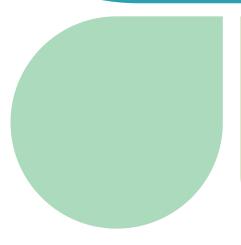
# FIT Forum for **Injection Technique** Canada



Recommendations for Best Practice in Injection Technique 3rd Edition



Optimizing injection technique in diabetes

#### **Objectives**

- Identify the injection techniques currently being used by people with diabetes in Canada.
- Raise awareness of the impact that existing and emerging research regarding injection technique may have on health outcomes.
- Facilitate opportunities in which best practice can be discussed, developed, implemented and evaluated across Canada.

#### Preface

Forum for Injection Technique (FIT) Canada provides evidence-based best practice recommendations for people with diabetes who are using injectable therapies. Through these recommendations, people with diabetes can achieve the best possible health outcomes by ensuring that the correct dose of medication is delivered to the correct injection site, using the proper technique. Dissemination initiatives will include education for both healthcare professionals and patients, and patient support and clinical research programs.

#### Introduction

The results of an international survey(1) led to an increased awareness among healthcare professionals of the issues associated with improper injection technique. The Canadian Forum for Injection Technique (FIT) initiative was developed in response to these concerns.

Following the precedent set by the United Kingdom FIT initiative, (2) as well as other international injection technique initiatives, (3-6) the recommendations presented in this document were designed to promote best practice in injection technique for healthcare professionals who are involved in diabetes care, and their patients. (5,6) They also aim to raise awareness of existing and emerging research regarding injection technique. Implementation of these recommendations may have a direct impact on the health outcomes of people with diabetes who are using subcutaneous injection therapies. This document continues to be distributed to all Canadian healthcare professionals who are involved in injection therapy for people with diabetes.

A meeting of Canadian diabetes education experts was convened to identify unmet educational needs regarding injection technique. The top 3 educational priorities identified were as follows:

- 1 Techniques to avoid intramuscular injection
- 2 Steps to ensure healthy injection sites

3 Provision of clear and concise direction to healthcare professionals regarding proper injection technique

Utilizing these priorities as a framework, this best practice document was developed by the Canadian FIT Board and has been reviewed by an expert committee of diabetes educators. Where evidence was unavailable, expert opinion guided the recommendation.

Since the initial FIT recommendations were published in October 2011, a Canadian injection practice survey was conducted.(7) Analysis of these data, new evidence regarding injection technique and – most importantly - new learnings regarding best practice, resulted in a revision to the document. Research regarding injection technique and the role of lipohypertrophy in glycemic variability has been increasing steadily since the launch of the international survey in 2009.(1) In 2013 and 2014, two trials examined enhanced glycemic control through improved injection technique(8) and cost analysis of improved injection technique.(9) Of note, the rate of lipohypertrophy in both of these studies was significant. Grassi and colleagues reported the incidence of lipohypertrophy as follows:(8) females, 48.1%; males, 51.9%. Blanco and colleagues observed a lipohypertrophy incidence of 64.4% in total participants.(9) In 2016, a well-conducted study of people with type 1 diabetes demonstrated that the action and absorption of insulin was considerably more variable with a blunted action when injections

were administered into areas of lipohypertrophy, which leads to a deterioration in postprandial glucose control.(10)

Most recently, another international injection survey was published, in which 329 Canadian patients were enrolled.(11) As a result, updated recommendations for patients and healthcare professionals have also been published.(12) The information acquired from these recommendations, as well as clinical experience since the publication of the first (2011) and second (2015) editions of the FIT Canada Recommendations, have guided the revisions to this document.

The evidence is compelling to continue to assess injection technique, examine patients for the presence of lipohypertrophy, and provide patient and healthcare professional education to ensure the prevention and management of lipohypertrophy. The development of FIT and the subsequent Canadian recommendations for injection technique are supported by BD Canada and endorsed by Canadian pharmaceutical companies that manufacture insulins and glucagonlike peptide-1 (GLP-1) receptor agonists.

#### The Canadian FIT Board – 3rd Edition

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#### **Endorsements**

As a company heavily committed to diabetes for the long term and with a large and diverse portfolio of medicines, AstraZeneca Canada endorses the FIT recommendations. Further educating healthcare professionals on better injection techniques is needed and will definitely benefit all those patients living with diabetes who require injectable medicines.

Neil Maresky MD, Vice-President, Scientific Affairs, AstraZeneca Canada

BD is proud to be a supporter of FIT worldwide. Through our ongoing research and collaboration with healthcare professionals, we strive to elevate the importance of injection technique practices for people living with diabetes who take injections, so that they can achieve the best possible diabetes outcomes. FIT Canada has done an outstanding job leveraging this new research to deliver a timely, comprehensive set of recommendations for best practice in injection technique.

Larry Hirsch MD, Worldwide Vice President, Medical Affairs, BD Medical – Diabetes Care

Utilizing the correct technique to administer injectable therapies for diabetes is critically important to help ensure patients benefit fully from their treatment. Eli Lilly Canada is dedicated to improving care for people with diabetes and welcomes this update to the FIT recommendations, as a means to improve both healthcare professional and patient understanding of good injection technique. The comprehensive, evidence-based guidelines provided through FIT will play an important role in supporting improved diabetes care in Canada.

Joanne Lorraine MD FRCPC MEd, Medical Director, Diabetes Care, Eli Lilly Canada

The burden of managing diabetes can be overwhelming for patients, families and healthcare providers. The FIT recommendations are a valuable way to support best practice sharing and ensure appropriate injection technique, which Novo Nordisk proudly endorses. Novo Nordisk is committed to supporting healthcare professionals to deliver the highest quality of care possible as their patients navigate the complexities of diabetes care. This includes the appropriate use of innovative devices, needles and therapeutics, as outlined in the FIT guidelines.

Hossam Ali Saad MD, Associate Director, Medical Affairs, Novo Nordisk Canada

Sanofi Canada is committed to improving diabetes management through our integrated offering of treatments, medical devices and services. We are proud to support the FIT Canada recommendations, whose goal is to promote best practice in diabetes injection technique. Proper injection technique is key to ensuring that patients receive the full benefit of injectable therapies. At Sanofi Canada, our focus is to simplify the management of a complex disease for people with diabetes and their healthcare providers. We are working hard, in partnership with everyone committed to diabetes care, to develop innovative solutions to help people with diabetes live as people, not as patients.

Hisham Mahmoud MD, Medical Head Canada, Diabetes and Cardiovascular, Sanofi Canada



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### 1.0 Preparing for injection

# 1.1 Psychological challenges of injections: Adults

- 1 The healthcare professional should inform all people with type 2 diabetes early after diagnosis that they will likely require injectable therapy in the future to treat their diabetes. It is important to explain the natural progression of diabetes and that initiation of injection therapy at any point during the course of the disease should not be seen as personal failure.(13)
- 2 Few adults have true needle phobia (i.e. a fear of needles); however, many experience anxiety regarding injecting, particularly when embarking on an injectable therapy regimen. The healthcare professional should explore a patient's anxieties regarding the injection process and address any concerns or barriers to treatment, with the goal of working together to improve treatment adherence and quality of life.(14-16)
- Both the short- and long-term advantages of achieving and maintaining target blood glucose levels should be emphasized to people with diabetes. Furthermore, it is important that healthcare professionals explain that finding the right combination of therapies – which may include injectable therapy – to achieve optimal glycemic targets is a primary treatment goal.(17,18)



Figure 1. Wash hands with soap and water



Figure 2. Wipe the cartridge or vial with an alcohol swab

#### 1.2 Injection site care

- Injections should be administered in a clean site on the body, using clean hands.(19)
- If necessary, people should clean their hands and the injection site with soap and water (Figure 1).(19)
- Disinfection of the injection 3 site is generally not required; however, alcohol swabs may be mandated for use prior to injections administered in a hospital or long-term care setting, or wherever nosocomial infections are more prevalent. If alcohol is used to clean the site, the skin must dry completely before the injection is administered.(20,21) Cleaning the medication cartridge or vial with an alcohol swab is required (Figure 2).(20)

#### 2.0 The correct use of devices

# 2.1 Use of syringes with an insulin vial

 Proper syringe selection is crucial. The decision regarding which syringe is appropriate should be based on the amount of insulin to be administered (volume: U-30, U-50 or U-100 syringes) and length of needle. Due to the need to pierce the insulin vial stopper, the current shortest available needle length of an insulin syringe is 6 mm.

The use of a 6-mm needle is recommended with or without a skin lift, depending on assessment of the site and amount of subcutaneous tissue. Ensure a skin lift with an 8-mm needle.(22) The use of 12-mm or 12.7-mm needles is not recommended, due to an increased risk of intramuscular injection.



Figure 3. Preparing an insulin syringe

- 2 When preparing to draw up the insulin, the air equivalent to the dose should be drawn up first and injected into the vial, to facilitate easier withdrawal (Figure 3).
- 3 If air bubbles are seen in the syringe, hold it with the needle pointed upwards, tap the barrel to bring them to the top, and then remove the bubbles by pushing the plunger to expel the air.
- 4 When using an 8-mm needle, injections should be administered into a skin lift at a 90-degree angle (Figure 4). To prevent intramuscular injection, lean individuals may need to inject into a skin lift at a 45-degree angle (Figure 5).(23-26)

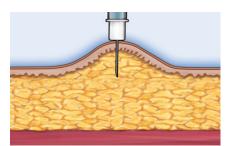


Figure 4. Proper injection into a skin lift at a 90-degree angle

This method may also be required with a 6-mm needle in particularly lean individuals.

- 5 When administering injections, the following steps should be taken if a skin lift is required:(27,28)
  - Insert the needle completely into the skin lift.
  - Depress the plunger completely.
  - Remove the syringe quickly, at the same angle that it was inserted.
  - Release the skin lift.
- 6 Syringes should be used only once.(29-31)

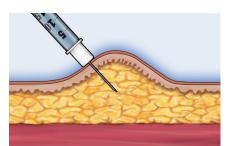


Figure 5. Proper injection into a skin lift at a 45-degree angle

### 2.0 The correct use of devices

#### 2.2 Use of pen devices

When teaching patients proper pen use, healthcare professionals should consult the instruction manual for the specific device being used. Obstruction of insulin flow in a pen is rare, but could lead to serious consequences. Understanding how to monitor movement of the rubber plunger within the pen is an important learning to ensure adequate insulin delivery.

- Insulin pen devices should always be primed (with doses as per the manufacturer's instructions) with the needle pointing upwards; a flow of insulin should be observed at the needle tip before each injection. Once flow is verified, the desired dose should be dialed and the injection administered.(1,32)
- 2 Pen devices and cartridges are for single-person use only and should never be shared, due to the risk of cross-contamination. (33,34)

- 3 Pen needles should be used only once. Using a new needle each time may reduce the risk of needle breakage in the skin, clogging of the needle, complications (e.g. lipohypertrophy, abscess) and inaccurate dosing.(29-31,35,36)
- 4 The insulin pen injection button should be touched only when the pen needle is fully inserted. The button should be pressed along the axis of the pen, not at an angle. After pushing in the injection button completely, the individual should count to 10 slowly (approximately 10 seconds, or as per the manufacturer's instructions) and maintain pressure on the thumb before withdrawing the needle, in order to: deliver the full dose; prevent aspiration of tissue into the cartridge; and prevent medication leakage (Figure 6). Counting higher than 10 may be necessary for higher doses. (27,28)
- 5 Pen devices with a dose window should be checked after each injection; the number o should be displayed when the desired dose has been injected. If a number other than o is showing, then the correct insulin dose has not been administered. In this event, replace the cartridge, attach a new pen needle, prime the pen (per the manufacturer's instructions) and administer the remainder of the dose.



Figure 6. Method for pushing in insulin pen injection button completely

#### 2.0 The correct use of devices

- 6 Needles should be safely disposed of immediately after use and should not remain attached to the pen. This prevents the entry of air or other contaminants into the cartridge or leakage of medication from the cartridge, both of which can affect subsequent dose accuracy. (27,37)
- 7 Non-disposable pen devices should not be stored in the refrigerator, as they contain parts (e.g. rubber) whose consistency is compromised by cold temperatures, which in turn affects pen function.
- 8 Individuals should keep a spare syringe or a second pen at hand in case of breakage or malfunction. A syringe should not be used to remove insulin from a pen with concentrated insulin, as the scale on insulin syringes is made for U-100 insulin only. The use of current insulin syringes with concentrated insulin (U-200 or U-300) could result in an overdose.

#### 2.3 Use of pen needles

- 1 Choose the right needle:
  - A shorter needle should be used at the initiation of insulin therapy.(26,38,39)
  - The needle gauge should be 30G, 31G or 32G (higher gauge = smaller needle diameter).
  - 4-mm, 5-mm and 6-mm needles are suitable for all people with diabetes, regardless of body mass index (BMI). An 8-mm needle may be preferred by some patients.
  - Current research across a wide range of BMIs (19 to 65 kg/m<sup>2</sup>) supports the use of 4-mm pen needles to avoid the risk of intramuscular injection.(40)
  - A recent study demonstrated that a 4-mm pen needle provides equivalent A1C control to 8-mm and 12-mm pen needles in obese people who are taking large doses of insulin.(41)

### 2.0 The correct use of devices

- 2 Injections with shorter needle lengths (i.e. 4 mm, 5 mm, 6 mm) should be administered in adults at a 90-degree angle to the skin surface.(23,42)
  - A skin lift may be warranted to prevent an intramuscular injection in a slim limb or abdomen, even when a shorter needle is used (Figure 7).(23,39)
  - A skin lift may not be required, particularly for patients who are using a 4-mm needle. (22,23,43)

- 3 Injection at a 45-degree angle with a 6-mm needle may be required in extremely lean adults, if no skin lift is used.
- 4 When using 8-mm needles, injections should be administered into a skin lift at a 90-degree angle. Lean individuals should administer injections into a skin lift at a 45-degree angle to prevent possible intramuscular injection. (23,39)
- 5 The use of 12-mm or 12.7-mm needles is not recommended.(39)





Figure 7. Correct (left) and incorrect (right) ways of performing a skin lift. To perform a skin lift correctly, lift the skin and subcutaneous tissue delicately between the thumb and index finger, leaving the muscle behind

#### 2.4 Injections should be administered into subcutaneous tissue

- To ensure proper injection technique (Figure 8), individuals should consult with a healthcare professional who is trained in appropriate injection techniques. (6,22)
- 2 When the needle is removed, check skin appearance for the following:
  - If the injection is administered correctly, the tissue beneath the skin (subcutaneous) appears normal.(22)

### 2.0 The correct use of devices

- A white area that appears when the needle is withdrawn (intradermal) may indicate that the insulin has not been injected deeply enough.
- Blood and/or bruising at the injection site may indicate that a minor capillary has been penetrated, with no resulting effect on absorption of the insulin.(6,25,44)



Figure 8. Proper injection technique for subcutaneous absorption of insulin and GLP-1 receptor agonists: 4-mm pen needle, no skin lift (left); 8-mm pen needle, skin lift (right)

# 2.5 Tips for making injections more comfortable

- Inspect and palpate the injection site prior to each injection. Any area with signs of lipodystrophy, inflammation, edema or infection should be avoided.(5,45)
- 2 Avoid injecting into hair roots, scars, moles, stretch marks or other skin abnormalities.
- 3 Keep injectable therapies currently in use at room temperature.(46,47)
- 4 Use a needle of shorter length and smaller diameter.(43)
- 5 Use a new needle for each injection.(35)
- 6 Insert the needle through the skin using a quick, smooth movement.(48)
- 7 Inject medication slowly and evenly. Ensure that the plunger (syringe) or injection button (pen) has been depressed fully.(48)

- 8 If using alcohol swabs, inject only when the alcohol has dried fully.
- 9 Avoid injection through clothing, particularly in individuals who are using shorter needles, as there is an increased risk of intradermal injection and the site cannot be inspected.(49)
- 10 In some cases, the insulin dose should be distributed between 2 injections sites, as discomfort at the injection site may decrease at doses <50 units for insulins with 100 units/mL concentration.(50) Higher-concentration basal and mealtime insulins are now available in Canada, which may permit higher doses to be administered in smaller volumes than was previously the case.
- 11 If needed, apply ice or analgesic cream to the site before administering an injection.
- 12 If needed, use such devices as NeedleAid<sup>®</sup>, Inject-Ease<sup>®</sup>, Insuflon<sup>®</sup> and i-port<sup>®</sup>.

### 3.0 Disposal of injection materials

#### 4.0 Injectable therapy – insulin

#### 4.1 Temperature of insulin

- All healthcare professionals, individuals with diabetes and caregivers should be aware of local regulations regarding sharps disposal and the consequences of inappropriate disposal (e.g. needle stick injuries to refuse workers). (51,52)
- 2 Proper disposal technique should be demonstrated upon initiation of injection therapy and reinforced at subsequent healthcare visits (Figure 9).
- 3 Where available, a needleclipping device can be used.
- 4 Needles should never be resheathed.(53)



Figure 9. All needles should be disposed of in an approved sharps container after use

- The temperature of insulin does not affect its pharmacokinetics or absorption, provided that it is stored at room or refrigeration temperature.(54)
- Insulin administered at room temperature may reduce irritation, burning or pain, and facilitates the re-suspension of cloudy insulin.(46,55-58)

#### 4.2 Storage of insulin

- Unopened insulin vials and cartridges should be stored at refrigeration temperature (2 to 8 degrees C). Once in use, insulin may be stored at room temperature.
- Insulin should never be frozen or exposed to extreme heat (>30 degrees C) for prolonged periods, as this will affect its potency and alter its action. Keep the caps on insulin pens to protect the insulin from the light. Do not store insulin in direct sunlight.
- 3 As per product monographs, once insulin is opened it should not be used for more than 28 days, with the exception of insulin detemir and insulin glargine U-300, which may be used for up to 42 days.
- 4 Insulin should never be used past its product expiry date.

#### 5.0 Site-related factors that may affect insulin absorption

#### 5.1 Intramuscular injection

- Intramuscular injection of all human insulin, as well as rapid- and long-acting analogues, should be avoided due to the risks of erratic blood glucose control and severe hypoglycemia.(59,60)
- 2 Accidental intramuscular injection into an arm, leg, or buttock prior to or during exercise may increase insulin absorption, and result in a faster action and more rapid decrease in blood glucose levels.(55,61)

# 5.2 Injection site-related factors

- Massaging the injection site immediately before or after an injection is not recommended, as it increases the absorption rate of insulin and results in an unpredictable time-action profile.(54,62)
- 2 Avoid damaged skin (e.g. from surgical scars or lipohypertrophy, as described in Section 9.0) when injecting insulin and GLP-1 receptor agonists.(5,54)
- 3 Injecting into an area that has an increased skin temperature (e.g. after a sauna or hot bath) can increase the absorption rate of insulin.(63,64)
- 4 Insulin is absorbed most consistently from the abdominal area.(65-71)
- 5 The upper arm and the lateral side of the thigh, not proximal to the knee, have moderate insulin absorption rates.(65-68,71)

- 6 The slowest absorption of insulin occurs when it is injected in the buttock; thus, this may be the preferred injection site if slow absorption is desired.(71)
- 7 Rapid- and long-acting insulin analogues may be administered at any injection site, as absorption rates do not appear to be site-specific.(67,72-76)
- 8 The abdomen is the preferred site for soluble human insulin (regular), since absorption of this insulin is fastest in this area.(69,70,77-80)
- 9 Premixed regular/NPH insulin should be injected in the abdomen to increase the speed of absorption of this short-acting insulin, in order to cover postprandial glycemic excursions.(81)

### 6.0 Ensuring proper preparation and administration of insulin

# 6.1 Re-suspension of cloudy insulin

When using cloudy insulin (i.e. NPH and premixed insulin) the vial, cartridge or pen device should first be gently rolled 10 times, then tipped (not shaken) 10 times; finally, it should be inspected to ensure the suspension has a consistently milky white appearance (Figure 10).(82-84)

# 6.2 Factors affecting volume of injection

- Larger doses of insulin are associated with more leakage and potentially more discomfort. (50,85,86)
- In obese patients, there is no difference in glycemic control, safety, leakage rates and patient ratings between 4-mm, 5-mm, 8-mm and 12.7-mm pen needle lengths.(41,43,87-89) In one study, the amount and rate of leakage appeared to increase related to a coinciding increase in BMI.(88)
- 3 The volume of leakage is generally <0.1 IU (or <1.0% of total insulin, for most patients) and hence almost always clinically insignificant.(86,90,91)

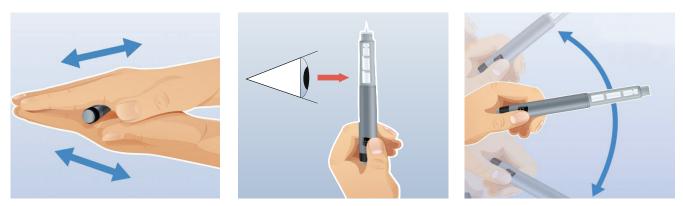


Figure 10. Method of mixing cloudy insulin: roll 10 times, tip 10 times, then perform a visual check for milky white appearance

### 6.0 Ensuring proper preparation and administration of insulin

# 6.3 Effect of volume of injection on insulin action (kinetics)

- 1 The larger the dose, the more delayed the action of NPH and short-acting (regular) human insulins. The clinical evidence regarding these human insulin formulations suggests a longer, flatter action profile with doses >50 units, which may compromise glycemic control. When injecting >50 units of short-acting (regular) or intermediate-acting (NPH) insulin per dose, it may be prudent to split the dose into 2 separate injections.(54,63,85,92,93)
- 2 The time-action profile of insulin analogues does not appear to be affected by the volume of injection. The decision to use 2 injection sites may be a function of the device (i.e. a maximum single dose of 80 units) or discomfort with injection volume, rather than a requirement to achieve a better pharmacokinetic profile.
- To date, no clinical trials have been conducted to determine at which dose insulin detemir (Levemir<sup>®</sup>) should physically be split into 2 volumes. However, since the currently marketed Novo Nordisk insulin delivery device administers a maximum dose of 80 units at one time, doses >80 units will require multiple, separate injections to administer a full dose. Insulin therapy should be individualized and in accordance with the needs of the individual patient; any changes made to the dose or regimen should be done under medical supervision, and close monitoring is recommended. (94) (This information was provided by Novo Nordisk Canada.)
- Clinical trials have shown that insulin glargine 100 units/mL (Lantus<sup>®</sup>) provides a constant concentration/time profile over 24 hours and achieves glycemic control over 24 hours with once-daily administration.

Splitting Lantus<sup>®</sup> into more than 1 injection would be a function of exceeding the maximum dose delivery of the device.(95)

- Insulin glargine 300 units/mL (Toujeo<sup>™</sup>) provides more even steady-state pharmacokinetic and pharmacodynamic profiles, with no pronounced peak and a longer duration of action than Lantus®. Splitting Touieo<sup>™</sup> into more than 1 injection would be a function of exceeding the maximum dose delivery of the device. Toujeo<sup>™</sup> is administered once daily, and there are currently no data to support dividing a large dose into a twice-daily regimen.(96) (This information was provided by Sanofi Global.)
- There are currently no data from clinical trials regarding splitting insulin glargine (rDNA origin) (Basaglar<sup>®</sup>) at a particular dose amount. Eli Lilly Canada concurs with Sanofi Global that if a patient requires more basal insulin

# 6.0 Ensuring proper preparation and administration of insulin

than the maximal deliverable dose from the insulin pen device, the dose should be split. Any other decisions regarding splitting the basal insulin dose should be made by the patient and their healthcare team, in consideration of individual patient characteristics and circumstances.(97) (This information was provided by Eli Lilly Canada.)

 Humalog<sup>®</sup> KwikPen<sup>®</sup> (insulin lispro) 200 units/mL provides similar kinetics to Humalog<sup>®</sup> 100 units/mL. Splitting Humalog<sup>®</sup> 200 units/mL into more than 1 injection would be a function of exceeding the maximum dose delivery of the device. (This information was provided by Eli Lilly Canada.)

#### 6.4 Concentrated insulin: practical tips and special considerations

- Concentrated insulin delivers the same dose with less volume. This concept requires further study to ascertain if there will be more, less, or no difference in rates of lipohypertrophy.
- 2 Concentrated insulin is available in a pre-filled pen device specifically designed for this type of insulin. The dosing window shows the number of units that will be delivered in a smaller volume.
- 3 There is no calculation required when switching or starting these insulins: 1 unit on the pen = 1 unit of insulin. It is delivered in less diluent.
- 4 Concentrated insulins are not available in vials; therefore, it is imperative that there is no pen-to-syringe transfer, to avoid dosing errors. It is also important that none of the concentrated insulins be removed from the prefilled pen device for use in a syringe, pump or other delivery device, in order to avoid potential overdose or hypoglycemia.

#### 7.0 Injectable therapy – GLP-1 receptor agonists

The injection technique for GLP-1 receptor agonists is similar to insulin; however, there are a few practical differences. While lipohypertrophy is largely associated with insulin therapy (e.g. incorrect site rotation, reuse of needles), insulin as a growth factor also contributes significantly to the development of lipohypertrophy. It is therefore not surprising that current evidence indicates that GLP-1 receptor agonist injections do not lead to lipohypertrophy; however, it is still important to rotate injection sites with these agents. The results of ongoing trials will provide further information.

While no studies have been published regarding the effect of injecting a GLP-1 receptor agonist into an area of lipohypertrophy, it may be hypothesized that, similar to insulin, erratic medication absorption may occur. Considering the time-action profile of current GLP-1 receptor agonists (i.e. dulaglutide(98) [Trulicity™], exenatide(99) [Byetta®], exenatide once-weekly(100) [Bydureon®] and liraglutide(101) [Victoza®]), the clinical implications of these absorption distortions would have less impact than with insulin. Still, patients should be advised to avoid injecting GLP-1 receptor agonists into lipohypertrophic areas.

Injection site nodules with Victoza® have been reported to occur at a rate of 1%. In long-term controlled trials, injection site reactions occurred in approximately 2% of patients. The most frequently reported reactions were bruising and pain. Discontinuation rates were low (0.2 to 0.4%).(99,101,102)

In clinical trials, injection site reactions with Trulicity<sup>™</sup> occurred at a rate of 1.7%, vs. 0.9% with placebo. The most frequently reported reactions – hematoma (0.8% vs. 0.4% placebo), injection site pain (0.3%) and erythema (0.2%) – were reported only in the Trulicity<sup>™</sup> group. Discontinuation rates due to injection site reactions were low (approximately 0.1%).(98) Injection site nodules (mild inflammation due to foreign body reaction) are an expected reaction to the poly-(D,L-lactide-coglycolide) microspheres contained in Bydureon<sup>®</sup>. The size of nodules ranges from 0.25 to 2.0 cm (on average, <0.75 cm in size). They are typically transient, and most are asymptomatic and resolve in 4 to 8 weeks. The incidence of injection site nodules in the clinical trial program was 6.8%, with a discontinuation rate of 0.4% due to nodules.(100)

In 3 separate clinical trials, injection site reactions with Byetta<sup>®</sup> occurred at a rate of 9.4% vs. 9.7% placebo, 9.8% vs. 6.8% placebo, and 7.4% vs. 4.5 % placebo, respectively. The most commonly reported reactions were injection site bruising, pruritus, erythema, hemorrhage, pain and swelling. In all 3 studies, no patients withdrew due to injection site reactions.(99)

While albiglutide (Eperzan®) has been approved for use in Canada, it is not available or marketed at this time. Hence, information about albiglutide has not been included in this update.

### 7.0 Injectable therapy – GLP-1 receptor agonists

# 7.1 Storage of GLP-1 receptor agonists

- GLP-1 receptor agonists should be stored in a refrigerator, at a temperature between 2 and 8 degrees C. They should not be stored directly adjacent to a refrigerator cooling element or in a freezer.
- 2 GLP-1 receptor agonists should not be frozen; if freezing occurs accidentally, the medication should be discarded.
- 3 After initial use of the reusable pen containing Victoza® or Byetta®, the products can be stored for 30 days at room temperature (no higher than 30 degrees C) or in a refrigerator (between 2 and 8 degrees C).
- 4 Single-use devices such as Trulicity<sup>™</sup> can be stored for 14 days at room temperature (no higher than 30 degrees C), while Bydureon<sup>®</sup> can be stored for 30 days at room temperature (no higher than 30 degrees C) or in a refrigerator (between 2 and 8 degrees C).

# 7.2 Practical tips and special considerations

- GLP-1 receptor agonists are absorbed equally from each of the usual injection sites (i.e. abdomen, arm and thigh). (99,101,103)
- Priming of reusable devices (Victoza<sup>®</sup>, Byetta<sup>®</sup>) with each injection is not required for GLP-1 receptor agonists. Due to the design of these pen devices, priming is required only once, prior to administration of the first dose.(99,101)
- 3 Trulicity<sup>™</sup> is a once weekly GLP-1 receptor agonist that is available in a ready-to-use (no reconstitution required) single dose/single use pen, with a hidden, pre-attached needle. The needle, which extends and retracts automatically, is 29 gauge, with a 5-mm injection depth. Both doses – 0.75 mg and 1.5 mg – are delivered in a 0.5 mL injection volume. No priming is required for Trulicity<sup>™</sup>.(98)
- Bydureon<sup>®</sup> is a GLP-1 4 receptor agonist that utilizes biodegradable microsphere technology for controlled extended release. Bydureon® is supplied in a dual chamber pen injector. The front chamber contains the 2-mg onceweekly dose of exenatide powder, while the rear chamber contains sufficient diluent to re-suspend the exenatide with microspheres (total volume: 0.65 mL). Reconstitution is required. A 23 gauge (7-mm) needle is used to deliver Bydureon® subcutaneously. Administration with a 7-mm needle should follow the same technique as with an 8-mm needle. No priming is required for Bydureon<sup>®</sup>.(90)

# 8.0 Injection area

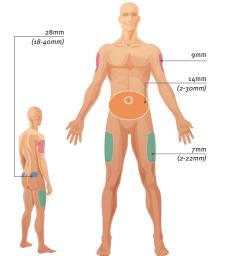
#### 8.1 Injection area selection

A plethora of research, using various imaging techniques, has demonstrated that – regardless of age, BMI, gender or race – skin thickness (epidermis and dermis) is relatively consistent; it ranges from 1.25 mm to 3.25 mm at its extremes, but averages approximately 2 mm.(22,104-110)

The thickness of subcutaneous tissue has a much wider variance, and is related to gender, body site and BMI. The subcutaneous layer increases proportionally with an increase in BMI (Figure 11). (22,66,106,111-113)

The buttocks are noted to have the thickest subcutaneous layer, followed by the abdomen, arm and thigh. The subcutaneous thickness can vary slightly within the same anatomical area.(109) Women are noted to have approximately 5 mm greater subcutaneous fat than men with the same BMI.(1,22,65,109-114) Best practice indicates that rates of unexplained hypoglycemia and increased glycemic variability are lower when the abdomen is used exclusively as an injection site.

- 1 To avoid intramuscular injection, and in consideration of safety and ease in self-injection, the abdomen, thighs and buttocks are the recommended selfinjection areas for adults. The buttocks are noted to have the thickest subcutaneous layer of these areas.(4,106,108-110)
- 2 The areas of injection are defined as:
  - Abdomen boundaries: 1 cm above symphysis, 1 cm below lowest rib, 1 cm away from umbilicus and laterally at the flanks
  - Thighs: upper 3rd anterior lateral aspect of both thighs
  - Buttocks: posterior lateral aspect of both upper buttocks and flanks



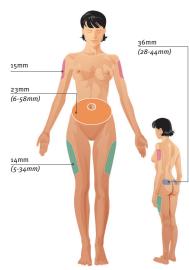


Figure 11. Subcutaneous tissue (in mm) in male and female adults: the mean values (bold) and ranges (in parentheses) are the result of a series of studies using ultrasound(4)

# 8.0 Injection area

- 3 The abdomen offers the most consistent absorption of regular and NPH insulin.(5)
- 4 The arm is not a preferred area for self-injection, due to difficulty accessing the correct zone, difficulty in handling the delivery device to achieve the necessary 90-degree angle and the lessened thickness of subcutaneous fat, which could create a greater potential for intramuscular injection. (4,5,106,113-115)

# 9.0 Lipohypertrophy

# 9.1 Identification of lipohypertrophy

Lipohypertrophy is the most common lipodystrophy found at injection sites.(116) Lipohypertrophic areas can develop under the skin where the same injection or infusion site is used repeatedly. Described as thickened or rubbery lesions (Figure 12),(2,6) lipohypertrophic areas may vary in size and shape; some are visually apparent, while others may require palpation for detection. Recent research suggests that some areas of lipohypertrophy may be detected only via ultrasound.(10,117)

When palpated with the fingertips, lipohypertrophic areas may feel dense and hard.(9,118-121) These lesions can also be identified by pinching the skin: while healthy skin can be pinched together tightly, lipohypertrophic lesions cannot (Figure 13).



Figure 12. Lipohypertrophic lesions



Figure 13. The pinch characteristics of normal (left) vs. lipohypertrophic (right) tissue(120)

### 9.0 Lipohypertrophy

#### 9.2 Factors contributing to the development of lipohypertrophy

- 1 Unlike other injectable agents (e.g. GLP-1 receptor agonists, heparin) insulin is a growth factor that contributes to the enlargement of adipocytes and swelling of the fat tissue when injected repeatedly into a small subcutaneous area. This anabolic activity of insulin is a significant contributor to the development of lipohypertrophy.(117,123)
- Although the exact causes 2 have not been substantiated. factors known to be associated with increased areas of lipohypertrophy include: longer duration of insulin use;(124) more frequent injections; higher dosage of insulin; the use of non-purified insulin (prior to the use of human insulin and insulin analogues); repeated injection or infusion into a small area (i.e. smaller than the size of a postage stamp); reuse of needles; and failure to inspect injection or infusion sites on a regular basis.(8,9,57,116,123-127)

# 9.3 Effects of lipohypertrophy

The effects of injecting or infusing insulin into a lipohypertrophic site have been documented as a decrease in the rate of insulin absorption, as well as a variable rate of absorption, thereby resulting in variable glycemic response and unexplained hypoglycemia.(10) Recent studies have shown that when insulin is injected into lipohypertrophic sites, larger daily doses of insulin are needed to achieve glycemic targets. This results in increased costs to the insulin user.(9) There is also potential for the development of disfiguring anatomical lesions. (8,9,123,127)

It has been noted that patients repeatedly choose lipohypertrophic sites for injections or infusions, as these areas have limited nerve innervations and result in relatively painless injections.(128,129)

Recent international trials have found that the prevalence of lipohypertrophy ranges from 49% to 64% among study participants. The strongest correlating factor in all studies was the lack of injection site rotation.(8-10,123)

A previous international survey found that 28% of participants could not remember ever having their injection sites checked by a healthcare professional. This clearly indicates the need for a heightened level of awareness among both healthcare professional and patients to check injection sites daily and rotate sites as necessary to reduce the risk of lipohypertrophy. (8,12,123,130)

Due to the potential for the thickness of the subcutaneous fat layer to vary, even within the same anatomical area (e.g. the abdomen),(109) the use of a 4-mm needle minimizes the potential for intramuscular injection and allows patients to use a larger area for injection, i.e. a postcard-sized area vs. a postage-stamp-sized area.

# 9.0 Lipohypertrophy

#### 9.4 Assessment, prevention and avoidance of lipohypertrophy

- Education regarding lipohypertrophy should be included during all insulin initiations and reinforced during all discussions with insulin-using patients.(8,121,131-133)
- 2 Injection or infusion sites should be inspected and palpated by a healthcare professional at each visit:
  - The inspection should be performed while the patient is in a standing(120) or supine position.
  - Adequate lighting should be ensured.
  - The injection area should be palpated in a circular, sweeping motion using the fingertips.
  - Assessment may be enhanced with the use of examination gel or lotion.
- Patients should be taught how to manually inspect and palpate their injection sites to detect lipohypertrophy (Figure 14).(134)

- 4 To prevent lipohypertrophy and maintain consistent medication absorption, patients should rotate their injections within an anatomical area, use larger injection zones and use a new needle with each injection. (5,6,9,32,128,130-132)
- 5 Patients should be instructed never to use lipohypertrophic sites when injecting medication. (121,132,133)
- 6 When changing from a lipohypertrophic injection site to a healthy site, patients should be cautioned to reduce their insulin dose initially and monitor their blood glucose levels more frequently.(8)

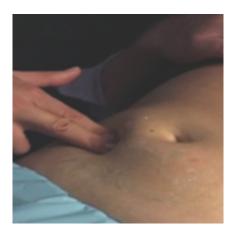


Figure 14. Proper palpation technique for detection of lipohypertrophy

### 10.0 Site rotation

#### 10.1 Implementation

Site rotation is essential to avoid lipohypertrophy and to facilitate consistent medication absorption, thereby contributing to a decrease in glycemic variability and unexplained hypoglycemia. (8,9,12,57,119,123-125,135,136)

- 1 To prevent lipohypertrophy and maintain consistent medication absorption, patients should be taught a personalized, structured rotation regimen for injection and insertion sites. (78,122)
- 2 For insulin injections, structured rotation is recommended in the same anatomical area (e.g. abdomen, thigh) at the same time of day, with injections administered at least 1 cm to 2 cm apart (i.e. the width of 1 finger) across the entire area (Figure 15, Figure 16). (9,66,78,137)

- 3 Patients should be encouraged to use as large a zone as possible in the anatomical area, i.e. a postcard-sized vs. a postage-stamp-sized zone (Figure 16).(8,9,108)
- 4 The abdomen remains the preferred injection/infusion area; however, patient preference remains an important consideration.(33) Care should be taken to avoid injecting or inserting within 2 to 3 cm of the umbilicus.
- 5 Injection or insertion site rotation should be discussed with, and demonstrated by, patients at every visit.(4,130,138) Documentation of this should be done in the patient's chart.(8)

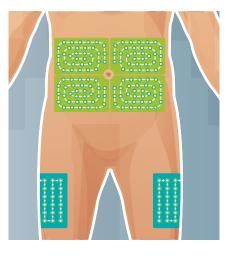


Figure 15. Injections within any quadrant should be spaced at least 1 to 2 cm from each other

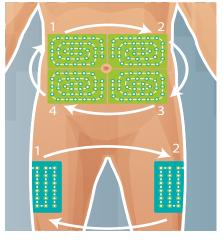


Figure 16. Sample structured rotation plan for abdomen and thighs: divide the injection area into quadrants or zones; use 1 zone per week and move clockwise(4)

### 11.0 Bruising and bleeding

#### 11.1 Recommendations

Local bruising and/or bleeding may occur occasionally at an injection site and is more common in patients who are taking antiplatelet therapy. Although bruising and bleeding do not impede medication absorption and do not appear to be associated with needle length or injection site – switching to a shorter, thinner needle may have positive psychological implications with respect to adherence.(12,127,139) The primary contributor to bruising and bleeding at the injection site is incorrect injection technique. (6,25,44,108)

- Patients should be reassured that occasional bruising or bleeding at an injection site will not affect medication efficacy. (12,43,133)
- 2 Avoid indenting the skin when injecting. Place the needle into the skin, while maintaining visibility of the needle hub (Figure 17).(12,133,139)
- 3 Frequent bruising or bleeding at an injection site warrants a review of injection technique.

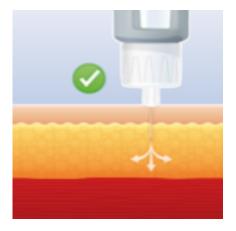


Figure 17. Avoid indenting the skin when injecting

#### 12.0 Pregnancy

Due to the paucity of evidence regarding insulin injection technique during pregnancy, the following recommendations are based upon available research and clinical experience.(25,44)During pregnancy, questions often arise from women regarding why, where and how insulin should be administered. The initial concerns of the mother regarding the effect of insulin injections or infusion on the fetus must be explored, to facilitate medication adherence. Ease of use and safety issues (e.g. hypoglycemia) should also be discussed.(140)

#### 12.1 Recommendations

- Education regarding insulin use during pregnancy is essential for all pregestational women and women with gestational diabetes who require insulin. This education should include discussion of the psychological adjustment to insulin use, changes to insulin requirements during pregnancy, appropriate injection sites and site rotation, and prevention of hypoglycemia.
- 2 The abdomen is the preferred area of injection for pregnant women.(141,142)
- 3 The thigh may be used as an alternate injection area.(108)
- 4 Shorter needles (4 mm or 5 mm) should be used, to decrease the potential for intramuscular injection.(12,104-106)
- 5 Injections within 2 to 3 cm of the umbilicus,(104,106) or areas on the abdomen where the skin is taut, should be avoided.

6 During the third trimester of pregnancy, when the skin is taut over the central abdomen, the lateral sides of the abdomen are the recommended areas for injection (Figure 18).



Figure 18. Recommended injection sites during the third trimester of pregnancy

### 13.0 Elderly

#### 13.1 Special considerations

Education and treatment approaches for the elderly population are challenged by both physical and psychological issues, including loss of muscle mass and strength, decreased skin integrity and changes in cognition, memory, sight and hearing. Impaired counterregulatory hormones reduce the recognition of hypoglycemia, creating a greater potential for falls and fractures.(143) The approach to elderly patients must be highly individualized, while integrating all aspects of their lives (i.e. physical, social and spiritual realms).(144,145)

Assessing cognitive and functional abilities affected by aging is a primary concern when evaluating safety in injection technique in the elderly.(144) should be done using standardized tests for cognitive and functional abilities.(144,146) The clock drawing test is recommended as an assessment tool to determine cognitive function.(147) Depression screening should be mandatory. (108,144,146,148)

- 2 A structured diabetes management and injection technique plan should be written, based upon a comprehensive physical and psychological assessment. (108,145,146)
- 3 The use of premixed insulin in the elderly results in greater accuracy in insulin dose, compared with self-mixed insulin.(149,150)
- 4 Pen use including the use of memory pens and other assistive devices – is recommended.(32)

- 5 Education of family members and friends is encouraged for support and safety. Encourage family members to be involved on a daily basis.(145,151) Telephone follow-up with this group is recommended.(145,151,152)
- 6 The recommended area for self-injection in elderly patients is the abdomen. The use of an insulin pen device with a 4-mm pen needle is encouraged, to avoid the need for a skin lift. Healthcare professionals may recommend the outer aspect of the arm as an alternate site for caregivers who are responsible for injecting, and have been trained in injection technique. Safety engineered devices are recommended for third-party caregivers, where there is a risk of disease transmission. (12,66,108,134,153)
- 7 All training regarding injection therapy should include a return demonstration.(134,146)

1 Individualized assessment

### 14.0 Pediatrics

#### Psychosocial Challenges 14.1 Thickness of subcutaneous fat

Many children and adolescents are emaciated at the time of diabetes diagnosis. As well, children aged 2 to 6 years, those who are slim and very lean teenage boys have minimal subcutaneous fat tissue. All of these factors render the administration of insulin into subcutaneous fatty tissue very challenging. Appropriate injection techniques are key to achieving optimal blood glucose control.

 The healthcare professional should conduct an individualized assessment to determine the amount of subcutaneous fat thickness at each injection site. This assessment will guide the choice of needle length and administration technique.(154)

- Insulin pens are the injection devices of choice, due to their shorter needle lengths (4 mm, 5 mm or 6 mm);(155) 4-mm needles are the safest needle length currently available.(107)
  - A 4-mm needle can be inserted at a 90-degree angle without a skin lift in adolescents and children >6 years of age; children aged 2 to 6 years require a skin lift in order to avoid intramuscular injection. (23,107)
  - If a child or adolescent is lean, 5-mm and 6-mm needles require a 45-degree angle injection with a skin lift. (90,156)
- 3 If a young child cannot remain immobile during the injection procedure – as is required with pen use – a syringe with a 6-mm needle may be used. In order to avoid intramuscular injection, it is critical to inject into a site with sufficient adipose mass, perform a skin lift and angle the injection. (155,156)

#### 14.2 Injection sites

Small children have less surface area at injection sites. As well, since many children and adolescents do not adhere to an adequate site rotation plan, lipohypertrophy is a common occurrence. Barriers to the use of multiple sites include fear that a new site will be painful to inject into and comfort with an existing routine.(157,158)

- The healthcare professional should educate parents, children and adolescents regarding the need for injection site rotation. Indeed, parents must reinforce the consequences of injecting into "favourite spots."
- 2 For children and adolescents who self-inject, supervision may be required in order to ensure adequate site rotation.

### 14.0 Pediatrics

#### Physiological Challenges 14.3 Needle anxiety and pain

Needle anxiety is common in children and adolescents, as well as their parents; younger children report greater fear and pain. Parents' attitudes are important for their child's acceptance of injections.(159-161)

- The healthcare professional should ask patients about needle fear and pain, as many do not report it voluntarily.(2)
- 2 At diagnosis of diabetes, the healthcare professional should consider intervention strategies for the child's parents, as follows:
  - Inform them that displayed distress and negative attitudes can influence their child's cooperation with the administration of insulin.
  - Have parents experience the injection regimen by performing a saline injection with a syringe or pen needle attached to an empty insulin pen.

- 3 Younger children may be helped by:(154)
  - Distraction therapy (provided it does not involve trickery), e.g. injecting while watching a favourite television show, blowing bubbles, or looking for hidden objects in picture books.
  - Play therapy, e.g. injecting a favourite stuffed toy.
- 4 Older children and adolescents experiencing needle anxiety may be helped by cognitive behavioural therapy, if available, including:(154)
  - Relaxation training
  - Guided imagery
  - Graded exposure
  - Active behavioural rehearsal
  - Modeling and reinforcement
  - Incentive scheduling

# 14.4 Preparing children for injections

Anticipatory fear is often worse than the actual experience of injection. Parents who are wellprepared beforehand will transmit less anxiety to a child. In fact, the presence of a calm and reassuring parent is the most effective support for a distressed child.(33,34)

### 14.0 Pediatrics

#### 14.5 Self-Injection

The age at which children can selfinject is related to developmental maturity rather than chronological age. Most children >10 years of age can either administer their own injections or help with them.(162)

 If self-injecting, young children should do so under supervision, and share the responsibility with their parents.(154,162)

# 14.6 Insulin under- and overdosing

Intentional under- and overdosing of insulin is common in children and adolescents, and can lead to severe hypoglycemia or diabetic ketoacidosis.(163-166)

- If insulin dose manipulation is suspected or confirmed, the healthcare professional should instruct parents to be more involved in insulin administration.(167)
- 2 If omission or overdosing remains an issue, parents should be instructed to assume the responsibility of injecting insulin.
- 3 Supervision of injections by parents or caregivers should include checking the dose prior to injection and ensuring the injection has penetrated the skin.

#### 14.7 Adolescence

Adolescence is defined as puberty through 18 years of age. During this stage of life, insulin resistance is more common, and higher doses of insulin are often required to achieve near-normal glucose control. Studies have demonstrated that insulin levels are higher during puberty than they are during adulthood or the years preceding puberty.(168)

Although the majority of adolescents with type 1 diabetes adapt well to the difficult challenges of puberty, it must be recognized that their healthcare and emotional needs are distinctly different from those of younger children or older adults. Adolescence involves training to become an independent adult and may result in failures and mistakes, as well as successes. Many adolescents have a greater tendency to skip insulin, due to peer pressure, rebellion, pain, depression or diabetes burnout. As well, some adolescents associate insulin with weight gain, and therefore choose to skip insulin doses.(168)

### 15.0 Institutions

The safety of patients and healthcare professionals in medical institutions and long-term care facilities is a primary consideration regarding injection technique.

Needle stick injuries are a frequent, yet largely preventable, occurrence among healthcare professionals. Consideration must be given to the safe disposal of all injection and infusion devices to prevent injury to healthcare workers.

Cross-contamination among patients is also preventable with appropriate use and disposal of injection or infusion devices. Institutions are encouraged to develop a 'safety culture' through staff education and increased awareness of best practice.

#### **CLINICAL TIP**

"One pen, one patient!"

#### 15.1 Special considerations

- Safety engineered devices

   (i.e. syringes or pen needles)
   should be used by healthcare
   professionals for all injections in
   an institutional setting, thereby
   eliminating the need to recap
   needles.(6,53,55)
- 2 Injectable delivery systems should be for individual use only. (6,34)
- 3 Injection sites should be clean and free of infection, edema, bruising or lipohypertrophy. (20,32,44)
- 4 Alcohol swabs may be used to clean the injection site (note, however, that this does not disinfect the site); the skin should be thoroughly dry before injecting.(20,30,32,45)
- 5 To avoid intramuscular injection, the use of a shorter, safetyengineered pen needle (5 mm) or an angled injection(22,104-106) (syringe only) is preferred over a skin lift, to reduce the risk of a needle stick injury.

- 6 Prior to injecting, all healthcare professionals should have a clear line of sight to the disposal unit they will be using.
- 7 All institutions should have clear policies and procedures that ensure a 'no blame' approach to the reporting of needle stick injuries.(169)
- 8 All institutions should have an established education program in injection technique to ensure best practice.(143)

### 16.0 Best practice recommendations

- Prepare patients regarding the need for injection therapy, provide proper education and ensure regular assessment of injection sites and techniques.
- 2 Rotation of injection sites within all zones of an anatomical area is essential to avoid lipohypertrophy.
- 3 Healthcare professionals and patients alike should be taught how to inspect and palpate injection sites, and how to prevent lipohypertrophy.
- 4 Shorter pen needles (e.g. 4 mm, 5 mm and 6 mm) are suitable for all people with diabetes, regardless of BMI; however, 6-mm needles are recommended, if syringe use is preferred.

- 5 The abdomen is the preferred injection area, for consistency of absorption and for ease of selfinjection. Instructions should be provided for caregivers for alternate site specifically the arm for a third-party injection.
- 6 Splitting insulin doses related to the volume of the injection should be individualized to each person after consideration of all factors.
- 7 Glycemic variability and poor glycemic control may be related to injection techniques. Careful assessment and management are required when encouraging use of healthy sites.
- 8 When using cloudy insulin, the vial or cartridge should be rolled gently 10 times and then tipped (not shaken) 10 times; the vial or cartridge should also be inspected visually to ensure the suspension has a consistent milky white appearance.

- 9 The injection technique for GLP-1 receptor agonists is similar to insulin, with a few practical differences. Patients should avoid injecting GLP-1 receptor agonists into areas of lipohypertrophy.
- 10 With respect to special populations:
  - The lateral sides of the abdomen are the preferred injection sites for pregnant women.
  - Safety is a primary consideration in the elderly population; as such, cognitive and functional abilities should be assessed.
  - Young children who selfinject, and older children and adolescents who are suspected of insulin under- or overdosing, should be closely supervised by a parent.

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### Glossary

- A1C (glycated hemoglobin): A test that measures the average level of blood glucose over the past 2 to 3 months. According to the Canadian Diabetes Association, the target A1C for most people with diabetes is 7.0%.
- Blood glucose: The concentration of glucose in the blood, which is represented in millimoles per litre (mmol/L) of blood.
- Blood glucose targets: The blood glucose level range recommended by a diabetes healthcare professional for successful diabetes management. According to the Canadian Diabetes Association, blood glucose targets for people with diabetes are as follows:
- Fasting blood glucose: 4.0 to 7.0 mmol/L
- 2-hour postprandial blood glucose: 5.0 to 10.0 mmol/L (5.0 to 8.0 mmol/L in those whose A1C remains above 7.0%)
- **Diabetes:** A metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action, or both.
- **Glycemic variability:** The degree to which a person's blood glucose fluctuates between high and low levels.
- Hyperglycemia: The presence of excessively high levels of glucose in the blood, which occurs when the body does not have enough insulin or cannot use the insulin it does have to turn glucose into energy. Chronic hyperglycemia in diabetes is associated with microvascular complications (i.e. retinopathy, nephropathy, neuropathy) and macrovascular complications (i.e. hypertension, acute coronary syndrome, stroke, heart failure).
- Hypoglycemia: An abnormally low concentration of glucose in the circulating blood. Hypoglycemia is defined as a blood glucose level <4.0 mmol/L

#### Injection area (anatomical area):

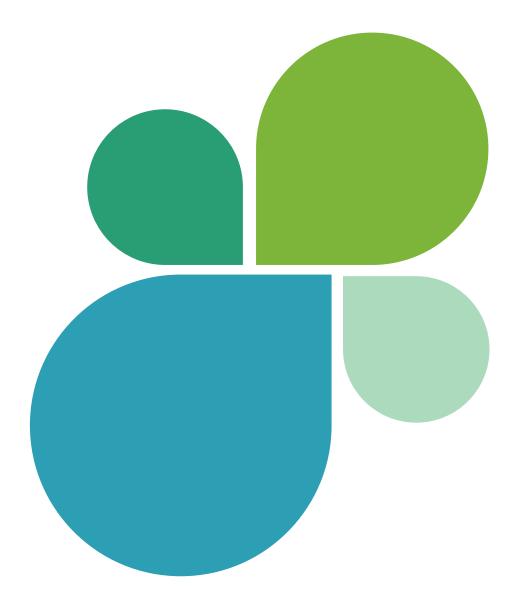
Appropriate Injection areas are as follows: abdomen, thighs, buttocks, back of arm.

Injection site: The point of insertion or injection of medication.

Injection site rotation: A system to ensure that people do not inject medication into the same site each time they administer an injection. Rotating injection sites is crucial for people who administer injectable medications, to prevent lipohypertrophy and to facilitate consistent medication absorption.

- Injection zone: The injection area divided into quadrants (abdomen) or halves (thighs).
- Insulin: A hormone produced in the pancreas that regulates the amount of sugar in the blood by stimulating cells – especially liver and muscle cells – to absorb and metabolize glucose. Insulin also stimulates the conversion of blood glucose into glycogen and fat, which are the body's chief sources of stored carbohydrates.
- Insulin analogues: A tailored form of insulin in which certain amino acids in the insulin molecule have been modified. The analogue acts in the same way as insulin, but with some beneficial differences for people with diabetes.
- Insulin pen: A pen-sized injection device that is used to inject insulin, and is composed of an insulin cartridge (either integrated or bought separately) and a dial to measure the dose.
- **Lipoatrophy:** The loss of subcutaneous fat from one area of the body.

- Lipodystrophy: A medical condition characterized by abnormal or degenerative conditions of the body's adipose tissue.
- Lipohypertrophy: An accumulation of subcutaneous fat tissue at a site where insulin has been injected continuously.
- Needle: A hollow, pointed instrument used to deliver injectable medications into the body. A needle can be used with an insulin syringe to deliver medication from a vial. A pen needle consists of a hollow needle which is embedded in a plastic hub and attaches to the end of an injection pen.
- Skin lift: A manoeuvre used when injecting insulin or other injectable medications to ensure optimal medication uptake. To perform a skin lift correctly, an individual should lift the skin and subcutaneous tissue delicately between the thumb and index finger, leaving the muscle behind.





Optimizing injection technique in diabetes

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