



# Medical Directive

<b>Title</b>	<b>Type 2 Diabetes Medical Management in Non-Pregnant Adults</b>	<b>Assigned Number:</b>	<b>003B</b>
<b>Activation Date:</b>	<b>July 1, 2011</b>	<b>Review By:</b>	<b>December 2025</b>
<b>Approval Signature &amp; Date</b>			
Medical Director: _____		Date Reviewed: Revised: May 25, 2024	
Clinical Services Director: _____		Date Reviewed: Revised: May 25, 2024	
<b>Order and/or Delegated Procedure:</b>	<b>Appendix Attached:</b> <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <b>Title:</b>		
Provision of Medications for the Management of Type 2 Diabetes Mellitus in non-pregnant adults by Registered Pharmacists (RPh).			
<b>Recipient Patients:</b>	<b>Appendix Attached:</b> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <b>Title:</b>		
All active non-pregnant adult patients of the Thames Valley Family Health Team who have Type 2 Diabetes.			
<b>Authorized Implementers:</b>	<b>Appendix Attached:</b> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <b>Title:</b>		
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.			
<b>Indications:</b>	<b>Appendix Attached:</b> <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <b>Title:</b>		
1. Non-pregnant adult patients 18 years of age and older identified with Type 2 Diabetes			
<b>Contraindications:</b>	<b>Appendix Attached:</b> <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <b>Title:</b>		
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.			

<b>Consent:</b>	<b>Appendix Attached:</b> <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <b>Title:</b>
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1. Verbal consent is obtained from the patient by the implementer prior to implementation of care.

<b>Guidelines for Implementing the Order/Procedure:</b>	<b>Appendix Attached:</b> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No <b>Title:</b> Appendix 1 – Oral/Injectable Non-Insulin Anti-Hyperglycemic Agents <b>Title:</b> Appendix 2 – Insulin Management
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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

<b>Documentation and Communication</b>	<b>Appendix Attached:</b> <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <b>Title:</b>
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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.



## 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**

<b>Oral/Non-insulin Injectable Antihyperglycemic Agent</b>  Dose (I = initial, U = usual, M = max, CI = contraindications)  Renal Dose Suggestions	<b>Indications for Adjustment</b>	<b>Contraindication/Precautions</b>
<b>Biguanides</b>		
<p><b><u>Metformin (Glucophage®)</u></b>  <b>I:</b> 250 –500 mg PO daily with food  <b>U:</b> 1000 mg PO BID with food  <b>M:</b> 2550 mg PO per day or 850 mg PO TID            CrCl 30- 45 mL per min (less than or equal to 1000 mg daily)  <b>CI:</b> eGFR less than 30 mL per min</p> <hr/> <p><b><u>Metformin Extended Release (Glumetza®)</u></b>  <b>I:</b> 250 –500 mg PO daily with food  <b>U:</b> 1000 – 2000 PO mg with food  <b>M:</b> 2500 PO mg daily            CrCl 30- 45 mL per min (less than or equal to 1000 mg daily)  <b>CI:</b> eGFR less than 30 mL per min</p>	<p>GI side effects</p> <p>Inadequate blood glucose control</p> <p>Frequent hypoglycemic event</p>	<p>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</p> <p>Hold for 48 hours if undergoing radiologic studies with administration of iodinated contrast material</p> <p>Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table</p>

<b>Oral/Non-insulin Injectable Antihyperglycemic Agent</b>  Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	<b>Indications for Adjustment</b>	<b>Contraindications/Precautions</b>  Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
<b>Insulin Secretagogues</b>		
<b>Sulfonylureas</b>  <u><b>Gliclazide (Diamicon)®</b></u> <b>I:</b> 40-80 mg PO daily in am with food <b>U:</b> 80 mg PO BID with food <b>M:</b> 160 mg PO BID with food <b>CI:</b> eGFR less than 30 mL per min  <hr/> <u><b>Gliclazide MR (Diamicon MR)®</b></u> <b>I:</b> 30 mg MR PO daily <b>U:</b> 60 mg MR PO daily <b>M:</b> 120 mg MR PO daily <b>CI:</b> 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
<b>Non-sulfonylureas</b>  <u><b>Repaglinide (GlucoNorm)®</b></u> <b>I:</b> [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 <b>U:</b> 1-4 mg PO BID-QID before meals <b>M:</b> 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

<b>Oral/Non-insulin Injectable Antihyperglycemic Agent</b>  Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	<b>Indications for Adjustment</b>	<b>Contraindications/Precautions</b>  Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
<b>Incretins</b>		
<b>DPP4 Inhibitors</b>  <b>Sitagliptin (Januvia)®</b> <b>I, U, M:</b> 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)	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
<b>Linagliptin (Trajenta)®</b> <b>I, U, M:</b> 5 mg PO daily No dosage adjustments eGFR less than 15 mL per min (use with caution)		
<b>Saxagliptin (Onglyza®)</b> <b>I, U, M:</b> 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	<b>GLP-1 Analogues</b>  <b>Liraglutide (Victoza)®</b> <b>I:</b> 0.6 mg subcut daily <b>U:</b> after greater than or equal to 1 week 1.2 mg subcut daily X 1 week, then 1.8 mg subcut daily <b>M:</b> 1.8 mg subcut daily Caution eGFR less than 30 mL per min, no dosage adjustment <b>CI:</b> eGFR less than 15 mL per min  <b>Dulaglutide (Trulicity)®</b> <b>I:</b> 0.75 mg subcut once weekly <b>U, M:</b> 1.5 mg subcut once weekly eGFR less than 15 mL per min (use with caution)	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

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

<b>Oral/Non-insulin Injectable Antihyperglycemic Agent</b>  Dose (I = initial, U = usual, M = max, CI = contraindications) Renal Dose Suggestions	<b>Indications for Adjustment</b>	<b>Contraindications/Precautions</b>  Renal dysfunction – see eGFR under CI for each of the medications in the first column of the table
<b>GIP and GLP1-RA</b>		
<b><u>Tirzepatide (Mounjaro)®</u></b> <b>I:</b> 2.5 mg subcut once weekly x 4 weeks, then increase to 5 mg once weekly <b>U:</b> May increase dose in 2.5 mg per week increments every 4 weeks if needed to achieve glycemic goals <b>M:</b> 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
<b>SGLT2 Inhibitors</b>		
<b><u>Canagliflozin (Invokana)®</u></b> <b>I, U:</b> 100 mg PO daily in the morning <b>M:</b> 300 mg PO daily in the morning eGFR 30 - 60 mL per min (100 mg daily) <b>CI:</b> eGFR less than 30mL per min		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/L; use with caution in patients predisposed to ketoacidosis – Canadian Black Box Warning (e.g., alcohol abuse, caloric restriction)
<b><u>Dapagliflozin (Forxiga)®</u></b> <b>I, U:</b> 5 mg PO daily in the morning <b>M:</b> 10 mg PO daily in the morning EGFR less than 45 mL per min (not recommended) <b>CI:</b> eGFR less than 25 mL per min	Hypoglycemia  Nausea and hyperkalemia  Discontinue if recurrent genital mycotic infection or if develops ketoacidosis	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
<b><u>Empagliflozin (Jardiance)®</u></b> <b>I, U:</b> 10 mg PO daily in the morning <b>M:</b> 25 mg PO daily in the morning eGFR less than 60 mL per min (caution) <b>CI:</b> eGFR less than 20 mL per min		May cause symptomatic hypotension due to intravascular volume depletion
<b>Combination Therapy</b> 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: <a href="https://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Metformin-LacticAcidosis-QandA.pdf">https://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Metformin-LacticAcidosis-QandA.pdf</a> , <a href="https://www.diabetes.ca/DiabetesCanadaWebsite/media/Health-care-providers/2018%20Clinical%20Practice%20Guidelines/Appendix-7-therapeutic-considerations-for-renal-impairment.pdf?ext=.pdf">https://www.diabetes.ca/DiabetesCanadaWebsite/media/Health-care-providers/2018%20Clinical%20Practice%20Guidelines/Appendix-7-therapeutic-considerations-for-renal-impairment.pdf?ext=.pdf</a>		



## 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 repaglinide 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 (sulfonylureas, 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
<b>Basal Insulin</b> Long-Acting and Ultra Long Acting (clear)				<p>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.</p> <p>General storage and stability information for all insulins: Store unopened vials/cartridges in refrigerator. Keep away from heat and sunlight; do not freeze.</p> <p>Use by expiration date.</p> <p>Store punctured or open vials or cartridges/pens at room temperature. Discard within 28 days of opening.</p> <p>Consult individual product monograph for product-specific details.</p>
Insulin detemir	1-2hrs	P: undiscernable D: 16-24hrs	Titrate to target based on fasting blood sugar	
Insulin glargine 100 units per mL	1-2hrs	P: undiscernable D: Up to 4hr	Hypoglycemia	
Insulin glargine 300 units per mL	Up to 6hrs	P: undiscernable D: Up to 30hrs	Switch to more concentrated product (e.g., glargine 300 units per mL or degludec 200 units per mL) for large volume doses	
Insulin degludec 100 units per mL, 200 units per mL	60-90mins	P: none D: More than 42hrs		
<b>Basal Insulin</b> Intermediate-Acting (cloudy)				
NPH	1-3hr	P: 5-8hr peak D: Up to 18hrs	<p>Hyperglycemia Hypoglycemia</p> <p>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</p>	
<b>Bolus (Prandial) Insulins</b> Rapid and Short-Acting (clear)				
<b>Ultra-fast acting</b> Insulin aspart (Fiasp® only)	5mins	P: 45-60min D: 3-5 hrs	<p>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)</p>	
<b>Rapid acting</b> Insulin aspart (all other products)	10-15mins	P: 1-2 hrs D: 3-5hrs		
Insulin glulisine				
Insulin lispro				

<b>Regular insulin</b> 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	
<b>Insulin Type</b>	<b>Onset</b>	<b>Peak (P) / Duration(D)</b>	<b>Indications for Adjustment</b>	<b>Therapeutic Considerations</b>
<b>Premixed Insulins</b>				
<b>Premixed regular</b> (cloudy) Insulin human and isophane	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
<b>Premixed analogues</b> (cloudy)  Insulin lispro and lispro protamine  Insulin aspart and aspart protamine				
<b>Combination Products with Insulin + GLP-1 Analogues</b>				
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](https://guidelines.diabetes.ca/CDACPG/media/documents/hcp-resources/Insulin_Prescription_EN_09_23.pdf)