



Your dose of drug information in between details

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 metformin’s glucose lowering effect, formulations, dose and cost?

The BC Provincial Academic Detailing (PAD) Service's 2021-2022 [Type 2 Diabetes Focused Update: SGLT2 Inhibitors and GLP1 Agonists](#) 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 recommend metformin as a first-line medication due to its glucose-lowering efficacy, low risk of hypoglycemia and weight gain, tolerability and cost.¹ An [ongoing trial](#) is comparing the effect of metformin to an SGLT2 inhibitor on diabetes-related complications in people with early type 2 diabetes, with results expected in 2025.²

Glucose lowering effect and dosing:

- Metformin lowers HbA1c by approximately 0.9%.³
- Higher doses \geq 2000 mg per day lower HbA1c only modestly (by an additional 0.26%) compared to doses of 1000 to 1500 mg per day.⁴
- Gradual dose titration is recommended to improve gastrointestinal tolerance, e.g., initiating at half or one 500 or 850 mg immediate-release (IR) tablet per day, then increasing by 500 or 850 mg increments every one to two weeks.
- While 2550 mg is the maximum daily dose for metformin IR, practically, metformin 850 mg BID achieves most of the HbA1c lowering effect with a lower pill burden and at a low drug cost.
- Metformin doses should be reduced in people with $eGFR < 45$ mL/min/1.73m² (e.g., half the maximum dose) and should be discontinued if $eGFR < 30$ mL/min/1.73m².⁵

Formulations:

- Metformin is available as an immediate-release (IR) formulation dosed 2-3 times a day ([Glucophage®](#), generics) or as an extended-release (ER) formulation dosed once a day ([Glumetza®](#), generics).^{6,7}
- The HbA1c lowering effects of the IR and ER formulations are similar but the ER formulation costs 20 times more than the IR formulation.^{8,9}
- The 2005 US Food and Drug Administration Review of the ER formulation concluded that the adverse event profile was comparable to the IR formulation, including similar risks of diarrhea, flatulence and nausea.⁸
- A 2021 systematic review also could not differentiate between the formulations for most gastrointestinal adverse events with the exception of dyspepsia which favoured the ER formulation.⁹

Metformin Products ¹⁰		
Generic Name (Brand Name) Available Tablet Strengths	Approximate Annual Drug Cost	BC PharmaCare Coverage
metformin IR (Glucophage®, generics) 500 mg, 850 mg	\$20-\$40	Regular Benefit
metformin ER (Glumetza®, generics) 500 mg, 1000 mg	\$400-\$800	Non-Benefit

¹LIPSCOMBE Can J Diabetes 2020 (PMID: 32972640); ²<https://clinicaltrials.gov/ct2/show/NCT03982381>; ³TSAPAS Ann Int Med 2020 (PMID: 32598218); ⁴BC PAD Service 2015 Glucose Lowering Medications Type 2 Diabetes; ⁵KDIGO Kidney International Guideline 2020 (PMID: 32998798); ⁶Health Canada [Metformin IR \(Glucophage\)](#); ⁷Health Canada [Metformin ER \(Glumetza\)](#); ⁸US FDA 2005 Review [Metformin ER \(Glumetza\)](#); ⁹ABRILLA Diabetes Res Clin Pract 2021 (PMID: 33887354); ¹⁰BC PAD Service 2021 T2DM Focused Update: SGLT2 Inhibitors & GLP1 Agonists