ANTIHYPERGLYCEMIC DRUGS for type 2 diabetes

Dr. Pierre McCabe, 2024 — Diabetes Québec

Rx		Dosage Form	Strength and Dosage Schedule	eGFR (mL/min/1.73m²) < 15 or dialysis	eGFR (mL/min/1.73m²) 15–29	eGFR (mL/min/1.73m²) 30–44	eGFR (mL/min/1.73m²) 45–59	↓ A1C (add-on to MET)	Weight (add-on to MET)	Hypo Risk	Major Adverse Cardiovascular Events‡	Cardiorenal Benefits	RAMQ ⚜ reimbursement criteria: Monotherapy MET + SU Contraindicated or not tolerated	RAMQ ⚜ reimbursement criteria: In conjunction If the other agent is contraindicated, not tolerated, or ineffective: + MET	RAMQ ⚜ reimbursement criteria: In conjunction If the other agent is contraindicated, not tolerated, or ineffective: + SU	RAMQ ⚜ reimbursement criteria: Combination treatment **EN 150:** SU contraindicated, not tolerated or ineffective; MET stable for 1 month **EN 219:** Recognized indication for Empa; MET stable for 1 month — Cardiovascular criterion **EN 179:** In combination with other drugs; presence of MCAS or MVAS; A1C ≥ 7%	NIHB reimbursement criteria (Non-Insured Health Benefits program for First Nations and Inuit): Coverage	NIHB reimbursement criteria (Non-Insured Health Benefits program for First Nations and Inuit): Combination treatment coverage
1* Metformin	**GLUCOPHAGE** (Metformin)		500 - 850 mg BID/TID (max. 850 mg TID/1000 mg BID)		500 mg QD (do not initiate)	500 mg BID		–	Neutral	Rare	–	–	**Covered**	–	**Covered**	–	**Open Benefit**	–
	GLUMETZA (Metformin)		500 - 1000 mg QD (max. 2000 mg QD)			1000 mg QD		–		Rare			Private ins.	–	Private ins.	–	Not listed	–
SGLT2i	**INVOKANA** (Canagliflozin)		100 - 300 mg QD		Continue treatment	100 mg (Recommended for cardiorenal benefits. Lower glycemic efficacy.)		↓↓↓ 0.8 to 0.9%	↓↓ 3.3 to 4.0 kg	Rare	POSITIVE [1] (Established atherosclerotic cardiovascular disease)	↓ Hospitalization for heart failure[3] ↓ Progression of nephropathy[4]	**EN 167**	**EN 148**	**EN 149**	**Invokamet** 50 - 150/500 - 1000 | Private ins.	Limited Use Uncontrolled T2D and intolerance to MET and SU	**Invokamet** (Not listed)
	JARDIANCE (Empagliflozin)		10 - 25 mg QD	< 20 ml/min	10 mg Continue treatment	(Recommended for cardiorenal benefits. Lower glycemic efficacy.)		↓↓↓ 0.7 to 0.8%	↓↓ 2.1 to 3.1 kg	Rare			**EN 167**	**EN 148**	Private ins.	**Synjardy** 5 - 12.5/500 - 850 - 1000 | EN 219 **Jardiance** | EN 179	**Open Benefit**	**Synjardy Open Benefit**
	FORXIGA (Dapagliflozin)		5 - 10 mg QD		Continue treatment			↓↓↓ 0.5 to 0.8%	↓↓ 2.9 to 3.2 kg	Rare	NEUTRAL		Private ins.	**EN 148**	**EN 149**	**Xigduo** 5/850 - 1000 | EN 150	**Open Benefit**	**Xigduo Open Benefit**
INCRETINS — 2** GLP-1 RA	**VICTOZA** (s.c. Liraglutide)		0.6 mg QD x 1 week 1.2 mg QD x 1 week 1.8 mg QD (optional)	NR				↓↓↓↓ 1.0 to 1.5%	↓↓ 2.6 to 3.4 kg	Rare	POSITIVE [2] (Established atherosclerotic cardiovascular disease AND/OR >60 yo with 2 CV risk factors)	↓ Albuminuria[5]	**Exception drugs** Not at target + MET; BMI >30; DPP-4i is ineffective, contraindicated, and/or not tolerated. 12 months per authorization (first continuation: ↓ A1C ≥ 0.5% or a value ≤ 7%)			–	Not listed	–
	TRULICITY (s.c. Dulaglutide)		0.75 mg Q1W x 2 weeks 1.5 mg Q1W (optional)	Caution				↓↓↓↓ 1.0 to 1.4%	↓↓ 2.7 to 3.1 kg	Rare						–	Not listed	–
	OZEMPIC (s.c. Semaglutide)		0.25 mg Q1W x 4 weeks 0.5 mg Q1W x 4 weeks 1 mg Q1W (optional)	NR	Caution			↓↓↓↓↓ 1.3 to 1.6%	↓↓↓ 4.2 to 5.8 kg	Rare			**Exception drugs** In association with MET, where a SU is contraindicated, not tolerated or ineffective			–	**Open Benefit**	–
	RYBELSUS (oral Semaglutide)		3 mg QD x 30 days 7 mg QD x 30 days 14 mg QD (optional)	NR				↓↓↓↓ 1.0 to 1.3%	↓↓ 2.2 to 3.8 kg	Rare	NEUTRAL (superiority study ongoing)	–				–	Limited Use Uncontrolled T2D and intolerance to MET and SU	–
	AR GIP + GLP-1 — **MOUNJARO** (Tirzepatide)		2.5 mg Q1W x 4 weeks ↑2.5 mg Q1W x 4 weeks ad 5 mg, 10 mg or 15 mg Q1W (optional)					↓↓↓↓↓↓ 2.0 to 2.3 kg	↓↓↓↓ 7.6 to 11.2 kg	Rare	(ongoing study)	–	**Private ins.**			–	Not listed	–
	DPP-4i — **JANUVIA** (Sitagliptin)		100 mg QD		25 mg		50 mg	↓↓ 0.7%	Neutral	Rare	NEUTRAL	–	**EN 167**	**EN 148**	Private ins.	**Janumet** 50/500 - 850 - 1000 | **EN 150** **Janumet XR** 50/500 - 1000; 100/1000 | **EN 150**	Limited Use Uncontrolled T2D and intolerance to MET and SU	**Janumet** Limited Use Uncontrolled T2D and intolerance to MET and SU
	TRAJENTA (Linagliptin)		5 mg QD	Caution				↓↓ 0.5 %	Neutral	Rare			**EN 167**	**EN 148**	Private ins.	**Jentadueto** 2.5/500 - 850 - 1000 | EN 150	**Open Benefit**	**Jentadueto Open Benefit**
	NESINA (Alogliptin)		25 mg QD		6.25 mg		12.5 mg	↓↓ 0.6 %	Neutral	Rare			**EN 167**	**EN 148**	**EN 149**	**Kazano** 12.5/500 - 850 - 1000 |EN 150	Not listed	**Kazano** (Not listed)
	ONGLYZA (Saxagliptin)		5 mg QD	Caution		2.5 mg		↓↓ 0.7 %	Neutral	Rare		↑ Hospitalization for heart failure	Private ins.	**EN 148**	**EN 149**	**Komboglyze** 2.5/500 - 850 - 1000 | EN 150	**Open Benefit**	**Komboglyze Open Benefit**
Alpha-glucosidase	**GLUCOBAY** (Acarbose)		50 - 100 mg TID					↓↓ 0.6 %	Neutral	Rare	NEUTRAL	–	**Covered**	**Covered**	**Covered**	–	**Open Benefit**	–
Secretagogues	**DIABETA** (Glyburide)		2.5 - 5 mg QD/BID (max. 10 mg BID)			Caution		↓↓ 0.5 to 1.0 %	↑ 1.5 kg	✚✚	–		**Covered**	**Covered**	–	–	**Open Benefit**	–
	DIAMICRON (Gliclazide)		80 mg (max. 160 mg BID) MR 30 - 60 mg (max. 120 mg QD)	NR				↓↓ 0.5 to 1.0 %	↑ 1.5 kg	✚			**Covered**	**Covered**	–	–	**Open Benefit**	–
	AMARYL (Glimepiride)		1 - 2 - 4 mg (max. 8 mg QD)	NR	Caution			↓↓ 0.5 to 1.0 %	↑ 1.5 kg	✚✚	NEUTRAL		**EN 23**	**EN 23**	–	–	Not listed	–
	GLUCONORM (Repaglinide)		0.5 - 1 - 2 mg TID (max. 4 mg QID)	Caution				↓↓ 0.5 to 1.0 %	↑ 1.6 kg	✚	–		**Covered**	**Covered**	–	–	**Open Benefit**	–
TZD	**ACTOS** (Pioglitazone)		15 - 30 - 45 mg QD	Caution				↓↓↓↓ 0.9 to 1.5 %	↑↑ 1.5 to 2.8 kg	Rare	NEUTRAL	↑ Heart failure	**EN 121**	**EN 118**	**EN 119**	**EN 117** (For patients with CKD) **EN 120** (In combination with MET + SU when insulin is indicated, but the patient is unable to receive it)	**Open Benefit** (generic only)	–
	AVANDIA (Rosiglitazone)		2 - 4 - 8 mg QD	Caution				↓↓↓↓ 0.9 to 1.5 %	↑↑ 1.5 to 2.8 kg	Rare			**EN 121**	**EN 118**	**EN 119**		Not listed	–

		Rx	Pens pre-filled	Delivery System and Maximum Single Dose	Dosage † Initiation	Dosage † Titration	Dosage † Switch	Hypo Risk	RAMQ Coverage	SSNA Coverage	Duration of Action
BASAL INSULIN	Long-acting	**TRESIBA U100** (Degludec) **TRESIBA U200**		FlexTouch (max. 80 U) FlexTouch (max. 160 U)	10 U at any time of day	2 U every 3–4 days OR 4 U once a week until targets reached (4 to 7 mmol/L)	1:1 (↓ by 20% when switched from TOUJEO or twice daily insulin)	✚	**Covered**	**Open Benefit**	
		TOUJEO U300 (Glargine)		SoloSTAR (max. 80 U) DoubleSTAR (max. 160 U)	10 U at bedtime or in the morning	1 U QD until targets reached (4 to 7 mmol/L)	1:1 (↓ by 20% when switched from twice daily insulin)	✚	**Covered**	**Open Benefit**	
		LANTUS U100 (Glargine)		Cartridge SoloSTAR (max. 80 U)	10 U at bedtime or in the morning	1 U QD until targets reached (4 to 7 mmol/L)	1:1 (↓ by 20% when switched from TOUJEO or twice daily insulin)	✚✚	Private ins. (Plan dependent)	**Open Benefit**	
		BASAGLAR (Biosimilar glargine)		Cartridge KwikPen (max. 80 U)					**Covered**	**Open Benefit**	
		SEMGLEE (Biosimilar glargine)		Semglee (max. 80 U)					**Covered**	**Open Benefit**	
		LEVEMIR (Detemir)		Cartridge	10 U at bedtime or in the morning	1 U QD until targets reached (4 to 7 mmol/L)	1:1 (↓ by 20% when switched from twice daily insulin)	✚✚	**Covered**	**Open Benefit**	
	Intermediary	**HUMULIN N**		Cartridge KwikPen (max. 60 U)	10 U at bedtime	1 U QD until targets reached (4 to 7 mmol/L)	1:1	✚✚✚	**Covered**	**Open Benefit**	
		NOVOLIN NPH		Cartridge							

Glucose Infusion Rate (mg/kg/min) — Time (hr): 0, 12, 24, 36

- TRESIBA U100 | U200 > 42 h
- TOUJEO U300 up to 36 h
- LANTUS U100 | BASAGLAR 24 h
- LEVEMIR up to 24 h
- HUMULIN N | NOVOLIN NPH 12-18 h

Hirsch IB. N Engl J Med. 2005; 352:174-83. Flood TM. J Fam Pract. 2007; 56(suppl1):S1–S12. Becker RH et al. Diabetes Care. 2015; 38:637–43. Tim Heise. Expert Opinion on Drug Metabolism & Toxicology: 2015; 11:8, 1193-1201.

		Rx	Pens pre-filled	Delivery System and Maximum Single Dose	Onset	RAMQ Coverage	NIHB Coverage
MEALTIME INSULIN	Fast	**FIASP** (Faster aspart)		Cartridge FlexTouch (max. 80 U)	4 min	Private ins. (Plan dependent)	Not listed
		NOVORAPID (Aspart)		Cartridge FlexTouch (max. 80 U)	10-20 min	Private ins. (Plan dependent)	**Open Benefit**
		TRURAPI (Biosimilar aspart)		Cartridge SoloSTAR (max. 80 U)		**Covered**	**Open Benefit**
		KIRSTY (Biosimilar aspart)		Kirsty (max. 80 U)		**Covered**	**Open Benefit**
		HUMALOG U100 (Lispro) **HUMALOG U200**		Cartridge KwikPen (max. 60 U) KwikPen (max. 60 U)	10–15 min	Private ins. (Plan dependent) **Covered**	**Open Benefit**
		ADMELOG (Biosimilar lispro)		Cartridge SoloSTAR (max. 80 U)		**Covered**	**Open Benefit**
		APIDRA (Glulisine)		SoloSTAR (max. 80 U)		**Covered**	**Open Benefit**
	Regular	**HUMULIN R**		Cartridge KwikPen (max. 60 U)	30 min	**Covered**	**Open Benefit**
		NOVOLIN GE TORONTO		Cartridge			

Recommendations based on Diabetes Canada guidelines.
1 * Metformin is the first line of treatment. **2**** SGLT2i and GLP-1 RA should be favoured after metformin in patients with CV comorbidity and/or in poorly controlled patients in whom it is desirable to promote CV benefits and/or weight loss while minimizing the risk of hypoglycemia.
† Patients on insulin should have an individualized fasting glucose targets. ǂ 3-point MACE is defined as a composite of nonfatal stroke, nonfatal myocardial infarction, and cardiovascular death.
Results of CV studies (evidence level A and B in italic). **1)** ↓ in MACE: if established Atherosclerotic Cardiovascular Disease OR if CKD. **2)** ↓ in MACE: if established Atherosclerotic Cardiovascular Disease OR if >60 yo with 2 risk factors (tobacco, HBP, DLD, obesity) OR if CKD. **3)** ↓ in Hospitalization for Heart Failure: if history of Heart Failure OR if CKD OR if established Atherosclerotic Cardiovascular Disease OR if >60 yo with 2 CV risk factors. **4)** ↓ progression of nephropathy: if CKD OR if established Atherosclerotic Cardiovascular Disease. **5)** ↓ Albuminuria: if established Atherosclerotic Cardiovascular Disease.

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CAD: coronary artery disease | **CKD**: chronic kidney disease | **CV**: cardiovascular | **DLD**: dyslipidemia | **eGFR**: estimated glomerular filtration rate | **HBP**: high blood pressure | **MET**: metformin | **NR**: not recommended **PAD**: peripheral artery disease | **QD**: once per day | **Q1W**: once weekly | **QID**: four times a day | **s.c.**: subcutaneous | **SU**: sulfonylurea
Reference: Efficacy on A1C and weight lowering data as add-on to metformin have been taken from product monographs or from head-to-head trials.
This guide reflects current standards and the author's opinion, Dr. Pierre McCabe, specialist in general internal medicine. It does not replace clinical judgement and should only be used as a reference. Some products are not represented on the chart as they are rarely prescribed. | 2020 © Photos by Vigilance Santé inc.