Elevating the role of basal insulin therapy in T2D management: From CGM use to fixed-ratio combinations and once-weekly regimens

Practice aid for the management of type 2 diabetes using basal insulin

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**Treatment intensification with basal insulin in T2D**

- Recommended in patients living with T2D who do not meet glycaemic targets with non-insulin glucose-lowering agents\(^1,2\)

Clinical inertia is the failure to initiate or intensify therapy according to the guidelines\(^3\)

### Delayed initiation leads to:

- Chronic hyperglycaemia\(^4\)
- Microvascular complications e.g. retinopathy and neuropathy\(^5-7\)
- Macrovascular complications e.g. CHD and stroke\(^5-7\)
- Reduced patient QoL and psychological wellbeing\(^5,7\)
- Increased risk of early mortality\(^7\)

### Barriers to daily insulin intensification:

#### Physician related:

- Complex dosing schedules\(^1\)
- Injection-site reactions\(^8\)
- Fear of hypoglycaemia\(^1,8,9\)

#### Patient related:

- Difficult administration\(^9\)
- Injection burden\(^1\)
- Social stigma\(^9\)
- Anticipation of pain\(^8\)
- Fear of weight gain\(^1,9\)
- Fear of hypoglycaemia\(^1,9\)

#### System related:

- Lack of time or resources for education\(^1\)

### Strategies to overcome clinical inertia:

- Implement **simpler titration regimens** e.g. fixed-ratio combinations\(^1,10\)
- Improve **patient and PCP education** to enhance communication enabling fears to be explored and resolved\(^9\)
- Use **videos to educate** patients to save time in consultations and allay patient fears e.g. on injection or titration technique\(^8,9\)
- Suggest **peer advisor and patient support groups** to enable patients to access continuous support\(^8\)
Using CGM and time-in-range to optimize patient outcomes in T2D

- CGM uses a subcutaneous sensor to measure interstitial glucose concentrations every few minutes.\(^{11}\)
- HbA1c testing at HCP follow-ups does not evaluate short-term glycaemic variability or daily fluctuations in blood glucose.\(^{5,12}\)
- CGM reveals high and low glucose levels that are not apparent with HbA1c alone.\(^{11}\)

International guidelines state *CGM may be considered to improve glycaemic control in T2D in patients on insulin therapy and not achieving their glucose targets*.\(^{2,13-15}\)

Guideline recommendations for glucose levels over 24 hours

- **Below range 1**
  - Aim for <4% of time
  - <3.9 mmol/L (70.0 mg/dL)\(^{2,16}\)

- **Below range 2**
  - Aim for <1% of time
  - <3.0 mmol/L (54.0 mg/dL)\(^{2,16}\)

- **Above range 1**
  - A TIR >70% is equivalent to a HbA1c <7%\(^2\)
  - Each 10% increase in TIR equates to a ~0.5% reduction in HbA1c.\(^{17}\)

- **Above range 2**
  - A TIR could be a predictor of micro- and macrovascular complications and is associated with better patient outcomes.\(^{17}\)

TIR – normal range

- 3.9-10.0 mmol/L (70.0–180.0 mg/dL)\(^2\)
Preparing for once-weekly basal insulins

Once-weekly basal insulins may be more suitable for patients with relatively low variation in basal insulin requirements and predictable lifestyles.

Example of dosing and titration of once-weekly basal insulins

<table>
<thead>
<tr>
<th>Initial dose</th>
<th>Dose 2</th>
<th>Dose 3+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin naive</td>
<td>70 U</td>
<td>70 U + titration</td>
</tr>
<tr>
<td>Prior basal insulin</td>
<td>10.5x daily basal dose</td>
<td>7x daily basal dose</td>
</tr>
</tbody>
</table>

Managing hypoglycaemia

In clinical trials, hypoglycaemia responded to standard corrective procedures, with severe hypoglycaemia successfully managed with oral carbohydrate alone.*18,22

Management of an acute episode should be similar to those experienced with daily basal insulins: administer calculated amounts of carbohydrates, monitor response and repeat as necessary.23

Management of special populations

- Further research is needed into how to adjust once-weekly insulin to manage exercise, sick days and surgery.18,19
- Patients requiring dosing assistance may benefit from once-weekly insulins, with the reduced injection burden and increased treatment flexibility - a dose can be missed without loss of efficacy.23
- Once-weekly insulins may prove safer than daily basal insulin (particularly if less aggressive glucose targets are used) in those requiring a caregiver to administer insulin, e.g. the elderly and those in care facilities.23

*Severe hypoglycaemia defined as hypoglycaemia associated with severe cognitive impairment requiring external assistance for recovery.21,22,24–27†Dosages of once-weekly insulins can be missed once a steady state has been achieved. Missed icodex doses should be taken as soon as possible, however, if 3 days or fewer remain before the next dose, that week’s dose should be skipped.23
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Abbreviations
CGM, continuous glucose monitoring; CHD, coronary heart disease; FPG, fasting plasma glucose; HbA1c, glycated haemoglobin; HCP, healthcare professional; no., number; PCP, primary care physician; QoL, quality of life; TIR, time-in-range; T2D, type 2 diabetes; U, units.

References

The guidance provided by this practice aid is not intended to directly influence patient care. Clinicians should always evaluate their patients’ conditions and potential contraindications and review any relevant manufacturer product information or recommendations of other authorities prior to consideration of procedures, medications, or other courses of diagnosis or therapy included here.

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