 mL/min.<sup>9\*</sup>

\* While in many cases eGFR will be sufficient to estimate renal function in patients taking metformin, the NZF recommends using the Cockcroft-Gault equation for a more accurate calculation of creatinine clearance, which may be particularly useful in people with more severe renal impairment.<sup>9</sup> A calculator is available here: [www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation](http://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation)

## Step 2: Prescribing combination treatment

If patients require intensification of pharmacological management, the recommended next step is to combine metformin with another non-insulin glucose-lowering medicine (or use two of these medicines if metformin is contraindicated or not tolerated). Funded options include:<sup>3,9</sup>

- A sodium-glucose co-transporter 2 (SGLT-2) inhibitor: **empagliflozin\*\***
- A glucagon-like peptide (GLP-1) receptor agonist: **dulaglutide†**
- A dipeptidyl-peptidase 4 (DPP-4) inhibitor: **vildagliptin\***
- A sulfonylurea: either **gliclazide** or **glipizide\*\***
- A thiazolidinedione: **pioglitazone**

\* Available in a single formulation and in combination with metformin

† Special Authority criteria apply. Dulaglutide funded from 1 September, 2021. For further information see: “New diabetes medicines funded: empagliflozin and dulaglutide”, Page 19.

\*\* Glibenclamide is another subsidised sulfonylurea, however, prescribing glibenclamide is generally not recommended as it is associated with a higher risk of hypoglycaemia than other sulfonylureas<sup>5</sup>

When prescribed in combination with metformin there are no clinically meaningful differences in the extent of HbA<sub>1c</sub> lowering between the non-insulin glucose-lowering medicines; adding one of these medicines to metformin treatment generally reduces HbA<sub>1c</sub> by approximately 8 – 11 mmol/mol.<sup>8, 10</sup> There are, however, other reasons for selecting one medicine over another (see: “Which medicine to choose?”).


**Acarbose** is another fully funded glucose-lowering medicine which could be added to metformin treatment if other medicines are not tolerated, however, available data suggest it is less effective at lowering HbA<sub>1c</sub> levels when added to

metformin than the medicines above.<sup>11</sup> Adverse effects include bloating, flatulence, diarrhoea and, rarely, deranged liver function tests.<sup>3</sup>

## Which medicine to choose?

Clinicians and patients can jointly decide which of the above options to add to treatment after considering any contraindications, co-morbidities, risk of hypoglycaemia, effects on weight, medicines interactions, adverse effects and eligibility for funding (Table 2).


**Empagliflozin** or **dulaglutide** are preferred for people with established or at high risk of CVD, or with heart failure or diabetic kidney disease, regardless of their HbA<sub>1c</sub> levels; currently only patients with HbA<sub>1c</sub> levels > 53 mmol/mol who are at high risk of CVD or renal complications are eligible for funded treatment.<sup>3</sup> A combination metformin + empagliflozin formulation is available fully funded with Special Authority.

 For further information on prescribing these medicines, see: “New diabetes medicines funded: empagliflozin and dulaglutide”, Page 19

**Vildagliptin** is preferred for patients who are not eligible for funded empagliflozin or dulaglutide treatment.<sup>3</sup> A combination formulation of metformin + vildagliptin is available fully funded without restriction.

Some guidelines favour the addition of vildagliptin or a sulfonylurea instead of pioglitazone due to potential adverse effects associated with pioglitazone.<sup>5</sup> Vildagliptin or pioglitazone may be preferred over a sulfonylurea if patients have problems with hypoglycaemia.

N.B. Prior to initiating vildagliptin, request baseline liver function tests (Table 2).<sup>3</sup>

 For further information on prescribing vildagliptin, see: “Prescribing vildagliptin for type 2 diabetes”, Page 28

## Escalating beyond dual treatment

Options for treatment intensification for patients who have HbA<sub>1c</sub> levels above the desired target despite optimal use of two non-insulin medicines and lifestyle approaches are:

- Initiating a third non-insulin medicine (either an oral medicine or an injectable GLP-1 receptor agonist [i.e. dulaglutide])
- Initiating insulin (i.e. Step 3 – see below)

Take into account the patient’s other prescribed medicines, which will often include an angiotensin-converting enzyme (ACE) inhibitor, statin, antihypertensives and aspirin, and consider whether triple oral therapy is likely to create difficulties with adherence.

**Table 2:** Funded glucose-lowering medicines and factors to consider when prescribing.<sup>3,9</sup>

Medicine	Effects on weight	Risk of hypoglycaemia	Use in patients with renal or hepatic impairment	Other factors and monitoring requirements
<b>Metformin</b>	Weight loss of approximately 2 – 3 kg over 12 months <sup>12</sup>	Low	<ul style="list-style-type: none"> <li>■ Avoid if CrCl &lt; 15 mL/min*</li> <li>■ Reduce doses if CrCl 15 – 59 mL/min*</li> <li>■ Avoid if severe hepatic disease (Child-Pugh grade C) and use with caution if mild hepatic impairment; impaired hepatic function can reduce lactate clearance and increase the risk of lactic acidosis</li> </ul>	<ul style="list-style-type: none"> <li>■ The preferred oral medicine in patients who are pregnant or breastfeeding</li> <li>■ May cause vitamin B12 deficiency; check levels if patients have symptoms of anaemia or peripheral neuropathy – supplementation may be required<sup>13</sup></li> <li>■ Up to 20% of patients experience gastrointestinal adverse effects; slow titration and taking metformin with food may help to avoid this<sup>13</sup></li> <li>■ Consider temporary cessation of metformin in situations that may lead to lactic acidosis, e.g. dehydration due to illness</li> </ul>
<b>Empagliflozin</b>	Weight loss of approximately 2 kg over six months <sup>14</sup>	Low	<ul style="list-style-type: none"> <li>■ Contraindicated for people with eGFR &lt; 30 mL/min/1.73m<sup>2</sup> as it is ineffective</li> <li>■ No dose adjustment required for people with mild renal impairment</li> </ul>	<ul style="list-style-type: none"> <li>■ Renal function should be assessed at least annually in patients taking empagliflozin (with or without metformin) and prior to initiating any medicines that may reduce renal function</li> <li>■ May cause diabetic ketoacidosis; treatment should be temporarily stopped during acute illness and prior to elective procedures. Use with caution in patients on a low carbohydrate or ketogenic diet.</li> <li>■ Avoid in patients with a history of severe genitourinary infections</li> </ul>
<b>Dulaglutide</b>	Weight loss of approximately 2 – 3 kg over 12 months <sup>15</sup>	Low	<ul style="list-style-type: none"> <li>■ No dose adjustment required</li> </ul>	<ul style="list-style-type: none"> <li>■ No additional monitoring requirements</li> <li>■ Common, but usually transient, adverse effects include gastrointestinal disturbance and injection site reactions</li> <li>■ Avoid in patients with a history of medullary thyroid cancer; and use with caution in patients with a family history</li> </ul>
<b>Vildagliptin</b>	No change	Low	<ul style="list-style-type: none"> <li>■ Reduce dose if eGFR &lt; 50 mL/min/1.73m<sup>2</sup> †</li> <li>■ Avoid in patients with hepatic dysfunction, e.g. ALT levels &gt; 2.5 times the upper limit of normal</li> </ul>	<ul style="list-style-type: none"> <li>■ Avoid use in patients with severe heart failure (New York Heart Association functional class IV)</li> <li>■ Assess liver function prior to initiation, every three months for the first year and then periodically</li> </ul>
<b>Sulfonylureas</b> (glipizide, gliclazide)	Weight gain of approximately 2 kg over 12 months <sup>16</sup>	High	<ul style="list-style-type: none"> <li>■ Other medicines are preferable in patients with increased risk of hypoglycaemia, including patients with renal impairment or severe hepatic impairment<sup>19,27</sup></li> <li>■ Contraindicated in patients with ketoacidosis or acute porphyria</li> </ul>	<ul style="list-style-type: none"> <li>■ Effects on HbA<sub>1c</sub> may not persist as long as other oral options, requiring a change in medicine earlier<sup>17</sup></li> </ul>
<b>Pioglitazone</b>	Weight gain of approximately 2 kg over 12 months <sup>16</sup>	Low	<ul style="list-style-type: none"> <li>■ Avoid in patients with hepatic impairment, e.g. ALT levels &gt;2.5 times the upper limit of normal</li> <li>■ Use is not advised in patients with renal failure</li> </ul>	<p>Increased risk of:</p> <ul style="list-style-type: none"> <li>■ Oedema and heart failure</li> <li>■ Fractures</li> <li>■ Bladder cancer; avoid use in patients with risk factors for or a history of bladder cancer</li> </ul>
<b>Insulin</b>	Weight gain of 3 – 9 kg over 12 months <sup>18</sup>	High	<ul style="list-style-type: none"> <li>■ Dose reduction not usually required in patients with hepatic or renal impairment</li> </ul>	<ul style="list-style-type: none"> <li>■ Injection site reactions are a common adverse reaction</li> </ul>

\* While in many cases eGFR will be sufficient to estimate renal function in patients taking metformin, the NZF recommends using the Cockcroft-Gault equation for a more accurate calculation of creatinine clearance, which may be particularly useful in people with more severe renal impairment.<sup>9</sup> A calculator is available here: [www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation](http://www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation)

† The combination vildagliptin + metformin formulation is not recommended in patients with eGFR < 60 mL/min/1.73m<sup>2</sup>; prescribing metformin and vildagliptin in separate tablets may be preferable to allow for an appropriate reduced dose of metformin.

There is very little clinical trial evidence to guide choice of which third non-insulin medicine to add. In general, the incremental effect of adding a third oral medicine is likely to be less than when these medicines are used alone or in dual treatment combinations.<sup>8</sup>

In international guidelines, adding a GLP-1 receptor agonist is the preferred next step for patients requiring escalation to injectable treatment, however, not all patients will be eligible for funded treatment in New Zealand.<sup>3,8</sup> Initiating dulaglutide may be more acceptable to patients than insulin. While both are injectable treatments, dulaglutide is administered once weekly and self-monitoring of blood glucose levels is not necessary (unless their regimen includes a sulfonylurea).


Combination SGLT-2 inhibitor and GLP-1 receptor agonist treatment, in addition to metformin, is the recommended next step for people at high risk of cardiovascular or renal complications who were previously treated with just one of these medicine classes, however, dual treatment is not currently funded.<sup>3</sup>

### Step 3: Insulin

Discuss insulin initiation with patients who have HbA<sub>1c</sub> levels above the desired target despite optimal use of two oral medicines and lifestyle approaches, or where a rapid escalation of pharmacological treatment is required because of high HbA<sub>1c</sub> levels. Insulin has the largest effect on reducing HbA<sub>1c</sub> levels of all glucose-lowering medicines, however, it is also associated with greater weight gain and a higher risk of hypoglycaemia than other glucose-lowering medicines (Table 2).<sup>8</sup> Weight gain typically plateaus after the first one to three years of treatment and is dose-dependent.<sup>19,20</sup>


Reassurance and advice is often required when discussing the possibility of initiating insulin with patients to ensure that any anxieties about insulin are addressed, e.g. feeling that it signifies an escalation in the seriousness of their condition, being worried or embarrassed about self-injection, needles or calculating doses, and fear of weight gain or hypoglycaemia. After discussing options some patients may wish to trial more intensive changes to their dietary or physical activity approaches instead of initiating insulin. If this is the case, agree to a time frame for review to ensure that insulin treatment is not unduly delayed.

#### Summary of key points for initiating patients with type 2 diabetes on insulin:<sup>3</sup>

 A detailed discussion on initiating and up-titrating insulin, including the different regimens, insulins and devices, is available in: "Initiating insulin for people with type 2 diabetes", Page 34

- Most patients are initiated on once-daily basal insulin, injected at night; isophane insulin (an intermediate-acting insulin) is an appropriate choice for most patients

- A weight-based approach is recommended to determine the initial basal insulin dose:
  - 0.1 units/kg daily if at least one of:
    - HbA<sub>1c</sub> < 64 mmol/mol
    - BMI < 18 kg/m<sup>2</sup> (less likely to have type 2 diabetes)
    - Older (e.g. aged > 65 years) or frailty
    - Renal or liver failure
  - 0.2 units/kg daily if HbA<sub>1c</sub> > 64 mmol/mol and BMI > 18 kg/m<sup>2</sup>
- Patients initiating basal insulin should begin self-monitoring blood glucose levels; a once daily measurement before breakfast (if insulin is taken at night) is sufficient; the aim of treatment is to achieve blood glucose levels between 6 – 8 mmol/L
- Patients will need to titrate the insulin dose upwards from this starting point based on their fasting blood glucose levels
- Patients who continue to have elevated HbA<sub>1c</sub> levels while using a basal insulin regimen may require intensification of insulin treatment. This could include switching to a biphasic insulin formulation, which includes long-acting and short-acting insulins in a premixed solution, or continuing with a basal insulin and adding a short-acting insulin at mealtimes.
- More frequent blood glucose monitoring is advised when introducing other insulin regimens, e.g. adding a fast-acting insulin at mealtimes. Monitoring before meals and before bed is useful.
- Ask patients to check their blood glucose levels if they experience symptoms consistent with hypoglycaemia. If an obvious cause is not apparent, e.g. missed meals, changes to carbohydrate intake or exercise regimen, patients should reduce their insulin dose by 10 – 20%.

 Patient information on recognising and responding to hypoglycaemia is available at: [www.healthnavigator.org.nz/health-a-z/l/low-blood-glucose](http://www.healthnavigator.org.nz/health-a-z/l/low-blood-glucose)

### Continuing other medicines

**Metformin is usually continued** when insulin is started as it can result in less weight gain and lower doses of insulin being required to meet HbA<sub>1c</sub> targets.<sup>21</sup>

**Empagliflozin is usually continued** when insulin is initiated; combining SGLT-2 inhibitor and insulin treatment can result in less weight gain and greater reduction in HbA<sub>1c</sub> levels without increasing the risk of hypoglycaemia.<sup>22</sup> Empagliflozin also provides cardiovascular and renal benefits independent of its actions on glycaemia.<sup>3</sup>

**Dulaglutide is usually continued** when insulin is initiated; combining GLP-1 receptor agonist and insulin treatment can result in less weight gain and greater reduction in HbA<sub>1c</sub> levels without increasing the risk of hypoglycaemia.<sup>23</sup> Dulaglutide also provides cardiovascular and renal benefits independent of its actions on glycaemia.<sup>3</sup>

**Vildagliptin may be continued** when insulin is initiated, but in practice is often withdrawn to simplify the regimen. The formulation of vildagliptin + metformin is also approved for use in combination with insulin.

**Sulfonylureas may be continued** if patients are using basal insulin as a lower dose of insulin is required to meet the HbA<sub>1c</sub> target.<sup>3</sup> However, there is an increased risk of hypoglycaemia when these medicines are used in combination.<sup>3</sup> Sulfonylureas are titrated down and withdrawn if treatment with a short-acting insulin is initiated.<sup>21</sup>

**Pioglitazone is typically discontinued** when insulin is initiated as combined use increases the risk of oedema.<sup>24</sup>


## Regularly revise treatment approaches and goals

Most people with type 2 diabetes will have it for the rest of their lives. Regular review of treatment is necessary to optimise individual goals of treatment and ensure medicine regimens remain appropriate.

**Measuring HbA<sub>1c</sub> levels at three to six month intervals** is recommended to determine the effect of lifestyle and pharmacological approaches (Figure 1).<sup>3</sup> Treatment can then be optimised by checking and reinforcing lifestyle approaches,

adjusting doses, adding or withdrawing medicines, or adjusting HbA<sub>1c</sub> targets, as appropriate. An annual check is sufficient for patients with stable, well controlled HbA<sub>1c</sub> levels.

**Discuss diet and physical activity.** For all patients, sustaining lifestyle changes and maintaining weight loss is required for long term improvements in HbA<sub>1c</sub> levels and cardiovascular risk factors. Achieving this can be difficult; offer regular encouragement and assess barriers the patient is experiencing. Monitor body weight and ideally waist circumference annually.<sup>3</sup>

 For further information on lifestyle management, see: “Weight loss for the prevention and treatment of type 2 diabetes”, Page 15

**Discuss medicine use and adverse effects.** Ask patients about adverse effects or any difficulties they are having with their prescribed medicines which could contribute to reduced adherence.


**Consider the simplicity of the patient’s medicine regimen,** including medicines prescribed for co-morbidities, and whether any changes are possible to improve adherence.<sup>5</sup>

**Ask about hypoglycaemia** if the patient is taking a sulfonylurea or insulin. If patients have symptoms of hypoglycaemia, discuss when they occurred, and the circumstances involved, e.g. a missed meal, acute illness. Ensure the patient is aware of symptoms of nocturnal hypoglycaemia, such as nightmares or disturbed sleep, being particularly hungry in the morning or waking with wet sheets due to sweating.<sup>3</sup> Problems with hypoglycaemia should prompt consideration of reducing doses of medicines, changing medicines or adjusting HbA<sub>1c</sub> targets.

## Diabetes medicines can affect fitness to drive

People with type 2 diabetes generally have no restrictions for holding a private vehicle licence (Class 1 or 6 licence). However, the NZTA advises that people taking sulfonylureas or insulin need to receive appropriate education regarding the possibility of hypoglycaemia, how to recognise it and how to respond. Avoiding driving for 24 hours is recommended if an episode of hypoglycaemia occurs. A person may need to stop driving for a few days after initiating insulin to check that they do not experience hypoglycaemia.


People with type 2 diabetes using either oral medicines or insulin may be considered fit to hold heavy vehicle licences (Classes 2 – 5) and endorsements P, V, I and O, however, assessments from both a general practitioner and a diabetes specialist (if taking insulin) are required and patients must meet specific conditions to continue driving.


 For further information on diabetes and driving, see: [www.nzta.govt.nz/assets/resources/medical-aspects/Medical-aspects-of-fitness-to-drive-a-guide-for-health-practitioners.pdf](http://www.nzta.govt.nz/assets/resources/medical-aspects/Medical-aspects-of-fitness-to-drive-a-guide-for-health-practitioners.pdf)



## Review management of cardiovascular and renal risk factors:

Annual review of cardiovascular and renal risk factors, including blood pressure and lipid levels, albumin:creatinine ratio and eGFR, is recommended.<sup>3</sup> In addition, an annual foot check and recall for retinopathy screening at least every two years is recommended. Many PHOs have funding for this review. N.B. More frequent review may be indicated depending on the patient's risk factors.

 A calculator to assess CVD risk in people with type 2 diabetes is available here: [www.nzssd.org.nz/calculators/calculator/1/cvd-risk-assessment/](http://www.nzssd.org.nz/calculators/calculator/1/cvd-risk-assessment/)

 For further information on an annual diabetes review, see: "The annual diabetes review: screening, monitoring and managing complications", Page 44

## Patient information

- Patient information on type 2 diabetes, the importance of diet and physical activity, and recognising and responding to hypoglycaemia is available from:
  - Diabetes New Zealand: [www.diabetes.org.nz](http://www.diabetes.org.nz)
  - Ministry of Health "Keeping well with diabetes" booklet, available in English, Māori, Cook Islands Māori, Samoan, Tongan and Niuean: [www.healthed.govt.nz/search?topic%5B0%5D=3&type=resource&mode=picture-view](http://www.healthed.govt.nz/search?topic%5B0%5D=3&type=resource&mode=picture-view)
  - Health Navigator: <https://www.healthnavigator.org.nz/health-a-z/d/diabetes-type-2/>
- A guide to initiating insulin for patients with type 2 diabetes, produced by the Waitematā District Health Board, is available in various languages: <http://www.saferx.co.nz/patient-guides/>

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## References

1. Ministry of Health. New Zealand health survey: annual data explorer. 2020. Available from: [https://minhealthnz.shinyapps.io/nz-health-survey-2019-20-annual-data-explorer/\\_w\\_f0eb173a/#/](https://minhealthnz.shinyapps.io/nz-health-survey-2019-20-annual-data-explorer/_w_f0eb173a/#/) (Accessed Mar, 2021).
2. PricewaterhouseCoopers New Zealand. The economic and social cost of type 2 diabetes. 2021. Available from: <https://healthierlives.co.nz/wp-content/uploads/2021/03/COT2D.pdf> (Accessed Mar, 2021).
3. New Zealand Society for the Study of Diabetes (NZSSD), Ministry of Health. Type 2 diabetes management guidance. 2021. Available from: <https://t2dm.nzssd.org.nz/> (Accessed Mar, 2021).
4. American Diabetes Association. 8. Obesity Management for the Treatment of Type 2 Diabetes: Standards of Medical Care in Diabetes—2021. *Dia Care* 2021;44:S100–10. doi:10.2337/dc21-S008
5. The Royal Australian College of General Practitioners. Management of type 2 diabetes: A handbook for general practice. 2020. Available from: <https://www.racgp.org.au/getattachment/41fee8dc-7f97-4f87-9d90-b7af337af778/Management-of-type-2-diabetes-A-handbook-for-general-practice.aspx> (Accessed Jul, 2020).
6. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes—2021. *Dia Care* 2021;44:S73–84. doi:10.2337/dc21-S006
7. Rawshani A, Rawshani A, Franzén S, et al. Risk factors, mortality, and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2018;379:633–44. doi:10.1056/NEJMoa1800256
8. American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes — 2021. *Dia Care* 2021;44:S111–24. doi:10.2337/dc21-S009
9. New Zealand Formulary (NZF). NZF v106. Available from: [www.nzf.org.nz](http://www.nzf.org.nz) (Accessed Apr, 2021).
10. Maruthur NM, Tseng E, Hutfless S, et al. Diabetes medications as monotherapy or metformin-based combination therapy for type 2 diabetes: a systematic review and meta-analysis. *Ann Intern Med* 2016;164:740. doi:10.7326/M15-2650
11. Palmer SC, Mavridis D, Nicolucci A, et al. Comparison of clinical outcomes and adverse events associated with glucose-lowering drugs in patients with type 2 diabetes: a meta-analysis. *JAMA* 2016;316:313. doi:10.1001/jama.2016.9400
12. Aroda VR, Knowler WC, Crandall JP, et al. Metformin for diabetes prevention: insights gained from the Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study. *Diabetologia* 2017;60:1601–11. doi:10.1007/s00125-017-4361-9
13. Waitematā District Health Board. Metformin - safe prescribing. 2016. Available from: <http://www.saferx.co.nz/assets/Documents/full/10d1b02e07/Metformin.pdf> (Accessed Apr, 2021).
14. Neeland IJ, McGuire DK, Chilton R, et al. Empagliflozin reduces body weight and indices of adipose distribution in patients with type 2 diabetes mellitus. *Diabetes and Vascular Disease Research* 2016;13:119–26. doi:10.1177/1479164115616901
15. Jendle J, Grunberger G, Blevins T, et al. Efficacy and safety of dulaglutide in the treatment of type 2 diabetes: a comprehensive review of the dulaglutide clinical data focusing on the AWARD phase 3 clinical trial program: Review of Dulaglutide Clinical Trial Program. *Diabetes Metab Res Rev* 2016;32:776–90. doi:10.1002/dmrr.2810
16. Khunti K, Chatterjee S, Gerstein HC, et al. Do sulphonylureas still have a place in clinical practice? *The Lancet Diabetes & Endocrinology* 2018;6:821–32. doi:10.1016/S2213-8587(18)30025-1
17. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Dia Care* 2018;41:2669–701. doi:10.2337/dci18-0033
18. Apovian CM, Okemah J, O'Neil PM. Body weight considerations in the management of type 2 diabetes. *Adv Ther* 2019;36:44–58. doi:10.1007/s12325-018-0824-8
19. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *The Lancet* 1998;352:837–53. doi:10.1016/S0140-6736(98)07019-6
20. Lindstrom T, Eriksson P, Olsson AG, et al. Long-term improvement of glycemic control by insulin treatment in NIDDM patients with secondary failure. *Diabetes Care* 1994;17:719–21. doi:10.2337/diacare.17.7.719
21. Lipscombe L, Booth G, Butalia S, et al. Pharmacologic glycemic management of type 2 diabetes in adults. *Canadian Journal of Diabetes* 2018;42:S88–103. doi:10.1016/j.cjcd.2017.10.034
22. Rosenstock J, Jelaska A, Zeller C, et al. Impact of empagliflozin added on to basal insulin in type 2 diabetes inadequately controlled on basal insulin: a 78-week randomized, double-blind, placebo-controlled trial. *Diabetes Obes Metab* 2015;17:936–48. doi:10.1111/dom.12503
23. Young LA, Buse JB. GLP-1 receptor agonists and basal insulin in type 2 diabetes. *The Lancet* 2014;384:2180–1. doi:10.1016/S0140-6736(14)61409-4
24. Philis-Tsimikas A. Initiating basal insulin therapy in type 2 diabetes: practical steps to optimize glycemic control. *Am J Med* 2013;126:S21–27. <http://dx.doi.org/10.1016/j.amjmed.2013.06.010>



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