Medical Directive

Title	**Type 2 Diabetes Medical Management in Non-Pregnant Adults**	**Assigned Number:**	**003B**
Activation Date:	**July 1, 2011**	**Review By:**	**December 2023**

Approval Signature & Date

Medical Director: _____ Date Reviewed: January 13, 2022

Clinical Services Director: _____ Date Reviewed: January 13, 2022

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 physicians who have Type 2 Diabetes, identified on the Authorizer Approval Form.

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

Thames Valley Family Health Team RPhs, who have undergone an Assessment of Competency accepted to the Thames valley Family Health Team that ensures competencies in the initiation of pharmacotherapy in the management of diabetes. Implementers must sign the Implementer Performance Readiness Form in HR Downloads, following the completion of all educational components.

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

1. Non-pregnant adult patients >= 21 yo identified with Type 2 Diabetes

Contraindications:	

1. Patients <21 yo or are identified having Type 1 Diabetes
2. No verbal consent obtained from the patient by the RPh, RPN, RN, or RD
3. Pregnancy and Lactation
4. Patients identified by the physician 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 RPh 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
- Appendix 2 – Insulin Management

1. RPh will educate and implement new medications as per (Appendix 1) Oral/Injectable Non-Insulin Antihyperglycemic Agents and (Appendix 2) Insulin Management.
2. A message via EMR will be sent to the patient's most responsible physician within 48 hours of initiating the new agent. If appropriate and clinically indicated, the pharmacist can also follow-up with a phone call to the patient's most responsible physician within 48 hours of initiating the new agent.
3. RPh will consult with the patient's family physician or on-call physician or nurse practitioner if patients 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. RPh will phone or write a new prescription as per usual standard with the family physician'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. RPh 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 physician.

∗ *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 physician/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 recommended 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:**
The directive remains in force until and unless amendment occurs. Review will occur biennially or if the following situations occur. 1. In the case the medical director identifies the need to change the medical directive, at least one (1) TVFHT member of the implementing discipline 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 (1) TVFHT member of the implementing discipline, 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 (1) implementing RN.	
Approving Physician(s)/Authorizer(s):	**Appendix Attached:** ☐ **Yes** ☒ **No** **Title:**
Authorize Approval Form	

Thames Valley Family Health Team

Appendix 1: Diabetes Education and Medical Management in Adults with Diabetes

Oral and Injectable Non-insulin Antihyperglycemic Agents

This directive will be implemented by RPhs who have been deemed authorized implementers.

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

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**	**Contraindications/Precautions**
Biguanides Metformin (Glucophage) I: 250 –500 mg PO daily cc U: 1000 mg bid cc M: 2550 mg per day or 850 mg PO TID CrCl 30- 45 mL/min (≤ 1000 mg daily) CI: eGFR < 30 mL/min Metformin (Glumetza - Extended Release) I: 250 –500 mg PO daily cc U: 1000 – 2000 mg cc M: 2500 mg daily CrCl 30- 45 mL/min (≤ 1000 mg daily) CI: eGFR < 30 mL/min	• GI side effects • Inadequate blood glucose control • Frequent hypoglycemic events	• Contraindications: Type 1 Diabetes, history of lactic acidosis, ketoacidosis, renal impairment (CrCl < 30 mL/min), excessive ETOH (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**
Insulin Secretagogues	• Frequent hypoglycemic events	• 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 • Check for drug interactions before using; avoid use with strong 3A4 and 2C8 inhibitors (due to increased risk of hypoglycemia) • Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
Sulfonylureas Gliclazide (Diamicron) I: 40-80 mg daily in am cc U: 80 mg bid cc M: 160 mg bid cc CI eGFR < 30 mL/min Gliclazide MR (Diamicron MR) I: 30 mg MR PO daily U: 60 mg MR daily M: 120 mg MR daily CI eGFR < 30 mL/min Glimepiride (Amaryl) I: 1-2 mg PO daily in am cc U: 1-4 mg daily in am cc M: 8 mg daily cc CI eGFR < 30 mL/min	• Inadequate blood glucose control • Renal impairment	
Non-sulfonylureas:		
Repaglinide (GlucoNorm) I: [A1C < 8%] 0.5 mg PO TID ac, [A1C ≥ 8%] 1-2 mg PO TID ac U: 1-4 mg PO bid-qid ac M: 16 mg daily EGFR < 30mL/min (caution)	• Dose adjustment hypoglycemia persists 1-2 times per week • Blood glucose remains above target (7 mMol/L) consistently Blood glucose below 4 mMol/L consistently	

Oral/Non-insulin Injectable Antihyperglycemic Agent Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	**Indications for Adjustment**	**Contraindications/Precautions**
GLP-1 Analogues Liraglutide (Victoza) I: 0.6 mg SC daily U: after ≥ 1 week 1.2 mg SC daily X 1 week, then 1.8 mg SC daily M: 1.8 mg SC daily CI eGFR < 15 – 30 mL/min Dulaglutide (Trulicity) I: 0.75 mg SC once weekly U, M: 1.5 mg SC once weekly EGFR < 15 mL/min (caution) Semaglutide (Ozempic) I: 0.25 mg SC once weekly U: after ≥ 4 weeks 0.5 mg once weekly X 4 weeks, then 1 mg SC once weekly as tolerated M: 1 mg SC once weekly EGFR < 30 mL/min (caution) Lixisenatide (Adlyxine) I: 10 mcg SC daily ac X 2 weeks U, M: 20 mcg once daily ac CI: eGFR < 15 –20 mL/min	• Nausea (extended duration) Inadequate glucose control	• 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 • 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**
SGLT2 Inhibitors Canagliflozin (Invokana) I, U: 100 mg PO daily am M: 300 mg PO daily am eGFR 30 - 60 mL/min (100 mg daily) CI : eGFR< 30 mL/min Dapagliflozin (Forxiga) I, U: 5 mg PO daily am M: 10 mg PO daily am EGFR < 45 mL/min (not recommended) CI : eGFR < 30 mL/min Empagliflozin (Jardiance) I, U: 10 mg PO daily am M: 25 mg PO daily am eGFR < 60 mL/min (not recommended) CI: eGFR < 30 mL/min Ertugliflozin (Steglatro) I, U: 5 mg PO daily am M: 15 mg PO daily am CI: eGFR < 45 mL/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 < 13.9mM; 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 • Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
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 CEP_Type2DiabetesNonInsulin_April12_1.pdf		

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

Key Adverse Effects

- Gastrointestinal upset, loose bowels (biguanide)
- Hypoglycemia (secretagogues – less with gliclazide, glimepride and replaglinide than with glyburide), GLP-1 analogues, SGLT2 inhibitors.
- Edema, fluid retention (insulin sensitizers)
- 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)

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

Insulin Management

This directive will be implemented by RPhs who have been deemed authorized implementers.

Insulin Type	Onset	Peak	Duration	Indications for Adjustment	Therapeutic Considerations
Basal insulins 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 Consult individual product monograph for product-specific details.
Insulin determir (levemir)	1-2hrs	Almost peak less	16-24hrs	Titrate to target based on fasting blood sugar Hypoglycemia	
Insulin glargine 100u/ml (Basaglar, Lantus)	1-2hrs		Up to 24hr		
Insulin glargine 300u/ml (Toujeo)	Up to 6hrs	n/a	Up to 30hrs		
Insulin degludec 100u/ml, 200u/ml (Tresiba)	60-90mins		More than 42hrs		
Basal Insulin Intermediate-acting (cloudy)					
Humulin-N Novolin ge NPH	1-3hr	5-8hr	Up to 18hrs	Hyperglycemia Hypoglycemia	
Bolus (Prandial) Insulins					
Ultra-fasting acting Insulin aspart (Fiasp)	5mins	45-60mins	3-5 hrs	Typically administered in multiple daily doses. Titrate based on 2- hour post-meal glucose measurement or next pre-meal measurement following the injection. Avoid hypoglycemia	
Rapid acting Insulin aspart (Novorapid) Insulin glulisine (Apidra) Insulin lispro (Humalog and Humalog U200)	10-15mins	1-2hrs	3-5hrs		
Regular insulin Toronto or Humulin R	30mins	2-3hrs	5-8hrs		
Entuzity (500u/ml)	15mins	4-8hrs	Up to 24hrs		

Insulin Type	Onset	Peak	Duration	Indications for Adjustment	Therapeutic Considerations
Premixed Insulins *Premixed regular- NPH (cloudy)* • Humulin 30/70 • Novolin ge 30/70, 40/60, 50/50 *Premixed analogues (cloudy)* • Biphasic insulin aspart (NovoMix 30) • Insulin lispro/lispro protamine (Humalog Mix25 and Mix50)	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.	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 Consult individual product monograph for product-specific details.
Combination with 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