Non-Insulin Pharmacotherapy *(Adapted from* ANTI-HYPERGLYCEMIC TYPE 2 DIABETES AGENTS: Drug Comparison Chart*)*[11]

Drug	A1C reduction %	Cardiovascular and Renal Outcomes	Weight	90 Day Cost*	Coverage	Exception Drug Status (EDS) Criteria
Metformin (Glumetza®)	1-1.5%	Decrease risk of MI in overweight patients greater than 120% ideal body weight; NNT=14 over 10.7 years (UKPDS-34) Observational follow up: decrease all-cause mortality NNT =14 per 100 patient years Decrease MI NNT=14 per 100 patient years (UKPDS-80)	Loss up to 2.9 kg over 4 years (Adopt)	500 mg 2 tabs BID: $9 850 mg BID: $6	Yes Part 1	N/A
				1000 mg SR daily: $120	No	
Gliclazide (Diamicron®)	1-1.5%	Neutral effect on CVD outcomes Microvascular benefit (ADVANCE, UKPDS-33)	Gain of 1.5-2.5 kg	30-120 mg MR daily: $6-12	Yes Part 1	N/A
				80 mg IR BID: $53		
DPP-4 Inhibitors						
Alogliptin (Nesina®)	0.5-0.7%	Neutral effect on mortality and CVD outcomes (TECOS, GRADE, SAVOR-TIMI 53, CARMELINA, EXAMINE)	Neutral effect or weight loss	6.25, 12.5, or 25 mg daily $208	No	N/A
Linagliptin (Trajenta®)				5 mg daily $225	Part 3 EDS	For the treatment of patients with type 2 diabetes who have previously been treated with metformin and a sulfonylurea. Should be used in patients with diabetes who are not adequately controlled on or are intolerant to metformin and a sulfonylurea, and for whom insulin is not an option.
Saxagliptin (Onglyza®)				2.5 mg daily $120 5 mg daily $144	Part 3 EDS	
Sitagliptin (Januvia®)				25, 50 or 100 mg daily $77	Part 3 EDS	
SGLT2 Inhibitors						
Canagliflozin (Invokana®)	0.5-0.7%	↓ MACE: NNT~ 220 per year (CANVAS)	Loss of 2-3 kg	100 or 300 mg daily $265	Part 3 EDS	For the treatment of patients with type 2 diabetes who have previously been treated with metformin and a sulfonylurea. Should be used in patients with diabetes who are not adequately controlled on or are intolerant to metformin and a sulfonylurea, and for whom insulin is not an option.

Drug	A1C reduction %	Cardiovascular and Renal Outcomes	Weight	90 Day Cost*	Coverage	Exception Drug Status (EDS) Criteria
		↓ CKD: NNT=23 over 2.6 years (CREDENCE)				
Dapagliflozin (Forxiga®)		↓ mortality: NNT=44 over 1.5 years (DAPA-HF) NNT=48 over 2.4 years (DAPA-CKD) MACE: Neutral (DECLARE but lower risk population) ↓ CKD: NNT = 19 over 2.4 years (DAPA-CKD) ↓ HF: NNT = 21 over 1.5 years (DAPA-HF)		5 or 10 mg daily: $65	Yes Part 1 (as of Aug 24, 2023)	*Note: important to continue to assess which PCH residents will actually benefit from dapagliflozin as the time to benefit from the evidence was 2-4 years. The required monitoring is also a critical component to consider.*
Empagliflozin (Jardiance®)		↓ Mortality: NNT=38 over 3.1 year (EMPA-REG) ↓ MACE NNT = 63 over 3.1 years (EMPA-REG) ↓risk of progression of CKD: EMPA-KIDNEY ↓ CV death and HF hospitalization NNT 19 over 1.3 years (EMPEROR Reduced)		10 or 25 mg daily: $255 12.5 mg (1/2 of 25 mg tab) daily $128	Part 3 EDS	For the treatment of patients with type 2 diabetes who have previously been treated with metformin and a sulfonylurea. Should be used in patients with diabetes who are not adequately controlled on or are intolerant to metformin and a sulfonylurea, and for whom insulin is not an option. **OR** As an adjunct to diet, exercise, and standard care therapy to reduce the incidence of cardiovascular (CV) death in patients with type 2 diabetes mellitus (T2DM) and established cardiovascular disease who have inadequate glycemic control, if the following criteria are met: • Patients have inadequate glycemic control despite an adequate trial of metformin • Patients have established cardiovascular (CV) disease as defined* in the EMPA-REG OUTCOME trial. ***NOTE: Established CV disease is defined on the basis of one of the following:** • History of myocardial infarction (MI) • Multi-vessel coronary artery disease in two or more major coronary arteries (irrespective of revascularization status) • Single-vessel coronary artery disease with significant stenosis and either a positive non-invasive stress test or discharged from hospital with a documented diagnosis of unstable angina within 12 months prior to selection

Drug	A1C reduction %	Cardiovascular and Renal Outcomes	Weight	90 Day Cost*	Coverage	Exception Drug Status (EDS) Criteria
						• Last episode of unstable angina > 2 months prior with confirmed evidence of coronary multi-vessel or single-vessel disease • History of ischemic or hemorrhagic stroke • Occlusive peripheral artery disease
GLP-1 Receptor Agonists						
Lixisenatide (Adlyxine®) *subcutaneous injection*	0.6-1.4%	MACE neutral: ELIXA	Loss of 1.6-3 kg	10 or 20 mcg daily $359	Part 3 EDS	For treatment of type 2 diabetes in combination with a basal insulin with or without metformin in patients who have been uncontrolled on, or are intolerant to, a sulfonylurea and metformin.
Dulaglutide (Trulicity®) *subcutaneous injection*		↓ MACE: NNT = 72 over 5.4 years (REWIND in patients with established CVD)		0.75 or 1.5 mg weekly $667	No	N/A
Liraglutide (Victoza®) *subcutaneous injection*		↓ Mortality: NNT=72 over 3.8 years (LEADER, GRADE) ↓ MACE: NNT = 53 over 3.8 years (LEADER)		1.2 mg daily $611 1.8 mg daily $917	No	N/A
Semaglutide (Ozempic®) *subcutaneous injection*	1.5-2%	↓ MACE: NNT = 44 over 2 years (SUSTAIN-6)	Loss of up to 4 kg in 2 years (SUSTAIN-6)	0.5 or 1 mg weekly $633	Part 3 EDS	For the treatment of type 2 diabetes in combination with metformin and a sulfonylurea, when diet and exercise plus dual therapy with metformin and a sulfonylurea do not achieve adequate glycemic control.
(Rybelsus®) 3mg, 7mg, 14mg oral tablets	1.1%	MACE: neutral (PIONEER-6)	Loss of up to 5kg in 1 year	3, 7, or 14 mg daily $681	No	N/A

CKD = chronic kidney disease, CVD = cardiovascular disease, HF = heart failure, MACE = major adverse cardiovascular event, NNT = number needed to treat; MI = myocardial infarct

*Cost obtained from Hypoglycemic Agents (page 8) Price Comparison of Commonly Prescribed Medications in Manitoba 2023 https://medsconference.files.wordpress.com/2023/05/price-comparison-commonly-rx-drugs-mb-may-9-2023.pdf and Manitoba Drug Interchangeability Formulary June 2023 https://residents.gov.mb.ca/file?id=6258244&key=LABEL_FILE_POLICY&index=0