

Antihyperglycemic Medications

Drug	Trade Name	Family	Dosage	Mechanism of Action	A1C Reductions
Sitagliptin	Januvia	Dipeptidase-4 inhibitor	100mg once daily ¹	Increase levels of glucagon-like peptide (GLP-1)	0.5-1.0%
Saxagliptin	Onglyza	Dipeptidase-4 inhibitor	5mg once daily ²	Increase levels of glucagon-like peptide (GLP-1)	0.5-1.0%
Liraglutide	Victoza	Glucagon-like Peptide-1 agonist	0.6mg-1.8mg once daily	Stimulate glucagon-like peptide effects in the body (GLP-1)	0.8-1.5%
Exenatide	NOC received – not yet marketed in Canada	Glucagon-like Peptide-1 agonist/ mimetic	5-10mcg bid ³	Stimulate glucagon-like peptide effects in the body (GLP-1)	<1%
Dapagliflozin	Undergoing Phase III trials	SGLT-2 inhibitor	10mg once daily	Inhibit the reabsorption of glucose at the sodium-glucose transporter-2 in the proximal kidney	<1%

1. Dosage reduction for renal dysfunction approved in the US only – CrCl 30-50mL/min use 50mg once daily, CrCl<30mL/min use 25mg once daily.
2. Dosage reduction for renal dysfunction approved in the US only – CrCL <50mL/min use 2.5mg once daily. Dosage reduction if patient is taking on a strong CYP 450 3A4/5 inhibitor use 2.5mg once daily.
3. Dosage reduction for renal dysfunction approved in the US – CrCl<30mL/min do not use, CrCl 30-50mL/min use maximum 5mcg bid, >50mL/min use 10mcg bid.

In Canada, these agents are approved only for renal function of CrCl>50mL/min in the doses given in the above table.

Approved Indications:

DPP-4 Inhibitors – combination with metformin or sulfonylurea or both. Sitagliptin also indicated as monotherapy in patients who do not tolerate both metformin and sulfonylurea.

Liraglutide – with metformin or in combination with metformin + sulfonylurea

Exenatide – received Notice of Compliance in Canada, not yet marketed

SGLT-2 Inhibitors – Phase III trials

Contraindications:

DPP-4 Inhibitors – renal impairment (in Canada), pregnant or breast-feeding, pediatrics

Liraglutide - with family history of medullary thyroid carcinoma or MEN-2 syndrome, pregnant or breast-feeding women

Side Effects:

DPP-4 Inhibitors – increased risk of some infections (nasopharyngitis, bronchitis, urinary tract infections), GI distress, rare hypoglycemia on own but can worsen hypoglycemia caused by other drugs

Liraglutide - ++ GI distress (nausea, vomiting, diarrhea), rare hypoglycemia (higher rates of hypoglycemia when used in combination with sulfonylureas), injection site reactions, Increase in heart rate/ PR interval prolongation. Rare cases of pancreatitis reported. Pts need to be warned about rare cases of medullary thyroid carcinoma in rats and mice; however, this has not been reported in humans.

Exenatide - +++ nausea/ vomiting, diarrhea, rare hypoglycemia (higher rates of hypoglycemia when used in combination with sulfonylureas), injection site reactions, hypersensitivity reactions, rare reports of pancreatitis, renal impairment

SGLT-2 Inhibitors - constipation, diarrhea, nausea, rare hypoglycemia, vaginal infections and urinary tract infections, decreased serum Mg, increased serum phosphate

Drug Interactions:

DPP-4 Inhibitors -

- Saxagliptin metabolised by CYP3A4/5
- Unlikely to alter metabolic clearance of coadministered drugs
- 3A4 inducers may decrease saxagliptin levels
- 3A4 inhibitors did not alter levels saxagliptin levels (but some strong CYP450 3A4/5 inhibitors can be a concern).

- Sitagliptin not likely to have drug interactions

Liraglutide – potential for decreased absorption of narrow therapeutic index meds

Exenatide - Warfarin – increase INR; potential for decreased absorption of narrow therapeutic index meds

Counselling Issues:

DDP-4 Inhibitors – may be taken with or without food

Liraglutide – inject once a day independent of meals, inject subcutaneously in abdomen, thigh, or upper arm. Store liraglutide pens in the refrigerator and keep out of sunlight; however, pen currently in use may be stored at room temperature for 30 days.

Exenatide – inject twice a day independent of meals, inject subcutaneously in abdomen, thigh, or upper arm.

SGLT-2 Inhibitors – take before morning meal

Average Monthly Cost Comparison

- Sitagliptin 100mg daily – \$100 (ODB coverage)
- Saxagliptin 5mg daily - \$100
- Liraglutide 1.2mg sc daily - \$170
- Liraglutide 1.8mg sc daily - \$250