Appendix D: Commonly Used Antihyperglycemic Agents and Adjunctive Agents for Use in Type 2 Diabetes[a]

Generic Name *Trade Name* Dosages	Adult Dosage	Cost/ 30 days[b]	PharmaCare Coverage	Therapeutic Considerations
Biguanides				
Metformin *Glucophage, G* Tabs: 500, 850 mg *Glumetza, G* ER tabs: 500, 1000 mg	**Initial**: 250 or 500 mg PO BID **Usual**: 1000 mg PO BID **Maximum**: 2550 mg/day[1] ER tabs: **Initial**: 1000 mg PO daily **Usual**: 2000 mg PO daily **Maximum**: 2000 mg PO daily	*G*: $3 *ER tabs*: $70	Regular benefit ER tabs: Non-benefit	**Pros**: first line drug for type 2 diabetes; low rates of hypoglycemia; weight loss (2.9 kg/4 years), lowers A1C by 1-1.5%, decrease mortality and MI. [2,3,4] **Cons**: GI side effects including diarrhea and nausea, Vitamin B12 deficiency. Use with caution / reduce dose if eGFR < 60 mL/min/1.73m^2.[1] **Administration**: Take with food to reduce GI side effects. ER tabs should be taken once daily with the evening meal. **Contraindications**: eGFR < 30 mL/min/1.73m^2, hepatic or cardiac failure.[1] **Notes**: Hold during acute illnesses associated with risk for dehydration or procedures associated with high risk of acute kidney injury.[2] Metformin: doses ≥ 2000 mg per day reduced A1C by an additional 0.26% compared to lower doses (1000 to 1500 mg per day); lactic acidosis 0.03 cases per 1000 patient years.[5]
Insulin Secretagogues, Sulfonylureas				
Glyburide *G* Tabs: 2.5, 5 mg	**Initial**: 5 mg PO daily **Usual**: 2.5-20 mg PO daily (divide BID if >10 mg) **Maximum**: 20 mg/day	$4	Regular Benefit	**Pros:** cost effective as a second line agent if patient has no CVD; extensive clinical experience, lowers A1C by 1-1.5%.[4] **Cons:** weight gain (1.5-2.5 kg), higher risk of hypoglycemia, especially in older or frail patients.[1] **Contraindications:** eGFR < 60 mL/min/1.73m^2 (glyburide), eGFR < 30 mL/min/1.73m^2 (gliclazide, glimepiride). **Notes**: Trials have shown microvascular benefit and similar, neutral CV outcomes with glimepiride when compared to linagliptin.[4]
Gliclazide *Diamicron, G* Tabs: 80 mg, *Diamicron MR, G* MR tabs: 30, 60 mg	**Initial**: 80-160 mg PO daily **Usual**: 80-320 mg PO daily (≥160 mg divide BID) **Maximum**: 320 mg/day MR Tabs: **Initial**: 30 mg PO daily at breakfast **Usual**: 30-120 mg PO daily **Maximum**: 120 mg/day	*G*: $6 *MR tabs*: $5	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	
Glimepiride *G* Tabs: 1, 2, 4 mg	**Initial**: 1 mg PO daily **Usual**: 1-4 mg PO daily **Maximum**: 8mg/day	$35	Non-benefit	

Generic Name *Trade Name* Dosages	Adult Dosage	Cost/ 30 days[b]	PharmaCare Coverage	Therapeutic Considerations
Sodium-Glucose Cotransporter 2 Inhibitors				
Empagliflozin *Jardiance* Tabs**:** 10, 25 mg	**Initial**: 10 mg PO daily in the am **Maximum**: 25 mg PO daily in the am	$90	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	**Pros**: reduce risk of major adverse cardiovascular events and death from any cause in patients with T2DM and CV risk factors, decrease risk of end stage kidney disease, demonstrated benefit for cardiorenal outcomes, reduce risk of hospitalization for heart failure and the progression of chronic kidney disease, weight loss (2-3 kg), low rates of hypoglycemia.[4,12] **Cons**: modest improvement in A1C (0.5-0.8%), decreased bone mineral density and increased risk of bone fractures (canagliflozin), reports of euglycemic diabetic ketoacidosis, volume depletion (more in age > 65 years), genital mycotic infections, UTI, increased LDL, glucose lowering is independent of beta cell function and insulin sensitivity.[4,9] **Contraindications**: pregnancy, renal impairment (refer to product monograph for details), dialysis.[9] **Notes**: SGLT2 inhibitors should not be used in individuals with type 1 diabetes or in individuals with type 2 diabetes who have factors predisposing to diabetic ketoacidosis.[9]
Empagliflozin plus Metformin *Synjardy* Tabs: 5/500 mg, 5/850 mg, 5/1000 mg, 12.5/500 mg, 12.5/850 mg, 12.5/1000 mg		$90	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	
Empagliflozin plus Linagliptin *Glyxambi* Tabs: 25/5 mg		$155	Non-benefit	
Canagliflozin *Invokana* Tabs: 100, 300 mg	**Initial**: 100 mg PO daily in the am **Maximum:** 300 mg PO daily	$95	Non-benefit	
Canagliflozin plus Metformin *Invokamet* Tabs: 50/500 mg, 50/1000 mg, 150/500 mg, 150/1000 mg		$110	Non-benefit	
Dapagliflozin *Forxiga* Tabs: 5, 10 mg	**Initial**: 5 mg PO daily am **Maximum**: 10 mg PO daily am	$90	Non-benefit	
Dapagliflozin plus Metformin *Xigduo* Tabs: 5/850 mg, 5/1000 mg		$85	Non-benefit	

Generic Name *Trade Name* Dosages	Adult Dosage	Cost/ 30 days[b]	PharmaCare Coverage	Therapeutic Considerations
Glucagon-Like-Peptide 1 (GLP-1) Receptor Agonists				
Semaglutide *Ozempic* Pre-filled pen: 2 mg/1.5 mL 4 mg/3 mL	**Initial:** 0.25 mg SC once weekly x 4 weeks, then increase to 0.5 mg SC weekly. May increase to 1 mg SC weekly after additional 4 weeks **Usual:** 0.5 – 1 mg SC once weekly **Maximum**: 1 mg SC once weekly	*Ozempic:* $220	*Ozempic* Limited Benefit (hyperlinked to Special Authority criteria and form)	**Pros**: reduce risk of major adverse cardiovascular events and death from any cause in patients with T2DM and CV risk factors (liraglutide, dulaglutide, semaglutide SC), modest weight loss, low risk of hypoglycemia, lowers A1C by 1-1.5% (semaglutide SC: 1.5-2%).[2,4,5,8] **Cons**: GI side effects, rare reports of pancreatitis, increased heart rate, injectable. Use with caution in patients with renal impairment.[8] **Contraindications:** pregnancy, history of pancreatitis, personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome type 2. Exenatide: contraindicated in eGFR<30 mL/min/1.73m.[28] **Notes:** Semaglutide: tablets should be taken by mouth on an empty stomach when waking up with a sip of plain water (no more than 4 ounces). Wait 30 minutes before taking anything else by mouth. Liraglutide: 1.8 mg per day and 1.2 mg per day were generally similar in reducing A1C across studies reviewed by the U.S. FDA.[5] Exenatide: differences in A1C lowering between exenatide 10 mcg BID and 5 mcg BID ranged from 0.22% to 0.40% across RCTs reviewed by the U.S. FDA.[5]
Rybelsus Oral tabs: 3 mg, 7 mg, 14 mg	**Initial:** 3 mg PO daily **Usual:** 7 mg PO daily **Maximum**: 14 mg PO daily	*Rybelsus:* $230	*Rybelsus:* Non-benefit	
Exenatide *Byetta* Prefilled pen: 250mcg/mL; 1.2mL, 2.4mL	BYETTA: **Initial**: 5 mcg SC BID AC (≥6hr apart) **Maximum:** 10 mcg SC BID	*Byetta*: $155	Non-benefit	
Bydureon: long-acting release (LAR) Pre-filled pen: 2 mg	BYDUREON: **Usual:** 2 mg SC once every 7 days	*Bydureon:* $220		
Dulaglutide *Trulicity* Pre-filled pen: 0.75 mg/0.5 mL 1.5 mg/0.5 mL	**Initial:** 0.75 mg SC once weekly **Maximum**: 1.5 mg SC once weekly	$230	Non-benefit	
Liraglutide *Victoza* pre-filled pen: 0.6 mg/0.1 ml; 3 mL	**Initial**: 0.6 mg SC once daily x 1 week **Usual:** Increase to 1.2 mg SC once daily **Maximum**: 1.8 mg SC once daily	$210	Non-benefit	
Lixisenatide *Adlyxine* Pre-filled pen: 0.15 mg/3 mL 0.3 mg/3mL	**Initial:** 10 mcg SC daily AC (for 14 days) **Usual**: 20 mcg SC daily AC	$130	Non-benefit	

Generic Name *Trade Name* Dosages	Adult Dosage	Cost/ 30 days[b]	PharmaCare Coverage	Therapeutic Considerations
Dipeptidyl Peptidase-4 Inhibitors (DPP4i)				
Linagliptin *Trajenta* Tabs: 5 mg	**Usual**: 5 mg PO daily	$80	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	**Pros**: low risk of hypoglycemia [4] **Cons**: Mortality and CVD outcomes neutral, modest lowering of A1C (0.5-0.7%), rare reports of pancreatitis, reports of severe joint pain, hospitalization for heart failure may increase in patients treated with saxagliptin.[4,7] **Contraindications**: pregnancy, hepatic failure, previous lactic acidosis.[7] **Notes**: Saxagliptin and sitagliptin: Dose reduction required for patients with renal impairment (refer to product monographs for details). Dose adjustment not required for linagliptin.[7]
Linagliptin plus metformin *Jentadueto* Tabs: 2.5/500 mg, 2.5/850 mg, 2.5/1000 mg		$80	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	
Saxagliptin *Onglyza, G* Tabs: 2.5, 5mg	**Usual**: 5 mg PO daily	$50	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	
Saxagliptin plus metformin *Komboglyze* Tabs: 2.5/500 mg, 2.5/850 mg, 2.5/1000 mg		$85	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	
Alogliptin *Nesina* Tabs: 6.25 mg, 12.5 mg, 25 mg	**Usual**: 25 mg PO daily	$70	Non-benefit	
Alogliptin-metformin *Kazano* Tabs: 12.5/500 mg, 12.5/850 mg 12.5 mg/1000 mg		$80	Non-benefit	
Sitagliptin *Januvia* Tabs: 25, 50, 100 mg	**Usual**: 100 mg PO daily	$105	Non-benefit	
Sitagliptin plus metformin *Janumet* Tabs: 50/500 mg, 50/1000 mg		$115	Non-benefit	
Sitagliptin plus metformin XR *Janumet XR* XR tabs: 50/500 mg, 50/1000 mg, 100 mg/1000 mg		$115	Non-benefit	
Insulin Secretagogues, Meglitinides				
Repaglinide *GlucoNorm, G* Tabs: 0.5, 1, 2 mg	**Initial**: 0.5 mg (treatment-naïve) or 1 mg PO TID AC **Usual:** 0.5mg to 4 mg PO TID AC **Maximum**: 16 mg/day	$25	Non-benefit	**Pros**: lowers A1C 1-1.5% [4] **Cons**: moderate risk of hypoglycemia (less than SU), weight gain (1 kg) **Contraindications:** pregnancy **Notes:** If meal is skipped, skip dose

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Alpha-glucosidase inhibitor				
Acarbose *Glucobay, G* Tabs: 50, 100 mg	**Initial**: 50 mg PO once daily with first bite of main meal **Usual:** 50 mg PO TID with first bite of main meal **Maximum:** 100 mg PO TID with first bite of main meal	$25	Non-benefit	**Pros:**low risk hypoglycemia, weight neutral to modest weight loss. **Cons:** modest reduction in A1C (0.5-0.8%, no additional A1C reduction at doses >150 mg/day), frequent GI side effects, not recommended if eGFR < 25 mL/min/1.73m^2. [4,5] **Contraindications:** IBS and IBD **Notes:** Must use glucose (dextrose) for hypoglycemia, not sucrose as complex sugars are ineffective. If meal is skipped, skip dose.
Thiazolidinediones (TZDs)				
Pioglitazone *G* Tabs: 15, 30, 45 mg	**Initial**: 15-30 mg PO daily **Usual:** 30 mg PO daily **Maximum**: 45 mg/day	$25	Limited Coverage[c] (hyperlinked to Special Authority criteria and form)	**Pros:** lowers A1C by 0.5 to 1.4%, low risk of hypoglycemia, increase HDL.[6] **Cons:** weight gain (2-5 kg), use with caution in patients with renal impairment, pioglitazone increases the risk of fractures in women[4] **Contraindications:** pregnancy, metabolic bone disease, heart failure, ischemic heart disease.[6] **Notes**: Pioglitazone is contraindicated in active bladder cancer, history of bladder cancer or uninvestigated macroscopic haematuria.[5,6] Rosiglitazone is not approved as a monotherapy unless metformin treatment is inappropriate. Rosiglitazone is not recommended for use in combination with metformin and sulfonylurea.[5,6]
Rosiglitazone *G* Tabs: 2, 4, 8 mg	**Initial**: 4 mg PO daily in 1-2 doses **Usual:** 4 mg PO daily **Maximum**:8 mg /day	$65	Non-benefit	

Abbreviations: AC=before meals; A1C=glycosylated hemoglobin; BID=twice a day; BC=British Columbia; CV=cardiovascular; eGFR=estimated glomerular filtration rate; ER=extended release; G=generic; GI=gastrointestinal; HDL=high density lipoprotein; HF=heart failure; IBD= inflammatory bowel disease; IBS=Irritable bowel syndrome; LDL=low density lipoprotein; MACE=major adverse CV events (nonfatal myocardial infarction, stroke or CV death); mg=milligram; MI= myocardial infarction; MR=Modified release; NPH=Neutral protamine hagedorn (e.g., Humulin N); NYHA=New York Heart Association Functional Classification; PO=orally; SC=subcutaneous; Tab=tablet; TID=three times a day; URTI=upper respiratory tract infection; UTI=urinary tract infection; XR=Extended Release

Footnotes: a Not an exhaustive list; b for reference only; pricing is approximate of usual dose as of September 2021 for generics, and does not include dispensing fees or additional markups; only include the lowest price for drugs with multiple dosage forms and package sizes; c Special Authority Required; please refer to this link for specific criteria: https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/prescribers/special-authority#_Special_Authority_drug
Note: Please review product monographs at hc-sc.gc.ca/dhp-mps/prodpharma/databasdon/index-eng.php and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

PharmaCare Coverage Definitions: **Regular Benefit**: Eligible for full reimbursement*; does not require Special Authority. **Limited Coverage**: Requires Special Authority to be eligible for reimbursement*. **RDP**: Reference Drug Program. Drugs included in the RDP are comparable agents of the same therapeutic class. **RDP Reference Drug**: Eligible for full reimbursement* within the therapeutic class, subject to Benefit status of the therapeutic class. **Partial Benefit RDP**: Eligible for limited reimbursement* under the RDP program up to the price of the Reference Drug. **Non-benefit**: Not eligible for coverage under any circumstances.