



---

## “Ultralong”-acting insulin for diabetes: How long is long enough?

### CLINICAL QUESTION

In patients with diabetes (type 1 or 2), how does the “ultralong”-acting insulin degludec compare to long-acting or NPH insulin?

---

### BOTTOM LINE

In both type 1 and 2 diabetes, insulin degludec reduces the risk of severe hypoglycemia compared to insulin glargine [number needed to treat (NNT)=17-59]. The risk of symptomatic hypoglycemia is either similar, or at best lower with degludec (NNT=19-29), with no other differences in clinical outcomes or hemoglobin A1c.

### EVIDENCE

- Degludec versus glargine 100 units/mL:
  - Five systematic reviews<sup>1-5</sup> compared degludec to glargine in individuals with type 1 diabetes [4 randomized controlled trials (RCTs), 1477 patients] and type 2 diabetes (10-15 RCTs, 9619-16,328 patients) with follow-up 12 weeks to 2 years:
    - Hemoglobin A1c: Differences not clinically significant ( $\leq 0.1\%$ ).<sup>1-5</sup>
    - Hypoglycemia:
      - Severe (requiring assistance) hypoglycemia: Most showed relative risk reduction (RRR)  $\sim 30\%$ <sup>1,3,4</sup> with degludec, whereas another found no statistically significant difference.<sup>5</sup>

- Symptomatic hypoglycemia: Range from no statistical difference<sup>1,4</sup> to RRR 18%.<sup>2</sup>
    - E.g., in blinded RCTs:<sup>6-8</sup> NNT=17-59 for severe hypoglycemia and NNT=19-29 for overall hypoglycemia.
  - No differences in severe adverse events, treatment discontinuation, death, cardiovascular events, or weight gain.
- Limitations:
  - Some meta-analyses<sup>1,4</sup> included RCTs with thrice-weekly degludec and mixed insulins. Symptomatic hypoglycemia would be statistically different without these RCTs;
  - Review of type 1 diabetes excluded hypoglycemia outcomes from largest RCT;<sup>5</sup>
  - All RCTs industry-funded and only 3 were blinded.<sup>6-8</sup>
- Degludec versus glargine 300 units/mL (1 RCT, 924 patients): No difference in any outcome.<sup>9</sup>
- Degludec versus detemir:
  - Type 1 diabetes (2 RCTs, 806 patients): No differences except in 1 RCT in 1 out of 5 nocturnal hypoglycemia outcomes.<sup>5</sup>
  - Type 2 diabetes: No RCTs.<sup>3</sup>
- Degludec versus NPH insulin: No RCTs.<sup>1-5,10</sup>

## CONTEXT

- Insulin degludec's longer half-life (24 hours versus glargine's ~12) increases administration time flexibility,<sup>11</sup> but takes 3-4 days to see the full effect of dose changes (versus glargine's 1-2 days).
- Guidelines suggest degludec over detemir/glargine 100 units/mL to reduce hypoglycemia in both type 1 and 2 diabetes.<sup>11,12</sup>
- Detemir/glargine do not consistently reduce severe hypoglycemia versus NPH insulin, with similar efficacy.<sup>13</sup>
- Costs/15mL: Degludec \$135, detemir \$135, glargine (Basaglar®) \$90, NPH \$65.<sup>14</sup>

---

## REFERENCES

1. Zhang XW, Zhang XL, Xu B, *et al.* Acta Diabetologica. 2018; 55:429-41.
2. Liu W, Yang X, Huang J. Int J Endocrinol. 2018; 2018:8726046.
3. Holmes RS, Crabtree E, McDonagh MS. Diabetes Obes Metab. 2019; 21:984-92.
4. Zhou W, Tao J, Zhou X, Chen H. Diabetes Ther. 2019; 10:835-52.
5. Hemmingsen B, Metzendorf MI, Richter B. Cochrane Database Syst Rev. 2021; 3:CD013498.
6. Lane W, Bailey TS, Gerety G, *et al.* JAMA. 2017; 318:33-44.
7. Marso SP, McGuire DK, Zinman B, *et al.* N Engl J Med. 2017; 377:723-32.
8. Wysham C, Bhargava A, Chaykin L, *et al.* JAMA. 2017; 318:45-56.
9. Rosenstock J, Cheng A, Ritzel R, *et al.* Diabetes Care. 2018; 41:2147-54.
10. Semlitsch T, Engler J, Siebenhofer A, *et al.* Cochrane Database Syst Rev. 2020; 11:CD005613.
11. McGibbon A, Adams L, Ingersoll K, *et al.* Can J Diabetes. 2018; 42:S80-S87.
12. Lipscombe L, Butalia S, Dagupta K, *et al.* Can J Diabetes. 2020; 44:575-91.

## AUTHORS

**Ricky D Turgeon**, BSc(Pharm)  
ACPR PharmD, **Justin Weresch**,  
MD

*Authors do not have any conflicts of interest to declare.*

13. Allan GM, Virani AS. Tools for Practice #35 online publication. October 26, 2010 (updated January 29, 2018). Available at: [https://gomainpro.ca/wp-content/uploads/tools-for-practice/1528907129\\_updatedtftp35insulinanalogues.pdf](https://gomainpro.ca/wp-content/uploads/tools-for-practice/1528907129_updatedtftp35insulinanalogues.pdf). Accessed March 14, 2022.
14. Alberta College of Family Physicians. 2020 Pricing Document. Available at: <https://pricingdoc.acfp.ca/pricing/>. Accessed January 13, 2022.

---

**TOOLS FOR PRACTICE  
PROVIDED BY**



---

**IN PARTNERSHIP WITH**



**Tools for Practice** are peer reviewed and summarize practice-changing medical evidence for primary care. Coordinated by **Dr. G. Michael Allan** and **Dr Adrienne Lindblad**, they are developed by the Patients, Experience, Evidence, Research (PEER) team, and supported by the College of Family Physicians of Canada, and the Alberta, Ontario, and Saskatchewan Colleges of Family Physicians. Feedback is welcome and can be sent to [toolsforpractice@cfpc.ca](mailto:toolsforpractice@cfpc.ca). Archived articles can be found at [www.toolsforpractice.ca](http://www.toolsforpractice.ca)

*This communication reflects the opinion of the authors and does not necessarily mirror the perspective and policy of the College of Family Physicians of Canada.*