TABLE 1A : 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 < 6yrs	No data available for use in pregnancy
• Insulin Lispro 100 u/ml (Humalog®)	◐[1]	◐[2]	◐[3]	●	✔	✔ No data < 3yrs	✔
• Insulin Lispro 200 u/ml (Humalog®)	○	○	○	○	✔	✔ No data < 3yrs	✔
Short-acting Insulins (clear)							
• Humulin® -R	●	●	●	●	✔	✔	✔
• Novolin® ge Toronto	●	●	●	●	✔	✔	✔
BASAL Insulins							
Intermediate-acting Insulins (cloudy)							
• Humulin® - N	●	●	●	●	✔	✔	✔
• Novolin® ge NPH	●	●	●	●	✔	✔	✔
Long-acting Insulin Analogues (clear)							Not indicated for use in pregnancy. The decision to continue this type of insulin in pregnancy should be made in discussion with the specialist physician. There is no evidence to suggest harm; however, high-grade safety data is lacking.
• Insulin Detemir 100 u/ml (Levemir®)	◐[4]	◐[4]	◐[4]	◐[4]	✔	✔	
• Insulin Glargine 100 u/ml (Lantus®)	◐[4]	◐[4]	◐[4]	◐[4]	✔	✔	
• Insulin Glargine 100 u/ml (Basaglar™)	○	○	○	○	✔	✔ > age 6	
• Insulin Glargine 300 u/ml (Toujeo™)	○	○	○	○	✔	No data <18yrs	
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)	○	○	○	○	✔	✔ No data <16yrs	
• Insulin Lispro/Lispro protamine (Humalog® Mix 25 and Mix 50)	○	○	○	○	✔	✔ No data < 3yrs	

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

× Reference: Product monograph

¥ Reference: Briggs GG, Freeman RK, Yaffe SJ. *Drugs in pregnancy and lactation*. Ninth edition. 2011

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

Key Interpretations:

◖[1] = ES[1]

Full benefit for children ≤18 years and younger under Community Services, Family Pharmacare, and Diabetes Assistance Programs

For the management of Type 1 and Type 2 diabetes mellitus in patients (>18 years old) 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 management of Type 1 or Type 2 diabetes in adult patients (>18 years old) who:
- have experienced frequent episodes of postprandial hypoglycemia,
- have unpredictable mealtimes,
- have insulin resistance, or
- 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.

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 (Novolin® ge Toronto) and the patient would be responsible for the difference).

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

NOTE: TABLE 1A was updated July 2017.

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

	Formulary Coverage				Indication for use with:				
NON-INSULIN THERAPIES	**NS**	**NB**	**NL**	**PE**	**ADULTS[x]**	**PEDIATRICS[x]**	**PREGNANCY**	**LACTATION[€]**	**Other Therapeutic Considerations**
ORAL ANTIHYPERGLYCEMIC AGENTS									
Alpha-glucosidase inhibitor									
• Acarbose (Glucobay®)	●	●	◖[1]	●	Type 2	Not for use < 18	Safety not established. [¥]	No data, probably compatible	
Insulin Secretagogues									
Sulfonylureas:									
• Gliclazide (Diamicron®, Diamicron® MR)	●	●	●	●			Safety not established. [§]	No data	**Glyburide may be considered** through the first trimester (under care of a specialist) until insulin is initiated - Diabetes Care Program Nova Scotia (DCPNS)
• Glimepiride (Amaryl®)	○	●	●	●	Type 2	Not for use <18	Safety not established. [¥]	No data, probably hazardous	
• Glyburide (Diabeta®, Euglucon®)	●	●	●	●			**Human data suggest low risk[¥]**	No data, probably compatible	
• Chlorpropamide	○	●	●	●	Type 2	Safety, efficacy not established	Human data suggest risk in 3rd trimester. [¥]	No data, probably compatible	
• Tolbutamide	●	●	●	●	Type 2	Safety, efficacy not established	Human data suggest risk in 3rd trimester. [¥]	Limited data, probably compatible	
Meglitinides:									
• Repaglinide (Gluconorm®)	○	◖[2]	◖[3]	○	Type 2	Not for use <18	Safety not established[¥]	No data, probably hazardous	
Biguanides									
• Metformin (generics Glucophage®, Glumetza® once-daily formulation)	●	●	●	●	Type 2	Safety & efficacy not established	**Human data suggest low risk[¥]**	**Limited data, compatible**	Use in Polycystic Ovarian Syndrome (PCOS). Use in the first trimester until insulin initiated. Increasing use in GDM and type 2 DM in pregnancy.
DPP-4 Inhibitor									
• Sitagliptin (Januvia®)	◖[4]	◖[5]	◖[4]	◖[4]			Safety not established [¥]	No data, probably compatible	
• Saxagliptin (Onglyza®)	◖[4]	◖[4]	◖[4]	◖[4]	Type 2	Not for use <18	Safety not established [¥]	No data	
• Linagliptin (Trajenta®)	◖[4]	◖[4]	◖[4]	◖[4]			Safety not established [¥]	No data, probably compatible	
• Alogliptin (Nesina®)	○	○	○	○			Safety not established [¥]	No data	

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

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NOTE: TABLE 1B was updated July 2017.

ORAL ANTIHYPERGLYCEMIC AGENTS (CONT)	NS	NB	NL	PE	ADULTS×	PEDIATRICS×	PREGNANCY	LACTATION€	
Thiazolidinedione									
• Pioglitazone (Actos®)	◖[6]	◖[7]	◖[7]	◖[6]	Type 2	Not for use < 18	Safety not established ¥	No data, probably compatible	
• Rosiglitazone (Avandia®)	○	○	○	○					
Sodium Glucose co-transporter (SGLT2) Inhibitors									
• Canagliflozin (Invokana®)	◖[4]	◖[4]	◖[4]	◖[4]	Type 2	Not for use < 18	Safety not established ¥	No data	
• Dapagliflozin (Forxiga®)	○	◖[4]	◖[4]	◖[4]					
• Empagliflozin (Jardiance®)	◖[4]	◖[4]	◖[4]	◖[4]					
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®)	◖[8]	◖[8]	◖[8]	◖[8]					
• Metformin + Sitagliptin (Janumet® XR)	◖[8]	◖[8]	◖[8]	◖[8]					
• Metformin + Linagliptin (Jentadueto®)	◖[9]	◖[9]	◖[9]	◖[9]					
• Metformin + Saxagliptin (Komboglyze®)	◖[10]	◖[10]	◖[10]	◖[10]					
• 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®)	○	○	○	○					
• Metformin + Empagliflozin (Synjardy®)	○	○	○	○					
• Linagliptin + Empagliflozin (Glyxambi®)	○	○	○	○					
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 ¥	No data	
• Albiglutide (Eperzan®)	○	○	○	○					
WEIGHT LOSS AGENTS									
• Orlistat (Xenical®)	○	○	○	○	Weight loss	Not for use < 12	Safety not established ¥	No data, probably compatible	
• Liraglutide (Saxenda®)	○	○	○	○		Not for use < 18	Safety not established ¥		

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

× Product monograph

¥ Reference: Briggs GG, Freeman RK, Yaffe SJ. *Drugs in pregnancy and lactation*. Ninth edition; With the exception of orlistat, all product monographs recommend no use in pregnancy.

§ Reference: *Micromedex Healthcare Series*. Thomson Micromedex. Available at: http://www.thomson hc.com. Accessed 2012 May 15

€ Reference: Hale TW and Rowe HE. *Medications and Mothers Milk*. Plano, TX: Hale Publishing; 2014.

TABLE KEY

◖ = ES	Exception Status Criteria
◖1	For patients who are not controlled satisfactorily, despite maximum doses of a biguanide and sulfonlyurea, or in whom these agents are contraindicated.
◖2	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.
◖3	For patients who have failed to respond to or have experienced hypoglycemia from sulfonylureas.
◖4	For the treatment of type 2 diabetes in addition to metformin and a sulfonylurea for patients with inadequate glycemic control on metformin and a sulfonylurea **AND** in whom insulin is not an option.
◖5	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.
◖6	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).
◖7	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.
◖8	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.
◖9	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.
◖10	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.

NOTE: TABLE 1B was updated July 2017.

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 (Reg or Toronto)	BASAL INSULIN	Intermediate-acting (NPH or Humulin N)	Long-acting IA • Detemir	Long-acting IA • Glargine	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 (Trajenta®)		X	X		X	X	X		X	X
Thiazolidinedione										
• Pioglitazone (Actos®)		X	X		X	X	X		X	X
• Rosiglitazone (Avandia®)		X	X		X	X	X		X	X
Sodium Glucose co-transporter (SGLT2) Inhibitors										
• Canagliflozin (Invokana®)[3]		✓	✓		✓	✓	✓		✓	✓
• Dapagliflozin (Forxiga®)[3]		✓	✓		✓	✓	✓		✓	✓
• Empagliflozin (Jardiance®)[3]		✓	✓		✓	✓	✓		✓	✓
Alpha-glycosidase inhibitor										
• Acarbose (Glucobay®)[3]		✓	✓		✓	✓	✓		✓	✓
Combined formulations										
• Metformin + Rosiglitazone (Avandamet ®)		X	X		X	X	X		X	X
• Metformin + Sitagliptin (Janumet®)		✓	✓		✓	✓	✓		✓	✓
• Metformin + Sitagliptin (Janumet®XR)		✓	✓		✓	✓	✓		✓	✓
• Metformin + Linagliptin (Jentadueto®)		X	X		X	X	X		X	X
• Metformin + Saxagliptin (Komboglyze®)		✓	✓		✓	✓	✓		✓	✓
• Metformin + alogliptin (Kazano®)		✓	✓		✓	✓	✓		✓	✓
• Metformin + Canagliflozin (Invokamet®)		✓	✓		✓	✓	✓		✓	✓
• Metformin + Dapagliflozin (Xigduo®)		✓	✓		✓	✓	✓		✓	✓
• Metformin + Empagliflozin (Synjardy®)		✓	✓		✓	✓	✓		✓	✓
• Linagliptin + Empagliflozin (Glyxambi®)		X	X		X	X	X		X	X
Injectable Antihyperglycemic Therapy: GLP-1 Receptor Agonist										
• Exenatide (Byetta®) [4]		X	X		✓	✓	✓		X	X
• Exenatide extended release (Bydureon®)		X	X		✓	✓	✓		X	X
• Liraglutide (Victoza®)[5]		X	X		✓	✓	✓		X	X
• Dulaglutide (Trulicity™)[5]		X	X		✓	✓	✓		X	X
• Albiglutide (Eperzan®)[5]		X	X		✓	✓	✓		X	X
Weight Loss Agents										
• Orlistat (Xenical®)		✓	✓		✓	✓	✓		✓	✓
• Liraglutide (Saxenda®)		X	X		✓	✓	✓		X	X

Key: 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: 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.

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

Note:

Several studies have compared the effects of oral antidiabetic agents (OADs) added to insulin compared with insulin monotherapy; however, there are no studies that have directly compared OADs in combination with insulin to help understand their relative effectiveness and tolerability in this context.

- A common limitation of currently available data on the use of OAD agents in combination with insulin is that most studies were designed to fulfill drug licensing requirements.

- Study design is influenced by when drugs are brought to market. Newer agents such as the SGLT2 inhibitors have been specifically studied in patients poorly controlled on high insulin doses plus OADs. The older oral agents were not studied in this way as practice patterns were very different at the time they came to market. Therefore, the relative efficacy and safety of the available oral agents in combination with insulin is largely unknown.

- Studies have either not evaluated the efficacy and tolerability of the addition of an OAD agent to insulin or, if evaluated, the comparator was placebo not other OAD agents plus insulin in combination (i.e., metformin + insulin).

- Study patients are not necessarily using basal insulin exclusively. Also full details on insulin regimens are not always provided.

- The bulk of trial data are only partially reflective of T2DM treatment with insulin as it exists in current clinical practice.

NOTE: TABLE 2A was updated July 2017.