

This tool is designed to support family physicians and primary care nurse practitioners to prescribe and manage insulin for adult patients with type 2 diabetes.

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## SECTION A: Role of insulin in type 2 diabetes

For many patients with type 2 diabetes, insulin is needed eventually. As the condition progresses, non-insulin pharmacotherapy may no longer be sufficient to maintain glycemic control over time.<sup>1</sup>

### Overview of insulin therapy for type 2 diabetes<sup>2</sup>

#### Consider starting insulin therapy if:

##### Non-insulin pharmacotherapy is inadequate or not feasible:

- Non-insulin pharmacotherapy cannot be used due to cost or tolerability issues
- End organ damage (e.g., poor renal function) that requires discontinuation or reduction of non-insulin pharmacotherapy
- During or when planning pregnancy<sup>1</sup> (**Note:** diabetes during pregnancy is outside of the scope of this tool)
- Fasting blood glucose and A1C are not at target when a patient is taking optimal non-insulin pharmacotherapy<sup>1,2</sup>
  - Target levels to consider:

##### Fasting blood glucose<sup>2,3</sup>

- 4.0-7.0 mmol/L (if A1C is not at target, consider a target of 4.0-5.5 mmol/L, balanced against the risk of hypoglycemia)
- Targets may be relaxed for frail or functionally dependent patients\*

##### A1C<sup>1</sup>

- ≤7.0% for most patients
- 7.1-8.0% for functionally dependent patients\*
- 7.1-8.5% for patients with frailty,\* dementia, limited life expectancy or history of recurrent severe hypoglycemia and hypoglycemia unawareness
- To individualize, consider benefit vs. harm and patient values

##### Patient shows severe/symptomatic hyperglycemia or metabolic decompensation:

- Severely elevated A1C and fasting blood glucose (e.g., A1C > 10% or blood glucose ≥ 16.7 mmol/L), even without symptomatic hyperglycemia and metabolic decompensation<sup>4,5</sup>
- Metabolic decompensation,\*\* symptoms include:
  - Symptomatic hyperglycemia (e.g., polyuria, polydipsia, nocturia, blurred vision, fatigue, headache)<sup>4,6</sup>
  - Marked hyperglycemia (blood glucose ≥16.7 mmol/L)<sup>2,4</sup>
  - Unintentional weight loss
  - Ketosis<sup>2,5</sup>

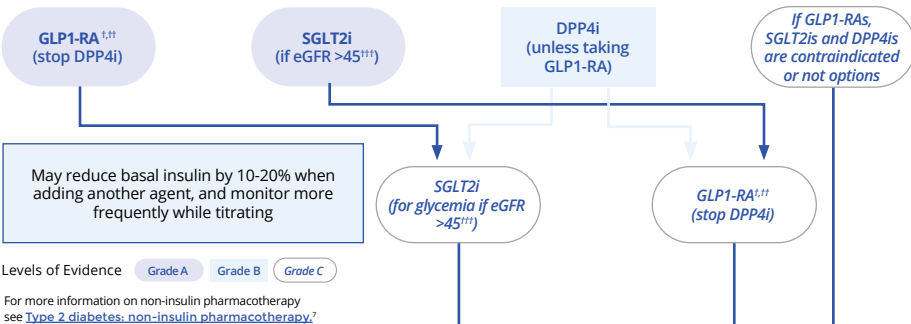
- Start basal insulin and titrate to achieve fasting blood glucose target (e.g., 4.0-7.0 mmol/L)
- Review and adjust other non-insulin agents
- Continue (or start) metformin unless contraindicated

- Start basal insulin +/- metformin, and titrate to achieve fasting blood glucose target (e.g., 4.0-7.0 mmol/L)

#### Regularly:

- Assess glycemic control, cardiovascular and renal status
- Screen for complications (i.e., eyes, feet, kidneys)
- Review the efficacy, side effects and safety of medications
- Assess the patient's ability to take current medications
- Reinforce and support healthy behaviour interventions

#### Consider adding one of the following non-insulin agents, (taking into account what has been tried before):



- Add prandial (bolus) insulin step-wise (beginning with one meal injection per day and advancing to an injection at each meal if needed)
- Consider the use of premixed insulin if patient not suited to more than 2 injections per day
- Stop sulfonylureas<sup>†††</sup> when prandial or premixed insulin started
- Review and adjust other non-insulin agents

Advance insulin therapy if A1C is not at target within 3-6 months, despite:

- Adequate titration of insulin to achieve fasting blood glucose target without hypoglycemia
- Lifestyle changes, and
- Pharmacotherapy support

\*Functionally dependent patients have a [Clinical Frailty Scale](#)<sup>8</sup> score of 4-5 on a 9-point scale. Patients with frailty have a [Clinical Frailty Scale](#)<sup>8</sup> score of 6-8 on a 9-point scale.

\*\*Some experts suggest using early, short-term (2-4 weeks) intensive insulin therapy in newly diagnosed type 2 diabetes patients with symptomatic hyperglycemia or those with high cardiovascular risk in acute care settings (e.g., acute MI, stroke, coronary artery bypass graft). This approach is associated with improvements in insulin resistance, beta cell function, quality of life and may induce remission when started within the first 2 years of diagnosis. It reflects expert opinion and is not included in current clinical practice guidelines.<sup>9,10</sup>

<sup>†</sup> And titrate dose of GLP1-RA as tolerated

<sup>††</sup> Or fixed-ratio combination




<sup>†††</sup> If eGFR >30ml/min/1.73m<sup>2</sup>, may be used for cardio-renal benefit

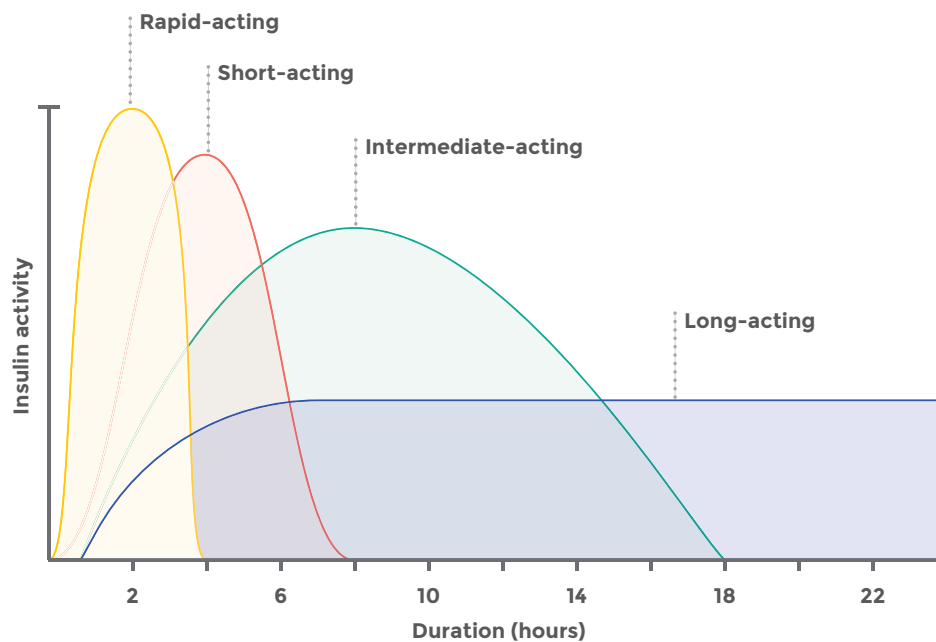
Notes: DPP4i = dipeptidyl peptidase-4 inhibitor, eGFR = estimated glomerular filtration rate, GLP1-RA = glucagon-like peptide-1 receptor agonist, SGLT2i = sodium-glucose cotransporter-2 inhibitor

**Bold** = agents with stronger evidence

## SECTION B: Selecting insulin

## Different types of insulin

 Basal insulin	 Prandial (bolus) insulin	 Premixed insulin
<b>What it is</b>		
<ul style="list-style-type: none"> <li>Intermediate- or long-acting insulin, usually injected once daily (usually at bedtime) and used to keep blood glucose levels stable during periods of fasting (e.g., between meals, while sleeping)</li> </ul>	<ul style="list-style-type: none"> <li>Short- or rapid-acting insulin injected at mealtime to control post-prandial (post-meal) glucose levels or for short-term correction of meal-related hyperglycemia</li> </ul>	<ul style="list-style-type: none"> <li>Premixed solutions that contain two types of insulin (e.g., prandial and basal insulin)</li> </ul>
<b>When to use it</b>		
<ul style="list-style-type: none"> <li>First-line treatment for insulin-naïve patients<sup>2</sup></li> <li>It is a simpler treatment regimen that causes less hypoglycemia and weight gain compared to premixed insulin or prandial-only regimens<sup>2</sup></li> </ul>	<ul style="list-style-type: none"> <li>May be added at mealtimes if glycemic control is suboptimal after 3-6 months on basal insulin (with other agents)<sup>3</sup></li> <li>Basal and prandial (bolus) insulin may be started together if the patient's blood glucose level is high (<math>\geq 16.7</math> mmol/L) and metabolic decompensation is present at initial diagnosis<sup>1</sup></li> </ul>	<ul style="list-style-type: none"> <li>Consider for patients who cannot accommodate &gt; 2 injections/day (e.g., those who require home care/caregiver support to administer insulin), or patients who would have difficulty adjusting insulin doses (e.g., due to cognitive ability or visual acuity)<sup>11,12</sup></li> <li>This dosing option is less flexible (requires a routine mealtime to prevent hypoglycemia) and offers less ability to correct for abnormal results<sup>11</sup></li> </ul>



## SECTION B: Selecting insulin (continued)

### Selecting which insulin to use

- There is not a simple reason to choose one insulin over another, within each type of insulin (basal, prandial and combination)
- When comparing insulin options, prioritize a patient's preference in the shared decision-making process

Common properties of insulin	Insulin specific properties	Other properties
<ul style="list-style-type: none"> <li>• A1C reduction</li> <li>• Cardiorenal outcomes</li> <li>• Impact on weight</li> <li>• Harms</li> </ul> <p>(See <a href="#">Common properties of insulin</a> table below for more information)</p>	<ul style="list-style-type: none"> <li>• Onset, peak and duration of action</li> <li>• Cost</li> <li>• Coverage (ODB, NIHB)</li> <li>• Hypoglycemia risk (for basal insulin)*</li> </ul> <p>(See <a href="#">Insulin specific properties</a> tables for more information)</p>	<ul style="list-style-type: none"> <li>• Properties (not well studied)<sup>13-16</sup> <ul style="list-style-type: none"> <li>• Mortality (exception for prandial: studies have not shown a significant difference in mortality between rapid- and short-acting insulin)<sup>17</sup></li> <li>• Quality of life</li> </ul> </li> </ul>

#### \*Hypoglycemia risk (for basal insulin)<sup>21-23</sup>

- Some patients benefit from choosing long-acting insulin over intermediate-acting insulin (e.g., those who do shift work, have inconsistent oral intake or those who would benefit from dosing less often)
- For most patients however, choosing basal insulin is not the primary factor in reducing hypoglycemia risk in a clinically meaningful way (i.e., absolute risk differences are small and the evidence is limited, making it difficult to compare basal insulins with confidence)
- Determining other ways to reduce hypoglycemia risk is essential (see [Managing hypoglycemia](#))

### Common properties of insulin

See the bottom of [page 5](#) for definitions of acronyms used throughout this table

<b>A1C reduction</b>	<ul style="list-style-type: none"> <li>• Effect on A1C is 0.9-1.2% or more<sup>2</sup></li> <li>• A1C reduction depends on dose and number of injections per day<sup>3</sup></li> <li>• Dose increases may be limited by hypoglycemia and cost<sup>2</sup></li> </ul>
<b>Cardiorenal outcomes</b>	<ul style="list-style-type: none"> <li>• Insulin has a neutral effect on cardiorenal outcomes (no risk reduction)<sup>1,2,18-20</sup></li> </ul>
<b>Weight</b>	<p>All insulin associated with weight gain:</p> <ul style="list-style-type: none"> <li>• Effects on weight are dose-related</li> <li>• Basal insulin is associated with a weight gain of 1-2 kg* (over 6-12 months)<sup>2,24-26</sup> <ul style="list-style-type: none"> <li>• Detemir and glargine 300 units/mL may lead to slightly less weight gain (<math>\leq 1</math>kg) than other options<sup>13,14</sup></li> </ul> </li> <li>• Prandial (bolus) insulin is associated with a weight gain (exact amount unknown)<sup>2</sup></li> <li>• Premixed insulins are associated with a weight gain of 3.5-5 kg* (over 6-12 months)<sup>2,24-26</sup></li> </ul>
<b>Harms</b>	<ul style="list-style-type: none"> <li>• Hypoglycemia</li> <li>• Lipohypertrophy</li> <li>• Local injection site reactions (exception: fewer with glargine vs. detemir)<sup>27</sup></li> <li>• Allergic reactions (rare)<sup>1</sup></li> </ul>

\*Unclear if it is causation or correlation.

## SECTION B: Selecting insulin (continued)



## Insulin specific properties - Basal insulin

See the bottom of [page 6](#) for definitions of acronyms and symbols used throughout this table

Agent (100 units/mL unless otherwise specified)	Onset <sup>1</sup>	Peak <sup>1</sup>	Duration <sup>1</sup>	Comments	Cover- age (ODB <sup>28</sup> , NIHB <sup>29</sup> )	Dosage forms <sup>28</sup>	Drug cost for dosage forms <sup>30</sup>	Drug cost for usual dose* (for 100 days supply)	
								50 units/day (basal alone)	25 units/day (basal + bolus; cost is for the basal component)
<b>Intermediate-acting</b>									
NPH (Humulin® N)	1-2h	5-8h	14-18h	<ul style="list-style-type: none"> <li>• More erratic absorption vs. long-acting analogues</li> <li>• If a patient is dosed bid, the need for a lunch dose of prandial (bolus) insulin may be delayed<sup>11</sup></li> <li>• Max units/dose:** 60 for prefilled and reusable pens<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$71	\$185	\$127
(Novolin®ge)						5x3mL cartridges	\$62	\$167	\$114
						10mL vial	\$36	\$143	\$89
						5x3mL cartridges	\$60	\$167	\$114
10mL vial	\$35	\$143	\$89						
†NPH pork (Hypurin®)	1-3h	6-12h	24-48h	<ul style="list-style-type: none"> <li>• Not often used in practice due to a lack of coverage, cost and inconvenience with vial/syringes</li> </ul>	ODB × NIHB ×	10mL vial	\$125	\$584	\$355
<b>Long-acting</b>									
Degludec (Tresiba®)	1h	No peak	>42h	<ul style="list-style-type: none"> <li>• Duration useful for shift workers<sup>1</sup></li> <li>• Can increase the dose by increments of 1 unit</li> <li>• Max units/dose:** 80 for prefilled pen<sup>31</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$129	\$370	\$250
Degludec 200 units/mL (Tresiba®)	1h	No peak	>42h	<ul style="list-style-type: none"> <li>• Duration useful for shift workers<sup>1</sup></li> <li>• 200 units/mL can be started if larger doses are required</li> <li>• Can increase the dose by increments of 2 units</li> <li>• Bioequivalent to degludec 100 units/mL<sup>31</sup></li> <li>• Max units/dose:** 160 for prefilled pen<sup>31</sup></li> </ul>	ODB ✓ NIHB ✓	3x3mL prefilled pens	\$153	\$442	\$298
Detemir (Levemir®)	1.5h	Al- most peak- less	6-24h	<ul style="list-style-type: none"> <li>• Duration of action may be shorter at lower doses and may require bid dosing (cut-off varies by patient)<sup>1</sup></li> <li>• If a patient is experiencing nocturnal hypoglycemia with a bedtime dose, lower the dose, inject the dose in the morning or split daily dose to bid</li> <li>• Max units/dose:** 80 for prefilled pen, 60 for reusable pen<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$129	\$370	\$250
						5x3mL cartridges	\$128	\$367	\$247
Glargine (Basaglar™)	1.5h	Al- most peak- less	24h	<ul style="list-style-type: none"> <li>• Acidic formulation may cause irritation<sup>32</sup></li> <li>• Basaglar™ is biosimilar to Lantus® (Health Canada: no clinically meaningful differences in pharmacokinetics, pharmacodynamics, clinical efficacy, safety or immunogenicity)<sup>33</sup></li> <li>• If a patient is experiencing nocturnal hypoglycemia with a bedtime dose, lower the dose or inject the dose in the morning</li> <li>• Max units/dose:** 80 for prefilled pens, 60 for Basaglar™ reusable pen, 80 for Lantus® reusable pen<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$84	\$234	\$159
(Lantus®)						5x3mL cartridges	\$84	\$234	\$159
						5x3mL prefilled pens	\$109	\$310	\$209
						5x3mL cartridges	\$109	\$310	\$209
10mL vial	\$75	\$209	\$142						
Glargine 300 units/mL (Toujeo®)	1.5h	No peak	Up to 36h	<ul style="list-style-type: none"> <li>• Recommend for patients who require &gt;20 units of basal insulin/day, and counsel on change of concentration</li> <li>• NOT bioequivalent to glargine 100 units/mL (longer duration and delayed peak; not interchangeable without a dose adjustment)<sup>34</sup></li> <li>• If a patient is experiencing nocturnal hypoglycemia with a bedtime dose, lower the dose or inject the dose in the morning</li> <li>• Max units/dose:** 80 for 1.5mL prefilled pen, 160 for 3mL prefilled pen<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓ (1.5mL) × (3mL)	3x1.5mL or 5x1.5mL prefilled pen	\$37	\$323	\$180
						3x3mL or 2x3mL prefilled pen	\$66	\$351	\$180

## SECTION B: Selecting insulin (continued)



## Insulin specific properties - Prandial (bolus) insulin

See the bottom of [page 5](#) for definitions of acronyms and symbols used throughout this table

Agent (100 units/mL unless otherwise specified)	Onset <sup>1</sup>	Peak <sup>1</sup>	Duration <sup>1</sup>	Comments	Coverage (ODB <sup>28</sup> , NIHB <sup>29</sup> )	Dosage forms <sup>28</sup>	Drug cost for dosage forms <sup>30</sup>	Drug cost for usual dose* (25 units/day for 100 days supply)
<b>Rapid-acting</b>								
Aspart (Novorapid®)	9-20 min	1-3h	3-5h	<ul style="list-style-type: none"> <li>Inject immediately (not more than 5-10 minutes) before or immediately after a meal</li> <li>Max units/dose:** 80 for prefilled pen, 60 for reusable pen<sup>11</sup></li> </ul>	ODB ✓ <a href="#">LU 388</a> , <a href="#">389, 390</a> <sup>35</sup> NIHB ✓	5x3mL prefilled pens 5x3mL cartridges 10mL vial	\$78 \$75 \$42	\$147 \$142 \$107
t(Fiasp®)	4 min	0.5-1.5h	3-5h	<ul style="list-style-type: none"> <li>Faster-acting insulin</li> <li>Suggested initial dose for type 2 diabetes in adults is 4 units at one or more meals</li> <li>Inject at the start of the a meal (up to 2 minutes before meal) or within 20 minutes after starting the meal</li> <li>Max units/dose:** 80 for prefilled pen, 60 for reusable pen<sup>11</sup></li> </ul>	ODB x NIHB x	5x3mL prefilled pens 5x3mL cartridges 10mL vial	\$84 \$81 \$45	\$157 \$152 \$115
Glulisine (Apidra®)	10-15 min	1-1.5h	3.5-5h	<ul style="list-style-type: none"> <li>Inject within 15 minutes before or within 20 minutes after starting a meal</li> <li>Max units/dose:** 80 for prefilled and reusable pens<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens 5x3mL cartridges 10mL vial	\$67 \$66 \$38	\$124 \$123 \$95
Lispro (Humalog®)	10-15 min	0.75-2.5h	3.5-4.75h	<ul style="list-style-type: none"> <li>Inject within 15 minutes before a meal or within 20 minutes after starting the meal</li> <li>Admelog® is biosimilar to Humalog® (Health Canada: no clinically meaningful differences in pharmacokinetics, pharmacodynamics, clinical efficacy, safety or immunogenicity)<sup>33</sup></li> <li>Max units/dose:** 60 for Humalog® prefilled and reusable pens, 80 for Admelog® prefilled and reusable pens<sup>11</sup></li> </ul>	ODB ✓ <a href="#">LU 599</a> <sup>36</sup> NIHB ✓	5x3mL prefilled pens 5x3mL cartridges 10mL vial	\$74 \$74 \$42	\$138 \$139 \$107
(Admelog®)					ODB ✓ NIHB x	5x3mL prefilled pens 5x3mL cartridges 10mL vial	\$63 \$63 \$37	\$112 \$112 \$87
Lispro 200 units/mL (Humalog®)	30-45 min	0.75-2.5h	3.5-4.75h	<ul style="list-style-type: none"> <li>Higher concentration requires a smaller volume</li> <li>Recommend for patients who require &gt;20 units of prandial (bolus) insulin/day, and counsel on change of concentration</li> <li>Max units/dose:** 60 for prefilled pen<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$129	\$129
<b>Short-acting</b>								
Regular insulin (Humulin® R)	30-60 min	2-4h	5-8h	<ul style="list-style-type: none"> <li>Inject 15-30 minutes before meals</li> <li>Entuzity® should be reserved for patients who require &gt; 200 units/day and delivers insulin in 5-unit increments</li> </ul>	ODB ✓ NIHB ✓	5x3mL cartridges 10mL vial	\$62 \$36	\$115 \$89
(Novolin®ge Toronto)						5x3mL cartridges 10mL vial	\$61 \$36	\$112 \$88
†Regular insulin 500 units/mL (Entuzity®)	3-58 min	0.5-8.0h	17-24h	<ul style="list-style-type: none"> <li>Entuzity® has a unique pharmacokinetic profile with an onset similar to regular insulin and a duration similar to some basal/premixed insulins</li> <li>Max units/dose:** 60 for Humulin-R® reusable pen, 60 for Novolin ge Toronto® reusable pen, 300 for Entuzity® prefilled pen<sup>11</sup></li> </ul>	ODB x NIHB x	2x3mL prefilled pens	\$120	\$120

## SECTION B: Selecting insulin (continued)

### Insulin specific properties - Premixed insulin

The choice of premixed insulin will depend on the patient's dosing requirements for basal and prandial (bolus) insulin and which type of prandial insulin is preferred by the patient and provider

See the bottom of [page 8](#) for definitions of acronyms and symbols used throughout this table

Agent (100 units/mL unless otherwise specified)	Comments (refer to individual components in previous tables for onset, peak and duration)	Coverage (ODB <sup>28</sup> , NIHB <sup>29</sup> )	Dosage forms <sup>28</sup>	Drug cost for dosage forms <sup>30</sup>	Drug cost for usual dose* (50 units/day for 100 days supply)
<b>Short-acting + intermediate-acting</b>					
Premixed regular/NPH (Humulin <sup>®</sup> 30/70)	<ul style="list-style-type: none"> <li>Contain both short-acting regular prandial (bolus) insulin and intermediate-acting NPH basal insulin</li> <li>The numbers in the product name (e.g., 30/70) refer to the percentage of each type of insulin contained in the product (e.g., Novolin ge 30/70<sup>®</sup> contains 30% regular insulin and 70% NPH insulin)</li> <li>Inject bid (or tid for 50/50) 30 minutes before eating</li> <li>Max units/dose:** 60 for reusable pen<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL cartridges	\$65	\$176
(Novolin <sup>®</sup> ge 30/70)			10mL vial	\$38	\$151
(Novolin <sup>®</sup> ge 40/60)			5x3mL cartridges	\$60	\$162
(Novolin <sup>®</sup> ge 50/50)			10mL vial	\$36	\$144
			5x3mL cartridges	\$60	\$163
			5x3mL cartridges	\$60	\$163
<b>Rapid-acting + intermediate-acting</b>					
Aspart/aspart protamine suspension (Novomix <sup>®</sup> 30)	<ul style="list-style-type: none"> <li>Contains 30% rapid-acting prandial (bolus) insulin aspart and 70% intermediate-acting insulin aspart protamine crystals</li> <li>Inject within 10 minutes before eating</li> <li>Max units/dose:** 60</li> </ul>	ODB ✓ NIHB ✓	5x3mL cartridges	\$70	\$191
Lispro/lispro protamine suspension (Humalog <sup>®</sup> Mix25)	<ul style="list-style-type: none"> <li>Contains a mix of rapid-acting prandial (bolus) insulin lispro (either 25% to 50%) and intermediate-acting insulin lispro protamine suspension (either 75% or 50%)</li> <li>Inject within 10 minutes before eating</li> <li>Max units/dose:** 60 for prefilled and reusable pens<sup>11</sup></li> </ul>	ODB ✓ NIHB ✓	5x3mL prefilled pens	\$74	\$205
(Humalog <sup>®</sup> Mix50)			5x3mL cartridges	\$75	\$206
			5x3mL prefilled pens	\$73	\$201
			5x3mL cartridges	\$74	\$203
<b>GLP1-RA + insulin combinations (not premixed insulins)</b>					
†Degludec/liraglutide (Xultophy <sup>®</sup> )	<ul style="list-style-type: none"> <li>Contains a mix of long-acting basal insulin degludec and GLP1-RA liraglutide</li> <li>Inject 16 units/0.58mg – 50 units/1.8mg SC daily</li> <li>Administer at any time of the day (but same time every day) independent of meals</li> <li>Max: 50 units insulin daily</li> </ul>	ODB x NIHB x	5x3mL cartridges	\$370	\$1,065
Glargine/lixisenatide (Soliqua <sup>®</sup> )	<ul style="list-style-type: none"> <li>Contains a mix of long-acting basal insulin glargine 100 units/mL and GLP1-RA lixisenatide</li> <li>Inject 15 units/5µg – 60 units/20µg SC daily</li> <li>Administer within 1 hour before the first meal of the day</li> <li>Max: 60 units insulin daily</li> </ul>	ODB ✓ NIHB ✓	5x3mL cartridges	\$215	\$624

\* Prices reflect the cost to the consumer and include a markup and dispensing fee (the cost per dosage form and the 100-day cost both include one dispensing fee and reflect the usual pharmacy practice of dispensing a full box or vial; e.g., 5x3mL pens). The cost for a usual dose assumes a 100 kg patient. The price for vials does not include the cost of syringes.

\*\* This reflects the maximum amount given for 1 injection, not the maximum amount of insulin that is required. Multiple injections may be required to achieve blood glucose targets.

† = not on Ontario drug formulary, ✓ = general benefit, x = not a benefit, **bid** = twice daily, **h** = hour, **kg** = kilogram, **LU** = limited use, **max** = maximum, **µg** = microgram, **mg** = milligram, **mL** = milliliter, **NIHB** = non-insured health benefits for First Nations and Inuit, **NPH** = neutral protamine Hagedorn, **ODB** = Ontario Drug Benefit, **SC** = subcutaneous

## SECTION B: Selecting insulin (continued)

### Consider the affordability of insulin

- Cost is an important factor for many patients
- Balance the consideration of cost against other factors when selecting insulin in the shared decision-making process
- Consider biosimilar insulin as it costs less. A biosimilar is a biologic drug that is highly similar to a biologic drug that was already authorized by Health Canada for sale<sup>33</sup>
- Patients' coverage (e.g., Ontario Drug Benefit [ODB], Non-Insured Health Benefits [NIHB]) plays into cost
  - ✓ All insulin options below have ODB and NIHB coverage unless otherwise specified

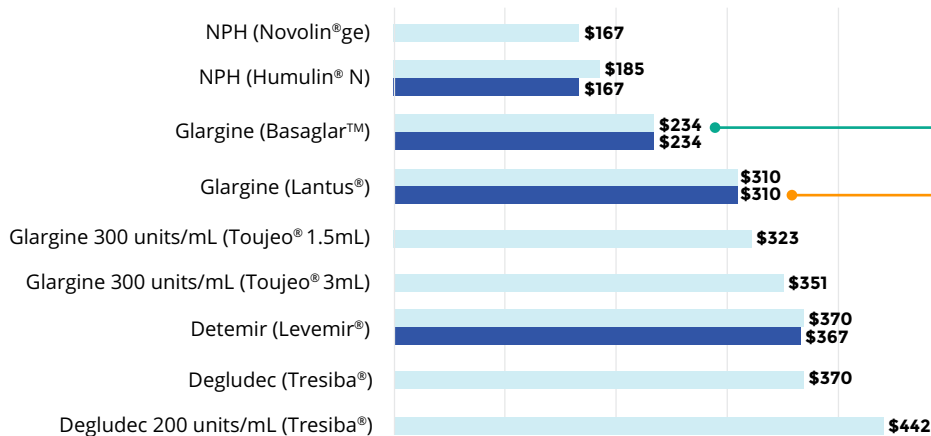
■ Prefilled pen

■ Cartridge

All insulin 100 units/mL, unless otherwise specified

#### Basal insulin

Drug cost for usual dose\* (50 units/day for 100 days supply [basal alone])

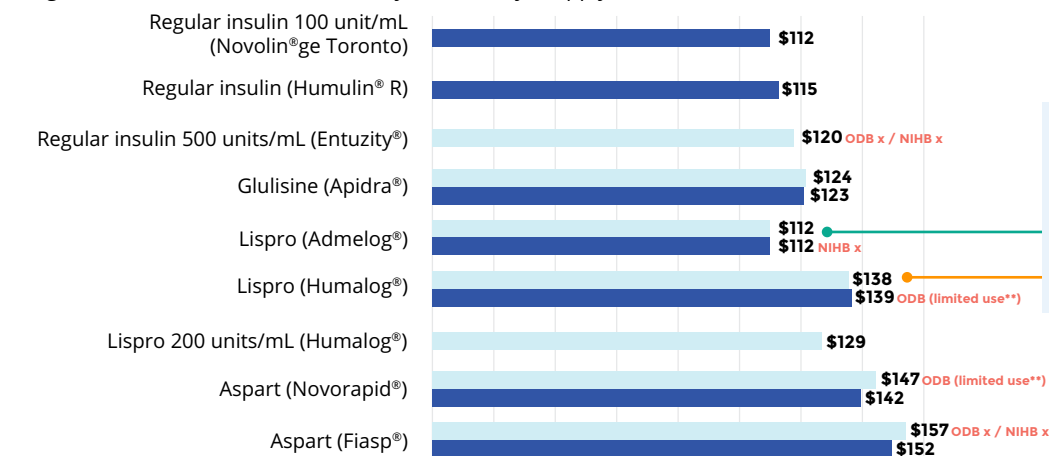


#### Consider biosimilar insulin

- Basaglar<sup>™</sup> is a biosimilar of Lantus<sup>®</sup> and costs 25% less
- Switching a patient on Lantus<sup>®</sup> to Basaglar<sup>™</sup> would save them ~\$277/year
- Switching all Ontarians on Lantus<sup>®</sup> to Basaglar<sup>™</sup> would save the provincial healthcare system ~\$5 million/year<sup>37</sup>

#### Prandial (bolus) insulin

Drug cost for usual dose\* (25 units/day for 100 days supply)

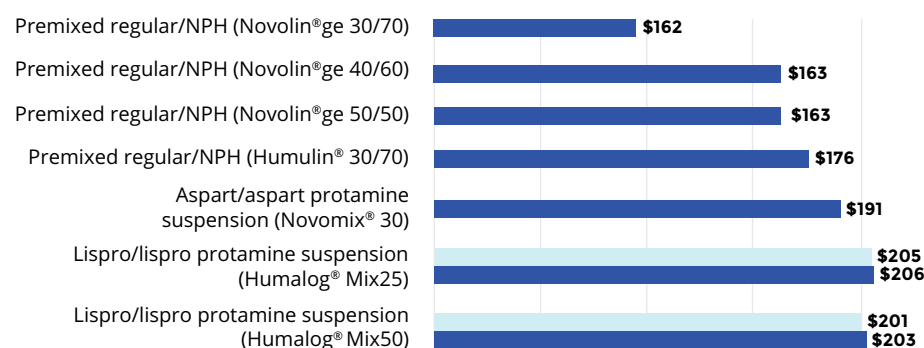


#### Consider biosimilar insulin

- Admelog<sup>®</sup> is a biosimilar of Humalog<sup>®</sup> and costs 19% less
- Switching a patient on Humalog<sup>®</sup> to Admelog<sup>®</sup> would save them ~\$99/year

#### Basal/prandial (bolus) premixed insulin

Drug cost for usual dose\* - (50 units/day for 100 days supply)



\* Prices reflect the cost to the customer and include markup and dispensing fee (the cost per dosage form and the 100-day cost both include one dispensing fee and reflect the usual pharmacy practice of dispensing a full box; e.g., 5x3mL pens). The cost for a usual dose assumes a 100kg patient.

\*\* See [Insulin specific properties- Prandial \(bolus\) insulin](#) table for details on the limited use restrictions.

## SECTION B: Selecting insulin (continued)

### Explore patient reimbursement opportunities

Support patients to explore reimbursement opportunities for blood glucose monitoring supplies, pen needles and syringes.

#### Diabetes Canada's Ontario Monitoring for Health Program<sup>38</sup>

- Offers patients of all ages 75% [reimbursement for](#):
  - Blood glucose test strips and lancets – up to a maximum of \$920/year
  - Blood glucose meter – up to a maximum of \$75/every 5 years
  - Talking blood glucose meter – up to a maximum of \$300/every 5 years (note: a letter from a doctor is required to confirm visual impairment)

#### Ontario Ministry of Health's Assistive Devices Program<sup>39</sup>

- Offers patients 65+ an annual grant (\$170/year) to [cover the costs of needles and syringes](#) used to inject insulin
- Consider less expensive insulin dosage forms (e.g., vials) for patients 65+ who obtain syringe coverage

#### Ontario Ministry of Health's Ontario Drug Benefit (ODB) program

- Offers all ODB recipients on insulin [reimbursement for a flash glucose monitoring system](#) (specifically, the FreeStyle Libre<sup>®</sup> system), including:<sup>40</sup>
  - 1 reader/patient (otherwise costs \$65)
  - 33 sensors/year/patient (otherwise costs \$2,457.54/year)
- Offers all ODB recipients coverage for a set [number of blood glucose test](#) strips annually, depending on their diabetes management approach:<sup>41</sup>
  - 3,000 test strips/year for patients on insulin
  - 400 test strips/year for patients on non-insulin pharmacotherapy with higher risk of causing hypoglycemia (e.g., glyburide, gliclazide)
  - 200 test strips/year for patients on non-insulin pharmacotherapy with lower risk of causing hypoglycemia (e.g., acarbose, metformin, canagliflozin, empagliflozin, linagliptin, saxagliptin, sitagliptin)
  - 200 test strips/year for patients on diet/lifestyle therapy only



### Consider the environmental impact of insulin

The environmental impact of insulin is important to some patients.

Suggestions to reduce the environmental impact of insulin include:

- ✓ Consider reusable insulin pens instead of single-use, prefilled insulin pens if available (see [Insulin specific properties](#) tables for insulin products that have reusable pens that take cartridges)<sup>30,42,43</sup>
- ✓ Disposing of pens, syringes, needles and cartridges in a clearly-labeled, closable, puncture-resistant sharps container (can be obtained from a pharmacy) to prevent the disposal of 'sharps' into landfills<sup>43-45</sup>
- ✓ If patients are using insulin exceeding amount allowed in 1 injection, consider a more concentrated insulin formulation (less volume required) and counsel the patient on appropriate dosing to avoid overdose<sup>30,34,44,46</sup>
- ✓ Recycle the paper boxes, pamphlets and inserts packaged with insulin<sup>47</sup>





## SECTION C: Initiating and titrating insulin

### Practical tips for discussing insulin initiation with patients

- ✓ Start the insulin discussion early (e.g., at diagnosis and regular follow-up appointments)
- ✓ Ensure patients understand that insulin is not a punishment or indication of treatment failure, and that many patients end up on insulin later in life
- ✓ Consider patient values regarding the benefits/harms of adding insulin relative to the intensity of glycaemic control (e.g., some patients may opt for moderate control without insulin)
- ✓ Provide information on the benefits of insulin therapy (e.g., lower blood glucose, no gastrointestinal upset, reduces nocturnal urination secondary to hyperglycemia)
- ✓ Understand the patient's barriers or concerns about starting insulin
- ✓ Consider framing starting insulin as a "trial", with a set duration (e.g., 1 month), with a plan to discuss and adjust as needed
- ✓ To increase their confidence before starting injection(s), give the patient time to try different insulin pens and needles



#### Talking points

"For most people living with diabetes, insulin is required at some point in their life as part of their management plan."  
 "Since you are not feeling well now, adding insulin may help you feel better." (Offer the patient examples of their symptoms, e.g., blurred vision, fatigue, low energy, increased urination)  
 "The insulin needle injection hurts less than a fingerprick when checking blood glucose."  
 "Would you be open to trying insulin for 1 month to see how it works for you?"

### Insulin initiation checklist

Counsel patients on:

- ✓ Insulin injection frequency and timing
- ✓ Proper and safe insulin injection techniques, pen needle use and insulin storage
  - Consider connecting the patient to a qualified person/program to provide this counselling (e.g., Certified Diabetes Educator, Diabetes Education Program/Centre or collaborative support [registered nurse, nurse practitioner, pharmacist, dietitian] in the office or community). See [Local services for patients living with type 2 diabetes](#)<sup>1</sup>
- ✓ Hypoglycemia prevention and treatment (see [Managing hypoglycemia](#))
- ✓ Frequency of self-monitoring of blood glucose (See [Self-monitoring blood glucose frequency and pattern tool](#))<sup>48</sup>
- ✓ Options for blood glucose self-monitoring devices/systems (e.g., blood glucose meter, flash glucose monitoring system, continuous glucose monitoring system)
- ✓ Changes to current non-insulin pharmacotherapy dosing, if applicable (see [Insulin initiation and titration process](#))

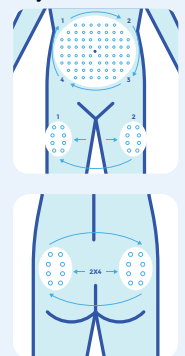
### Storing insulin<sup>49, 50</sup>

- Unopened insulin:
  - Should be stored in the fridge between 2°C and 8°C
  - Is safe to use until the expiration date
- In-use insulin:
  - Should be stored at room temperature, avoiding contact with direct sunlight
  - Is safe to use for up to 28 days (detemir and glargine 300 units/mL are safe at room temperature for 42 days, and degludec is safe at room temperature for 56 days) - counsel patient to write the first date of use on the label
- Discard insulin that has been frozen, kept out of the fridge for longer than the specified period, exposed to temperatures greater than 30°C or expired

### Safe insulin injection techniques and pen needle use<sup>51</sup>

- Injection sites and rotation (proper injection technique can significantly improve A1C and reduce erratic insulin effects and hypoglycemia)
  - Divide injection area into zones, use 1 zone per week and move clockwise, spacing out each injection within any zone by 1-2 cm
  - Avoid intramuscular injection
    - Abdomen, thighs and buttocks are the preferred self-injection areas
    - Avoid the arms
  - Avoid injecting within 2-3 cm of the umbilicus
  - Avoid injecting in altered skin (e.g., skin with surgical scars, stretch marks, lipohypertrophy, tattoos, moles, skin conditions)
- Pen needles
  - Insulin should be brought to room temperature before injecting
  - Inject pen needles at a 90° angle
  - Avoid reusing pen needles or syringes
  - Use pen needle sized 4-6 mm for all patients regardless of body mass index (4 mm pen needles provide the equivalent A1C control as both as 8 mm and 12 mm pen needles in people with obesity who are taking large doses of insulin)<sup>52</sup>
- See [FIT technique plus](#)<sup>ii</sup> for a series of patient educational tools on best practice injection technique and pen needle use

Injection site rotation

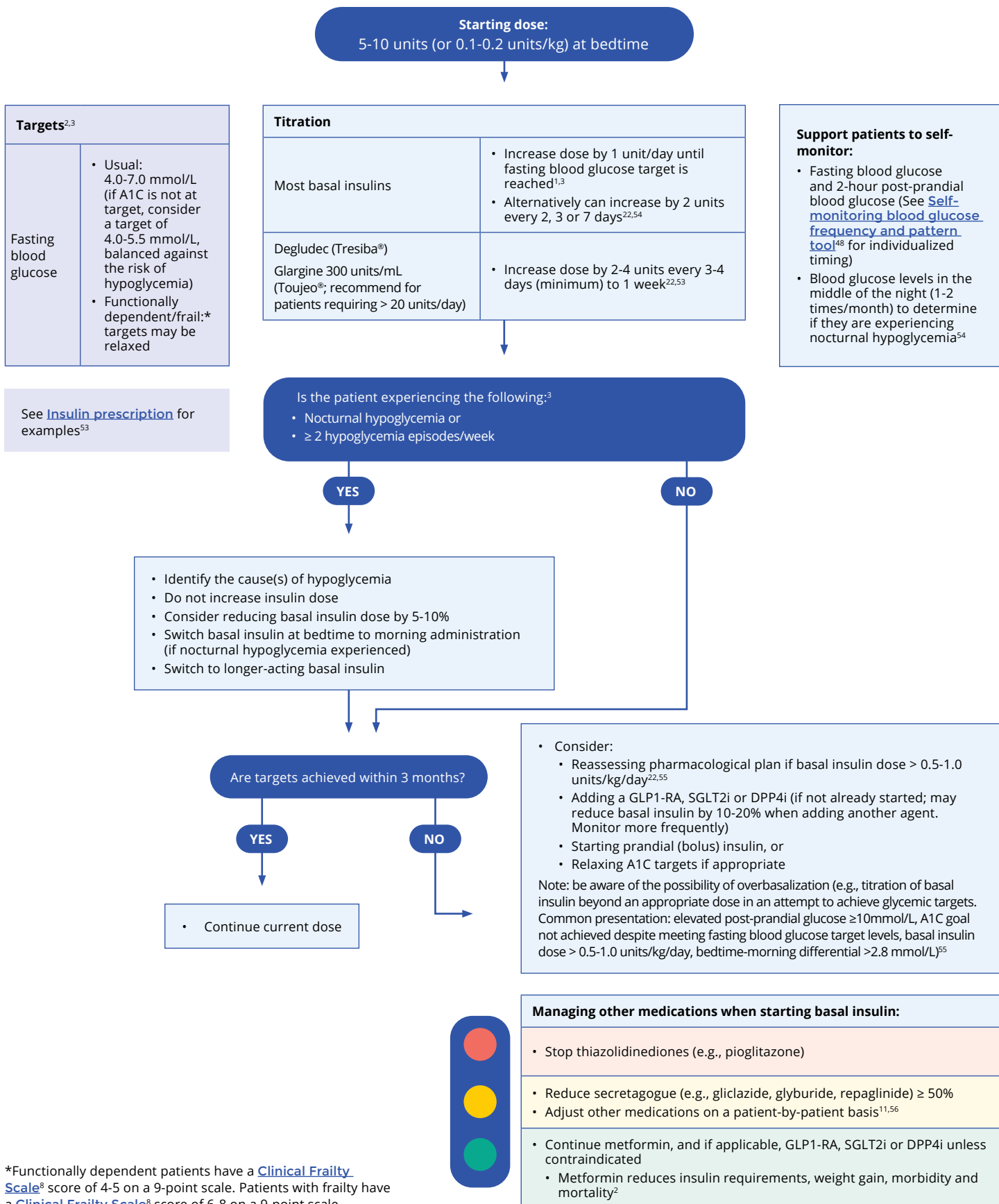


Pen needle wear after use



**SECTION C: Initiating and titrating insulin (continued)**

**Insulin initiation and titration process - Basal insulin**



**SECTION C: Initiating and titrating insulin (continued)**

**Insulin initiation and titration process - Prandial (bolus)**

**Usual approach – add prandial to basal insulin**

- Maintain basal insulin dose
  - Use clinical judgment; may need to reduce basal insulin by 10-20% when adding prandial insulin based on blood glucose and hypoglycemia risk
- Add prandial insulin, starting with one meal/day\* containing containing largest amount of carbohydrates (see [Glycemic index food guide](#)<sup>11</sup>)
  - Starting dose = 10% of basal dose

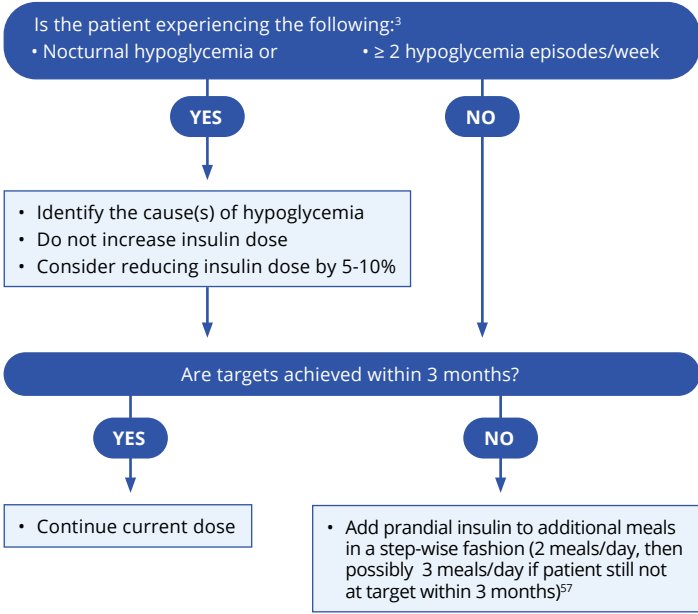
Targets <sup>2,3</sup>	
Fasting blood glucose	<ul style="list-style-type: none"> <li>• Usual: 4.0-7.0 mmol/L (if A1C is not at target, consider a target of 4.0-5.5 mmol/L, balanced against the risk of hypoglycemia)</li> <li>• Functionally dependent/ frail:** targets may be relaxed</li> </ul>
Pre-prandial blood glucose	<ul style="list-style-type: none"> <li>• Usual: 4.0-7.0 mmol/L</li> <li>• Functionally dependent:** 5.0-8.0 mmol/L</li> <li>• Frail/dementia:** 6.0-9.0 mmol/L</li> </ul>
Post-prandial blood glucose	<ul style="list-style-type: none"> <li>• Usual: 5.0-10.0 mmol/L</li> <li>• Functionally dependent:** &lt; 12.0 mmol/L</li> <li>• Frail/dementia:** &lt; 14.0 mmol/L</li> </ul>

Titration	
Adjust one insulin at a time	
Prandial (bolus) insulin	<ul style="list-style-type: none"> <li>• Increase dose by 1-2 units/week until pre- and post-prandial blood glucose targets reached<sup>11</sup></li> </ul>
Basal insulin (existing regime)	<ul style="list-style-type: none"> <li>• Increase dose by 1 unit/day until fasting blood glucose target is reached<sup>1,3</sup></li> <li>• Alternatively can increase dose by 2 units every 2, 3 or 7 days<sup>22,54</sup></li> <li>• For degludec (Tresiba®), Glargine 300 units/mL (Toujeo®) – increase by 2-4 units every 3-4 days (minimum) to 1 week<sup>22,53</sup></li> </ul>

**Example (100 kg patient)**

- Basal dose = 0.5 units/kg = 50 units
- Prandial (bolus) dose = 5 units/meal (starting with meal containing largest amount of carbohydrates)

See [Insulin prescription](#) for examples<sup>53</sup>



**Support patients to self-monitor:**

- Fasting blood glucose and 2-hour post-prandial blood glucose (See [Self-monitoring blood glucose frequency and pattern tool](#)<sup>48</sup> for individualized timing)
- Blood glucose levels in the middle of the night (1-2 times/month) to determine if they are experiencing nocturnal hypoglycemia<sup>54</sup>

**Other approaches**

- Start prandial insulin with all 3 meals
  - Calculate the total daily insulin (TDI) dose as 0.3-0.5 units/kg, then distribute:
    - 40-50% of TDI as basal
    - 50-60% of TDI as prandial
- Start premixed insulin (see [Premixed insulin](#))
- Basal and prandial (bolus) insulin may be started together if the patient's blood glucose level is high (>16.7 mmol/L) and metabolic decompensation is present at initial diagnosis<sup>1</sup>

**Example (100 kg patient)**

- TDI = 0.5 units/kg = 50 units
- Basal dose (50% of TDI) = 25 units daily
- Prandial (bolus) dose (50% of TDI) = 25 units daily (split over 3 meals, 8 units/meal, starting with the meal containing largest amount of carbohydrates)

\*As effective as starting prandial insulin at all meals, but with lower risk of hypoglycemia and greater patient satisfaction at 1 year<sup>57</sup>

\*\* Functionally dependent patients have a [Clinical Frailty Scale](#)<sup>8</sup> score of 4-5 on a 9-point scale. Patients with frailty have a [Clinical Frailty Scale](#)<sup>8</sup> score of 6-8 on a 9-point scale.



**Managing other medications when starting prandial (bolus) insulin:**

- Stop sulfonylureas, meglitinides and fixed-ratio combinations<sup>2</sup>
- Continue metformin, and if applicable, GLP1-RA, SGLT2i or DPP4i unless contraindicated
- Metformin reduces insulin requirements, weight gain, morbidity and mortality<sup>2</sup>

**SECTION C: Initiating and titrating insulin (continued)**

**Insulin initiation and titration process**

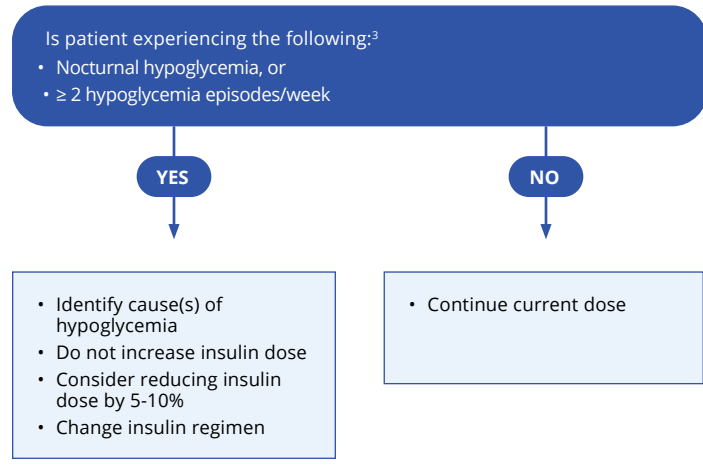
**Premixed insulin**

**GLP1-RA + insulin combinations**

Starting dose and titration	
Premixed regular/NPH (Humulin® 30/70) (Novolin®ge 30/70, 40/60, 50/50)	<ul style="list-style-type: none"> <li>Have the patient monitor blood glucose a minimum of 4 times/day for 1 week to determine the appropriate premixed insulin to use<sup>54</sup></li> <li><b>Starting dose:</b> <ul style="list-style-type: none"> <li>Patients currently on basal insulin or not on insulin:                             <ul style="list-style-type: none"> <li>Start on 5-10 units 1-2 times/day (pre-breakfast and/or dinner, premixed regular/NPH insulins need to be given 30 mins pre-meal)</li> </ul> </li> <li>Patients currently on basal and prandial (bolus) insulin:                             <ul style="list-style-type: none"> <li>Divide current basal dose into 2/3 pre-breakfast and 1/3 pre-dinner OR 1/2 pre-breakfast and 1/2 pre-dinner (premixed regular-NPH insulins need to be given 30 mins pre-meal)</li> <li>Consider a dose 10-20% lower than current basal and prandial (bolus) doses<sup>58</sup></li> </ul> </li> </ul> </li> <li><b>Titration:</b> <ul style="list-style-type: none"> <li>Dose titration depends on clinical judgment</li> <li>Suggest increasing pre-breakfast OR pre-dinner dose by 1 unit/day until pre-prandial blood glucose targets are reached<sup>53</sup></li> </ul> </li> </ul>
Aspart/aspart protamine suspension (Novomix® 30)	
Lispro/lispro protamine suspension (Humalog® Mix25, Mix50)	

Starting dose and titration	
Degludec/liraglutide (Xultrophy®)	<ul style="list-style-type: none"> <li>Starting dose: 16 units daily</li> <li>Titration: increase by 2 units every 3-4 days based on fasting blood glucose</li> </ul>
Glargine/lixisenatide (Soliqua®)	

Targets <sup>2,3</sup>	
Fasting blood glucose	<ul style="list-style-type: none"> <li>Usual: 4.0-7.0 mmol/L (if A1C is not at target, consider a target of 4.0-5.5 mmol/L, balanced against the risk of hypoglycemia)</li> <li>Functionally dependent/frail:* targets may be relaxed</li> </ul>
Pre-prandial blood glucose	<ul style="list-style-type: none"> <li>Usual: 4.0-7.0 mmol/L</li> <li>Functionally dependent:* 5.0-8.0 mmol/L</li> <li>Frail/dementia:* 6.0-9.0 mmol/L</li> </ul>
Post-prandial blood glucose	<ul style="list-style-type: none"> <li>Usual: 5.0-10.0 mmol/L</li> <li>Functionally dependent:* &lt; 12.0 mmol/L</li> <li>Frail/dementia:* &lt; 14.0 mmol/L</li> </ul>



**Example (100 kg patient)**

- Basal dose = 100 units daily
- Premixed insulin
  - 2/3 pre-breakfast and 1/3 pre-dinner with 10-20% reduction = 55-60 units every pre-breakfast, 25-30 units every pre-dinner
  - 1/2 pre-breakfast and 1/2 pre-dinner with 10-20% reduction = 40-45 units 2 times/day

See [Insulin prescription](#) for examples<sup>53</sup>

**Support patients to self-monitor:**

- Fasting blood glucose and 2-hour post-prandial blood glucose (See [Self-monitoring blood glucose frequency and pattern tool](#)<sup>48</sup> for individualized timing)
- Blood glucose levels in the middle of the night (1-2 times/month) to determine if they are experiencing nocturnal hypoglycemia<sup>54</sup>
- Blood glucose at least 2 times/day to safely titrate premixed insulin<sup>3</sup>

**Managing other medications when starting premixed insulin:**

- Stop sulfonylureas (if on twice-daily premixed insulin), meglitinides, thiazolidinediones (e.g., pioglitazone) and duplicate insulins<sup>2,22</sup>
- Consider dose reduction of agents other than metformin
- Adjust other medications on a patient-by-patient basis<sup>11,56</sup>
- Continue metformin, and if applicable, GLP1-RA, SGLT2i or DPP4i unless contraindicated
  - Metformin reduces insulin requirements, weight gain, morbidity and mortality<sup>2</sup>



\*Functionally dependent patients have a [Clinical Frailty Scale](#)<sup>8</sup> score of 4-5 on a 9-point scale. Patients with frailty have a [Clinical Frailty Scale](#)<sup>8</sup> score of 6-8 on a 9-point scale.

## SECTION D: Switching insulin

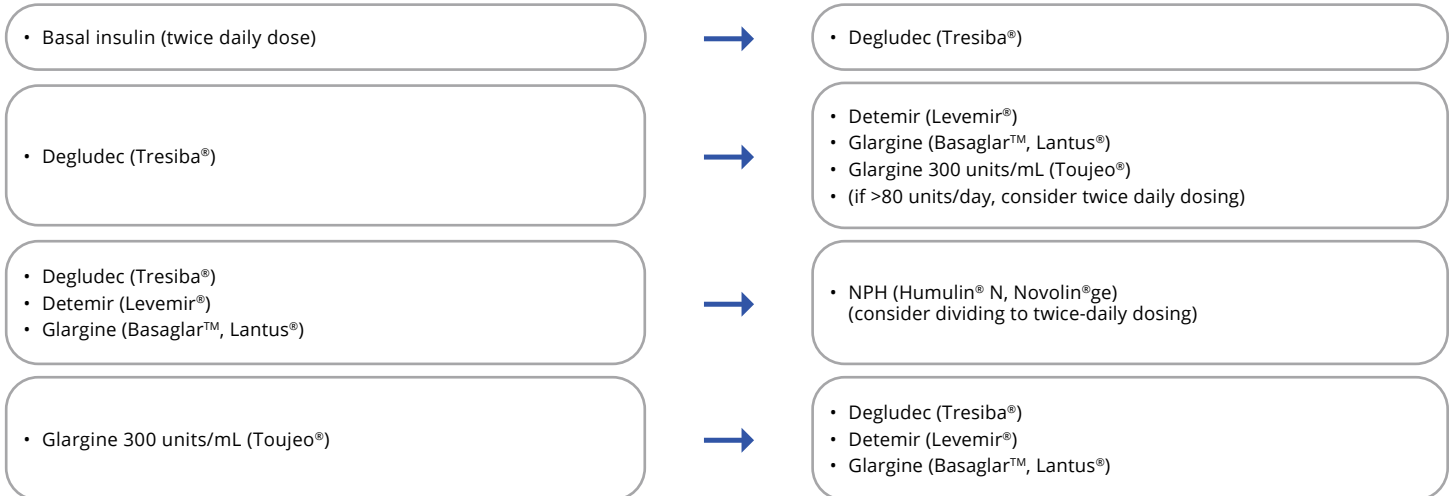
### How to switch insulin<sup>11,22</sup>

- Confirm current insulin dose, including agent, concentration and dosage form used
- Switching insulin often involves switching insulin pen devices
- Counsel patients to temporarily increase the frequency of blood glucose monitoring during switch
- Two approaches to switch insulin: 20% dose reduction or 'unit-to-unit'

#### 1. Switch insulin using a 20% dose reduction<sup>11,22</sup>

- **Use this technique (unless otherwise specified) to minimize the risk of hypoglycemia**
- May be used for the following insulin (100 units/mL unless otherwise specified)

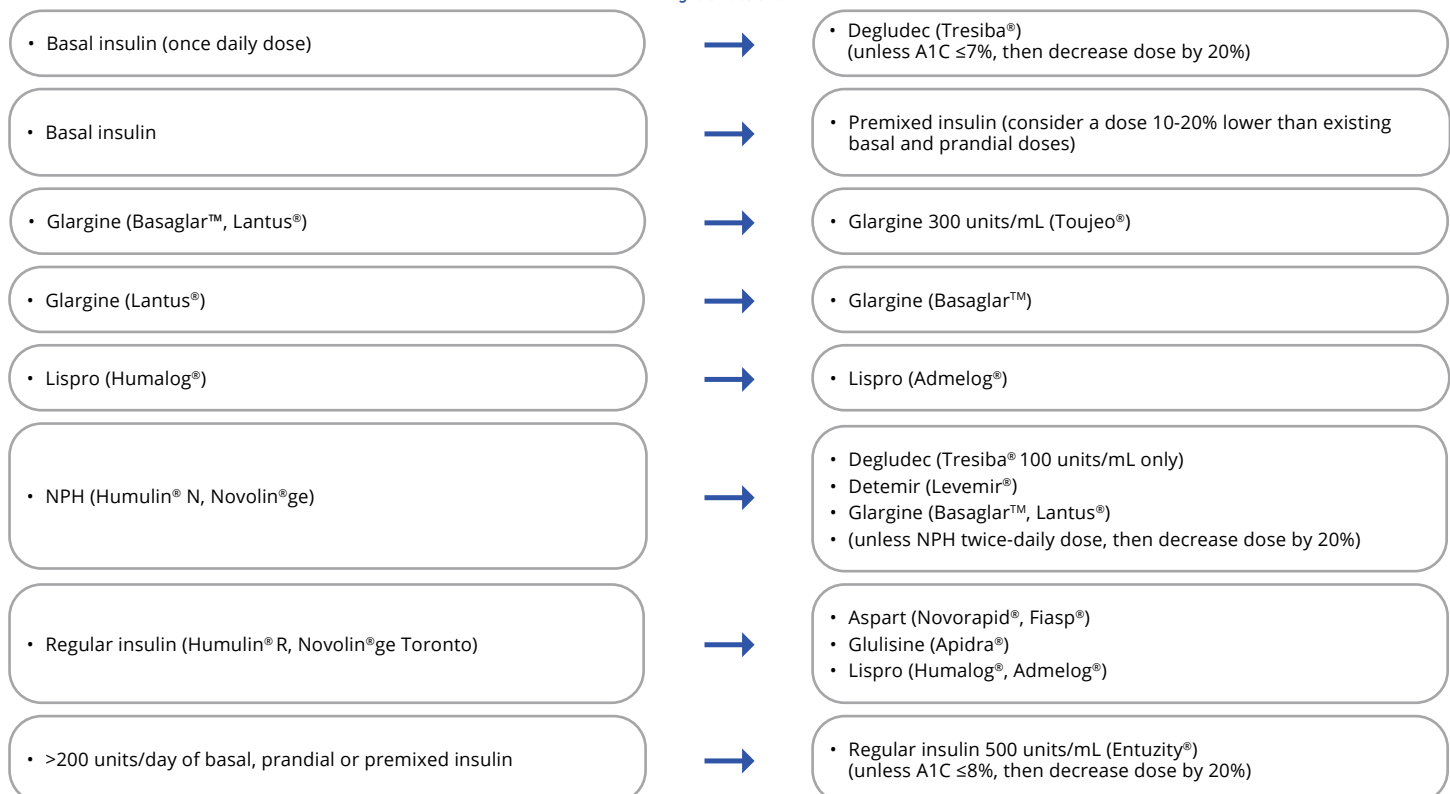
The insulin on the left may be switched to the insulin on the right using a 20% dose reduction



#### 2. Switch insulin 'unit-to-unit'<sup>11,22</sup>

- May be used for the following insulin (100 units/mL unless otherwise specified)

The insulin on the left may be switched to the insulin on the right 'unit to unit'



## Patient resources

- [i] [Centre for Effective Practice local services for patients living with type 2 diabetes](#)
- [ii] [Forum for Injection Technique \(FIT\) technique plus](#)
- [iii] [Diabetes Canada Glycemic index food guide](#)
- [iv] [Diabetes Canada Hypoglycemia low blood sugar in adults](#)
- [v] [RxFiles Type 2 diabetes and sick days: Medications to pause](#)
- [vi] [Diabetes Canada Drive safe with diabetes](#)
- [vii] [Diabetes Canada Air travel: Traveling can be a breeze if you follow a few tips](#)

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