Optimising pharmacological management of HbA$_{1c}$ levels in patients with type 2 diabetes: from metformin to insulin

A variety of subsidised medicines are available to help manage HbA$_{1c}$ levels in patients with type 2 diabetes, all of which can be prescribed by clinicians in primary care. Managing HbA$_{1c}$ levels can reduce a patient’s risk of microvascular complications associated with diabetes, but treatment regimens and target HbA$_{1c}$ levels need to be tailored to the individual. Lowering HbA$_{1c}$ levels is only one aspect of managing type 2 diabetes; other essential components are managing cardiovascular and renal risk factors and helping patients with dietary and physical activity approaches.

**KEY PRACTICE POINTS:**

- Lifestyle interventions are crucial at all stages of managing patients with type 2 diabetes and reduce the need for pharmacological treatment; help patients by providing regular advice, encouragement and referral to appropriate support programmes.
- Recent evidence shows that in some patients, weight reduction can induce remission of type 2 diabetes.
- The overall aim of pharmacological treatment with glucose-lowering medicines is to help reduce HbA$_{1c}$ levels and the risk of complications.
- HbA$_{1c}$ targets and the choice of pharmacological treatment should be individualised taking into account overall health status, co-morbidities and risks associated with hypoglycaemia; targets may need to change over time.
- Check HbA$_{1c}$ levels at three to six monthly intervals.
- A recommended approach to initiating glucose-lowering medicines is:
  - Initiate metformin at diagnosis; if HbA$_{1c}$ levels are > 75 mmol/mol, additional oral treatment or insulin may be required.
  - If treatment with metformin alone does not reduce HbA$_{1c}$ levels to the desired target, add vildagliptin, a sulphonylurea (glipizide or gliclazide) or pioglitazone.
  - If further intensification is required, initiate insulin. Alternatively, combine three oral glucose-lowering medicines.
  - Prior to intensifying any pharmacological regimen, check the patient’s adherence to their existing medicine regimen and diet and physical activity approaches.
- A basal insulin regimen is the preferred option in most clinical situations. Subsidised options are isophane insulin (usual first choice) and insulin glargine.

This article covers the management of patients with type 2 diabetes. Guidance on the management of patients with type 1 diabetes will be included in a future bpac article.
Lifestyle measures underpin pharmacological treatment

A combined approach of optimising both non-pharmacological and pharmacological management of type 2 diabetes and cardiovascular risk factors is recommended to provide the greatest health improvements for patients. Cardiovascular disease 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.

Key lifestyle goals for patients to aim for include at least 150 minutes per week of moderate intensity exercise, weight loss in those who are overweight, eating foods with a high fibre content, such as fruits, vegetables and whole grains, and avoiding sugar-sweetened beverages or foods with added sugars.

Reducing doses of medicines or withdrawing them may be possible in some patients who make significant alterations to their lifestyle; evidence shows that sufficient weight loss in people who are overweight can induce remission of type 2 diabetes, i.e. HbA1c levels below the threshold for a diagnosis without the use of glucose-lowering medicines.

Explaining the aim of lifestyle interventions can help

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.

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 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.

Connect patients to services that can assist with lifestyle changes

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 or Māori health provider.

Pharmacological treatment to reduce HbA1c levels

Prescribing medicines to reduce HbA1c levels in patients with type 2 diabetes is a balancing act, which aims to reduce HbA1c levels as far as possible without causing harm. Hypoglycaemia is the main limiting adverse effect associated with reducing HbA1c 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.

Choosing a target: the first step

A HbA1c target should be individualised and determined by factors such as the patient’s co-morbidities, history of hypoglycaemia and overall health status (Table 1).

Reaching and maintaining target HbA1c levels can reduce a patient’s risk of microvascular complications. Reducing HbA1c 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.

Aiming for a very low target is not always best if the risks associated with reducing HbA1c levels outweigh the benefits. Three major clinical trials, the ACCORD, ADVANCE and VADT studies, assessed the effects of treating patients with type 2 diabetes with intensive reduction and maintenance of HbA1c levels to 46–52 mmol/mol, compared with reducing HbA1c levels to 58–68 mmol/mol. Patients in these trials were prescribed a range of medicines to reduce HbA1c levels, including many of the medicines currently subsidised in New Zealand. These studies found that intensive reduction of HbA1c levels was associated with a 20% reduction in renal outcomes, such as new or worsening nephropathy, and a 13% reduction in ocular outcomes, such as new or worsening retinopathy; absolute risk reductions were 1–3%. However, rates of hypoglycaemia were two or more times higher in patients treated to intensive HbA1c targets and one of the studies, the ACCORD trial, was stopped early due to a higher rate of mortality in patients treated intensively.

Prescribing glucose-lowering medicines

An algorithm to guide the use of fully subsidised glucose-lowering medicines is shown in Figure 1. The intensity of pharmacological treatments required to reduce and maintain HbA1c at target levels varies greatly between patients and also depends on the extent of lifestyle changes adopted, the length of time they have had diabetes and their particular circumstances and preferences.

Many patients with type 2 diabetes eventually require or benefit from insulin treatment. Introducing this idea to patients early on may help ease the transition into initiating insulin injections should they become necessary.
Regular review is needed to optimise treatment

Measuring HbA₁c levels at three to six month intervals is recommended to determine the effect of lifestyle and pharmacological approaches (Figure 1). Treatment can then be optimised by checking and reinforcing lifestyle approaches, adjusting doses, adding or withdrawing medicines, or adjusting HbA₁c targets, as appropriate.

Discuss diet and physical activity. For all patients, sustaining lifestyle changes and maintaining weight loss is required for long term improvements in HbA₁c levels and cardiovascular risk factors. Achieving this can be difficult; offer regular encouragement and assessment of any barriers the patient is experiencing.

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.

Table 1: Patient characteristics to consider when selecting an example HbA₁c target

<table>
<thead>
<tr>
<th>Target range</th>
<th>48–53 mmol/mol</th>
<th>53–58 mmol/mol</th>
<th>58–64 mmol/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reasons for choosing target</td>
<td>Greatest reduction in risk of microvascular complications. Appropriate if can be achieved without adverse effects.</td>
<td>Reasonable balance between reduction in risk of microvascular complications with risks of treatment</td>
<td>Appropriate if benefits from treating to lower levels are outweighed by risks.</td>
</tr>
</tbody>
</table>

Characteristics of patients who may benefit from this target

- Younger
- Treated with only lifestyle or metformin
- Newly diagnosed
- Most patients
- Older patients at risk of falls and fractures
- Frailty
- Hypoglycaemia experienced at lower targets
- Live alone and are at risk of severe hypoglycaemia
- Short life expectancy
- Already have advanced diabetes complications
- Require multiple medicines to achieve lower HbA₁c targets and have complications caused by polypharmacy.

Ask about hypoglycaemia. 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. Problems with hypoglycaemia should prompt consideration of reducing doses of medicines, changing medicines or adjusting HbA₁c targets.

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

Hypoglycaemia most often occurs in patients prescribed insulin or a sulphonylurea; the use of metformin, vildagliptin, pioglitazone or acarbose is associated with low rates of hypoglycaemia, with little to no differences in rates compared to treatment with diet alone. Self-monitoring of blood glucose levels is recommended in patients with type 2 diabetes injecting insulin, and may be useful for some patients prescribed sulphonylureas to help identify episodes of hypoglycaemia.
Patients with newly diagnosed diabetes (HbA\textsubscript{1c} > 50 mmol/mol)

- Initiate metformin at, or soon after, diagnosis for all patients with type 2 diabetes
  - If patients have contraindications to using metformin, initiate an alternative oral hypoglycaemic medicine
- If patients have high HbA\textsubscript{1c} levels at diagnosis, e.g. > 75 mmol/mol consider prescribing two oral medicines or initiating metformin + insulin

Patients with HbA\textsubscript{1c} levels 46–49 mmol/mol

- Consider initiating metformin in combination with lifestyle advice

Emphasise non-pharmacological approaches

Determine an appropriate HbA\textsubscript{1c} target

Review management

- Measure HbA\textsubscript{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

If additional glucose-lowering medicines are required to meet HbA\textsubscript{1c} targets, options include:

**Dual oral therapy:**
Initiate any one of the following subsidised medicines* *in combination with metformin:
- Vildagliptin†
- A sulphonylurea
- Pioglitazone

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

**Triple therapy:**
A combination of three oral hypoglycaemic medicines

* Acarbose is another oral glucose lowering medicine available subsidised. It may be useful for some patients, however, when added to metformin treatment it is less effective at lowering HbA\textsubscript{1c} levels than other oral medicines\textsuperscript{12,18}
† A vildagliptin + metformin combination formulation is available subsidised

**Figure 1:** Optimising the management of HbA\textsubscript{1c} levels in patients with type 2 diabetes\textsuperscript{1,5,6}
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 are recommended. In addition, an annual foot check and recall for retinopathy screening every two to three years is recommended.

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 HbA1c levels and may assist with weight loss (Figure 1 and Table 2). Metformin should be initiated in all patients at, or soon after, diagnosis unless they have contraindications, such as creatinine clearance (CrCl) < 15 mL/min. People who have contraindications to using metformin, or cannot tolerate it, can initiate an alternative hypoglycaemic medicine.

Initiate metformin treatment 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. A higher maximum dose of 3 g, daily may be prescribed for patients with creatinine clearance > 120 mL/min.

Metformin use is associated with gastrointestinal adverse effects in up to 20% of patients. Slow titration may help to avoid this. These adverse effects may improve with continued use, or a temporary decrease in dose could be trialled. Vitamin B12 deficiency occurs in a minority of patients taking metformin; a meta-analysis found that metformin treatment reduces vitamin B12 levels by an average of approximately 60 pmol/L, which may lead to deficiency in some patients.

* The NZF recommends that the Cockcroft-Gault equation should be used to estimate renal function in patients using metformin. A calculator is available here: www.nzf.org.nz/nzf/resource/Creatinine%20Clearance%20Calculator.htm

Consider initiating insulin with metformin in patients with high HbA1c levels at diagnosis. For patients with particularly high levels of HbA1c at diagnosis, e.g. > 75 mmol/mol, initiating treatment with metformin in combination with insulin is recommended. Alternatively, a second oral glucose-lowering medicine could be added to metformin. Once HbA1c levels have reduced sufficiently, it may be possible to simplify treatment by withdrawing insulin or reducing doses of oral medicines.

Prescribing combination treatment with two oral medicines

If patients require intensification of pharmacological management, the recommended second-line treatment is to combine metformin with another oral glucose-lowering medicine (or use two of these medicines if metformin is contraindicated or not tolerated). Subsidised options include:

- **Vildagliptin**
  - A sulphonylurea: either gliclazide or glipizide
- **Pioglitazone**
  - Subsidised in a single formulation and in combination with metformin
  - Glibenclamide is another subsidised sulphonylurea, however, prescribing glibenclamide is generally not recommended as it is associated with a higher risk of hypoglycaemia than other sulphonylureas

When prescribed in combination with metformin there are no clinically meaningful differences in the extent of HbA1c lowering between vildagliptin, a sulphonylurea or pioglitazone; adding one of these medicines to metformin treatment generally reduces HbA1c by approximately 8–11 mmol/mol.

**Acarbose** is another subsidised glucose-lowering medicine which could be added to metformin treatment, however, available data suggest it is less effective at lowering HbA1c levels when added to metformin than the medicines above.

**Unsubsidised** medicines which could be added to metformin, recommended in international guidelines, include oral sodium glucose cotransporter-2 (SGLT-2) inhibitors and injectable glucagon-like peptide-1 (GLP-1) agonists.

Which medicine to choose?

Clinicians and patients can jointly decide which of the above options to add to treatment after considering any contraindications, medicines interactions or adverse effects (Table 1). Some guidelines favour the addition of vildagliptin or a sulphonylurea instead of pioglitazone due to potential adverse effects associated with pioglitazone. A combination formulation of metformin + vildagliptin is available subsidised, which may be the simplest second-line approach to help patients achieve their HbA1c target with less pill burden.

Vildagliptin or pioglitazone may be preferred over a sulphonylurea if patients have problems with hypoglycaemia or wish to avoid weight gain.

N.B. Prior to initiating vildagliptin, assess liver health by requesting liver function tests (Table 2).

For further information on prescribing vildagliptin, see: www.bpac.org.nz/2018/vildagliptin.aspx

Escalating beyond single or dual oral treatment

Discuss insulin initiation with patients who have HbA1c 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 HbA1c levels.
Table 2: Subsidised oral glucose-lowering medicines and factors to consider when prescribing.14, 15

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Effects on weight</th>
<th>Risk of hypoglycaemia</th>
<th>Use in patients with renal or hepatic impairment</th>
<th>Other factors and monitoring requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metformin</td>
<td>Weight loss of approximately 2–3 kg over 12 months14</td>
<td>Low</td>
<td>■ Avoid if CrCl &lt; 15 mL/min15</td>
<td>■ The preferred oral medicine in patients who are pregnant or breastfeeding</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>■ Reduce doses if CrCl 15–60 mL/min15</td>
<td>■ May cause vitamin B12 deficiency; check levels if patients have symptoms of anaemia or peripheral neuropathy.16 Monitor vitamin B12 levels periodically, e.g. annually or as appropriate depending on patient characteristics.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>■ Avoid if severe hepatic disease and use with caution if mild hepatic impairment; impaired hepatic function can reduce lactate clearance and increase the risk of lactic acidosis25</td>
<td></td>
</tr>
<tr>
<td>Vildagliptin</td>
<td>No change</td>
<td>Low</td>
<td>■ Reduce dose if eGFR &lt; 50 mL/min/1.72 m2 *</td>
<td>■ Avoid use in patients with severe heart failure (New York Association functional class IV)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>■ Avoid in patients with hepatic dysfunction, e.g. ALT levels &gt;2.5 times the upper limit of normal23</td>
<td>■ Assess liver function prior to initiation, every three months for the first year and then periodically23</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td>Weight gain of approximately 2 kg over 12 months26</td>
<td>High</td>
<td>■ Other medicines are preferable in patients with increased risk of hypoglycaemia, including patients with renal impairment or severe hepatic impairment19, 27</td>
<td>■ Effects on HbA1c may not persist as long as other oral options, requiring a change in medicine earlier5</td>
</tr>
<tr>
<td>(glipizide, gliclazide)</td>
<td></td>
<td></td>
<td>■ Use is not advised in patients on renal dialysis28</td>
<td></td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>Weight gain of approximately 2 kg over 12 months26</td>
<td>Low</td>
<td>■ Avoid in patients with hepatic impairment, e.g. ALT levels &gt;2.5 times the upper limit of normal28</td>
<td>■ Increased risk of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>■ Use is not advised in patients on renal dialysis28</td>
<td>■ Oedema and heart failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>■ Fractures</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>■ Bladder cancer; avoid use in patients with risk factors for or a history of bladder cancer 6</td>
</tr>
</tbody>
</table>

* The combination vildagliptin + metformin formulation is not recommended in patients with eGFR < 60 mL/min/1.73 m2; prescribing metformin and vildagliptin in separate tablets may be preferable to allow for an appropriate reduced dose of metformin.

When discussing the possibility of initiating insulin with a patient, reassurance and advice is often required 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 limit for review to ensure that insulin treatment is not unduly delayed.

The use of three oral hypoglycaemic medicines is an alternative to initiating insulin. However, there is little evidence available from clinical trials to guide this practice; 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.5 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.
Initiating insulin

Insulin has the largest effect on reducing HbA1c levels of all glucose-lowering medicines. There are a range of insulin formulations and delivery devices available, with regimens involving one injection per day to five or more per day. Consider a patient’s ability to administer injections, their lifestyle and work schedules, cognitive abilities and ability to recognise and address any potential hypoglycaemia when deciding which regimen to initiate.

Continuing oral 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 HbA1c targets.

Vildagliptin may also be continued when insulin is initiated. The formulation of vildagliptin + metformin is also approved for use in combination with insulin.

Sulphonylureas are often continued if patients are using basal insulin, but this can increase the risk of hypoglycaemia. Sulphonylureas are titrated down and withdrawn if treatment with a short-acting insulin is initiated.

Pioglitazone is typically discontinued when insulin is initiated as combined use increases the risk of oedema.

Basal insulin is typically the first insulin regimen used

There is no universally preferred insulin regimen: all regimens reduce HbA1c, and clinicians should recommend an approach that will optimise adherence and persistence.

A reasonable initial approach is to prescribe a once daily basal insulin. Basal insulin reduces HbA1c by controlling hepatic glucose production. Either an intermediate or long-acting insulin formulation can be prescribed as a basal insulin regimen. In contrast short-acting insulin formulations reduce HbA1c by decreasing glucose levels after a meal (post-prandial).

Once daily injections of a basal insulin are usually administered in the evening and help reduce high blood glucose levels in the morning. However, administering the injection in the morning may be appropriate for some patients who have increases in blood glucose levels throughout the day (Table 3). For example, older people with type 2 diabetes can have greater increases in glucose levels after a meal and lower fasting glucose levels compared to younger people.

For some patients self-monitoring of blood glucose levels (see below) may be useful before initiating insulin to determine their daily pattern of glycaemia. For example, a patient may measure levels before and after main meals for three days prior to initiation.

Education is key for patients initiating insulin

Ongoing advice and education are paramount to ensure patients are confident with their prescribed insulin regimen.

An initial session for patients starting insulin should cover:

- Self-monitoring of blood glucose levels
- How to use their injection device, injection technique and rotation of injection sites
- Appropriate storage of insulin and disposal of injection devices and needles
- What to do during disruptions to their typical daily routine, such as if they are acutely unwell, miss meals or are travelling
- Managing hypoglycaemia, including how diet and exercise can affect the risk, recognising symptoms, testing blood glucose levels during suspected hypoglycaemia and how to respond if levels are too low
- Driving safely while using insulin and any impact using insulin may have on their fitness to drive (see: “Diabetes medicines can affect a patient’s fitness to drive”)
- Use of a Medic Alert bracelet

Consider referral to a diabetes nurse specialist or education programme covering the above points if offered by the local DHB or PHO.

An information sheet for patients initiating insulin is available at: www.saferx.co.nz/assets/Documents/fe520032b2/insulin-english.pdf
Table 3: Patient characteristics to guide once daily dosing of basal insulin

<table>
<thead>
<tr>
<th>Once daily injections at night are suitable for patients:</th>
<th>Once daily injections in the morning are suitable for patients with:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- With high blood glucose levels in the morning</td>
<td>- Blood glucose levels that increase throughout the day</td>
</tr>
<tr>
<td>- At lower risk of nocturnal hypoglycaemia</td>
<td>- Increased risk of nocturnal hypoglycaemia</td>
</tr>
<tr>
<td>- Who can respond to a nocturnal hypoglycaemic event, e.g. have no mobility issues or can rely on assistance from others</td>
<td>- Increased risk of consequences of a nocturnal hypoglycaemia event, e.g. living alone, frailty, risk of falls</td>
</tr>
</tbody>
</table>

Most patients can be prescribed isophane insulin

Two types of basal insulin are available fully subsidised in New Zealand:

- Isophane insulin, also known as neutral protamine Hagedorn (NPH) insulin, is an intermediate-acting insulin
- Insulin glargine, an insulin analogue, is a long-acting insulin

Patients can typically be initiated on isophane insulin. Although isophane insulin has a shorter duration of action, both of these insulin formulations result in the same extent of HbA₁c reduction and are associated with similar rates of severe hypoglycaemia. Clinicians could consider switching a patient to insulin glargine if they experience problems with hypoglycaemia, as the use of insulin glargine is associated with lower rates of symptomatic and nocturnal hypoglycaemia. However, switching is not necessary unless there are clinical reasons for doing so.

Patients using insulin should begin self-monitoring of blood glucose

Self-monitoring of blood glucose is recommended to help guide insulin dosing and meal planning. For patients with type 2 diabetes initiating basal insulin, a once daily measurement is sufficient, taken either:

- Before breakfast (fasting) if initiating insulin injections in the evening; OR
- Prior to evening dinner if initiating insulin injections in the morning

The aim of treatment is to achieve blood glucose levels between 6–8 mmol/L at these times.

Start low and increase slowly

Start patients on a basal insulin dose of 10 IU per day: Patients will need to titrate the insulin dose upwards from this starting point. Having patients adjust their own doses, rather than waiting for instructions from a clinician, is usually a more successful approach for achieving HbA₁c targets.

There are different methods for titration; one example is for patients to start taking 10 IU per day, and then increase the dose by 2 IU every third day until blood glucose levels before breakfast or before dinner are between 6–8 mmol/L.

If fasting blood glucose levels < 6 mmol/L are recorded, insulin doses should be reduced:

- Between 4–6 mmol/L: decrease insulin dose by 2 IU
- < 4 mmol/L: decrease insulin dose by 4 IU

If high doses of basal insulin are being used, e.g. approaching or over 1.0 IU/kg, consider switching patients to an alternative regimen which includes short-acting insulin formulations.

Weight gain and hypoglycaemia are the most common adverse effects

Rates of weight gain and hypoglycaemia are dose-dependent. Data from randomised controlled trials of long-acting insulin regimens report that patients have an average weight gain of 2–3 kgs within the first six months of treatment and 2.5% of patients have an episode of severe hypoglycaemia. Continuing the use of metformin can help reduce the amount of weight gain when insulin is initiated.

Ask patients to check their blood glucose levels if they experience symptoms consistent with hypoglycaemia. If episodes of hypoglycaemia occur, consider possible causes, e.g. missed meals, changes in usual carbohydrate intake, sudden changes in exercise. If an obvious cause is not apparent, patients should reduce their insulin dose by 10–20%. If patients have fasting blood glucose results < 4.0 mmol/L without experiencing symptoms of hypoglycaemia, insulin should be reduced by 10%.

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

Intensifying insulin treatment

Patients who continue to have elevated HbA₁c 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. When intensifying insulin regimens, additional self-monitoring...
of blood glucose before and after meals is likely to be necessary to check levels and calculate insulin doses.\textsuperscript{16}

In general, insulin regimens used to manage blood glucose levels in patients with type 1 diabetes can be used in patients with type 2 diabetes. Various regimens and injection devices are available; treatment should be tailored to each patient’s need for glucose lowering and their ability to manage administering insulin and calculating dose requirements. Insulin intensification can be managed in primary care, however referring patients to or discussing options with an endocrinologist or diabetes nurse specialist may be appropriate in some situations.\textsuperscript{6}

Further information on biphasic and short-acting insulin regimens will be available in a future bpac\textsuperscript{\textregistered} article on the management of type 1 diabetes.

**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. Nutrition and physical activity should be discussed with patients at all stages of management. These approaches can help reduce the dose and number of medicines needed to control cardiovascular risk factors and maintain target HbA\textsubscript{1c} levels. For some patients who manage to make significant lifestyle changes, withdrawing medicines may be possible. As patients age or develop co-morbidities, revise HbA\textsubscript{1c} targets and the choice or dose of glucose-lowering medicines, as necessary.

**Diabetes medicines can affect fitness to drive**

People with type 2 diabetes generally have no restrictions for holding a passenger vehicle licence (Class 1 or 6 licence). However, the NZTA advises that people taking sulphonylureas 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), however, assessments from both a general practitioner and a diabetes specialist are required and patients must meet specific conditions to continue driving.

bpac\textsuperscript{\textregistered} will be publishing future articles on providing weight loss advice for patients and relaxing HbA\textsubscript{1c} targets in older patients with type 2 diabetes.

**Patient information**

- Patient information on type 2 diabetes, the importance of diet and physical activity, and recognising and responding to hypoglycaemia is available from:
  - 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)

- A guide to initiating insulin for patients with type 2 diabetes, produced by the Waitemata District Health Board, is available in various languages:
  - English: [www.saferx.co.nz/assets/Documents/fe520032b2/insulin-english.pdf](http://www.saferx.co.nz/assets/Documents/fe520032b2/insulin-english.pdf)
  - Samoan: [www.saferx.co.nz/assets/Documents/83a47fde72/insulin-samoan.pdf](http://www.saferx.co.nz/assets/Documents/83a47fde72/insulin-samoan.pdf)

For further information on diabetes and driving, see: [www.nzta.govt.nz/driver-licences/getting-a-licence/medical-requirements/information-for-health-practitioners/](http://www.nzta.govt.nz/driver-licences/getting-a-licence/medical-requirements/information-for-health-practitioners/)
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References:


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