



## Long shot: Can weekly insulin replace daily doses?

### CLINICAL QUESTION

**How does once-weekly insulin icodec compare to daily long-acting insulins in type 2 diabetes?**

### BOTTOM LINE

**Once-weekly insulin icodec is as effective as daily long-acting insulin (glargine or degludec) in lowering hemoglobin A1c (HbA1c). Safety and hypoglycemia risk appear similar, though data are limited for patients or situations at risk for hypoglycemia such as sick days or in frail patients.**

### EVIDENCE

- Results statistically significant unless mentioned otherwise.
- Eleven systematic reviews of randomized controlled trials (RCTs).<sup>1-11</sup> Focus on participant-level meta-analysis looking at major RCTs of type 2 diabetics (5 RCTs, 526–1,085 participants):<sup>11</sup>
  - 3765 participants (mean age ~60, baseline HbA1c 8.6%, 86% on metformin, ~70% insulin naive) randomized to weekly insulin icodec or to daily glargine or degludec insulin for 26 to 78 weeks. Insulin titrated to fasting morning blood glucose of 4.7-7.2mmol/L. Non-insulin antidiabetic agents allowed except for sulfonylureas and glinides (example repaglinide) which were stopped or reduced.
    - Change in HbA1c from baseline: -1.45% (icodec) versus -1.25% (control). Difference of 0.2% not clinically relevant.<sup>12</sup>

- Proportion of participants achieving A1c <7.0%: 49% versus 40% (control). Number Needed to Treat (NNT)=11.
- Significant hypoglycemia (blood glucose <3mmol/L): 1.15 versus 1.00 (control) episodes/year.
- Hypoglycemia requiring assistance: 0.007 versus 0.01 (control) episodes/year.
- Limitations: RCTs industry funded; all but one RCT open-label; no other patient-oriented outcomes; low number of moderate or severe hypoglycemic events.
- Other systematic reviews found similar.<sup>1-10</sup>

## CONTEXT

- Insulin icodec (Awiqli™ 700 units/mL, 2100units/pen) is an ultra-long-acting insulin approved for treating diabetes mellitus in adults.<sup>13</sup>
- In insulin naive patients, initial recommended dosage is 70 units once per week, equivalent to 10 units daily.<sup>13</sup> Maximum dose per injection 700 units.
- When switching from another long-acting insulin, use the equivalent total weekly dose. A one-time 50% higher loading dose may be considered.<sup>13</sup>
- Data on risk and management of severe or prolonged hypoglycemia in certain situations is lacking (examples: elderly, acute illness, surgery).
- Icodec is more expensive than other long-acting insulins.<sup>14</sup> Approximate costs per month for 40 units/day or 280/week:
  - Glargine: \$55
  - Degludec: \$80
  - Icodec: \$90

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