Thames Valley
Family Health Team

Medical Directive

Title	**Type 2 Diabetes Medical Management in Non-Pregnant Adults**	**Assigned Number:**	**003B**
Activation Date:	**July 1, 2011**	**Review By:**	**December 2025**

Approval Signature & Date

Medical Director: _____ Date Reviewed: Feb 23, 2024

Clinical Services Director: _____ Date Reviewed: Feb 23, 2024

Order and/or Delegated Procedure:

Appendix Attached: ☐ **Yes** ☒ **No**
Title:

Provision of Medications for the Management of Type 2 Diabetes Mellitus in non-pregnant adults by Registered Pharmacists (RPh).

Recipient Patients:

Appendix Attached: ☒ **Yes** ☐ **No**
Title:

All active non-pregnant adult patients of the Thames Valley Family Health Team who have Type 2 Diabetes.

Authorized Implementers:

Appendix Attached: ☒ **Yes** ☐ **No**
Title:

Thames Valley Family Health Team Registered Pharmacists (RPh)* herein referred to as the implementer.

∗ The implementer must receive orientation from the Educator with regards to the task. The implementer must have completed orientation and educational requirements of Diabetes Level 2 medical directive The implementer must sign the Implementer Performance Readiness Form electronically via HR Downloads after successful completion of the orientation (and quiz, if applicable) indicating acceptance of this medical directive.

Indications:

Appendix Attached: ☐ **Yes** ☒ **No**
Title:

1. Non-pregnant adult patients 18 years of age and older identified with Type 2 Diabetes

Contraindications:

Appendix Attached: ☐ **Yes** ☒ **No**
Title:

1. Patients under 18 years of age or are identified having Type 1 Diabetes
2. No verbal consent obtained from the patient by the implementer
3. Pregnancy and lactation
4. Patients identified by the provider who are not candidates for management under this medical directive.

Consent:	**Appendix Attached:** ☐ **Yes** ☒ **No** **Title:**

1. Verbal consent is obtained from the patient by the implementer prior to implementation of care.

Guidelines for Implementing the Order/Procedure:	**Appendix Attached:** ☒ **Yes** ☐ **No** **Title:** Appendix 1 – Oral/Injectable Non-Insulin Anti-Hyperglycemic Agents **Title:** Appendix 2 – Insulin Management

1. The implementer will educate, implement, and adjust new medications as per (Appendix 1) Oral/Injectable Non-Insulin Antihyperglycemic Agents and (Appendix 2) Insulin Management.
   - Adjust, hold, discontinue, or start oral or injectable antihyperglycemic agents per the appendices to this directive
   - Prescribe and refill up to 400 days of diabetic medication and supplies (e.g., 100 days with 3 refills)
2. A message via EMR will be sent to the patient's most responsible provider within 48 hours of initiating the new agent and for any dose adjustments. If appropriate and clinically indicated, the implementer can also follow-up with a phone call to the patient's most responsible provider within 48 hours of initiating the new agent.
3. The implementer will consult with the patient's provider if they are experiencing severe adverse drug events that require further medical evaluation (e.g., signs and symptoms consistent with pancreatitis, retinopathy, etc.) or if there are concerns regarding immediate safety and well-being of the patient due to the stability of their diabetic condition
4. The implementer will phone or write a new prescription as per usual standard with the provider's name on the prescription to the patient's pharmacy of choice*. Preferences will be for medications covered under a provincial or private drug plan.
5. The implementer will ensure follow-up plan that may include one or more of: self-monitoring blood glucose, HbA1c follow-up laboratory investigation in 3-6 months, or follow-up appointment with the most responsible provider.

∗ Potter, P.A. & Perry, A.G. (2006). Fundamentals of Nursing. St. Louis: Mosby. College of Nurses of Ontario (2008). CNO Practice Standard: Documentation

Documentation and Communication	**Appendix Attached:** ☐ **Yes** ☒ **No** **Title:**

1. Documentation in the patient medical records need to include name and number of the directive, name of the implementer (including credential(s)), and name of the authorizer responsible for the directive and patient.
2. Information regarding implementation of the procedure and the patient responses should be documented in accordance with standard documentation practice.
3. Standard documentation is required for prescriptions, requisitions, and requests for consultation. *

∗ Potter, P.A. & Perry, A.G. (2006). Fundamentals of Nursing. St. Louis: Mosby. College of Nurses of Ontario (2008). CNO Practice Standard: Documentation

Review and Quality Monitoring Guidelines:	**Appendix Attached:** ☐ **Yes** ☒ **No** **Title:**

1. The Directive remains in force until and unless amendment occurs. Review will occur biennially. In case the Medical Director identifies the need to change the Medical Directive, at least one TVFHT member of the implementing disciplines will be consulted.
2. At any such time that issues related to the use of this directive are identified, the team must act upon the concerns immediately by identifying these concerns to the Medical Director. The Medical Director will review these concerns and consult with at least one TVFHT member of the implementing disciplines, before necessary changes are made.
3. If new information becomes available between routine renewals, and particularly if this new information has implications for unexpected outcomes, the directive will be reviewed by the Medical Director and a minimum of one TVFHT member of the implementing disciplines.

Approving Authorizer(s):	**Appendix Attached:** ☐ **Yes** ☒ **No** **Title:**

Authorizer Approval Form signed in HR Downloads.

Thames Valley Family Health Team	**Appendix 1: Diabetes Education and Medical Management in Adults with Diabetes**

Oral and Injectable Non-insulin Antihyperglycemic Agents

Note: Medications discontinued or placed on hold should be reviewed within 24-48 hours by the implementer in collaboration with the provider.

TABLE 1: List of Medications Implemented Under this Directive with Detailed Indications/ Contraindications

Oral/Non-insulin Injectable Antihyperglycemic Agent Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	**Indications for Adjustment**	**Contraindication/Precautions**
Biguanides		
Metformin (Glucophage®) **I:** 250 –500 mg PO daily with food **U:** 1000 mg PO BID with food **M:** 2550 mg PO per day or 850 mg PO TID CrCl 30- 45 mL per min (less than or equal to 1000 mg daily) **CI:** eGFR less than 30 mL per min **Metformin Extended Release** (Glumetza®) **I:** 250 –500 mg PO daily with food **U:** 1000 – 2000 PO mg with food **M:** 2500 PO mg daily CrCl 30- 45 mL per min (less than or equal to 1000 mg daily) **CI:** eGFR less than 30 mL per min	GI side effects Inadequate blood glucose control Frequent hypoglycemic event	Contraindications: Type 1 Diabetes, history of lactic acidosis, ketoacidosis, renal impairment (CrCl less than 30 mL/min), excessive alcohol consumption (acute or chronic), hepatic dysfunction, pregnancy, or gastrointestinal side effects Hold for 48 hours if undergoing radiologic studies with administration of iodinated contrast material Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table

Oral/Non-insulin Injectable Antihyperglycemic Agent Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	**Indications for Adjustment**	**Contraindications/Precautions** Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
Insulin Secretagogues		
Sulfonylureas **Gliclazide** (Diamicron)© **I:** 40-80 mg PO daily in am with food **U:** 80 mg PO BID with food **M:** 160 mg PO BID with food **CI**: eGFR less than 30 mL per min **Gliclazide MR** (Diamicron MR) © **I:** 30 mg MR PO daily **U:** 60 mg MR PO daily **M:** 120 mg MR PO daily **CI:** eGFR less than 30 mL per min	Frequent hypoglycemic events Inadequate blood glucose control Renal impairment	Contraindications: Type 1 Diabetes, hypersensitivity to sulfonamides, severe renal or hepatic impairment, diabetic ketoacidosis, pregnancy, breastfeeding Hypoglycemia and weight gain are more common with glyburide Consider using other class(es) of oral antihyperglycemic agents first in patients at high risk of hypoglycemia (i.e., the elderly) Hypoglycemia with insulin
Non-sulfonylureas **Repaglinide** (GlucoNorm) © **I:** [A1C less than 8%] 0.5 mg PO TID before meals, [A1C greater than or equal to 8%] 1-2 mg PO TID before meals **U:** 1-4 mg PO BID-QID before meals **M:** 16 mg PO daily eGFR less than 30mL per min (caution)	Frequent hypoglycemic events Inadequate blood glucose control Renal impairment	Check for drug interactions before using; avoid use with strong 3A4 and 2C8 inhibitors (due to increased risk of hypoglycemia) Repaglinide contraindicated when co-administered with clopidogrel or with gemfibrozil Less risk of hypoglycemia than sulfonylureas due to short action and mealtime administration

Oral/Non-insulin Injectable Antihyperglycemic Agent Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	**Indications for Adjustment**	**Contraindications/Precautions** Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
Incretins		
DPP4 Inhibitors **Sitagliptin** (Januvia)© **I, U, M:** 25-100 mg PO daily eGFR 30-49 mL per min (50 mg PO daily) eGFR less than 30 mL per min, hemodialysis, peritoneal dialysis, CKD (25 mg PO daily) **Linagliptin (**Trajenta) © **I, U, M:** 5 mg PO daily No dosage adjustments eGFR less than 15 mL per min (use with caution) **Saxagliptin** (Onglyza®) **I, U, M:** 2.5 – 5 mg PO daily eGFR 15-50 mL per min (2.5mg PO daily) eGFR less than 15 mL per min use alternative agent	Nasopharyngitis Inadequate glucose control May need to reduce dose of insulin or insulin secretagogue if used in combination therapy	Contraindications: Hypersensitivity, Type 1 Diabetes Cases of acute pancreatitis have been reported, monitor for signs and symptoms of pancreatitis, and use with caution in patients with history of pancreatitis' CYP 3A4 inhibitors may increase the serum concentration of saxagliptin. U.S. saxagliptin product labelling recommends limiting adult dose to 2.5 mg PO daily when used with a strong CYP 3A4 inhibitor, monitor for increased saxagliptin effects. A similar recommendation is not made in the Canadian product labeling
GLP-1 Analogues **Liraglutide** (Victoza) © **I:** 0.6 mg subcut daily **U:** after greater than or equal to 1 week 1.2 mg subcut daily X 1 week, then 1.8 mg subcut daily **M:** 1.8 mg subcut daily Caution eGFR less than 30 mL per min, no dosage adjustment **CI:** eGFR less than 15 mL per min **Dulaglutide** (Trulicity) © **I:** 0.75 mg subcut once weekly **U, M:** 1.5 mg subcut once weekly eGFR less than 15 mL per min (use with caution)	Persistent and/or bothersome GI adverse effects Inadequate glucose control May need to reduce dose of insulin or insulin secretagogue if used in combination therapy	Contraindications: Hypersensitivity, pregnancy, breast-feeding, personal or family history of Medullary Thyroid Cancer, Multiple Endocrine Neoplasia syndrome type 2 (MEN2) Caution of us use in patients with hepatic impairment, especially liver cirrhosis Cases of acute and chronic pancreatitis have been reported, monitor for signs and symptoms of pancreatitis, and use with caution in patients with history of pancreatitis

Semaglutide (Ozempic) © **I:** 0.25 mg subcut once weekly **U:** after at least 4 weeks 0.5 mg once weekly X 4 weeks, then 1 mg subcut once weekly as tolerated **M:** 2 mg subcut once weekly Caution eGFR less than 30 mL per min, no dosage adjustment CI eGFR less than 15 mL per min		Caution in patients with pre-existing diabetic retinopathy, GERD, or gastroparesis (risk of worsening these conditions)
Semaglutide (Rybelsus) © **I:** 3 mg PO daily 30min before meals with 120mL of water **U:** After 30 days, increase dose to 7 mg daily 30min before meals with 120mL of water. **M:** 14 mg PO daily 30min before meals with 120mL of water **CI:** eGFR less than 30 mL per min		
Lixisenatide (Adlyxine) © **I:** 10 mcg subcut daily before meals X 2 weeks **U, M:** 20 mcg subcut once daily before meals **CI**: eGFR less than 15 –20 mL per min		

Oral/Non-insulin Injectable Antihyperglycemic Agent Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	**Indications for Adjustment**	**Contraindications/Precautions** Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
GIP and GLP1-RA		
Tirzepatide (Mounjaro) © **I:** 2.5 mg subcut once weekly x 4 weeks **U:** After greater than or equal to 4-8 weeks 15 mg subcut once weekly if additional glycemic control is needed then titrate by 2.5 mg subcut weekly x 4 weeks as tolerated **M:** 15 mg subcut once weekly	Frequent hypoglycemic events Inadequate glucose control May need to reduce dose of insulin or insulin secretagogue if used in combination therapy	Contraindications personal or family history of Medullary Thyroid Cancer, Multiple Endocrine Neoplasia syndrome type 2 (MEN2) Loss of up to 11.3 kg over 26 weeks (caution in frail elderly) Caution in patients with GI disease (e.g., GERD, gastroparesis) due to risk of worsening of symptoms
SGLT2 Inhibitors		
Canagliflozin (Invokana)© **I, U:** 100 mg PO daily in the morning **M:** 300 mg PO daily in the morning eGFR 30 - 60 mL per min (100 mg daily) **CI:** eGFR less than 30mL per min	Hypoglycemia Nausea and hyperkalemia Discontinue if recurrent genital mycotic infection or if develops ketoacidosis	Contraindications: Type 1 Diabetes, hypersensitivity, renal impairment) Canagliflozin: lower extremity amputation (avoid if prior amputation – Canadian Black Box Warning). May cause ketoacidosis, even with glucose values less than 13.9 mmoL; use with caution in patients predisposed to ketoacidosis – Canadian Black Box Warning (e.g., alcohol abuse, caloric restriction) May Increase risk of genital mycotic infections and urinary tract infections that may become serious (urosepsis, pyelonephritis); assess patients with symptoms suggestive of UTI and consider discontinuation of drug May cause symptomatic hypotension due to intravascular volume depletion
Dapagliflozin (Forxiga)© **I, U:** 5 mg PO daily in the morning **M:** 10 mg PO daily in the morning EGFR less than 45 mL per min (not recommended) **CI:** eGFR less than 25 mL per min		
Empagliflozin (Jardiance)© **I, U:** 10 mg PO daily in the morning **M:** 25 mg PO daily in the morning eGFR less than 60 mL per min (caution) **CI:** eGFR less than 20 mL per min		
Combination Therapy Any combination therapy of individual agents listed above	As per information listed for individual agents above	As per information listed for individual agents above

***Adapted from:** https://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Metformin-LacticAcidosis-QandA.pdf, https://www.diabetes.ca/DiabetesCanadaWebsite/media/Health-care-providers/2018%20Clinical%20Practice%20Guidelines/Appendix-7-therapeutic-considerations-for-renal-impairment.pdf?ext=.pdf

Summary of Therapeutic Notes for Oral and Injectable Non-Insulin Antihyperglycemic Agents:

Key Adverse Effects

- Gastrointestinal upset, loose bowels (biguanide, GLP-1 analogues)
- Hypoglycemia (secretagogues – less with gliclazide, glimepride and replaglinide than with glyburide), GLP-1 analogues, SGLT2 inhibitors.
- Moderate weight gain (insulin secretagogues, insulin sensitizers)
- Urinary tract infections, genital mycotic infections, euglycemic diabetic ketoacidosis with or without hyperglycemia (SGLT2 inhibitors)
- Canagliflozin fracture risk (NNH =285/~3 years), lower extremity amputation (NNH = 345/ ~ 3 years); avoid if prior amputation

Key Precaution / Contraindications

- Hepatic disease (glyburide, biguanide, insulin sensitizers, DPP-4i, GLP-1 analogues)
- Significant renal insufficiency (biguanide, sulfonylureas, DPP-4i, GLP-1 analogues, SGLT2-inhibitors)
- Pancreatitis history (GLP-1 analogues, DPP4-inhibitors)
- Personal/family history of medullary thyroid cancer or multiple endocrine neoplasia syndrome type 2 (GLP-1 analogues, DPP4-inhibitors)
- Retinopathy history (Semaglutide) ©
- Caution with renal dysfunction, loop diuretics in older adults (SGLT2-inhibitors)
- Bladder cancer (Dapagliflozin) ©
- Sick day management – caution in acute illness/dehydration (sulfonylrueas, metformin, SGLT-2 inhibitors) – see https://www.rxfiles.ca/rxfiles/uploads/documents/SADMANS-Rx.pdf

Appendix 2 - Diabetes Education and Medical Management in Adults with Diabetes

Insulin Management

Insulin Type	Onset	Peak (P) / Duration(D)	Indications for Adjustment	Therapeutic Considerations
Basal Insulin Long-Acting and Ultra Long Acting (clear)				The most common adverse effect of insulin is hypoglycemia. The timing of hypoglycemia may vary, depending on the insulin formulation and extrinsic factors such as timing of meals, exercise, or combination with other anti- hyperglycemic agents. General storage and stability information for all insulins: Store unopened vials/cartridges in refrigerator. Keep away from heat and sunlight; do not freeze. Use by expiration date. Store punctured or open vials or cartridges/pens at room temperature. Discard within 28 days of opening. Consult individual product monograph for product-specific details.
Insulin determir	1-2hrs	P: undiscernable D: 16-24hrs	Titrate to target based on fasting blood sugar Hypoglycemia Switch to more concentrated product (e.g., glargine 300 units per mL or degludec 200 units per mL) for large volume doses	
Insulin glargine 100 units per mL	1-2hrs	P: undiscernable D: Up to 4hr		
Insulin glargine 300 units per mL	Up to 6hrs	P: undiscernable D: Up to 30hrs		
Insulin degludec 100 units per mL, 200 units per mL	60-90mins	P: none D: More than 42hrs		
Basal Insulin Intermediate-Acting (cloudy)				
NPH	1-3hr	P: 5-8hr peak D: Up to 18hrs	Hyperglycemia Hypoglycemia For twice daily dosing: Increase evening dose if high fasting and rebound hyperglycemia has been ruled out. Increase or decrease morning dose if readings 4-6 hours after injection are out of target	
Bolus (Prandial) Insulins Rapid and Short-Acting (clear)				
Ultra-fast acting Insulin aspart (Fiasp® only)	5mins	P: 45-60min D: 3-5 hrs	Typically administered in multiple daily doses. Patients should eat within 10-15 min of injection (with the exception of ultra-fast acting aspart which is given no sooner than 2 minutes before the meal and up to 20 min after)	
Rapid acting Insulin aspart (all other products)	10-15mins	P: 1-2 hrs D: 3-5hrs		
Insulin glulisine				
Insulin lispro				

Regular insulin Insulin human	30mins	P: 2-3 hrs D: 5-8hrs	Titrate based on 2- hour post-meal glucose measurement or next pre-meal measurement following the injection. May also be adjusted if carbohydrate to insulin ratio is changed Avoid hypoglycemia	
Insulin Type	**Onset**	**Peak (P) / Duration(D)**	**Indications for Adjustment**	**Therapeutic Considerations**
Premixed Insulins				
Premixed regular (cloudy) Insulin human and isophane **Premixed analogues** (cloudy) Insulin lispro and lispro protamine Insulin aspart and aspart protamine	Each single vial/cartridge contains insulin in fixed ratio of rapid/short-acting to intermediate-acting. See above onset, peak, and duration times for individual components.		Typically administered in 2 daily doses.	See therapeutic considerations above for individual components
Combination Products with Insulin + GLP-1 Analogues				
Any combination therapy of individual agents listed above and GLP-1s listed in Appendix 1	As per information listed for individual agents above as well as per monograph information for the combination therapy		Typically administered subcutaneously once a day within the hour prior to the first meal of the day	As per information for individual agents listed above and GLP-1s listed in Appendix 1

Summary of Therapeutic Notes for Insulins

1. The usual total daily requirement is approximately 0.5 unit per kg of body weight.
2. Most patients new to insulin are started at 0.1 – 0.3 units per kg per day or 5-10 units QHS however, individual consideration (e.g. during pregnancy) needs to be assessed. Those patients who are hypoglycemic unaware or have a fear of insulin-induced hypoglycemia can be initiated on a smaller dose.
3. Under certain circumstances patients may need insulin adjusted greater or less than evidence-based recommendation of 5 –10% total daily dose (TDD)
4. Determine a plan for the frequency of communication with the pharmacist for further adjustments. Depending on clinical situation, may adjust insulin by 5-10% of total daily dose (TDD) and adjust every 3-4 days. Alternatively, for basal insulin, one can increase the dose by 1 unit daily until fasting plasma glucose target is reached with the exception of degludec & glargine (300 units/mL). Change one type of insulin at a time unless this change could cause hypoglycemia then adjust accordingly.
5. The dose of degludec can be titrated +/- 2 units every 3 - 4 days to target the individualized fasting glucose range. Alternatively, it can be titrated +/- 4 units once weekly to target the individualized fasting glucose range.
6. In the event a patient has high and low glucose results, always adjust insulin for hypoglycemia first.
7. Consult the Diabetes Canada Insulin Prescription Tool for further guidance https://guidelines.diabetes.ca/CDACPG/media/documents/hcp-resources/Insulin_Prescription_EN_09_23.pdf