TABLE 1A: Provincial Formulary Coverage of Insulin Therapies & Indications for Use in Various Populations

	Formulary Coverage				Indication for use with:		
INSULIN THERAPY	**NS**	**NB**	**NL**	**PE**	ADULTS◊	PEDIATRICS◊	PREGNANCY¥
BOLUS (Prandial/Meal Time) Insulins							
Rapid-acting Insulin Analogues (clear)							
• Insulin Aspart 100u/ml (NovoRapid®)	●	●	●	●	✔	✔	✔
• Insulin Aspart 100u/ml (Fiasp®)	○	○	○	○	✔	No data < 18yrs ▪	No data available for use in pregnancy ▪
• Insulin Glulisine 100 u/ml (Apidra®)	●	●	●	●	✔	✔	No data available for use in pregnancy
• Insulin Lispro 100 u/ml (Humalog®)	◐[1]	◐[2]	◐[3]	●	✔	✔	✔
• Insulin Lispro 200 u/ml (Humalog®)	○	○	◐[3]	○	✔	✔	✔
Short-acting Insulins (clear)							
• Insulin Regular 100 u/ml (Humulin® -R)	●	●	●	●	✔	✔	✔
• Insulin Regular 100 u/ml (Novolin® ge Toronto)	●	●	●	●	✔	✔	✔
• Insulin Regular 500 u/ml (Entuzity®)	○	○	○	○	✔	No data < 18yrs ▪	No data available for use in pregnancy ▪
BASAL Insulins							
Intermediate-acting (cloudy)							
• Insulin NPH 100 u/ml (Humulin® - N)	●	●	●	●	✔	✔	✔
• Insulin NPH 100 u/ml (Novolin® ge NPH)	●	●	●	●	✔	✔	✔
Long-acting Insulin Analogues (clear)							
• Insulin Detemir 100 u/ml (Levemir®)	◐[4]	◐[4]	◐[6]	◐[7]	✔	✔	✔
• Insulin Glargine 100 u/ml (Lantus®)	◐[4]	◐[5]	○	◐[7]	✔	✔	✔
• Insulin Glargine 100 u/ml (Basaglar™)	●	●	●	●	✔	✔	✔
• Insulin Glargine 300 u/ml (Toujeo® SoloSTAR®)	○	○	○	◐[8]	✔	No data <18yrs ▪	✔ Only if potential benefit justifies potential risk to fetus ▪
• Insulin Degludec 100 u/ml & 200 u/ml (Tresiba®)	○	●	○	●	✔	✔	No human data available for use in pregnancy
PREMIXED Insulins							
Premixed Regular and NPH							Not recommended in pregnancy. These do not allow for precise dosing as required to attain and maintain blood glucose targets.
• Humulin® 30/70	●	●	●	●	✔	✔	
• Novolin® ge 30/70, 40/60, 50/50	●	●	●	●	✔		
Premixed Insulin Analogues							
• Biphasic insulin Aspart (NovoMix® 30)	○	○	○	○	✔	✔	
• Insulin Lispro/Lispro protamine (Humalog® Mix 25)	○	○	○	●	✔	✔	
• Insulin Lispro/Lispro protamine (Humalog® Mix 50)	○	○	○	○	✔	✔	

◐= Exception Status; ●=Full Benefit; ○=Not a benefit

◊ Check marks indicate common use/clinical practice. Data for safe use in various ages in pediatrics varies by product. ¥ Reference: Briggs GG, Freeman RK, Towers, CV, Forinash AB. *Drugs in pregnancy and lactation a reference guide to fetal and neonatal risk. Eleventh edition.* 2017. ▪ Reference: Product Monograph

TABLE 1A: Provincial Formulary Coverage of Insulin Therapies & Indications for Use in Various Populations

◖[1] = ES[1]

Regular benefit for children 18 years and younger under Community Services, Family Pharmacare, and Diabetes Assistance Programs (full benefit for children 18 years and younger).

For the management of Type I and Type II diabetes mellitus in patients 19 years of age and older, who are:

- undergoing intensive therapy; i.e., administering three or more injections of insulin per day including basal insulin, **AND**
- testing blood glucose levels 4-6 times per day.

◖[2] = ES[2]

For patients with type 1 or type 2 diabetes who:

- have experienced frequent episodes of postprandial hypoglycemia, **OR**
- have unpredictable mealtimes, **OR**
- have insulin resistance, **OR**
- who are using continuous subcutaneous insulin infusion.

Claim Notes:

- Prescriptions written by New Brunswick endocrinologists and internists do not require special authorization.
- Subsequent refills ordered by other practitioners will not require special authorization.

◖[3] = ES[3]

For patients with insulin-dependent diabetes on multiple insulin dosing (≥ 3 injections of regular insulin per day) and who are experiencing frequent hypoglycemia or poor glycemic control on their current regimen.

For patients with insulin-dependent diabetes who are using an insulin pump. [**Please Note: HUMALOG KWIKPEN 200 unit/ml should not be administered via a subcutaneous infusion pump or mixed with any other insulin (including HUMALOG 100 units/mL)**].

For patients with insulin-dependent diabetes who, for convenience purposes, wish to use this insulin and are willing to pay the difference in price from traditional regular insulin (i.e., NLPDP will pay the cost normally reimbursed for regular insulin (Humulin R) and the patient would be responsible for the difference). (**HUMALOG 100 UNIT/ML VIAL, PEN only**)

◖[4] = ES[4]

For the treatment of patients who have been diagnosed with type 1 or type 2 diabetes requiring insulin and have previously taken insulin NPH and/or pre-mix daily at optimal dosing, and have:

- experienced unexplained nocturnal hypoglycemia at least once a month despite optimal management, **OR**
- documented severe or continuing systemic or local allergic reaction to existing insulin(s).

◖[5] = ES[5]

For the treatment of patients who have been diagnosed with type 1 or type 2 diabetes requiring long-acting insulin.

Claim Note:

- New requests for coverage of Lantus will not be considered. Basaglar brand of insulin glargine is listed as a regular benefit.

◖^{6} = ES^{6}

For patients who have been diagnosed with Type 1 or Type 2 diabetes AND

- who have experienced unexplained nocturnal hypoglycemia at least once a month despite optimal management with insulin glargine **OR**
- have documented severe or continuing systemic or local allergic reactions to both NPH insulin and insulin glargine **OR**
- who have experienced unexplained nocturnal hypoglycemia at least once a month despite optimal management with NPH insulin and who have documented severe or continuing systemic or local allergic reactions to insulin glargine

◖^{7} = ES^{7}

For the treatment of patients who have been diagnosed with type 1 or type 2 diabetes requiring insulin and have previously taken all open benefit long acting insulin analogues daily at optimal dosing

AND

- have experienced unexplained nocturnal hypoglycaemia at least once a month despite optimal management

OR

- have documented severe or continuing systemic or local allergic reaction to existing insulin(s)

◖^{8} = ES^{8}

For the treatment of patients who have been diagnosed with type 1 or type 2 diabetes requiring insulin and have previously used all eligible open benefit long acting insulin analogues at optimal dosing AND have experienced unexplained hypoglycemia at least once a month despite optimal management

OR

For the treatment of patients who have been diagnosed with type 1 or type 2 diabetes requiring high dose insulin.

NOTE: TABLE WAS UPDATED MAY 2019

Table 1B: Provincial Formulary Coverage of Non-Insulin Therapies (oral and injectable) and Indications for Use in Various Populations

NON-INSULIN THERAPIES	Formulary Coverage NS	NB	NL	PE	Indication for use with: ADULTS▪	PEDIATRICS▪	PREGNANCY	LACTATION	Other Therapeutic Considerations
ORAL ANTIHYPERGLYCEMIC AGENTS									
Alpha-glucosidase inhibitor									
• Acarbose (Glucobay®)	●	●	●	●	Type 2	Safety, efficacy not established	Safety not established. Limited human data ¥	No data, probably compatible € ¥	
Insulin Secretagogues									
Sulfonylureas:									
• Gliclazide (Diamicron®, Diamicron® MR, generics)	●	●	●	●		Not for use <18	Safety not established Limited Human data§	No data, alternative preferred. € ¥	
• Glimepiride (Amaryl®, generics)	○	●	●	●		Safety, efficacy not established	Safety not established Limited human data ¥	No/limited data, alternative preferred €▲ ¥	
• Glyburide (Diabeta®, generics)	●	●	●	●	Type 2	Not for use <18	**Human data suggest low risk¥**	Limited data, probably compatible €¥	
• Chlorpropamide	○	○	●	○		Safety, efficacy not established	Human data suggest risk in 3rd trimester ¥	No/limited data, alternative preferred €▲ ¥	**Glyburide may be considered** through the first trimester (under care of a specialist) until insulin is initiated - Diabetes Care Program Nova Scotia (DCPNS)
• Tolbutamide	●	●	●	●		Safety, efficacy not established	Human data suggest risk in 3rd trimester ¥	No/limited data, alternative preferred €▲ ¥	
Meglitinides:									
• Repaglinide (Gluconorm®, generics)	○	◖[1]	◖[2]	○		Not for use <18	Safety not established¥	No data, possibly hazardous/potential toxicity €¥	
Biguanides									
• Metformin (Glucophage®, generics)	●	●	●	●	Type 2	Safety & efficacy not established	**Human data suggest low risk¥** May have non-glycemic benefits including **less**: • gestational weight gain, • pregnancy-induced hypertension, • neonatal hypoglycemia • NICU admissions > 24 hrs.	**Limited data, compatible** € ¥	Use in Polycystic Ovarian Syndrome. Use in the first trimester until insulin initiated. Approximately 85% will require add-on insulin. Increasing use in women with GDM and Type 2 DM.
• Metformin once daily formulation (Glumetza®)	○	○	○	○					
DPP-4 Inhibitor									
• Sitagliptin (Januvia®)	◖[3]	◖[4]	◖[3]	◖[3]			Safety not established ¥	No data, probably compatible € ¥	
• Saxagliptin (Onglyza®)	◖[3]	◖[3]	◖[3]	◖[3]	Type 2	Not for use <18	Safety not established ¥	No data, alternative preferred▲ ¥	
• Linagliptin (Trajenta®)	◖[3]	◖[3]	◖[3]	◖[3]			Safety not established ¥	No data, probably compatible € ¥	
• Alogliptin (Nesina®)	○	○	○	○			Safety not established ¥	No data, alternative preferred▲ ¥	
Thiazolidinedione									
• Pioglitazone (Actos®)	◖[5]	◖[6]	◖[6]	◖[7]	Type 2	Not for use < 18	Safety not established ¥	No data, probably compatible€¥	
• Rosiglitazone (Avandia®)	○	○	○	○					

◖= Exception Status; ●=Full Benefit; ○=Not a benefit

ORAL ANTIHYPERGLYCEMIC AGENTS (CONT)	NS	NB	NL	PE	ADULTS▪	PEDIATRICS▪	PREGNANCY	LACTATION	
Sodium Glucose co-transporter (SGLT2) Inhibitors									
• Canagliflozin (Invokana®)	◖[3]	◖[3]	◖[3]	◖[3]	Type 2	Not for use < 18	Safety not established ¥	No data, potential toxicity ¥	
• Dapagliflozin (Forxiga®)	◖[8]	◖[3]	◖[3]	◖[3]					
• Empagliflozin (Jardiance®)	◖[9]	◖[3]	◖[3]	◖[3]			Not for use in pregnancy▪	Not for use in lactation, may affect developing human kidney ▪	
• Ertugliflozin (Steglatro™)	○	○	○	○					
Combined formulations									
• Metformin + Rosiglitazone (Avandamet ®)	○	○	○	○	Type 2	Not for use < 18	See recommendations for individual agents, page 1	See recommendations for individual agents, page 1	
• Metformin + Sitagliptin (Janumet®)	◖[10]	◖[10]	◖[10]	◖[10]					
• Metformin + Sitagliptin (Janumet® XR)	◖[10]	◖[10]	◖[10]	◖[10]					
• Metformin + Linagliptin (Jentadueto®)	◖[11]	◖[11]	◖[11]	◖[11]					
• Metformin + Saxagliptin (Komboglyze®)	◖[12]	◖[12]	◖[12]	◖[12]					
• Metformin + Alogliptin (Kazano®)	○	○	○	○					
• Metformin + Canagliflozin (Invokamet®)	○	○	○	○	Type 2	Not for use < 18	See recommendations for individual agents, page 1	See recommendations for individual agents, page 1	
• Metformin + Dapagliflozin (Xigduo®)	◖[13]	◖[13]	◖[13]	◖[13]					
• Metformin + Empagliflozin (Synjardy®)	◖[14]	○	○	○					
• Metformin + Ertugliflozin (Segluromet™)	○	○	○	○					
• Linagliptin + Empagliflozin (Glyxambi®)	○	○	○	○					
• Sitagliptin + Ertugliflozin (Steglujan™)	○	○	○	○					
INJECTABLE ANTIHYPERGLYCEMIC THERAPY									
GLP-1 Receptor Agonists:									
• Exenatide (Byetta®)	○	○	○	○	Type 2	Not for use <18	Safety not established ¥	No data, probably compatible€¥	
• Exenatide extended release (Bydureon®)	○	○	○	○					
• Liraglutide (Victoza®)	○	○	○	○					
• Dulaglutide (Trulicity ™)	○	○	○	○	Type 2	Not for use <18	Safety not established ¥ Not for use in pregnancy, toxic in animal studies ▪ Not for use in pregnancy▪	No data, alternative preferred ¥▲ Not for use in lactation, no data, unknown if excreted in breastmilk▪ Not for use in lactation▪	
• Lixisenatide (Adlyxine™)	○	○	○	○					
• Semaglutide (Ozempic®)	○	○	○	○					
WEIGHT LOSS AGENTS									
• Orlistat (Xenical®)	○	○	○	○	Weight loss	Not for use < 12	Contraindicated ¥	No data, alternative preferred €▲¥	
• Liraglutide (Saxenda®)	○	○	○	○		Not for use < 18	Contraindicated ▪	No human data, not for use▪	

◖= Exception Status; ●=Full Benefit; ○=Not a benefit

▪ Product monograph ¥ Reference: Briggs GG, Freeman RK, Towers, CV, Forinash AB. *Drugs in pregnancy and lactation a reference guide to fetal and neonatal risk.* Eleventh edition, 2017.

§ Reference: Micromedex Solutions. *IBM Micromedex*. Available at: http://www.micromedexsolutions.com. Accessed: 2019 January 28

€ Reference: Hale TW, Rowe, HE. *Medications & Mothers' Milk*. Seventeenth edition. New York, NY: Springer Publishing Company, 2017.

▲ Reference: U.S. National Library of Medicine. *Lactmed: A TOXNET DATABASE*. Available at: https://www.toxnet.nlm.nih.gov/newtoxnet/lactmed.htm. Accessed: 2019 February 22

TABLE KEY

◖ = ES	Exception Status Criteria, Key Interpretations
◖1	For patients with type 2 diabetes who are not adequately controlled by diet and exercise and glyburide and/or metformin or who have frequent or severe hypoglycemic episodes despite dosage adjustment of glyburide.
◖2	For patients who have failed to respond to or have experienced hypoglycemia from sulfonylureas. Note: Coverage may be considered WITHOUT a Special Authorization request as long as the beneficiary's medication history in the NLPDP database has had a paid (non-reversed) claim for Gluconorm (repaglinide), glimepiride, gliclizide, tolbutamide, chlorpropamide or glyburide in the past year. If there is no history of a previous claim for glimepiride, gliclizide, tolbutamide, chlorpropamide or glyburide the normal Special Authorization Process will be required.
◖3	For the treatment of type 2 diabetes mellitus, in addition to metformin and a sulfonylurea, in patients who have inadequate glycemic control on metformin and a sulfonylurea and for whom insulin is not an option. NB: Linagliptin: For patients with type 2 diabetes mellitus with inadequate glycemic control while on optimal doses of metformin and a sulfonylurea, and for whom **NPH insulin** is not an option, when added as a third agent.
◖4	For the treatment of Type 2 diabetes mellitus in patients for whom NPH insulin is not an option **AND**: • who have inadequate glycemic control while on optimal doses of metformin and a sulfonylurea when added as a third agent; **OR** • In combination with metformin when a sulfonylurea is not suitable due to contraindications or intolerance; **OR** • As monotherapy when metformin and sulfonylurea are not suitable due to contraindications or intolerance
◖5	For treatment of Type 2 diabetes in patients who have: • inadequate glycemic control on optimal doses of sulfonylurea and metformin; **OR** • demonstrated intolerance or contraindication to metformin and are on optimal doses of sulfonylurea; **OR** • demonstrated intolerance or contraindication to sulfonylurea and are on optimal doses of metformin Patients must have a recent A1C of < 10% unless insulin therapy is inappropriate for the patient. Duration of initial approval will be 6 months; further coverage will require demonstrated evidence of efficacy (a reduction of A1C of 0.7 observed to continue coverage).
◖6	For patients with type 2 diabetes who are not adequately controlled by diet, exercise, and drug therapy. Drug therapy should include a trial of a sulfonylurea and metformin, alone and in combination, unless one of these agents is not tolerated or is contraindicated. NL: For the treatment of type II diabetes in patients who are inadequately controlled on a combination of a sulfonylurea and metformin, at maximum dosages, or in whom these agents are contraindicated or not tolerated.
◖7	For the treatment of patients diagnosed with Type II diabetes, and who have: a)Inadequate glycemic control[1] on optimal doses[2] of Sulfonylurea and Metformin; OR b)Demonstrated intolerance or contraindication to Metformin[3] and are on optimal doses[2] of Sulfonylurea; OR c)Demonstrated intolerance or contraindication to Sulfonylurea[4] and are on optimal PEI Pharmacare doses[2] of Metformin. 1. Most recent (within the past 12 months) HbA1Crequired: >7% and <10%. The addition of a thiazolidinedione would not be expected to decrease the HbA1Cto satisfactory levels in patients with a HbA1Cgreater than 10. 2. Maximum doses: Metformin 2500mg/day, Chlorpropamide 500mg/day, Gliclazide regular tablets 320mg/day, Gliclazide modified-release tablets 120mg/day, Glimepiride 4mg/day, Glyburide 20mg/day. 3. Metformin: Intolerance -GI adverse effects; Contraindications -renal impairment (SrCr> 130mmol/L) or hepatic failure, acute or chronic metabolic acidosis. 4. Sulfonylureas: Intolerance -Hypoglycemia; Contraindications -sulfa allergy, severe renal insufficiency (CrCl < 50mL/min).
◖8	For the treatment of Type II diabetes when: Added on to metformin for patients: who have inadequate glycemic control on metformin; and who have a contraindication or intolerance to a sulfonylurea; and for whom insulin is not an option. Added on to a sulfonylurea for patients: Who have inadequate glycemic control on a sulfonylurea; and who have a contraindication or intolerance to metformin; and for whom insulin is not an option.
◖9	For the treatment of Type 2 diabetes mellitus for patients with inadequate glycemic control on 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 death in patients with type 2 diabetes mellitus and established cardiovascular disease (details must be provided as per clinical note below) who have inadequate glycemic control despite an adequate trial of metformin.

TABLE KEY (cont'd)

◖10	For the treatment of type 2 diabetes in patients for whom insulin is not an option **AND** who are already stabilized on therapy with metformin, a sulfonylurea and sitagliptin, to replace the individual components of sitagliptin and metformin in these patients.
◖11	For the treatment of patients with type II diabetes for whom insulin is not an option **AND** who are already stabilized on therapy with metformin, a sulfonylurea and linagliptin, to replace the individual components of linagliptin and metformin for these patients.
◖12	For the treatment of patients with type II diabetes for whom insulin is not an option **AND** who are already stabilized on therapy with metformin, a sulfonylurea and saxagliptin, to replace the individual components of saxagliptin and metformin for these patients.
◖13	For the treatment of patients with type II diabetes for whom insulin is not an option **AND** who are already stabilized on therapy with metformin and dapagliflozin, to replace the individual components of metformin and dapagliflozin for these patients. NS: Claim note: must have met criteria for dapagliflozin. PE: For the treatment of type II diabetes for patients for whom insulin is not an option and who are already stabilized on therapy with **metformin, a sulfonylurea and dapagliflozin**, to replace the individual components of dapagliflozin and metformin in these patients.
◖14	For the treatment of type 2 diabetes mellitus in patients who are already stabilized on therapy with empagliflozin and metformin, to replace the individual components of empagliflozin and metformin. Patients must meet coverage criteria for empagliflozin.

NOTE: TABLE 1B REVISED MAY 2019

TABLE 1C: Provincial Formulary Coverage of Injectable Combination Therapies & Indications for Use in Various Populations

	Formulary Coverage				Indication for use with:				
INJECTABLE COMBINATION THERAPY	**NS**	**NB**	**NL**	**PE**	ADULTS▪	PEDIATRICS▪	PREGNANCY▪	LACTATION▪	Therapeutic Considerations▪
Long acting BASAL insulin + GLP-1 Agonist • Insulin degludec/liraglutide (Xultophy®) • Insulin glargine/lixisenatide (Soliqua™)	○ ○	○ ○	○ ○	○ ○	Type 2	Not for use <18	Contraindicated	Contraindicated	These agents have not been studied in combination with prandial (short acting) insulin.

◖= Exception Status; ●=Full Benefit; ○=Not a benefit

▪ Reference: Product Monograph

Table 2A: Non-Insulin Therapies and Insulin - Considerations for Use

The recommendations in the following table are made based on varying levels of evidence, ranging from randomized controlled trial (RCT) data to existing clinical practice. Each agent is referenced to indicate the rationale for the recommendations made regarding their use with insulin. Recommendations may change as evidence evolves.

NON-INSULIN THERAPIES Use with Insulin (in combination)	BOLUS INSULIN	Rapid-acting IA	Short-acting (Regular insulin)	BASAL INSULIN	Intermediate-acting (NPH or Humulin N)	Long-acting IA • Detemir	Long-acting IA • Glargine	Ultra-long-acting IA • Degludec	PREMIXED	Premixed Reg and NPH	Premixed IAs
ORAL ANTIHYPERGLYCEMIC AGENTS											
Biguanides											
• Metformin[1] (Generics, Glucophage®, Glumetza® once-daily formulation)		✔	✔		✔	✔	✔	✔		✔	✔
INSULIN SECRETAGOGUES[2]											
• Sulfonylureas (Gliclazide®, Glimepiride®, Glyburide®, chlorpropamide and tolbutamide)		X	X		✔	✔	✔	✔		X	X
• Meglitinides: Repaglinide (Gluconorm®)		X	X		✔	✔	✔	✔		X	X
DPP-4 INHIBITOR											
• Sitagliptin[3] (Januvia®)		✔	✔		✔	✔	✔	✔		✔	✔
• Saxagliptin[3] (Onglyza®)		✔	✔		✔	✔	✔	✔		✔	✔
• Alogliptin[3] (Nesina®)		✔	✔		✔	✔	✔	✔		✔	✔
• Linagliptin[4] (Trajenta®)		X	X		X	X	X	X		X	X
THIAZOLIDINEDIONE											
• Pioglitazone (Actos®)		X	X		X	X	X	X		X	X
• Rosiglitazone (Avandia®)		X	X		X	X	X	X		X	X
SODIUM GLUCOSE CO-TRANSPORTER (SGLT2) INHIBITORS											
• Canagliflozin (Invokana®)[3]		✔	✔		✔	✔	✔	✔		✔	✔
• Dapagliflozin (Forxiga®)[3]		✔	✔		✔	✔	✔	✔		✔	✔
• Empagliflozin (Jardiance®)[3]		✔	✔		✔	✔	✔	✔		✔	✔
• Ertugliflozin (Steglatro™)[5]		X	X		X	X	X	X		X	X
ALPHA-GLYCOSIDASE INHIBITOR											
• Acarbose (Glucobay®)[3]		✔	✔		✔	✔	✔	✔		✔	✔
COMBINED FORMULATIONS											
• Metformin + Rosiglitazone (Avandamet ®)		X	X		X	X	X	X		X	X
• Metformin + Sitagliptin (Janumet®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Sitagliptin (Janumet®XR)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Linagliptin (Jentadueto®)		X	X		X	X	X	X		X	X
• Metformin + Saxagliptin (Komboglyze®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + alogliptin (Kazano®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Canagliflozin (Invokamet®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Dapagliflozin (Xigduo®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Empagliflozin (Synjardy®)		✔	✔		✔	✔	✔	✔		✔	✔
• Metformin + Ertugliflozin (Segluromet™)[5]		X	X		X	X	X	X		X	X
• Linagliptin + Empagliflozin (Glyxambi®)		X	X		X	X	X	X		X	X
• Sitagliptin + Ertugliflozin (Steglujan™)[5]		X	X		X	X	X	X		X	X
INJECTABLE ANTIHYPERGLYCEMIC THERAPY: GLP-1 RECEPTOR AGONIST											
• Exenatide (Byetta®)[6]		X	X		✔	✔	✔	✔		X	X
• Exenatide extended release (Bydureon®)		X	X		✔	✔	✔	✔		X	X
• Liraglutide (Victoza®)[7]		X	X		✔	✔	✔	✔		X	X
• Dulaglutide (Trulicity™)[7]		X	X		✔	✔	✔	✔		X	X
• Lixisenatide (Adlyxine™)[8]		X	X		✔	✔	✔	✔		X	X
• Semaglutide (Ozempic®)[9]		X	X		✔	✔	✔	✔		X	X
WEIGHT LOSS AGENTS											
• Orlistat (Xenical®)		✔	✔		✔	✔	✔	✔		✔	✔
• Liraglutide (Saxenda®)[10]		X	X		X	X	X	X		X	X

IA = insulin analogue; **X** = Not recommended for use with insulin - either due to lack of data or proof of harm; ✔= Used with insulin in clinical practice

FOOTNOTES:

1. RCT data supports metformin as the standard of care in combination with insulin in T2DM.

2. Existing clinical practice: Insulin secretagogues may be continued while taking basal insulin to limit initial deterioration of glycemic control and because of their insulin-sparing effect, but the combination should be avoided later if hypoglycemia occurs and/or when bolus insulin regimens are added. RCT data to inform the secretagogues optimal place in therapy with insulin are lacking.

3. Monograph states: Indicated as add-on combination therapy with insulin.

4. Monograph states: Use in combination with insulin is not indicated due to a cardiovascular risk which cannot be excluded.

5. Monograph states: not indicated for use in combination with insulin.

6. Monograph states: Indicated as add-on combination therapy with glargine insulin [based on RCT data]. Exenatide is combined with detemir and intermediate-acting insulin in clinical practice despite a lack of RCT data examining these combinations [existing/emerging clinical practice]. The combination of exenatide and bolus insulin has not been studied.

7. Monograph states: Indicated as add-on combination therapy with basal insulin. The combination of liraglutide and bolus insulin has not been studied.

8. Monograph states: indicated in combination with basal insulin (alone or with metformin).

9. Monograph states: indicated in combination with basal insulin WITH metformin when diet and exercise plus basal insulin with metformin do not achieve adequate glycemic control

10. Monograph states: Saxenda® should not be used with insulin, as this combination has not been studied.
    Note: Victoza® (also liraglutide) is indicated as add-on with basal insulin.

NOTE:

Clinical trials have studied the effects of newer non-insulin therapies (oral and injectable agents) combined with insulin, in treating high blood sugar levels, as compared to insulin monotherapy; however, at present, evidence is limited for all possible insulin combination therapies, in particular combinations with older oral agents.

NOTE: TABLE 2A WAS UPDATED MAY 2019