



Drug information question: Now that some of the newer type 2 diabetes medications are prioritized in patients with specific comorbidities, what do I need to know about sulfonylurea medications' glucose lowering effect, dose and cost?

The BC Provincial Academic Detailing (PAD) Service's 2021-2022 [Type 2 Diabetes Focused Update: SGLT2 Inhibitors and GLP1 Agonists](#)<sup>1</sup> addresses:

- Changes to available evidence and clinical practice guidelines, informing medication choices beyond HbA1c lowering.
- Clinical considerations which support treatment decisions including doses, adverse events, dosage forms, cost and coverage.

The [2020 Diabetes Canada Clinical Practice Guideline](#) continues to include sulfonylureas, by consensus, as an option for reducing glucose levels and improving HbA1c, while noting that sulfonylureas have no proven cardiorenal benefits.<sup>2</sup>

Glucose lowering effect and dosing:

- Sulfonylureas lower HbA1c by approximately 1-1.5%.<sup>3,4</sup>
- While they are approved by Health Canada and the US Food and Drug Administration with wide daily dosage ranges, (see table)<sup>5,6</sup> increasing to maximum daily doses does not typically lower HbA1c further compared to lower doses.<sup>3,7</sup>
- Gliclazide and glyburide are the most commonly prescribed sulfonylureas in British Columbia and they have similar mean elimination half-lives (10 hours, 16 hours for gliclazide MR) which are prolonged in renal impairment.<sup>8-10</sup>
- Diabetes Canada recommends that;<sup>2,11</sup>
  - Gliclazide can be used cautiously when eGFR < 60 mL/min. Reduce dose or avoid use if eGFR < 30 mL/min.
  - Glyburide should be avoided if eGFR < 60 mL/min.
  - Patients should be advised to temporarily hold sulfonylureas in cases of acute illness or dehydration (vomiting, diarrhea), as renal clearance is decreased and hypoglycemia risk is increased. [DC Sick Day List](#)

Hypoglycemia:

- Compared to other metformin drug combinations, metformin plus a sulfonylurea increases hypoglycemia risk.<sup>12</sup>
- Other patient factors that are associated with increased risk of sulfonylurea induced hypoglycemia include advanced age, renal impairment, and higher sulfonylurea doses.<sup>8,13</sup>
- Adding SGLT2 inhibitors or GLP1 agonists to sulfonylureas can enhance the risk of sulfonylurea induced hypoglycemia; when combining consider decreasing the dose of sulfonylurea.<sup>14,15</sup>
- Genetic polymorphisms of CYP2C9 may result in slower clearance of glyburide, and increased risk of hypoglycemia.<sup>8</sup>

Sulfonylureas <sup>8-10, 16</sup>			
Generic Name (Brand Name) Available Tablet Strengths	Dosage Range	Approximate Annual Drug Cost	BC PharmaCare Coverage
glyburide, glibenclamide (Diabeta®, generics) 2.5, 5 mg	1.25-20 mg/day	\$5-\$90	Regular Benefit
gliclazide (Diamicon®, generics) 80 mg	80-320 mg/day	\$35-\$150	Limited Coverage Plan W Regular Benefit
gliclazide MR (Diamicon MR®, generics) 30, 60 mg	30-120 mg/day	\$15-\$50	
glimepiride (Amaryl®, generics) 1, 2, 4 mg	1-8 mg/day	\$325-\$825	Non-Benefit

Practical tip: Gliclazide MR 60 mg tablets can be halved and used for the full 30 – 120 mg dosing range.<sup>10</sup>

<sup>1</sup>BC PAD Service 2021 T2DM Focused Update: SGLT2 Inhibitors & GLP1 Agonists; <sup>2</sup>Diabetes Canada Can J Diabetes 2020 (PMID: 32972640); <sup>3</sup>HIRST Diabetologia 2013 (PMID: 23494446); <sup>4</sup>TSAPAS Ann Int Med 2020 (PMID: 32598218); <sup>5</sup>Health Canada Drug Product Database; <sup>6</sup>US Food and Drug Administration Drugs@FDA; <sup>7</sup>US FDA Metformin Glyburide 2000 Review; <sup>8</sup>Health Canada Glyburide (Diabeta); <sup>9</sup>Health Canada Gliclazide (Diamicon); <sup>10</sup>Health Canada Gliclazide MR (Diamicon MR); <sup>11</sup>Diabetes Canada Can J Diabetes 2018 (PMID: 29650116); <sup>12</sup>COCHRANE 2019 CD012368; <sup>13</sup>VAN DALEM BMJ 2016 (PMID:27413017); <sup>14</sup>Health Canada Empagliflozin (Jardiance); <sup>15</sup>Health Canada Semaglutide (Ozempic); <sup>16</sup>Health Canada Glimepiride (Amaryl)