



# Refills

Your dose of drug information in between sessions

## Why does a recent guideline recommend against the use of DPP4 inhibitors such as linagliptin (Trajenta®) in people with type 2 diabetes?

**Conclusion: The American College of Physicians 2024 guideline advises against adding a DPP4 inhibitor (DPP4i) to metformin because they do not improve patient-important outcomes (morbidity, mortality). DPP4i are relatively costly and people are more likely to benefit from SGLT2 inhibitors (SGLT2i) or GLP1 agonists (GLP1a).**

The BC Provincial Academic Detailing (PAD) service continues to deliver the topic [T2DM Focused Update: SGLT2 Inhibitors & GLP1 Agonists](#). This topic highlights the evidence of SGLT2i and GLP1a in improving morbidity and mortality in people with type 2 diabetes.

- What does the 2024 guideline recommend?** The American College of Physicians recommends against adding a DPP4i to metformin in people with type 2 diabetes (strong recommendation).<sup>1</sup> Their systematic review demonstrates with high certainty that DPP4i do not improve cardiovascular or kidney outcomes or survival (refer to table below).<sup>2</sup> This review replicates findings of other systematic reviews published in 2021 and 2023.<sup>3,4</sup>
- What does linagliptin (Trajenta) cost?** The annual drug cost of linagliptin is ~\$940. For comparison, dapagliflozin costs ~\$270 per year, empagliflozin ~\$1090 and semaglutide subcutaneous 1 mg ~\$2960.<sup>5</sup>
- Can linagliptin (Trajenta) be used in renal impairment?** Based on small pharmacokinetic studies, no dosage adjustment is required in people with renal impairment.<sup>6</sup> However, linagliptin does not reduce the risk of progression of chronic kidney disease in people with type 2 diabetes.<sup>2</sup> Further, in a cohort study of older adults, new use of an SGLT2i was associated with a lower risk of acute kidney injury than DPP4i and SGLT2i can be initiated in patients with low eGFRs (20-30 mL/min/1.73<sup>2</sup>).<sup>7,8</sup> For more specific information, refer to the December 2022 PAD Refill [SGLT2 inhibitors in patients with reduced kidney function](#).
- How much does linagliptin (Trajenta) lower HbA1c?** When added to metformin in people with a baseline HbA1c of approximately 8%, a DPP4i lowers HbA1c by ~0.5%.<sup>9</sup>
- Is linagliptin (Trajenta) “insulin sparing”?** Compared to placebo, linagliptin reduces the daily insulin requirement by a small amount (1.6 units per day on average) at 1 year.<sup>10</sup> When added to usual care, 3 fewer people out of 100 in the linagliptin group had insulin initiated over 2 years of follow up compared to placebo.<sup>11</sup>

DPP4 inhibitors compared with placebo or usual care in people with type 2 diabetes <sup>2</sup>		
Death from any cause	RR 1.01 (95%CI 0.94 to 1.08)	no difference; high certainty of evidence
Major adverse cardiovascular events	RR 1.00 (95%CI 0.94 to 1.06)	
Hospitalization for heart failure	RR 1.06 (95%CI 0.96 to 1.17)	
Chronic kidney disease	RR 1.07 (95%CI 0.95 to 1.21)	

<sup>1</sup>QASEEM Ann Intern Med 2024 Apr 29 (PMID:38639546); <sup>2</sup>DRAKE Ann Intern Med 2024 Apr 19 (PMID:38639549); <sup>3</sup>Cochrane Database Syst Rev 2021;10:CD013650 (PMID: 34693515); <sup>4</sup>SHI BMJ 2023;381:e074068 (PMID:37024129); <sup>5</sup>McKesson Pharmacia; <sup>6</sup>Health Canada Drug Product Database Trajenta®; <sup>7</sup>ISKANDER CMAJ 2020;192:E351-60 (PMID:32392523); <sup>8</sup>BC PAD Service PAD Refill Dec 2022; <sup>9</sup>TSAPAS Ann Intern Med 2020;173:278-86 (PMID:32598218); <sup>10</sup>YKI-JARVINEN Diabetes Care 2013;12:3875-81 (PMID:24062327); <sup>11</sup>CARMELINA JAMA 2019;321:69-79 (PMID:30418475)