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CLINICAL PRACTICE UPDATE IN
ENDOCRINOLOGY & DIABETES

Shifting Paradigms: Introducing Weekly Basal Insulin for Type 2 Diabetes

Alexander Abitbol MDCM, FRCPC
Endocrinologist, LMC
Toronto, Ontario, Canada

Diabetes is a significant public health problem in Canada, with an estimated 9% of the Canadian population diagnosed with the disease. Treatment options for type 2 diabetes (T2D) include lifestyle modification, antihyperglycemic agents, and insulin therapy. In the summer of 1921, Frederick Banting and Charles Best were the first to extract insulin from the pancreases of dogs and proved that it can lower blood glucose in dogs. Progressive advancements led to the evolution of basal insulins with new options emerging that had longer duration of actions. Now, just over 100 years after the discovery of insulin, a weekly basal insulin, icodec (Awiqli®), is finally available to patients in Canada. Icodec has the longest half-life of any approved basal insulins through its increased albumin binding. This practical option will also help clinicians overcome some of the barriers to insulin initiation and thus benefit more patients affected with diabetes.

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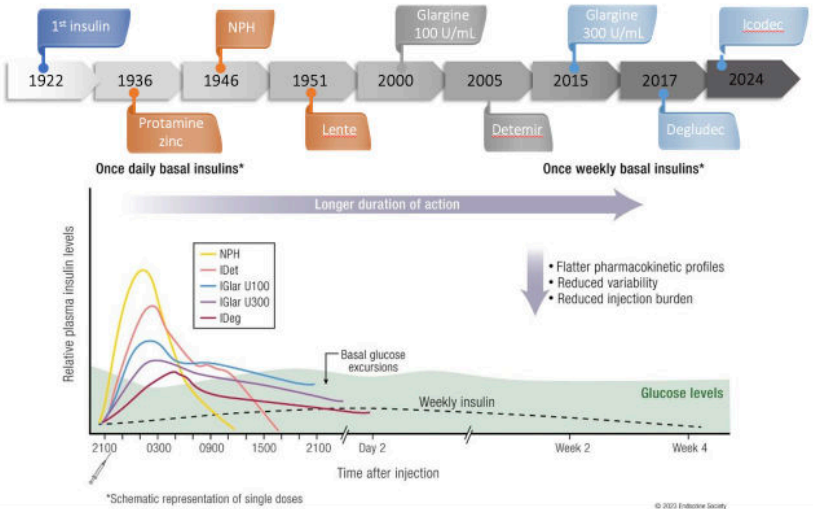
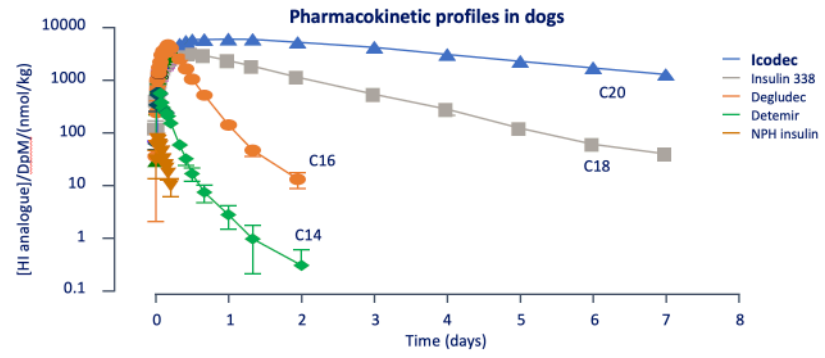
Evolution of Basal Insulins



Preclinical studies show increased albumin binding with icodec gives longer half-life



Initiating Insulin

Due to the progressive nature of diabetes, up to 40% of people with T2D eventually require insulin therapy. Unfortunately, clinical inertia is especially common with insulin initiation. A recent survey of Canadian family physicians found that the average A1C before starting insulin was 9.5%, and the mean time from diagnosis of T2D to insulin initiation was 9.2 years. The major barriers (identified by health care providers themselves) to insulin initiation included an overestimation by clinicians of their quality of care and adherence to guidelines, a fear of potential adverse effects (hypoglycemia and weight gain), and concerns over patient adherence and the ability to manage complex regimens. Insulin icodec may help overcome some of the barriers by providing greater convenience to patients, reduced clinical inertia, better adherence, less overwhelming sense of treatment, and will be easier for individuals with treatment regimens in need of medical/family assistance. The ONWARDS phase 3 clinical program has demonstrated the effectiveness and safety of insulin icodec.

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ONWARDS 1, 3 and 5 evaluated the benefits amongst insulin naïve individuals and demonstrated superior A1C reduction compared to daily basal insulin, and similar rates of clinically significant or severe hypoglycemia.

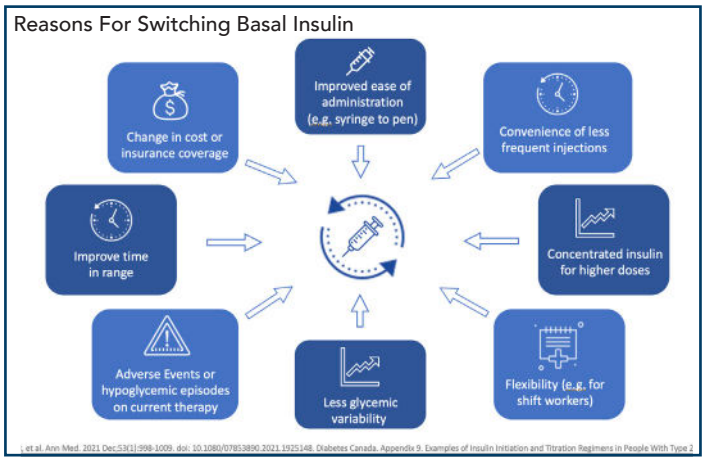
ONWARDS 1, 3 and 5 evaluated the benefits amongst insulin naïve individuals and demonstrated superior A1C reduction compared to daily basal insulin, and similar rates of clinically significant or severe hypoglycemia. The recommended starting dose of icodec is 70 units weekly. Patients are instructed to look at 3 pre-breakfast capillary blood glucose or continuous glucose monitor readings (2 days before and on day of titration), and target glucose between 4.4-7.2mmol/L. If mean glucose > 7.2mmol/L, it is recommended to increase dose of icodec by 20 units. If mean glucose <4.4 mmol/L, it is recommended to decrease dose of icodec by 20 units. In clinical practice, the titration values need to be individualized. A smaller titration increment of 10 units is also an option.

Switching Insulin

There are many reasons for switching an individual's basal insulin including an improved ease of administration (ex. hypodermic syringe to pen needle), adverse effects or hypoglycemic episodes on current therapy, the convenience of less frequent injections, flexible dosing options (ex: for shift worker), less glycemic variability, improved effectiveness (A1C/TIR), or changes in cost or insurance coverage. To switch from daily basal insulin to icodec, the current basal insulin dose is multiplied by 7. For the first dose, an extra 50% is administered as a loading dose (or 10.5x basal insulin dose). This one time additional dose is optional, depending on the patient's glycemic control and history of hypoglycemia (Awiqli® product monograph 2024). For the second week, 7x the daily basal insulin dose is adminis-tered. Starting in week 3, the dose of icodec administered in week 2 is titrated similarly to when starting icodec (as outlined above). Icodec is seven times concentrated (U-700) so the volume injected subcutaneously is similar to the volume injected with daily basal insulin. One unit of icodec provides the same glucose lowering as one unit of comparator daily basal insulins. Awiqli® is available

To switch from daily basal insulin to icodec, the current basal insulin dose is multiplied by 7.

Prescribe the 3ml pen when the dose of icodec exceeds 170 units weekly.



in 3 FlexTouch pens: 1ml (only available as sample), 1.5ml and 3ml. Prescribe the 3ml pen when the dose of icodec exceeds 170 units weekly.

ONWARDS 2 evaluated insulin-experienced participants with type 2 diabetes who switched basal insulin to weekly icodec or daily degludec. This trial demonstrated superior A1C reduction with icodec compared to degludec. There were similar rates of clinically signifi cant or severe hypoglycemia in both groups. Changes in diabetes treatment satisfaction questionnaire (DTSQ) scores favoured icodec over degludec. ONWARDS 4 evaluated insulin-experienced participants with type 2 diabetes treated with multiple daily injections (basal-bolus) of insulin who switched their basal insulin to weekly icodec or daily glargine U-100. This trial demonstrated a non-inferior A1C reduction and similar rates of clinically significant or severe hypoglycemic events for both groups.

Summary

Weekly insulin is now available in Canada. Icodec has demonstrated similar glucose-lowering efficacy and safety endpoints compared with first- and second-generation daily basal insulins, and better treatment satisfaction in the ONWARDS clinical trial program. The clinical discussion to start basal insulin is not an easy one to have with your patient. Breakthroughs in diabetes also don't come along very often. About 100 years after the discovery of insulin, a growing number of individuals today are still burdened with type 2 diabetes, many eventually require insulin therapy, and some are still developing diabetes-related complications due to poor glycemic control. Icodec is positioned to prevent complications by combating clinical inertia to insulin initiation and overcoming poor adherence through its more convenient week-ly administration.

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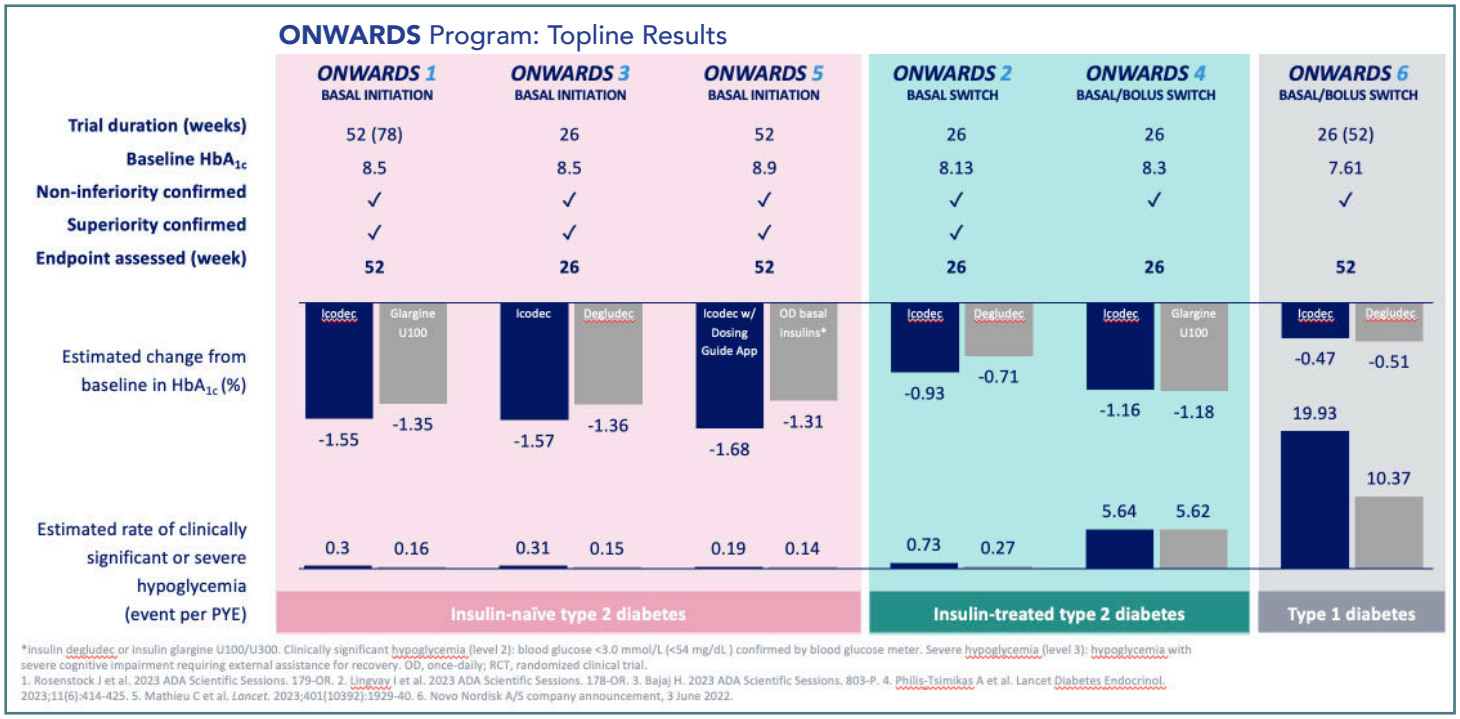
Individuals who are start insulin earlier and more appropriately, and establish better adherence to therapy will maintain adequate glycemic control and, ultimately, develop fewer complications from diabetes.



*insulin degludec or insulin glargine U100/U300. Clinically significant hypoglycemia (level 2): blood glucose <3.0 mmol/L (<54 mg/dL) confirmed by blood glucose meter. Severe hypoglycemia (level 3): hypoglycemia with severe cognitive impairment requiring external assistance for recovery. OD, once-daily; RCT, randomized clinical trial.

1. Rosenstock J et al. 2023 ADA Scientific Sessions. 179-OR. 2. Lingvay I et al. 2023 ADA Scientific Sessions. 178-OR. 3. Bajaj H. 2023 ADA Scientific Sessions. 803-P. 4. Philis-Tsimikas A et al. Lancet Diabetes Endocrinol. 2023;11(6):414-425. 5. Mathieu C et al. *Lancet*. 2023;401(10392):1929-40. 6. Novo Nordisk A/S company announcement, 3 June 2022.

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