

Taddle Creek

Family Health Team

Title:	Diabetes Management in Adults	Number:	TCFHT-MD05
Activation Date:	12-June-2012	Review Date:	12-June-2021
Next Review Date:	_12-June-2022		

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Order and/or Delegated Procedure: Appendix Attached: ____ No __X_ Yes

Title: Appendix C – Performed Controlled Acts and Procedures

The implementers are authorized to perform the following activities, in accordance with Appendix C when all conditions in this directive and the attached appendices are met:

- 1) Start, Adjust, Hold and Discontinue Basal Insulin already prescribed by Primary Care Provider/Endocrinologist
- 2) Start, Adjust, Hold and Discontinue Intensive Insulin Therapy already prescribed by Primary Care Provider/Endocrinologist
- 3) Adjust, Hold and Discontinue Oral Antihyperglycemic Agents
- 4) Adjust, Hold and Discontinue Injectable Antihyperglycemic Agents
- 5) Dispense Insulin prescribed by Primary Care Provider or Endocrinologist

Recipient Patients: Appendix Attached: ____ No _X_ Yes

Title: Appendix A – Authorizer Approval Form Recipients must:

- Be active patients of a TCFHT primary care provider/endocrinologist who has approved this directive by signing the Authorizer Approval Form
- Have a diagnosis of diabetes mellitus (type 1 or type 2) or pre-diabetes
- Meet the conditions identified in this directive.

Authorized Implementers:

Appendix Attached: <u>No X</u> Yes

Title: Appendix B – Implementer Approval Form; Appendix D – Competency Checklist Implementers must be TCFHT employed Regulated Health Care Providers or Physician Assistant (under the supervision of a physician).

Implementers must complete the following preparation and sign the Implementer Approval Form:

- Must become a certified diabetes educator (CDE) as per the Canadian Diabetes Educator Certification Board
- Practice according to Diabetes Canada's (DC's) most current Clinical Practice Guidelines
- Assess their own knowledge, skill, and judgment to competently perform these directives

In addition, to implement delegated procedures 1-4 (start, adjust, hold or discontinue basal or intensive insulin therapy to adjust, hold and discontinue oral antihyperglycemic agents, and to adjust, hold and discontinue injectable antihyperglycemic agents):

- Must have at least 1600 practice hours in providing direct diabetes education with patients living with diabetes
- Must be mentored by an authorized implementer, demonstrate the competencies and review all of the DC's Best Practice Guidelines, as outlined in Appendix D
- Must be supervised by Endocrinologist with at least 3 patient cases involving adjustments to insulin, oral antihyperglycemic agents, and injectable antihyperglycemic agents and complete and sign competency performance checklist (Appendix D)

Indications: Appendix Attached: ____ No _X _ Yes Title: Appendix C – Performed Controlled Acts and Procedures

- In general, each action/procedure under each directive will be implemented in the context of the existing physician/nurse practitioner relationship and as part of the medical diagnosis and plan of care established by the physician/nurse practitioner. These actions/procedures will be implemented without specific prior discussion (but as part of the plan of care) as per the indications and contraindications for each of these directives (Appendix C).
- Communication to primary care provider/endocrinologist regarding medication/insulin adjustments made following implementation of medical directive (see documentation and communication)

Contraindications:

• Indications described in Appendix C are not met

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Consent: Appendix Attached: <u>X</u> No Yes
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- Title:
- Patient's consent is implied, as patient has presented seeking support with diabetes management, and is a Family Health Team patient, where interprofessional practice is expected
- The implementer fully explains potential risks and benefits prior to initiating/adjusting insulin therapy and with any changes to oral or injectable antihyperglycemic medications

Guidelines for Implementing the Order/Procedure: Title: Appendix C – Performed Controlled Acts and Procedures As per Appendix C. Appendix Attached: <u>No X</u> Yes

Documentation and Communication: Appendix Attached: <u>X</u> No <u>Yes</u> Title:

- Documentation in the patient's eMR needs to include: name and number of the directive, patient's Capillary Blood Glucose (CBG) and/or Flash Blood Glucose (FBG) patterns (if applicable), current medications, self-management skills and learning needs, clinical findings and the plan of care, patient's response to the procedure or directions provided
- Implementer will send a message in Practice Solutions to patient's primary care provider, notifying him/her that patient was seen, recommendations were made and that eMR note needs review for details.
- Primary care provider responsible for entering newly prescribed medications into medication list in practice solutions. Implementer responsible for updating medication list in eMR and informing the patient's pharmacy via fax and/or phone call.
- Implementer will arrange a follow up plan in collaboration with patient and primary care provider/endocrinologist with any medication/insulin adjustments.

Review and Quality Monitoring Guidelines: Appendix Attached: _____No __X Yes Title: Appendix D – Competency Checklist Appendix Attached: ____No __X Yes

- Routine review will occur annually on the anniversary of the activation date. Review will involve a collaboration between the authorizing primary care providers and the authorized implementers.
- At any such time that issues related to the use of this directive are identified, TCFHT must act upon the concerns and immediately undertake a review of the directive by the authorizing primary care providers and the authorized implementers.
- If new information becomes available between routine renewals, such as the publishing of new Diabetes Canada Best Practice Guidelines, and particularly if this new information has implications for unexpected outcomes, the directive will be reviewed by the authorizing primary care providers and the authorized implementers.
- This medical directive can be placed on hold if routine review processes are not completed, or if indicated for an ad hoc review. During the hold, implementers cannot perform the procedures under authority of the directive and must obtain direct, patient-specific orders for the procedure until it is renewed.
- Implementer's competencies will be reviewed on a yearly basis as part of their performance review. Clinicians must consistently demonstrate competency in order to remain an authorized implementer of this directive see Appendix D

References:

Diabetes Canada. (2010). Building Competency in Diabetes Education: Advancing Practice.

Diabetes Canada. (2020). Building Competency in Diabetes Education: The Essentials (5th Edition).

Diabetes Canada. (2018). Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Retrieved from <u>http://guidelines.diabetes.ca/cpg</u>

Canadian Insulin Injection Recommendations: FIT Technique Plus, 2020. Retrieved from <u>http://www.fit4diabetes.com/canada-english/fit-technique-plus/</u>

Fit Forum for Injection Technique Canada. (2020). Fit Forum for Injection Technique Canada: Recommendations for Best Practice in Injection Technique 4th Edition. Retrieved from <u>http://fit4diabetes.com/canada-english/fit-recommendations/#</u>

Health Canada. Drug Product database. Retrieved from <u>https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html</u>

Ontario College of Family **Physicians Insulin** Prescription Tool - March 2014. Retrieved from <u>https://www.diabetes.ca/DiabetesCanadaWebsite/media/Managing-My-</u> <u>Diabetes/Tools%20and%20Resources/insulin-prescription-fillable-EN.pdf?ext=.pdf</u>

Up to Date. Retrieved from <u>uptodate.com</u>

NOTE:

This medical directive is based on TCFHT's previous medical directive DEP1 entitled, "Diabetes Management in Adults Medical Directive," which required revision in formatting to reflect the growth of the TCFHT organization. The majority of the content of DEP1 has remained the same for the revised TCFHT-MD05 version. Therefore, all approved Implementers and Authorizers for medical directive DEP1 "Diabetes Management in Adults Medical Directive" have grandfathered approval for TCFHT-MD05 "Diabetes Management in Adults."

Appendix A:

Authorizer Approval Form

Name	Signature	Date

Appendix B:

Implementer Approval Form

To be signed when the implementer has completed the required preparation, and feel they have the knowledge, skill, and judgement to competently carry out the actions outlined in this directive.

Delegated Procedures 1-4:

- Start, Adjust, Hold and Discontinue Bedtime Insulin
- Start, Adjust, Hold and Discontinue Intensive Insulin Therapy
- Adjust, Hold and Discontinue Oral Antihyperglycemic Agents
- Adjust, Hold and Discontinue Injectable Antihyperglycemic Agents

Name	Signature	Date

Delegated Procedures 5:

• Dispense Insulin or Injectable antihyperglycemics prescribed by Primary Care Provider or Consulting Endocrinologist

Name	Signature	Date
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Appendix C

Performed Controlled Acts and Procedures

Table 1: List of Medications (Insulin) Implemented under this Directive with Detailed Indications/Contraindications

Insulin Type	Onse t	Peak/ Duration	Indications for Adjustment	Tİ	herapeutic Considerations
 Rapid-Acting Lispro (Humalog) Aspart (Novorapid) Glulisine (Apidra) Lispro 200 (Humalog 200) Aspart (Fiasp) 	2-15 minute s	1-2 hours/ 3-5 hours	 2 hr post-meal and/or pre-meal blood sugars (lunch, dinner) are either elevated or hypoglycemia occurs 	 m. book do /ul>	pr current basal insulin users, aintain the basal dose and add olus insulin with each meal at a ose equivalent to 10% of the basal ose. For example, if the patient is on 0 units of basal insulin, add 5 units bolus insulin with each meal. or new insulin users starting a full asal + Bolus regimen, calculate Total aily Insulin dose (TDI) as 0.3 to 0.5 hits/kg, then distribute as follows: – 0% of TDI dose as basal insulin antus, Levemir, ToujeoTM, Humulin Novolin ge NPH) at bedtime. 20% of TDI dose as prandial (bolus) sulin prior to each meal. attents should eat within 0-15 inutes after injection certain circumstances injecting nortly after eating is appropriate e.g. disturbance resulting in early tiety, vomiting etc. or Patients on MDI (multiple daily jections) using a rapid-acting insulin is recommended that they self- onitor blood glucose (SMBG) at ast QID for safe titration of doses umalog 200 must only be used in e pre-filled pen. It must not be rawn up in a syringe asp is best injected 2 minutes efore and up to 20 minutes after a eal. It may not be best in people ith delayed gastric emptying & has ot been studied in pregnancy

 Short-Acting Humulin R Novolin Toronto 	30 minute s	2-3 hrs/6.5 hours	 Pre-meal blood sugars (lunch, supper) and/or bedtime are elevated or hypoglycemia occurs 	 Same initiation recommendations as rapid-acting insulin (see above) Rapid-acting insulin usually preferable to short-acting due to better post-prandial glycemic control and lower risk for hypoglycemia Patients should inject insulin 30 minutes prior to eating For Patients on MDI (multiple daily injections) using a short-acting insulin it is recommended that they SMBG at least QID for safe titration of doses
Intermediate- Acting • Humulin N • Novolin NPH	1-3 hours	5-8 hours/up to 18hours	 Increase evening dose if high fasting blood sugar (if rebound hyperglycemia has been eliminated) Decrease dose if hypoglycemia (recommend CBG testing in the night to rule out nocturnal hypoglycemia) Increase or decrease morning dose if 5-8 hour pre-meal blood sugars are out of target 	 To be injected once to twice daily in the morning and/or before bed Start at 10u daily or 0.2u/kg Long-acting basal insulins are typically preferred due to longer action profile and lower risk for hypoglycemia but intermediate-acting may be appropriate in some cases e.g., affordability/, glycemic management of hyperglycemia due to steroid therapy etc. Must be adequately re-suspended before injecting Recommended for Patients to SMBG OD-BID for safe titration of doses

TCFHT-MD05_Diabetes Management in Adults

Pre-Mix Analogues NovoMix 30 Humalog Mix 25 Humalog Mix 50 Regular Insulin Novolin 30/70, 40/60, 50/50 Humulin 30/70	10-15 minute s 30-60 minute s	Contains a fixed ratio of insulin (% of rapid- acting or short-acting insulin to % of intermediat e-acting insulin: see above for information about peak actions based on insulin contained	•	Increase/ decrease morning dose if lunch/supper readings are out of target Increase/decrease evening dose if HS or fasting sugars are out of target Recommend CBG testing in the night to rule out nocturnal hypoglycemia	•	To be injected once to twice daily before breakfast and dinner Typically started at 5-10u bid (or 50/50 split of current basal insulin regime) Must be adequately re-suspended before injecting Patients should eat within 0-15 min after injecting Mix 30, Mix 25 or Mix 50 Patients should inject 30/70, 40/60 or 50/50 30 minutes prior to eating Recommended for Patients to SMBG at least BID (AC breakfast and dinner) for safe titration of doses
 Long-Acting Detemir (Levemir) Glargine (Lantus, Basaglar) Glargine 300 (Toujeo) Degludec (Tresiba) U-100, U- 200 	90 minute s	No peak/16- 24hrs No peak/up to 24 hrs No peak/ up to 30hrs No peak/up to 42h	•	Increase/decrease dose by 1u if fasting or pre- supper sugars (if injecting in the morning) are out of target Tresiba and Toujeo should be adjusted by q3-4 days by 2- 3u	•	To be injected once daily at the same time each day (Detemir and Glargine may be injected twice daily in the morning and before bed) Start at 10u daily or 0.2-0.4u/kg Do not mix with another insulin in the same syringe Recommended for patients to SMBG at least OD (FBG or AC meals) for safe titration of dose Toujeo can be stored for 6 weeks at room temperature Tresiba can be stored for 8 weeks at room temperature Toujeo and Tresiba U-200 must only be used in the pre-filled pen. They must not be drawn up in a syringe Use a 1:1 conversion using total daily dose when switching from intermediate or long-acting insulin to Tresiba Use a 1:1 conversion using total daily dose when switching from long- acting insulin to Toujeo or 80% of total daily intermediate dose

Table 1 Notes:

- The implementer will adhere to the indications and contraindications outlined in Table 1
- The implementer is responsible for teaching patient safe injection technique according to FIT 2020 guidelines.
- A prescription is required from the primary health care provider and/or endocrinologist prior to insulin initiation.
- Individual considerations need to be assessed with insulin initiation i.e. patients who are hypoglycemia unaware or have a fear of insulin-induced hypoglycemia can be initiated on a smaller dose etc.
- Evidence-based recommendations are to adjust insulin by 1-2u q 3-4 days or by 1u per day. Under certain circumstances patients may need insulin adjustment greater or less than 5-10% of total daily dose i.e. extreme hyperglycemia, medications and/or lifestyle factors that can increase/decrease glycemic levels.
- Implementer should determine a communication plan with the patient for further insulin adjustment and encourage self-titration if possible.
- Implementer will instruct a patient starting insulin around hypoglycemia treatment, driving instructions and instruct family/caregivers on using a glucagon kit when applicable i.e. type 1 diabetes and high risk for hypoglycemia.
- In the case of high CBG readings and low CBG readings, always correct for hypoglycemia first.
- Patients should be instructed as to how to adjust insulin during times of illness, travel and physical activity following current best practice guidelines.
- Allergic reactions are rare but can occur with a few patients. Reactions may be local (i.e. rash/weal at site) or systemic (i.e. shortness of breath, wheezing or severe weakness).
 Implementer should instruct Patient to hold insulin and get in contact with primary care provider a.s.a.p. and/or proceed to the nearest emergency department.
- Patient should be instructed to store unopened insulin vials/cartridges in the refrigerator, store open insulin vials/cartridges at room temperature, not expose insulin to heat or direct sunlight, not freeze insulin, and to use by expiration date.
- The primary care provider or endocrinologist must be available to provide consultation as required.
- Primary care provider and/or endocrinologist should be consulted in the following circumstances:
 - Recurrent or severe hypoglycemia with no apparent cause
 - Glycemic control is not improving or is deteriorating despite adjustments made to insulin or other component of the treatment plan
 - \circ Total daily dose exceeds what is generally expected for age/body type
 - Patient shows signs and symptoms of Diabetic Ketoacidosis (DKA), dehydration or other serious problems *send to the Emergency Department immediately
 - o Recurring/persistent vomiting/diarrhea
 - Disordered eating pattern resulting in calorie restriction
 - o Significant error in dose or timing of insulin administered by person or caregiver

- Change in brand or type of insulin
- Change in frequency of injections i.e., BID to TID
- For patients with additional complex medical or endocrine disorders which may influence insulin requirements or patient safety
- In all situations that are beyond the implementer's scope of practice and/or competency level

Table 2: Non-Insulin Antihyperglycemic agents: List of Medications Implemented under this Directive with Detailed Indications/Contraindications

Antihyperglycemic Agent	Indications for Adjustment	Contraindications/Precautions
Alpha-Glucosidase Inhibitor Acarbose (Glucobay, Prandase) Initial Dose: 25-50 mg daily Average Dose (Max dose): 50-100 mg tid (300 mg) Special Instructions: Take with first bite of meal Onset/peak/duration: 1h/2h/4-6h Expected HbA1C reduction: 0.6% ODB Coverage: limited use	 Gastrointestinal (GI) side effects Inadequate blood glucose control Very low frequency of hypoglycemia unless combined with a sulfonylurea Initiate therapy with 25mg OD- BID and titrate slowly by 25mg/day every 2-4 weeks as tolerated Maximum effectiveness with at 50mg TID; higher doses associated with increased adverse events 	 Not recommended as initial therapy in people with severe hyperglycemia (AIC ≥8.5%) Gastrointestinal side effects in approx. 30% of Patient's i.e. cramps, diarrhea, abdominal distension, flatulence (effects usually decrease with continued use but there is a high discontinuation rate based on GI side effects) Treat hypoglycemia with Dextrose tablets, milk or honey as Acarbose interferes with glucose absorption Contraindicated in Patient's with DKA, inflammatory bowel disease, intestinal ulcers, cirrhosis, partial intestinal blockage or predisposed to blockage Renal dosing: discontinue use if creatinine clearance (CrCl) <25ml/min or eGFR <30 mL/min In patients with known liver impairment or liver disease, liver enzymes should be monitored prior to start of Acarbose, and monitored on a regular basis within the first year Case reports of reduction in absorption of digoxin and increased absorption of warfarin Maximum doses based on weight <132 lbs: 50mg TID; >132 lbs: 100mg TID

Antihyperglycemic Agent	Indications for Adjustment	Contraindications/Precautions
Biguanides Metformin (Glucophage) Initial Dose: 250-500 mg daily Average Dose (Max dose): 500-1000 mg bid or 850 mg tid (2550 mg) Special Instructions: Take with meals to reduce GI side effects Onset/peak/duration: 1-2h/6h/6-12h Expected HbA1C reduction: 1-1.5% ODB Coverage: Yes Glumetza (Metformin HCL ER) Initial Dose: 500 mg daily (ideally with dinner) Average Dose (Max dose): 1000-2000 mg daily (2500 mg) Onset/peak/duration: 1-2h/4-8h/17.6-19.8h Expected HbA1C reduction: 1-1.5% ODB Coverage: No	 Initiate Glucophage 500mg twice daily or 850mg OD Initiate Glumetza 500mg once or twice daily GI side effects in 20-30% of Patient's (Glumetza associated with fewer GI side effects than short-acting Metformin). Side effects can be reduced by slow titration (500mg/day every 2 weeks and taking medication with meals Decrease in FBG levels seen within 3-5 days; maximal effect in 1-2 weeks 80-85% of glucose lowering effect is seen with 1500mg/day Maximum effective dose is 2000mg/day Renal insufficiency Hypoglycemia (rare as monotherapy) Blood glucose remains above target Biguanides should be put on hold in patients with severe dehydration (i.e., vomiting and unable to keep down fluids) 	 Contraindicated in people with a history of lactic acidosis, severe hepatic dysfunction, severe infection/dehydration, trauma or cardiorespiratory insufficiency, surgery or in excessive alcohol intake, whether acute or chronic Reduced dose recommended if CrCl/eGFR <45mL/min and contraindicated if CrCl/eGFR <30 mL/min due to risk of accumulation Glucophage should not be initiated if eGFR 30-44, but can be maintained 5-10% of people are unable to tolerate due to substantial GI side effects (upset stomach, nausea, diarrhea, anorexia, metallic taste) Metformin should be stopped during acute illness (severe infections, trauma, surgery) and the recovery phase afterwards. Should also be put on hold in patients with severe dehydration (i.e., vomiting and unable to keep down fluids) Should do baseline liver function tests (LFT's) Higher doses (above 2000mg/day) associated with increased risk of adverse events with no additive effect Hold for 48 hours if undergoing radiologic studies with administration of iodinated contrast material (hold on day of procedure until 2-3 days after) Not recommended in the elderly (over 80yrs) unless CrCl/eGFR is >60 mL/min due to decreased muscle mass Recommend conservative dosing in the elderly Lactic acidosis is rare 0.03/1000 patients and 0.015 fatal cases/1000 patients; more likely to occur in patients with renal insufficiency, alcohol or liver disease. Hold dose in hypoxic states, shock, severe infection or septicemia Measurements of serum vitamin B12 are advisable at least every 1 to 2 years in patients on

Insulin Secretagogues Sulfonylureas: Frequent hypoglycemia • • (decrease or discontinue if modifications are made) **Diamicron (Gliclazide)** hypoglycemia persists 1-2 times • Initial Dose: per week) 40-80 mg daily or bid with meals ٠ Inadequate blood glucose Average Dose (Max dose): control (blood glucose remains • 80-160 mg bid (320 mg) above target consistently) *Onset/peak/duration:* Dose should be started low and 1-2h/4-6h/10-14h •

Expected HbA1C reduction: 0.8% ODB Coverage: Yes

Diamicron MR (Gliclazide MR)

Initial Dose: 30 mg daily with first meal Average Dose (Max dose): 30-120 mg daily (120 mg) *Onset/peak/duration:* 1-2h/6-12/>24h Expected HbA1C reduction: 0.8% **ODB** Coverage: Yes

Diabeta (Glyburide)

Initial Dose: 2.5 mg – 5.0 mg daily or bid with meals Average Dose (Max dose): 5-10 mg bid with meals (20 mg) Special Instructions: Take 30min prior to meal) Onset/peak/duration: 1-2h/4-6h/10-14h *Expected HbA1C reduction:* 0.8% **ODB** Coverage: Yes

Amaryl (Glimepiride)

Initial Dose: 1 mg daily with first meal Average Dose (Max dose): 1-4 mg daily (8 mg) *Onset/peak/duration:* 20min/2-4h/24h Expected HbA1C reduction: 0.8% ODB Coverage: No

- titrated every 1-2 weeks until glycemic targets are met
- Sulfonylureas should be put on hold in patients with severe dehydration (i.e., vomiting and unable to keep down fluids)

- Associated with weight gain (unless dietary
- Associated with hypoglycemia; annual rate of any hypoglycemia is 20%. Major hypoglycemic events occur in 1-2 % of individuals
- Consider using other class(es) of oral antihyperglycemic agents first in patients at high risk of hypoglycemia i.e. the elderly
- Requires lower dose and slower titration in patients with hepatic/renal impairment and the elderly
- Increased risk for hypoglycemia with insulin
- Glyburide not recommended with eGFR <60 • mL/min.
- Gliclazide and Glimepiride should be used with caution if eGFR 30-59 mL/min, not recommended with eGFR <30 mL/min

Antihyperglycemic Agent	Indications for Adjustment	Contraindications/Precautions
Insulin Secretagogues Non-Sulfonylureas: Meglatinides <u>Gluconorm (Repaglinide)</u> Initial Dose: 0.5-1mg tid with meals Average Dose (Max dose): 0.5-4 mg tid (16 mg) Special Instructions: take 1- 30min before meals Onset/peak/duration: 30min/1h/4-5h Expected HbA1C reduction: 0.7% ODB Coverage: Exceptional Access Program (EAP)	 Frequent hypoglycemia (decrease or discontinue if hypoglycemia persists 1-2 times per week) Less hypoglycemia compared to sulfonylurea's and are ideal for patients with irregular meal times Inadequate blood glucose control (blood glucose remains above target consistently) Doses should be titrated weekly as required to obtain glycemic targets 	 Less likely to cause weight gain and hypoglycemia than sulfonylureas Safe to use in renal impairment and mild hepatic impairment but requires slower dose titration In the elderly Repaglinide should be initiated at 0.5mg TID and titrate dose slowly (especially with CrCl 20-39mL/min) Preferred for use in elderly individuals with erratic eating patterns The concomitant use of Repaglinide and Clopidogrel (Plavix) is contraindicated as it may lead to a significant decrease in blood glucose levels due to a drug-drug interaction

Thiazolidinediones (TZD's)

Actos (Pioglitazone)

Initial Dose: 15 mg daily Average Dose (Max dose): 15-45 mg daily (45 mg) Onset/peak/duration: 30min/2-4h/4 weeks Expected HbA1C reduction: 0.8% ODB Coverage: EAP

Avandia (Rosiglitazone)

Initial Dose: 4 mg daily Average Dose (Max dose): 2-8 mg daily (8 mg) Onset/peak/duration: 30-60min/1-2h/4 weeks Expected HbA1C reduction: 0.8% ODB Coverage: EAP

Edema

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- Shortness of breath
- Discontinue TZD if insulin is initiated
- Titrate every 2-4 weeks
- Full BG-lowering effect seen within 6-12 weeks
- Discontinue if ALT >3 X upper limit of normal
- Should do baseline LFT's prior to initiation, every 2 months for the first year and then periodically
- May induce edema, fluid retention (recommended to monitor weight)
- Pioglitazone may increase risk of bladder cancer and is not recommended for use with Patient's who have or have had bladder cancer, are at high risk, have blood or a red color in their urine. Patient's taking pioglitazone should be assessed regularly for potential symptoms of bladder cancer i.e. blood or red color in urine, painful urinate etc.
- Can cause weight gain (subcutaneous fat + fluid retention) 1.5-4.84kg but decrease in visceral and hepatic fat. Weight gain is generally dose dependent
- Associated with increased risk for bone loss and fractures in women 55yrs or older (0.78 per 100)
- Used in combination with insulin may increase risk of edema and CHF. The combination of a TZD plus insulin is currently not an approved treatment in Canada
- Rosiglitazone is no longer approved for use alone to treat DM2 except when Metformin use is contraindicated or not tolerated and all other oral agents have been tried alone or together and targets are not reached
- Rosiglitazone is not indicated for triple therapy and is only indicated in combination with Metformin or a sulfonylurea
- Pioglitazone is no longer approved for use with Metformin and a sulfonylurea
- Can be used safely in mild to severe renal impairment
- Contraindicated for people with CHF New York Heart Association (NYHA) Class I to IV cardiac status; evidence of left ventricular dysfunction or serious hepatic impairment (ALT 2.5 X upper limit of normal)
- Prior to prescribing Avandia practitioners must 1) document the individual's eligibility to meet the above criteria; 2) counsel the individuals on the risks and benefits of Avandia, including the CV risks; and 3) obtain the person's written informed consent to take the drug

DPP4 Inhibitors

Sitagliptin (Januvia)

Initial Dose: 100 mg daily qam with/without food Average Dose (Max dose): 100 mg daily (100 mg) Onset/peak/duration: Rapidly absorbed/1-4h/24h Expected HbA1C reduction: approx. 0.7% ODB Coverage: Yes

Saxagliptin (Onglyza)

Initial Dose: 5 mg daily with/without food Average Dose (Max dose): 5 mg daily (5 mg) Onset/peak/duration: Rapidly absorbed/2.5h/26.9h Expected HbA1C reduction: approx. 0.7% ODB Coverage: Yes

Linagliptin (Trajenta)

Initial Dose: 5 mg daily with/without food Average Dose (Max dose): 5 mg daily (5 mg) Onset/peak/duration: Rapidly absorbed/1.5h/24h Expected HbA1C reduction: approx. 0.7% ODB Coverage: Yes

Alogliptin (Nesina)

Initial Dose: 25 mg daily with/without food Average Dose (Max dose): 25 mg daily (5 mg) Onset/peak/duration: Rapidly absorbed/1-2h/approx. 24h Expected HbA1C reduction: approx. 0.7% ODB Coverage: No Nasopharyngitis, cough and headache (rare cases)

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- Severe joint pain (rare cases), usually within 1 month of initiation
 - Inadequate glucose control
- Increased risk for hypoglycemia if combined with a sulfonylurea
 - Discontinue if suspicion of pancreatitis i.e. severe ongoing stomach or back pain with/without vomiting
- Linagliptin can be used in renal insufficiency (eGFR <15 mL/min and dialysis)
- Saxagliptin dose should be decreased to 2.5 mg od if eGFR <50 mL/min, and discontinued if eGFR <15 mL/min. It should not be used in patients on dialysis (assess renal function prior to treatment and periodically after)
- Sitagliptin dose should be decreased to 50 mg od if eGFR is 30-49 mL/min, and decreased further to 25 mg od if eGFR <30 mL/min (assess renal function prior to treatment and periodically after)
- Alogliptin dose should be decreased to 12.5 mg if eGFR is 30-59 mL/minute, 6.25 mg od if eGFR <30 mL/ and can be used at 6.25mg in ESRD with hemodialysis (has not been studied with peritoneal dialysis)
- Use in caution in the elderly (as per renal guidelines)
- Safety profile has not been studied and is unclear in individuals who are immunocompromised e.g. lymphocyte abnormalities, HIV, or people who have undergone organ transplant
- Approved for use with Metformin and a sulfonylurea
- Approved for use with insulin except for Linagliptin
- Linagliptin , Sitagliptin and Alogliptin are not recommended in severe hepatic insufficiency and Saxagliptin is not recommended in moderate to severe hepatic impairment (monitor hepatic function before initiating treatment and periodically after)
- Not recommended if history of pancreatitis
- Caution if history of alcoholism, high triglycerides (higher risk for pancreatitis)
- Not recommended for people with heart failure
- Contraindicated for use for patients with personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome 2

Antihyperglycemic Agent	Indications for Adjustment	Contraindications/Precautions
GLP-1 Receptor Agonist (oral) Semaglutide (Rybelsus) Initial Dose: 3 mg daily without food Average Dose (Max dose): 7 mg daily (14 mg) Onset/peak/duration: rapidly aborbed/1 hour/approx 1 week Expected HbA1C reduction: approx. 1.2-1.4% ODB Coverage: No	 Gastrointestinal (GI) side effects Inadequate blood glucose control low frequency of hypoglycemia unless combined with a sulfonylurea or insulin Initiate therapy with 3mg OD. After 30 days, increase to a maintenance dose of 7mg once daily. If additional glycemic control is needed after at least 30 days on the 7 mg dose, the dose can be increased to a maintenance dose of 14mg once daily. This regimen is intended to mitigate gastrointestinal symptoms during dose escalation Regular self-monitoring of blood glucose is not needed in order to adjust the dose of Rybelsus on its own. However, when used in combination with a Sulfonylurea or insulin, SMBG testing may be necessary in order to reduce the risk of hypoglycemia 	 Most frequent adverse reactions include: nausea, abdominal pain, diarrhea and vomiting Rybelsus must be taken on an empty stomach at least 30 min before the first food, beverage or other oral medications of the day. Waiting less than 30 min is likely to decrease the amount of semaglutide absorbed Rybelsus should be taken with more than half a glass of water equivalent to 120 mL. A larger volume of water is likely to decrease the amount of Semaglutide absorbed. Rybelsus should be swallowed whole. Do not split, crush or chew If a dose is missed, the missed dose should be skipped, and the next dose should be taken the following day Contraindicated for use for patients with personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome 2 Rybelsus should not be used for patients with Type 1 Diabetes or in DKA or in pregnancy Women of childbearing potential are recommended to use contraception when treated with Semaglutide. If a patient wishes to become pregnant or pregnancy occurs. Rybelsus should be discontinued at least 2 months before a planned pregnancy due to the long half-life of Semaglutide Caution for use with those with cardiac conditions that might be worsened by an increased in HR (i.e. tachyarrhythmias) Semaglutide causes a prolongation of the PR interval, and caution should be observed in patients with pre-existing conduction system abnormalities (first/second/third degree AV block) Rare cases of pancreatitis have been reported. Should be discontinued in the presence of persistent severe abdominal pain sometimes radiating to the back and which may or may not be accompanied by vomiting Caution for use with ESRD, GI problems, hepatic liver disease, diabetic retinopathy

GLP-1 Receptor Agonist (injectable)

Liraglutide (Victoza)

Initial Dose: 0.6 mg SC daily Average Dose (Max dose): 1.2-1.8 mg SC daily (1.8 mg) Expected HbA1C reduction: 1-1.5% ODB Coverage: No

Dulaglutide (Trulicity)

Initial Dose: 0.75mg (0.5 mL) SC qweekly Average Dose (Max dose): 1.5mg (1.5mg) Special Instructions: - Can be taken with or without meals Onset/peak/duration:24 hrs/48hrs/120hrs Expected HbA1C reduction: 1-1.5% ODB Coverage: No

Semaglutide (Ozempic)

Initial Dose: 0.25mg SC qweekly X 4 weeks (not a therapeutic dose) to be increased to 0.5mg SC qweekly Average Dose (Max dose): 0.5mg (1mg) Special Instructions: - Can be taken with or without meals Onset/peak/duration:24 hrs/24-72hrs/1 week Expected HbA1C reduction: 1-1.5% ODB Coverage: Yes

- Liraglutide to be increased to ideal therapeutic dose of 1.2mg OD after 1 week as tolerated. Can further increase to 1.8mg OD if needed based on response after 1 week at 1.2mg
- Dulaglutide to be increased to ideal therapeutic dose of 1.5mg q 1week after 1 week as tolerated.
- Semaglutide to be increased to ideal therapeutic dose of 0.5mg in 4 weeks. Can increase further to 1mg in another 4 weeks if tolerating well.

- Common adverse effects are nausea (10.7-18.6%), diarrhea (8.3-14.9%), headache (5.4-12.4%), vomiting (5.4-7.4%) and dyspepsia (2.1-7.0%)
- Side effects usually improve over time
- Should be stored in the refrigerator and unused medication discarded after 30 days
- Increase in heart rate/ PR interval prolongation. Caution should be observed in patients with preexisting conduction system abnormalities (first/second/third degree AV block)
- Liraglutide is only approved for use with Metformin and/or a sulfonylurea in Canada
- Semaglutide has been studied with Metformin, Metformin +Sulfonylurea, Metformin + SGLT2i, Metformin + Basal insulin
- Dulaglutide can be used with Metformin, with Metformin & a Sulfonylurea, with mealtime insulin.
- Dulaglutide has not been studied in combination with a basal insulin
- Rare cases of pancreatitis have been reported. Should be discontinued in the presence of persistent severe abdominal pain and vomiting
- Contraindicated with type 1 diabetes, DKA, personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome
- May slow absorption of medications; caution with medications that require rapid absorption (acetaminophen, pain medications)
- Increased risk of hypoglycemia if used with sulfonylurea (assess need to decrease sulfonylurea dose by 50%)
- In clinical trials, insulin dose was decreased by 20% at onset of Semaglutide treatment
- Assess renal function prior to treatment and periodically thereafter
- Semaglutide and Exanatide not recommended with eGFR <30, Liraglutide and Dulaglutide not recommended with eGFR <15 mL/min
- Caution in patients with recent MI, unstable angina, CHF, IBS or gastroparesis (no studies)
- Dulaglutide's day of weekly administration can be changed, if necessary, as long as the last dose was at least 3 days before
- Semaglutide's day of weekly administration can be changed, if necessary, as long as the time between two doses is at least 2 days
- Caution for use with ESRD, GI problems, hepatic liver disease, diabetic retinopathy

SGLT2 Inhibitors Canagliflozin (Invokana) Initial Dose: 100 mg daily qam ideally before meal Average Dose (Max dose): 300mg daily (300mg) Onset/peak/duration: Rapidly absorbed/1-2 hrs/approx. 24 hrs Expected HbA1C reduction: 0.77-1% * up to 2.56% with HbA1C >10% ODB Coverage: Yes Dapagliflozin (Forxiga) Initial Dose: 5 mg daily with/without food Average Dose (Max dose): 10 mg daily (10 mg) Onset/peak/duration: Rapidly absorbed/2h/approx. 24 hrs Expected HbA1C reduction: 0.7- 0.99% * up to 2.04% with HbA1C >9% ODB Coverage: No Empagliflozin (Jardiance) Initial Dose: 10 mg daily with/without food Average Dose (Max dose): 25 mg daily (25 mg) Onset/peak/duration: Rapidly absorbed/1.5h/approx. 24 hrs Expected HbA1C reduction: 0.7- 0.99% * up to 2.04% with HbA1C >9% ODB Coverage: Yes	 Start Canagliflozin at 100mg and increase to 300mg if well tolerated and eGFR >60 mL/min Start Dapagliflozin at 5mg od and increase to 10mg od if well tolerated and eGFR >60 mL/min Start Empagliflozin at 10mg od and increase to 25mg od if well tolerated and eGFR >45mL/min Canagliflozin should be discontinued when eGFR is <45 mL/min as it would not be effective in these patients and adverse reactions are more severe Dapagliflozin should be discontinued when eGFR is <60 mL/min Empagliflozin should be used with caution if eGFR 30-44 mL/min, discontinued when eGFR is <30 mL/min SGLT2 inhibitors should be put on hold in patients with severe dehydration (i.e., vomiting and unable to keep down fluids) 	 Indicated as monotherapy in patients with type 2 diabetes for whom Metformin is inappropriate due to contraindications or intolerance Indicated in combination therapy with Metformin, sulfonylureas or insulin (with or without Metformin) Invokana and Forxiga are indicated in combination with Januvia Common adverse effects are increased serum potassium >5.4 mEq/ml (12-27%) and >6.5 mEq/ml (12%), genital mycotic infections (7-11% in women and 3-4% in men), urinary tract infections (4-6%), nasopharyngitis (6-7%), polyuria (3-5%) SGLT2 inhibitors can be added for glycemic control if eGFR >45 mL/min SGLT2 inhibitors may be used for cardiorenal benefits in those with clinical CVD, A1C above target and eGFR >30 mL/min Renal function should be assessed prior to initiation of and regularly after with more frequent monitoring for patients taking Canagliflozin or Empagliflozin with eGFR 45-60 mL/min Monitor serum potassium levels periodically after initiating in patients with impaired renal function and in patients with of hyperkalemia due to medications or other medical conditions May increase the risk for ketoacidosis. Patients experiencing signs and symptoms of ketoacidosis (e.g., difficulty breathing, nausea, vomiting, abdominal pain, confusion, unusual fatigue or sleepiness) should be discontinued if acidosis is confirmed LDL levels should be monitored due to dose dependent increases in LDL-C seen with therapy Dapagliflozin is not recommended in combination with pioglitazone (Actos) Dapagliflozin and Canagliflozin tablets contain lactose May cause symptomatic hypotension due to intravascular volume depletion especially in patients with renal impairment (eGFR <60 mL/min), elderly, patients on other antihypertensives, or those with low systolic blood pressure. Assess volume status prior to inititation in patients at risk of hypotension and correct if
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	depleted; monitor for signs and symptoms of
	 hypotension after initiation Not recommended for use with patients on loop diuretics
	 Can be used in mild-moderate hepatic impairment Elderly patients (≥65 years) may have an increased risk of symptoms related to intravascular volume depletion (e.g., hypotension, orthostatic hypotension, dizziness, syncope, and dehydration) during therapy, especially with higher doses; elderly patients ≥75 years may experience a more pronounced risk. HbA1c reductions may be less in patients >65 years compared to younger patients. Patients should be educated about the increased risk for genital mycotic infections and/or urinary tract infections Patients should be advised about the possible side effect of increased urination and encouraged to drink sugar-free liquids during the day to avoid dehydration Increased risk for hypoglycemia if combined with sulfonylurea or insulin (may need to adjust
	diabetes medications)

Combination Medications	See the indications for medications included in	See contraindications/precautions for medications included in combination tablet
Janumet (Januvia and	combination tablet	included in combination tablet
Metformin)		
Initial Dose:	Initiate at higher doses (not initial dose) if along the tabling	
	initial dose) if already taking	
50/500mg bid	Metformin at higher doses and	
Average Dose (Max dose):	tolerating well	
50/1000mg bid (50/1000mg bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: Yes		
Janumet XR (Januvia and		
<u>Glumetza)</u>		
Initial Dose:		
50/1000mg daily ideally with		
dinner		
Average Dose (Max dose):		
50/2000mg od (50/2000mg od)		
Special Instructions:		
Take with meal to reduce GI side		
effects		
ODB Coverage: Yes		
Jentadueto (Trajenta and		
Metformin)		
Initial Dose:		
2.5/500mg bid		
Average Dose (Max dose):		
2.5/1000mg bid (2.5/1000mg		
bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: Yes		
Komboglyze (Onglyza and		
Metformin)		
Initial Dose:		
2.5/500mg bid		
Average Dose (Max dose):		
2.5/1000mg bid (2.5/1000mg		
bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: Yes		
Kazano (Nesina and Metformin)		
Initial Dose:		
12.5/500mg bid		

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Average Dose (Max dose):		
12.5/1000mg bid (12.5/1000mg		
bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: No		
obb coverage. No		
Xigduo (Forxiga and Metformin)		
Initial Dose:		
5/850mg bid		
_		
Average Dose (Max dose):		
5/1000mg bid (5/1000mg bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: No		
Invokamet (Invokana and		
<u>Metformin)</u>		
Initial Dose:		
50/500mg bid		
Average Dose (Max dose):		
150/1000mg bid (150/1000mg		
bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: No		
Synjardy (Jardiance and		
Metformin)		
Initial Dose:		
5/500mg bid		
Average Dose (Max dose):		
12.5/1000mg bid (12.5/1000mg		
bid)		
Special Instructions:		
Take with meals to reduce GI		
side effects		
ODB Coverage: No		
Xultophy (Degludec and		
Liraglutide)		
Initial Dose:		
10u SC daily (pts naïve to basal		
insulin or GLP1 receptor agonist)		
OR		
16u SC daily (pts currently using		
basal insulin or GLP1 receptor		
agonist)		
Average Dose (Max dose):		
	<u> </u>	

N/A (50u daily)	
Special Instructions:	
-Take once daily at the same time	
with or without meals	
-Dose should be titrated up or	
down by 2u q3-4days to achieve	
fasting blood glucose targets	
-Basal insulin and/or GLP1	
Receptor Agonist should be	
discontinued prior to starting	
Xultophy	
Soliqua (Glargine and	
<u>Lixisenatide)</u>	
Initial Dose:	
15u SC daily (pts taking <30u	
basal insulin daily) OR	
30u SC daily (pts taking30-60u	
basal insulin daily)	
Average Dose (Max dose):	
N/A(60u)	
Special Instructions:	
-Take once daily within an hour	
prior to the first meal of the day	
-Dose should be titrate dup or	
down by 2-4u every week to	
achieve fasting blood glucose	
targets	
-Basal insulin and/or GLP1	
receptor agonist should be	
discontinue prior to starting	
Soliqua	
See dosing information for	
medications included in	
combination tablet for	
more information	

Table 2 Notes:

- The implementer will adhere to the indications/contraindications outlined in this table
- The primary care provider or endocrinologist must be available to provide consultation as required
- The implementer will recommend hold of medication and contact the physician/nurse practitioner immediately if suspicion of a hypersensitivity reaction i.e. anaphylaxis, hives, rash etc.
- Implementer should follow up with the patient regarding medications discontinued or placed on hold in collaboration with physician/nurse practitioner.
- Women with type 2 diabetes who are planning a pregnancy should switch from noninsulin antihyperglycemic agents to insulin for glycemic control. Women with pregestational diabetes who also have PCOS may continue metformin for ovulation induction.
- Metformin and glyburide may be used during breastfeeding.

	Indications	Contraindications
Providing Insulin Samples	 The patient has obtained an Rx from their primary health care provider (PHCP) for the insulin to be provided or the RD or RN has been given a verbal or written order from the PHCP Samples will be provided (as able) when needed for the timely initiation of insulin or due to the financial constraints of the patient. The RN or RD will attempt to link the patient to any relevant financial assistance programs available for insulin and other diabetes management supplies i.e. trillium drug plan etc. The insulin samples will be kept in a fridge with temperatures ranging from 2 – 8 degrees Celsius. The temp. will be monitored and recorded twice per day Insulin samples should be inspected by the RD or RN prior to providing them to a patient to check expiration date and clarity of insulin (see contraindications) The RN or RD will document expiry date, & lot # of the insulin dispensed 	 Insulin storage fridge temp. has dropped below freezing (insulin will need to be discarded) Insulin has expired Insulin has clumps, solid white particles or clear insulin appears cloudy

Table 3 Notes: Insulin samples cannot be donated by patients.

Appendix D

Implementer Competency Checklist

Implementer Name: _____

CDA Guidelines Chapter Reviews		
Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada	Date Reviewed	Signature
Pharmacologic Management of Type 2 Diabetes (including updated resource for 2020)		
Diabetes and Driving		
Appendix 9: Examples of Insulin Initiation and Titration Regimes in People with Type 2 Diabetes		
Appendix 5: Self-Monitoring of Blood Glucose (SMBG) Recommendation Tool for Healthcare Providers		
Appendix 7: Therapeutic Consideration for renal impairment		
Appendix 8: Sick Day Medication List		
CDA Building Competency in Diabetes Education: The Essentials	Date Reviewed	Signature
Chapter 6 - Treatment Modalities: Pharmacological Therapy		
Chapter 12 – Intensive Insulin Therapy		
Diabetes Canada Building Competency in Diabetes Education: Advancing Practice	Date Reviewed	Signature
Chapter 2 – Advanced Insulin Therapy		
Chapter 3 - Acute Care Issues: Driving Employment and Insurance Issues		
Canadian Injection Recommendations: FIT, 2020		

	Performance Criteria	Observed ex. through mentoring or chart audits (Date)	Not Observed ex. discussion of cases (Date)	Comments
1.	Able to identify the action, dosing, indications & contraindications, possible side effects of all antihyperglycemic oral medications identified in this directive			
2.	Able to identify the pharmacokinetics and action times of all insulins described in this medical directive including onset, peak, duration			
3.	Identifies potential side effects of insulin therapy and how to avoid/minimize and manage them (i.e., hypoglycemia, lipohypertrophy, weight gain, in rare cases allergy)			
4.	Able to counsel Patient's on private and commercial driving recommendations when there is a higher risk for hypoglycemia i.e., taking insulin and/or sulfonylurea			
5.	Identifies lifestyle factors, medications and/or medical conditions that can impact patient's glycemic control			
6.	Describes basic physiologic insulin requirements in type 1 and type 2 diabetes in adults as well as usual starting doses based on age, weight, diagnosis, etc.			

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7.	Completes and documents comprehensive assessment of learning needs & provides timely, patient-centered education on diabetes management including insulin and medications		
8.	Calculates, uses and evaluates insulin: carbohydrate ratios		
9.	Calculates, uses and evaluates insulin sensitivity factor and correction doses		
10.	Describes the purposes of consistent CHO intake and/or CHO counting and identifies potential advantages/disadvantages of each, according to patient's situation		
11.	Identifies effect of alcohol consumption on blood glucose values and provides education and advice to minimize risk and prevent hypoglycemia		
12.	Identifies dietary and/or insulin recommendations for physical activity.		
13.	Identifies patterns of hyperglycemia or hypoglycemia or changes in routine that require adjustment of insulin, medications and/or other components of treatment plan		
14.	Describes and/or has provided sick day management recommendations including dietary, medication/insulin adjustments as necessary		
15.	Describes and/or has provided education and guidance for travelling with diabetes, including medication/insulin adjustment as needed		

16.	Builds relationships with patients to promote self-care and learning; does not encourage ongoing dependence on health professionals for insulin adjustment i.e., increased patient confidence to self-adjust insulin		
17.	Able to counsel patient around glucose meter usage and checking for accuracy i.e., lab/meter check or control solution		
18.	Able to document process according to established standards and consult referring primary care provider for non-standard situations and/or failure of insulin dose adjustment to improve control.		
19.	Familiarity with insulin pens and injections technique based on Canadian Recommendations FIT.		

Endocrinologist and Implementer Signature Sheet

۱ha	ave supervised
(Name of endocrinologist)	(Name of Implementer)
•	at they have achieved competency to adjust insulin for patients with diabetes according to medical ent in Adults".
Signed	_ Endocrinologist
Signed	_ DEP Coordinator and/or Preceptor
Signed	_ Implementer
Date	-