Forum for Injection Technique Malaysia

FIT-MY

Recommendations for Best Practice in Injection Technique

Optimising Diabetes Care

Malaysian Endocrine & Metabolic Society

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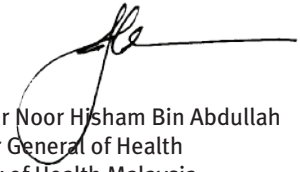
PREFACE

First and foremost, the Ministry of Health would like to acclaim the Malaysian Diabetes Educators Society for their efforts in developing the Injection Technique Guideline. The aim of this guideline is to provide evidence-based injection technique recommendation for healthcare professionals who care for people with diabetes in Malaysia.

Diabetes mellitus is a major public health problem that is approaching epidemic proportions globally. It is one of the strongest predictors for heart disease, stroke and kidney disease. A good glycaemic control is important to prevent these complications and ensure long-term survival in people with diabetes mellitus. Self-management of diabetes requires improved awareness on the importance of lifestyle modifications, self-monitoring of blood glucose and methods of insulin delivery.

The use of insulin therapy is in line with the *Malaysian Clinical Practice Guidelines on the Management of Type 2 Diabetes Mellitus,* where an early insulin therapy is recommended for people with suboptimal glycaemic control either at presentation or when treatment with oral anti-diabetic agents failed. The National Diabetes Registry, which tracks the care and management of diabetes mellitus in primary care clinics, reported an increase of over 80% in insulin use from 2009 to 2012. In tertiary care hospitals, findings from the DiabCare Malaysia cohort also found a similar uptrend in insulin use from 2008 to 2013. Nonetheless, there are still fears and concerns regarding insulin or injectable therapy among healthcare professionals and the public. This Injection Technique Guideline is a timely piece of production. Enlisting the role of diabetes educators and healthcare professionals in this aspect can help in addressing these challenges.

The Ministry of Health commends the Malaysian Diabetes Educators Society for their work and commitment towards developing this useful guideline for the Malaysian diabetes community. This guideline shall serve its purpose in promoting a better standard of diabetes care in the country.



Datuk Dr Noor Hisham Bin Abdullah
Director General of Health
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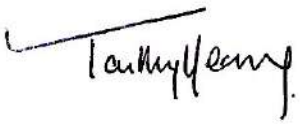
FOREWORD

Diabetes mellitus is a significant contributor to global morbidity and mortality. The most recent statistics by the International Diabetes Federation estimate that in 2015 there are 415 million people living with diabetes mellitus globally. In Malaysia, the reported prevalence of diabetes mellitus has increased significantly from 11.6% in 2006 to 17.5% in 2015.

Insulin and non-insulin therapies have a significant role in the treatment of diabetes especially for people with type 2 diabetes mellitus. Studies have reported its benefits in helping to achieve glycaemic control and reduce the risk of long-term diabetes complications. However, studies have shown concerns and barriers to initiation of treatment, particularly the errors or inaccuracies associated with the injectable therapies across the lifespan of people living with diabetes. Therefore, a proper education on the injection technique is imperative to enhance treatment adherence and promote overall improvement in glycaemic control. The predominant role of healthcare professionals is to provide initial and follow-up education with support to ensure understanding of the importance, rationale and evolving role of injectable therapies in individualised self-treatment regimens.

This Injection Technique Guideline for diabetes educators and healthcare professionals is aimed at standardizing educational practices to enable effective and accurate administration of injectable therapies for people with diabetes mellitus to enhance clinical outcomes. Topics covered include indications for injectable therapies particularly insulin therapy, correct injection techniques, issues related to injectable therapies such as medication storage, safety issues, potential complications, special populations and psychosocial challenges.

As the Chairperson of the Forum for Injection Guideline Malaysia, I would like to express my sincerest gratitude to the Ministry of Health Malaysia and the working committee as well as the external reviewers in this guideline development for their immense support and contribution.



Dr Tan Ming Yeong, RN CDE
Chairperson, Forum for Injection Technique – Malaysia

OBJECTIVE, TARGET POPULATION, TARGET GROUP

OBJECTIVE

To develop an Injection Technique Guideline based on current evidence practice for healthcare professionals (HCPs) who care for people with diabetes in Malaysia.

TARGET POPULATION

This guideline provides the evidence-based injection technique recommendations for people with diabetes who use injectable therapy in their daily management.

TARGET GROUP

This guideline may be used by HCPs who provide diabetes education related to injectable therapy for people with diabetes, including diabetes educators, nurses, assistant medical officers, dietitians, pharmacists and medical practitioners.

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INTRODUCTION

The latest results of the National Health and Morbidity Survey (NHMS) 2015 showed that diabetes prevalence among adults (≥18 years old) was 17.5%, with an estimate of about 3.3 million people living with diabetes in the country. The prevalence of known or presumably treated diabetes was 8.3% or an estimated 1.6 million people. Out of this number, at least 25.1% (400,000 people) were treated with insulin therapy in Malaysia.[1]

In recent years, there is a continued rise in the rates of insulin use among individuals with diabetes in Malaysia, as a result of treatment-specific guidelines along with healthcare provider training. Recent public healthcare statistics have shown that insulin use in the primary care had almost doubled from 11.7% in 2009 to 21.4% in 2012, with further steady increases in the subsequent years.[2] In hospital-based diabetes care, insulin therapy was used increasingly from 23.6% in 1998 to 53.6% in 2008 and subsequently 65% in 2013.[3,4,5]

Other non-insulin injectable agents for diabetes management such as glucagon-like peptide (GLP-1) receptor agonists (GLP-1 RA) have been available in Malaysia for some years, but their accessibility and use remains limited where these agents are mainly prescribed in private healthcare.

References

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SECTION 2

INJECTABLE THERAPIES IN DIABETES

There are several types of injectable therapies used for glycaemic lowering in diabetes. These are insulin, GLP-1 RA and amylin agonists. Amylin agonists are not available in Malaysia.

2.1 Insulin Injection Therapy

Insulin therapy is an integral part of diabetes management in both type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM). In T1DM, insulin therapy is required from the time of diagnosis and continued to be required over the lifetime of an individual. For T1DM, intensive insulin therapy with multiple dose injections to mimic physiological insulin secretion are the standard of care, with some people with T1DM requiring insulin pump therapy where indicated.

In T2DM, insulin therapy is used either during acute illness associated with hyperglycaemia and hyperglycaemic emergencies, perioperatively or during pregnancy and lactation. Long-term insulin therapy in T2DM is indicated following the failure of combination anti-diabetic therapy with oral or non-insulin injectables to maintain optimal glycaemic control.[1] Insulin therapy is usually initiated gradually, progressing from once daily basal insulin regimens to either premixed, basal-plus or basal bolus insulin regimens while the patient is maintained on certain oral anti-diabetic therapies as pancreatic beta cell failure progresses (Refer to Table 1 and 2*).*

2.1.1 Insulin – Classification and Types

Two types of insulin are currently in used in Malaysia, i.e. **human insulin** derived by recombinant technology or **insulin analogues** which are genetically modified human insulin, in which the amino acid sequence have been altered to change the pharmacokinetic profile.

The types of insulin available according to their pharmacokinetic profiles are shown in Table 1.

- **Prandial insulin,** which is rapid or short-acting insulin. It is administered pre-meal because of its short or rapid onset of action in controlling post-prandial glucose excursion.
- **Basal insulin,** which is intermediate or long-acting analogue insulin. It is administered once or twice daily and covers the basal insulin requirements in between meals and overnight.
- **Premixed insulin,** which is biphasic insulin that incorporates both the short or rapid-acting insulin with intermediate-acting insulin/long-acting insulin analogue in a single preparation to cover for both post-prandial glucose excursion as well as basal insulin needs.

Table 1: Classification and Types of Insulin

Insulin preparation	Onset of action	Peak action (hours)	Duration of action (hours)	Timing of insulin administration
Prandial				
Short-acting, regular Actrapid Humulin R Insuman R Insugen R	30 – 60 min	2 – 4	6 – 10	30 min before meal
Rapid analogue Aspart (NovoRapid) Lispro (Humalog) Glulisine (Apidra)	0 – 20 min	1 – 3	3 – 5	5 to 15 min before or immediately after meal
Basal				
Intermediate-acting, NPH Insulatard Humulin N Insuman N Insugen N	1 – 2 hrs	4 – 8 hrs	8 – 12 hrs	Pre-breakfast/ Pre-bed
Long-acting analogue Basalog Determir Degludec	 30 – 60 min 30 – 60 min 30 – 60 min	 Less peak Less peak Less peak	 16 – 24 16 – 24 16 – 24	 Same time everyday Flexible once-daily injection (maximum interval up to 40 hrs)
Glargine 100 U/ml (Lantus)	30 – 60 min	Less peak	16 – 24	Same time everyday
Glargine 300 U/ml (Toujeo)	30 – 60 min	Peakless	24 – 36	Same time daily, ±3 hrs flexible dose window
Premixed insulins				
Mixtard 30 Humulin 30/70 Insugen 30/70	30 min 30 min 30 min	Dual Dual Dual	18 – 23 16 – 18 18 – 23	30 min before meal
NovoMix 30 Humalog mix 25/75 Humalog mix 50/50	10 – 20 min 15 min 15 min	1 – 4 0.5 – 2.5 0.5 – 2.5	16 – 20 16 – 18 16 – 18	5 – 15 min before meal
IdegAsp 30 Insuman Comb	10 – 20 min 30 min	1 – 4 Dual	24 – 40 12 – 19	5 – 15 min before meal

(Adapted from Clinical Practice Guideline: Management of Type 2 Diabetes 2015)

2.1.2 Insulin Regimens

- An ideal insulin regimen should mimic the physiological insulin response to meals and endogenous hepatic glucose production. The choice of insulin regimen should be individualised, based on the individual's glycaemic profile, dietary pattern and lifestyle (Refer to Table 2).

Table 2: Insulin Regimens

No. of injections per day	Insulin regimen	Type of insulin and timing
1	**BASAL**	Intermediate-acting (NPH) insulin pre-bed
	BASAL	Long-acting anologue once daily
	PREMIXED OD	Premixed analogue pre-dinner
2	**BASAL**	Intermediate-acting (NPH) pre-brekfast and pre-dinner
	PREMIXED BD	Prandial insulin pre-breakfast and pre-dinner
	BASAL-PLUS 1	Basal insulin once daily + 1 prandial insulin
3	**BASAL-PLUS 2**	Basal insulin once daily + 2 prandial insulin
	PRANDIAL	Prandial insulin pre-breakfast, pre-lunch and pre-dinner
	PREMIXED TDS	Premixed pre-breakfast, pre-lunch and pre-dinner
	PREMIXED-PLUS 1	Premixed insulin pre-breakfast and pre-dinner + 1 prandial insulin pre-lunch
	PREMIXED-PLUS 2	Prandial insulin pre-breakfast and pre-lunch + 1 premixed insulin pre-dinner
4	**BASAL-BOLUS 1**	Basal insulin once daily + prandial insulin pre-breakfast, pre-lunch and pre-dinner
5	**BASAL-BOLUS 2**	Intermediate-acting (NPH) insulin pre-breakfast and pre-dinner + prandial insulin pre-breakfast, pre-lunch and pre-dinner

OD: once a day; BD: two times a day; TDS: three times a day
(Adapted from Clinical Practice Guideline: Management of Type 2 Diabetes 2015)

2.1.3 Insulin therapy — Initiation, Optimisation and Intensification

- Insulin initiation can be done safely in an outpatient setting. At initiation, the insulin dose prescribed is usually low to avoid hypoglycaemia. All people with diabetes prescribed with insulin therapy should be advised to perform self-monitoring of blood glucose (SMBG) and empowered to self-adjust their insulin doses.

- Insulin dose optimisation requires gradual, safe and prompt titration of insulin dose according to SMBG. The insulin dose should be adjusted at least weekly within the first 3 months of starting insulin to achieve optimal glycaemic targets. Adjustment of the insulin dose should be an interactive process between HCPs and the people with diabetes (including their caregivers) and can be done at diabetic resource centres, or via telephone calls or text messages.

- Often, the initiated insulin regimens may need modification if glycaemic control remains suboptimal despite dose adjustment. In such scenario, intensification of insulin therapy is then required by switching to a more intensive insulin regimens (usually by increasing the number of injections) to achieve better glycaemic control. Insulin pump therapy may be considered in people with diabetes who are still not controlled despite basal-bolus regimen at optimal doses (Refer to Figure 1).

- To ensure successful insulin intensification, the following key elements of ideal care are important: continuous patient education, a dedicated diabetes healthcare team (consists of diabetes educator, physician, pharmacist and dietitian), SMBG, frequent contact with healthcare team and a peer support group.

Notes:
- Metformin should be continued while on insulin therapy unless contraindicated or intolerant.
- Sulphonylureas/meglitinides should be withdrawn once prandial insulin is used regularly with meals.
- Insulin dose should be optimised prior to switching/intensifying regimens.

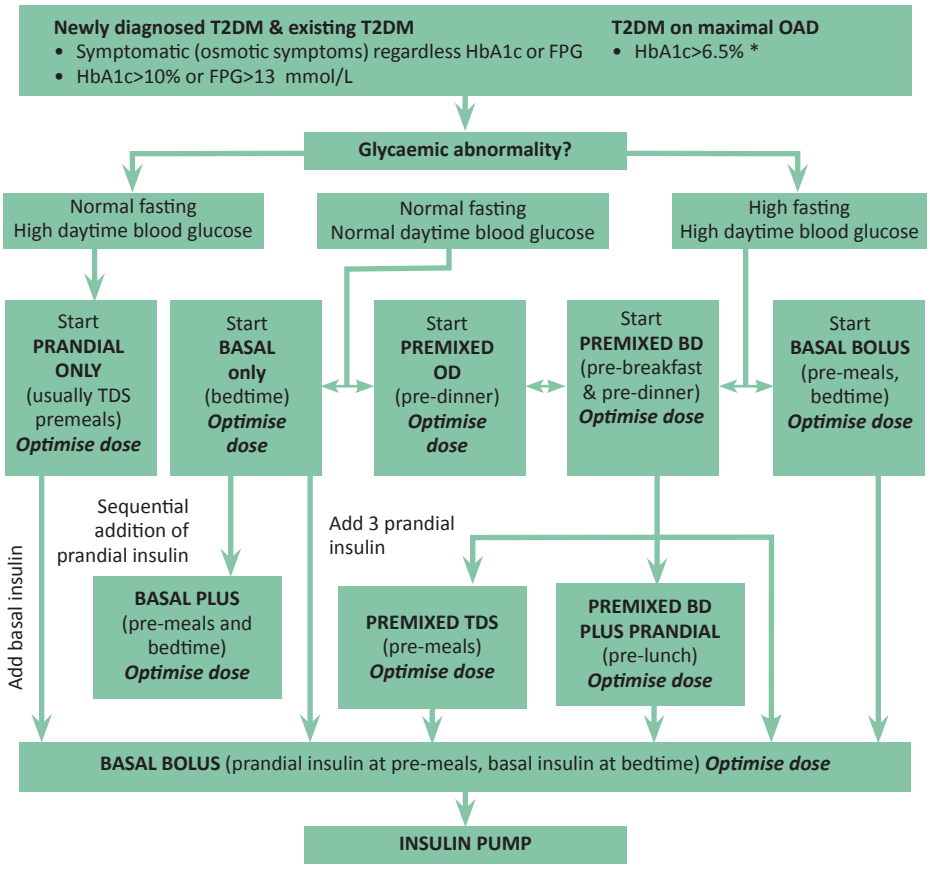
2.2 Insulin Pump Therapy or Continuous Subcutaneous Insulin Infusion (CSII)

- Insulin pump therapy is an alternative method of administering insulin subcutaneously by providing continuous delivery of rapid acting insulin via an infusion (tubing) set and a battery operated hand-held pump device. The infusion set is connected to the reservoir, which is filled with insulin and stored inside the pump device. The other end of the infusion set is connected to a needle called the cannula which is placed subcutaneously and secured by adhesive skin covering. The pump is programmed to deliver insulin at variable rates to mimic basal (background insulin for overnight and between meals) and bolus insulin (for meals and correction doses).

SECTION 2

- Insulin pump therapy is usually prescribed for people with T1DM who have frequent hypoglycaemia or hypoglycaemia unawareness and have poor glycaemic control. Recently, there are increasing numbers of insulin-treated people with T2DM who experience improved glycaemic control with insulin pump therapy. Selecting the suitable candidate for pump therapy is most important, as successful outcome with this form of insulin therapy requires adequate understanding of the disease, close blood glucose monitoring and the use of advanced carbohydrate counting.

Figure 1: Algorithm of Insulin Initiation, Optimisation and Intensification



*HbA1c threshold to initiate insulin need to be individualised according to an individual characteristic and comorbidity
(Adapted from Clinical Practice Guideline: Management of Type 2 Diabetes Mellitus 2015)

- Complications that may occur are infusion site reactions, infusion/tubing set problems and pump malfunction that may lead to glucose variability. Infusion site reactions include inflammation, infection, pain, lipohypertrophy, nodules and swelling which can potentially affect insulin flow and absorption. Infusion set problems include occlusion or flow interruption, disconnection and leakage. Pump malfunction includes failure of insulin delivery, keypad and battery problems. Silent occlusion is a situation of pump malfunction where insulin flow is interrupted for indeterminate length of time and for unknown reasons, and without an alarm trigger. This can lead to glycaemic variability.

2.2.1 Infusion Sites

- The preferred infusion site is at the abdomen, with alternative sites at the upper arms and thighs.
- Every new site should be at least 2.5 cm away from the previous site.
- People with diabetes should be taught to rotate infusion sites along the same principles of injection sites rotation.
- People with diabetes should have their infusions sites checked frequently for lipohypertrophy and nodules by healthcare providers.
- People with diabetes who develop hypersensitivity reaction to adhesives may need alternative options of tapes or skin barriers.

2.2.2 Insertion and Infusion Sets

- Plastic cannula sets are generally preferred. However, some people with diabetes may experience frequent kinking or hypersensitivity reaction.
- Steel needle sets are recommended in pregnancy or for people with diabetes with hypersensitivity reaction to plastic cannulae or who experience frequent kinks in plastic cannulae.
- The smallest diameter needle/cannula should be used to reduce pain.
- Shorter needles will prevent intramuscular infusions.
- A mechanical insertion device may be used by people with diabetes who experience difficulty inserting their infusion set manually.
- Any person with diabetes who experiences unexplained glucose variability or frequent hypoglycaemia should be evaluated for the presence of silent occlusion.

2.2.3 Angle of Insertion

- The needle or cannula should be inserted either at a 90° angle or a 30°–45° angle.
- The insertion angle of 90° is widely used.
- 30°–45° angled insertion sets may be considered in people with diabetes who experience infusion site complications with 90° insertion set.

- People with diabetes who are lean, muscular and active may benefit from 30°–45° angled insertion, as there is less risk of the cannula and tubing being dislodged.

2.2.4 Optimal Frequency for Changing Infusion Sets

- Infusion set and injection site problems occur more frequently after the 3rd day of infusion and insertion set use.
- Potency of insulin, and consequently, glucose control are diminished with a deterioration in pump performance, especially if infusion sets are used for longer periods at a time.
- Insulin pump insertion and infusion sets should only be used for 48–72 hours to avoid adverse events and potential metabolic deterioration.

2.3 GLP-1 RA Therapy

- GLP-1 RAs are non-insulin injectable therapies that are used in combination with oral anti-diabetic (OAD) agents and occasionally with insulin. These agents promote post-prandial glucose lowering by increasing incretin-mediated pancreatic insulin secretion, inhibiting glucagon secretion as well as delaying gastric emptying. There is an additional central effect on stimulating satiety, which results in reduced food intake and promotes weight loss.[1]

- There are currently three approved GLP-1 RA preparations available in Malaysia which are:
  - Exenatide Immediate Release (Byetta) – twice-daily injections
  - Liraglutide (Victoza) – once-daily injections
  - Exenatide extended release (Bydureon) – once-weekly injections

- GLP-1 RAs are available in specific prefilled pen devices and are administrated subcutaneously, just like insulin.

Reference

1. Malaysia Ministry of Health. Clinical Practice Guidelines on the Management of Type 2 Diabetes 5th edition; 2015.

THERAPEUTIC EDUCATION

Most people with diabetes express fear and concern when told the necessity to commence insulin or injectable treatment. A study done in Malaysia reported that 51% of people with T2DM were reluctant to commence insulin therapy when needed.[1] A systematic review reported that barriers to insulin initiation were multifactorial that included patient, HCPs and system-related barriers. The common barriers for people with diabetes were fear of needles and pain, side effects like hypoglycaemia and weight gain, lifelong dependency, inconvenience, personal failure, low self-efficacy and the myth that insulin therapy causes organ damage (e.g. kidney failure). [2,3,4]

3.1 Initial Education

- At the initiation of insulin or injectable therapy, people with diabetes and their caregivers should be given time to explore their anxiety, perception, beliefs and barriers to injectable therapy. HCPs should also ask about fear of needle-related pain early and explore the possible strategies to overcome this pain perception through the use of pen devices, smaller needles, injection pot and injectable tool. Younger children may be helped by distraction, play therapy or Cognitive Behavioural Therapy. [5]

- Starting insulin or injectable therapy should be a shared decision by people with diabetes and their caregivers. HCPs can use the tool 'Should I start insulin?' which is available in 4 local languages: English, Bahasa Malaysia, Mandarin and Tamil that can be accessed via http://dmit.um.edu.my/?modul=DMIT_PDA&pilihan=Book.[6]

- The role of HCPs is to provide education and support as well as ensuring that the individuals understand the indications for commencing insulin or injectable therapy. For people with T2DM, the possible need for insulin and injectable therapy should be addressed early, preferably at the initial diagnosis of the condition and at subsequent follow-up educations. The individuals should be reassured that starting insulin or injectable therapy is not an indicator of their personal failure in controlling their condition. On the contrary, it is an indicator of the natural progression of diabetes and that oral therapy may not be adequate to achieve good glycaemic control in preventing and delaying chronic complications. Finding the right combination of treatment to achieve good glycaemic control usually include insulin therapy.

- Other educational topics at initial insulin or injectable therapy include:
  - Indication for insulin or injectable therapy
  - How insulin or injectable therapy works

- Prescribed insulin or injectable regimen
- Choice and management of devices used including blood glucose monitoring
- Individualised target
- Correct injection techniques
- Care and self-examination of injection sties
- Possible injection complications and prevention
- Psychosocial issues related to insulin or injectable therapy

- The above instructions should be given in verbal and written form to both individuals with diabetes and their caregivers at initiation of insulin and injectable therapy.

3.2 Follow-up Education

- Adherence and potential barriers to insulin and injectable therapy as well as solutions to overcome them should be addressed on each follow-up visits[7] (Refer to Table 3).

Table 3: Potential Barriers and Suggested Solution of Insulin and Injectable Therapy

Barriers	Suggested solutions
Poor understanding of diabetes, its complications, and the role of insulin	• Provide comprehensive education • Explain the reduction of risk for complications with better glycaemic control • Explain the role of insulin in glucose regulation
Seeing insulin or non-insulin therapy as treatment failure	• Explain that insulin production decreases with ageing; most people with diabetes will eventually need insulin to maintain glucose control
Fear of needle	• Provide reassurance that today's needles are much smaller and are coated with silicon, allowing them to slide in more easily. In fact, most people say that it is almost painless and less uncomfortable than a finger prick to monitor blood glucose level • Use trial injection
Fear of side effects of insulin (i.e. hypoglycaemia and weight gain)	• Provide education on how to prevent, recognise and treat hypoglycaemia • Refer to a dietitian before starting insulin
Lifelong medications/ change in lifestyle	• Provide reassurance that many people with diabetes experience higher energy level and feel better when they achieve good glucose control after starting insulin

(Adapted from Diabetes Education Manual 2016)

- The follow-up education should be reviewed regularly and recorded in the care plan.
- By facilitating the acceptance of injectable treatment, this can enhance the adherence to therapy and quality of life.

Key Points

1. At initiation of insulin or injectable therapy, people with diabetes and their caregivers should be given time to explore their anxiety, concern and barriers to injectable therapy.
2. The decision to commence insulin or injectable therapy should be a shared decision between HCPs and individuals with diabetes (and their caregivers)
3. The roles of HCPs are to provide initial and supportive follow-up education to ensure people's understanding of the indications for insulin or injectable therapy and that they practice the recommended injection technique.

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7. Malaysia Ministry of Health. Diabetes Education Manual 1st edition; 2016.

SECTION 4

INJECTION TECHNIQUE

For people with diabetes, injection therapy can be insulin or non-insulin therapy such as GLP-1 RA. Proper injection technique is vital to avoid intradermal or intramuscular injections and ensures the appropriate delivery of insulin to the subcutaneous tissue.

4.1 Insulin Injection

4.1.1 Insulin Appearence

- Both rapid/short-acting insulin and long-acting analogue appear as a clear solution. Premixed insulin and intermediate-acting insulin appear as a cloudy solution.

4.1.2 Insulin Formulation

- Insulin is available in different formulations such as pen-fills and vials. For pen devices, there are disposable and prefilled pens (usually for insulin analogues).
- Currently, all the insulin in use in Malaysia is U-100 in strength or concentration, i.e. consisting of 100 units of insulin per milliliter of solution. Other formulations available overseas include U-300 (insulin glargine U-300, brand name Toujeo) and U-500 (Humulin–R U-500) strength.

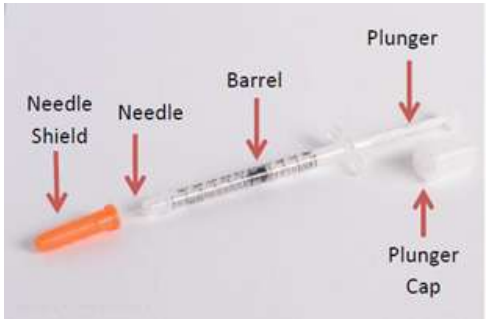
4.1.3 Insulin Delivery Devices

- There are various ways to administer insulin, including syringes, insulin pens and insulin pumps. Insulin pens are the primary injecting device used by people with diabetes in Malaysia. However, syringes are still often been used in healthcare settings.

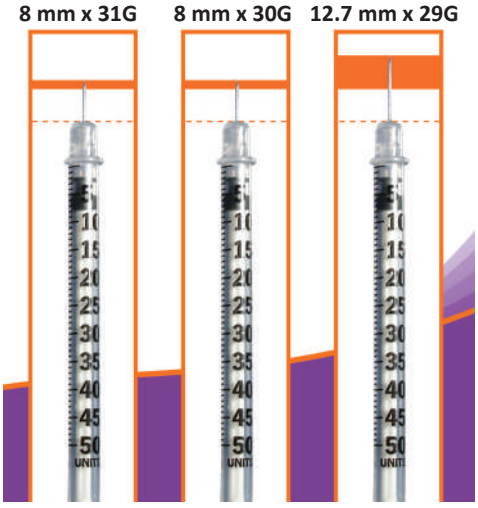
4.1.3.1 Syringe and Vial

- Syringes are often used in healthcare settings in Malaysia. Before injecting, choose the right size of syringe (volume U-100 is widely used in our local healthcare setting) and the length of the needle (Refer to Picture 1 and 2). A 6 mm and 8 mm needle is recommended over a 12.7 mm needle due to a higher risk of intramuscular injection.[9]

Picture 1: Component of an Insulin Syringe



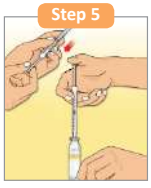
Picture 2: Syringe Size and Needle Length



SECTION 4

- **Administration using syringes and vials** — Before injecting, the insulin vial should be taken out from the refrigerator 30 minutes prior to injection to ensure that the insulin is at room temperature. Table 4 shows the steps while injecting insulin using vial and syringe.

Table 4: Steps for Injecting Insulin Using Syringe and Vial

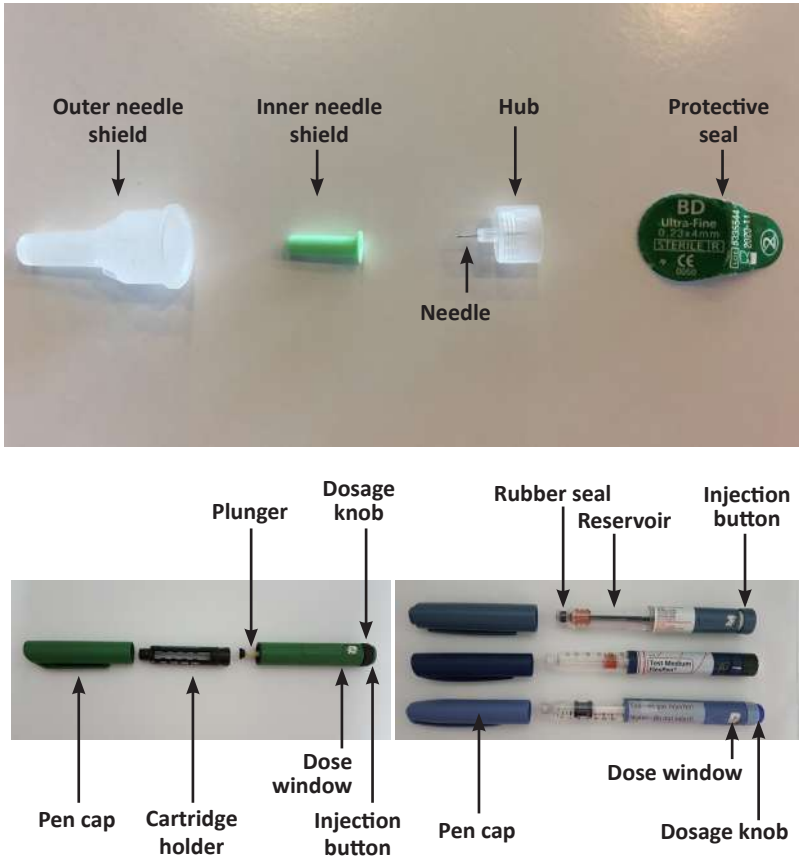
	• Wash your hands before handling syringe and vial.
	• Warm the insulin by rolling the insulin vial between your hands. • When injecting cloudy insulin (e.g. NPH and premixed insulin), the vial need to be gently rolled 10 times and inverted 10 times until it becomes evenly milky white. • Do not shake the vial.[1,3,10]
	• Wipe the top of the insulin bottle/vial with an alcohol swab.
	• Remove the cap from the plunger and the shield from the needle. • Pull the plunger back to draw air into the syringe equal to the dose of insulin to be injected.
	• Insert the needle through the rubber stopper of the insulin vial at a 90° angle. • Press down the plunger to inject the air into the vial.

	• Turn the vial upside down. • Pull the plunger back to draw the desired dose into the syringe. • To remove air bubbles (if present) in the syringe, draw up several more units of insulin, tap the barrel to move them to the top then expel them by pushing the plunger.
	• Remove the needle straight out of the vial.
	• Clean the site of injection with an alcohol swab. Wait till alcohol has completely dry before injecting.[11,12,13,14] • Gently pinch up the skin using your thumb and index finger.
	• Inject the insulin at 45° angle for needle length ≥8 mm.[15] • Depress the plunger in completely. • Remove the syringe quickly and then release the pinch.
	• Dispose the syringe according to local regulation (Please refer to Section 7 Safety Issues). • Syringes should only be used once.[5,16]

4.1.3.2 Pen/Prefilled Pen

- Insulin pen devices or injectors are a common and discreet way of administering insulin. The pen has three components: a built-in dial that allows the individual with diabetes to determine the amount of insulin to be injected, a short needle at one end and a plunger at the other end. Some pens are disposable and do not need to be assembled before use, while others have a replaceable insulin cartridge on penfill that needs to be inserted (Refer to Picture 3).

Picture 3: Components of Pen Devices and Insulin Needle



- **Administration using pen devices** — An insulin pen offers the benefits of accuracy, convenience and confidence to people with diabetes. Table 5 shows the steps on how to use insulin pen devices safely and easily.

Table 5: Step-by-step of Using Insulin Pen Devices

Step 1 	• Wash your hands before handling insulin pen devices. • Make sure you have a clean site and clean hands.
Step 2a  Step 2b  Step 2c 	• Cloudy insulin (e.g. NPH and premixed insulin) must be resuspended prior to each injection to ensure the suspension has a consistently milky white appearance (Picture 4).[1,2,3,4] a. Gently roll in between your palms for 10 times (for cold insulin only). b Tip up and down for 10 cycles. c. Visually check for milky white appearance. ▪ Vigorous shaking should be avoided since this produces bubbles which reduce dose accuracy. ▪ Inadequate resuspension of cloudy insulin (e.g. NPH and premixed insulin) before pen injection may lead to varying concentration of medication dosage that can cause unpredictable clinical responses. **Picture 4: Suspension of NPH Insulin Before and After 10 Cycles of Electronic Tipping**  Before (after 24 hours sedimentation) — After 7 cycles — After 10 cycles
Step 3 	• Place a new needle onto the pen device. • Using a new needle each time may reduce the risk of needle breakage in the skin, clogging of the needle, inaccurate dosing and complications (e.g. lipohypertrophy, abscess).[5,6]

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	• Remove the outer and inner cap. • Discard the inner cap and keep the outer cap.
	• Prime insulin pen device with the needle pointing upwards. • Observe at least a drop of insulin at the needle tip before each injection.
	• Dial the desired dose.
	• Insert pen needle into the skin at 90°, push down the dose button completely.
	• Count to 10 slowly before withdrawing the needle from the skin. • Counting past 10 may be necessary for higher insulin doses.[7] • This is to ensure full dose delivery and prevent insulin leakage.
	• Recap the used pen needle using the outer cap. • Remove pen needle and dispose it safely. • Used pen needle should not be left attached to the pen. This allows the entry of air and other contaminants into the cartridge, or leakage of insulin from the cartridge, which can affect subsequent dose accuracy.[8]

4.1.3.3 Insulin Pump

- Insulin pump therapy is an alternative method of administering insulin subcutaneously by providing continuous delivery of rapid-acting insulin via an infusion (tubing) set and a battery operated hand-held pump device. The infusion set is connected to a reservoir that is filled with insulin and stored inside the pump device. The other end of the infusion set is connected to a needle called the cannula which is placed subcutaneously and secured by adhesive skin covering (Refer to Picture 5). The pump is programmed to deliver insulin at variable rates to mimic basal (background insulin for overnight and between meals) and bolus insulin (for meals and correction doses).

Picture 5: Components of an Insulin Pump

4.2 Non-insulin Injectable Therapy

- Non-insulin injectable therapies such as GLP-1 RA are also administered with a prefilled pen device or injector, which is usually disposable after complete use (Refer to Appendix).

4.3 Needle Length

The choice of needle length should be appropriate for adults, adolescents and children to ensure the that insulin and non-insulin injectable (e.g. GLP-1 RA) are administered into the subcutaneous layer and avoiding the intradermal and intramuscular spaces.[17]

Ultrasound and other research technologies have shown that the subcutaneous fat layer may vary within a particular anatomical area, e.g. the abdomen.[18] The use of a 4 mm needle minimizes the potential for intramuscular injection and allows individuals to use a larger area for injection, i.e. a postcard-size area as opposed to a postage stamp-sized area.[19]

4.3.1 Adults

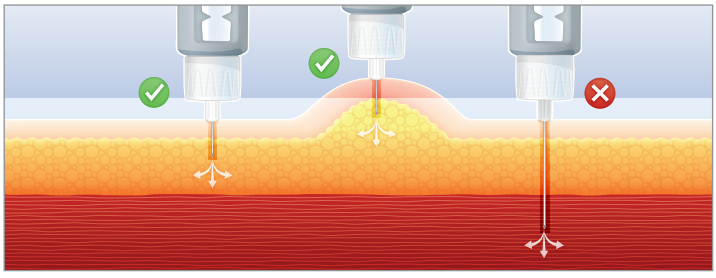
- The needle lengths available in Malaysia are 4, 5, 6 and 8 mm with different gauge (G) as shown in Table 6.

Table 6: Needle Lengths Available in Malaysia

Needle	4 mm	5 mm	6 mm	8 mm
BD	32G	31G	-	31G
Novofine	32G	-	31G, 32G	-
Ypsomed	32G	-	31G	31G
Terumo	32.5G	-	-	-

- Shorter needles (4, 5, 6 mm) provide equal efficacy and safety when compared with the longer needle (8 mm), even in obese individuals.[21]
- 4, 5 and 6 mm needles are suitable for all people with diabetes regardless of body mass index (BMI).[22,23]
- Injections with shorter length needles (4, 5, 6 mm) should be administered in adults at 90° to the skin surface.[22]
- The safest pen needle for all individuals with diabetes is 4 mm in length. The 4 mm needle inserted at 90° to the skin surface is long enough to penetrate the skin and enter the subcutaneous tissue, with little risk of intramuscular injection.[24,25]
- For extremely thin adults with diabetes (BMI <19), the proper injection technique is to use the 4 mm needle accompanied with lifting of skin fold when injecting to avoid the intramuscular injection.[22,23,24]
- Shorter and finer-gauge needles help to reduce pain. The 5-bevel needle tip has less penetration force in a skin hence provides more comfort and easier to insert.[26, 27]
- 8 mm needles should be discouraged to prevent the risk of intramuscular injection (Refer to Diagram 1).

Diagram 1 : Needle Length and Risk of Intramuscular Injection



- Individuals who have to continue using ≥8 mm needles should always lift a skin fold and/or inject at 45° in order to avoid intramuscular injections.[27]

4.3.2 Children and Adolescents

- Refer to Section 9 Special Populations.

4.4 Lifted Skin Folds

- The lifted skin fold should not be squeezed too tightly until it causes skin blanching or pain.
- The optimal sequence should be:
  - Make a lifted skin fold. Only the thumb, index finger and middle finger should be used.
  - Insert needle into skin at 90°.
  - Administer the therapy.
  - Leave the needle in the skin for at least 10 seconds after the dose button is fully depressed.
  - Withdraw needle from the skin.
  - Release lifted skin fold.
  - Dispose of used needle safely.
- A proper skin-fold technique should take up the skin and subcutaneous tissue only, leaving the muscle layer behind (Refer to Diagram 2).

Diagram 2: Correct and Incorrect Technique of Performing Skin Fold

4.5 Reused Needle

- Pen needles and syringes should only be used once. Picture 6 shows how reusing needles damages the tip of the needle.[19,20,28]
- There is a probable association between reused needle and the presence of lipohypertrophy, although a direct causal relationship has not been proven.
- Reused needles and syringes may cause pain, bleeding and bruising at injection sites.

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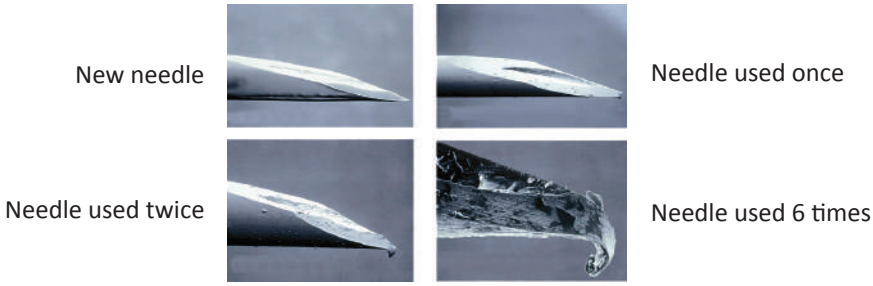
- Reused needles may cause the insulin in the barrel to crystalise and block its flow during the next injection.
- Reusing pen needles and syringes is not an optimal injection practice. People with diabetes should be discouraged from doing so.
- Needles should be disposed immediately after use. It should not be left attached to the pen. This allows the entry of air and other contaminants into the cartridge, or leakage of insulin from the cartridge, which can affect subsequent dose accuracy.[8]

Picture 6: Comparing the Tips of New and Reused Needles



Key Points

1. Shorter length pen needles (4, 5, 6 mm) are suitable for all people with diabetes regardless of BMI and provide equal efficacy and safety.
2. 4 mm insulin pen needles inserted at 90° to the skin surface is long enough to penetrate the skin and enter the subcutaneous tissue with little risk of intramuscular injection.
3. Pen needles and syringes should only be used only.
4. Cloudy insulin (e.g. NPH and premixed insulin) must be resuspended prior to each injection to ensure the suspension has a consistently milky white appearance.
5. Insulin Injection using syringe in healthcare setting should be administered at 45° angle for needle length ≥8 mm.

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SECTION 5

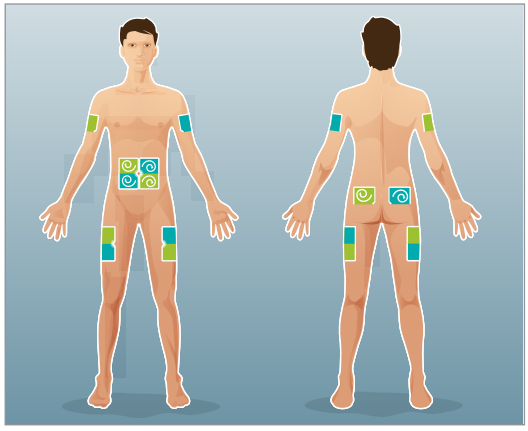
INJECTION SITES

Besides proper injection technique, education should also include the importance of site rotation and inspection of injection sites for better glycaemic control. For consistent absorption, insulin and non-insulin injectable agents should be injected into the subcutaneous layer in the abdomen, buttocks and thighs if self-administered, or arms and buttocks if given by caregivers.

5.1 Injection Sites Selection

Diagram 3 shows the current recommendation on insulin injection sites.

Diagram 3: Recommended Injection Sites



For ease of self-injection, the **abdomen** and **thighs** are the two main recommended injection sites for adults.[20]

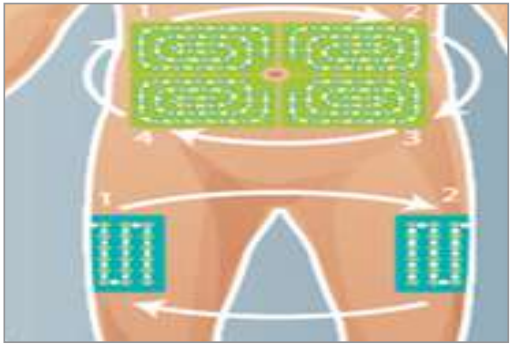
- **Abdomen** – Abdominal sites are within the following boundaries: ~1 cm above the symphysis pubis, ~1 cm below the lowest rib, ~1 cm away from the umbilicus and laterally at the flanks.[16]
- **Thighs** – use the upper 3rd anterolateral aspect.
- ***Buttocks and flanks** – Posterolateral aspect of both upper buttocks and flanks.
- ***Arm** – mid 3rd posterior aspect of upper arm.

*These sites are not the preferred site for self-injection in view of the difficulty in accessing the correct zone, difficulty in injecting at 90° and lessened thickness of subcutaneous fat, all of which are potential risk factors for intramuscular injection. Caregivers' assistance are required for administering injection to these sites.[16,20,21]

5.2 Rotation of Injection Sites

- Individuals with diabetes should be educated on the importance of injection site rotation to prevent lipohypertrophy and ensure the consistency of insulin absorption.[1,2,3,4]
- The pattern of site rotation that has been shown to be effective involves dividing the injection site into quadrants (or halves when using thighs and buttocks). Use one quadrant per week and rotate in a consistent direction (e.g. clockwise).[4]
- Injection sites rotation within any quadrant or half should be done systematically with spacing of at least 1 cm apart from each injection in order to prevent repeat tissue trauma as shown in Diagram 4 below.[4]

Diagram 4: Systematic Rotation Within the Recommended Injection Sites



5.3 Insulin Absorption

- Optimal absorption of insulin depends on injection into subcutaneous tissue. Absorption rate can be affected by various factors such as type of insulin, insulin storage, skin temperature, site of injection and exercising.

5.3.1 Factors Affecting Absorption Rates

- **Type of insulin**
  Insulin type affects the rate of absorption from the injection site. Rapid and short-acting insulin are absorbed faster than intermediate- and long-acting insulin.

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- **Site of insulin injection**
  Insulin absorption is fastest and most consistent when injected on the abdomen, followed by moderate absorption rate in the upper arm and lateral thigh. The slowest rate of absorption is at the buttock area. However, insulin absorption also differs based on the type of insulin, as shown in Table 7.

Table 7: Injection Site and Absorption Rate

Prandial insulin	Basal insulin	Premixed insulin
Short-acting, regular: Abdomen preferred due to fastest absorption rate.[7,8,9]	**Intermediate-acting, NPH**: Thigh and buttocks preferred due to slowest absorption rate.[19]	**Human or analogue, morning dose:** Abdomen preferred to increase speed of absorption to cover post-breakfast glycaemic excursion.[11]
Rapid analogue: May be given at any of the recommended sites of injection; absorption rates do not appear to be site specific.[12,13]	**Long-acting analogue:** May be given at any of the recommended sites of injection; absorption rates do not appear to be site specific.[12,13]	**Human or analogue, evening dose:** Preferred in the thigh or buttock for slower absorption and to lower the risk of nocturnal hypoglycaemia for high-risk individuals.[10]

- **Others Factors:**
  - Rotation of injection sites within the selected area is crucial to ensure optimal and consistent insulin absorption.
  - Intramuscular injection may accelerate the absorption rate of insulin.[14,15,16]
  - Massaging the site before or after injection may speed up the absorption. Hence, it is not recommended.[17,18]
  - Higher skin temperature (e.g. sauna or hot bath) may increase the absorption rate of insulin.[6]
  - Injecting into an exercising limb may increase the absorption of insulin which may fasten blood glucose-lowering effect.[5,6]

SECTION 5

Key Points

1. For ease of self-injection, abdomen and thighs are the two main recommended injection sites for adults.
2. Injection sites showing signs of lipohypertrophy, inflammation, oedema, ulceration or infection should be avoided.
3. Injection site rotation should be done systematically (using one quadrant per week and rotate in a consistent direction with at least 1 cm apart).
4. The absorption of insulin differs based on the type of insulin, site of insulin injection, skin temperature and exercising.

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SECTION 6

MEDICATION STORAGE

Proper storage of insulin and non-insulin injectable agents is important to ensure the potency and effectiveness of the medication.

6.1 Injection Storage

- All injectable medications have expiry dates printed on them. The expiry date indicates the date before which the unopened vial, pen or cartridge should be used.
- Unopened injectable medications should be stored at refrigeration temperature between 2°C–8°C. (Check the manufacturer's storage instructions as there may be possible differences from one manufacturer to the other).
- Once insulin is opened, it should not be used for more than 28 days, except for insulin determir which may be used for up to 42 days (Follow the manufacturer's recommendation).
- Write the opening date on the injectable medications to keep track of the date (Recommended practice for institution or hospital).
- In-use insulin pen can be stored at room temperature of <30°C. However if the room temperature is >30°C, in-use insulin pen should be stored in the refrigerator. It should be taken out and kept at room temperature for at least 30 minutes before use.
- Insulin or non-insulin injectable medications should never be frozen or exposed to extreme heat (>30°C) for prolonged periods; this will affect its potency and action. Avoid extreme temperatures such as direct sunlight, kitchen, closed cars, top of a radiator or a television.[1]
- Keep the caps on insulin pens to protect the insulin from light.
- Never leave the pen needle attached to the injectable pen as varying temperatures may cause leakage from the pen or possible air entry into pen hence affecting dosage delivery.[32]
- Injectable medications should never be used after the product expiry date.
- Injectable medications should be kept out of the reach of children.

6.2 Injection Storage During Travel

6.2.1 Travel: On Land

- Insulin should be stored in a proper container.
- Insulin should never be kept in the glove compartment of a car, or left in a locked car.[3]

6.2.2 Travel: Air

- Insulin should be stored in a proper container in personal bag or hand luggage.
- Insulin should not be placed in the baggage hold of the plane due to the risk of exposure to extreme temperatures.[3]
- Carry an extra insulin pen or vial for any unforeseen circumstances that may occur.[4]

Key Points

1. Follow the manufacturer's recommendation for storage of insulin and non-insulin injectable.
2. Always store unopened injectable medication at refrigeration temperature between 2°C–8°C.
3. In-use insulin can be stored at room temperature <30°C.
4. Avoid exposing insulin and other injectable medications to extreme temperatures of either too cold or too hot.
5. Injectable medications should never be used past the product expiry date.

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SECTION 7

SAFETY ISSUES

Insulin and other injectable therapy require people with diabetes to handle needle pen or insulin syringes to administer the medication effectively. Thus, it is important to educate individuals with diabetes and caregivers on safety issues pertaining to handling of injection materials and sharp items properly.

7.1 Safety

- Sharp devices represent a risk for the transmission of blood-borne pathogens to the user in the event of a needle stick injury (NSI) or blood exposure.
- Any healthcare setting which uses injectable pens should follow a strict one-person/one-pen policy.[1]
- All people at risk must receive appropriate education and training on ways to minimize risk, including the importance of following optimal injection or lancing techniques as well as using the available safety engineered devices and Personal Protective Equipment.

7.2 Disposal of Injection Material/Sharps

- All healthcare professionals, individuals with diabetes and caregivers should be aware of proper disposal of sharps and the consequences of inappropriate disposal (e.g. NSI).
- Proper disposal technique should be demonstrated at initiation of injection therapy and reinforced at subsequent visits.
- Needle recapping should not be done for insulin syringes.
- To discard pen needles, recap the outer needle cap using the scoop technique as shown in Picture 7 followed by careful removal of the pen needle and disposal into a sharp bin or a puncture proof container (for home user).

Picture 7: Scooping Technique of Outer Needle Cap

- Sharp materials should never be disposed into public trash bins.
- Use a sharp container or a puncture proof/metal container with lid to store used pen needles. Seal the container properly and label as "SHARP" before disposal. Keep the container out of the reach of children.
- Empty pen devices can be disposed in normal household refuse after the needle is removed.

7.3 NSI/Blood-borne Infection Risk

- To minimize the risk of NSI through a skin fold, the use of shorter needles (e.g. 4 and 5 mm pen needles, 6 mm insulin syringe) without lifting a skin fold upon injecting is recommended.
- If a lifted skin fold is used, do ensure that the finger and thumb making the skin fold are approximately 1 inch (25 mm) apart and the needle should be inserted into the centre of the fold thus minimizing the risk of through-skin fold NSI (Refer to Section 4 Lifted Skin Fold).
- HCPs and caregivers should use Personal Protective Equipment (e.g. glove) when administering injectable therapies or monitoring blood glucose for people with diabetes known to be seropositive for Human immunodeficiency virus (HIV), Hepatitis B virus (HBV) and Hepatitis C virus (HCV).

7.4 Institutional Practice

- The safety of individual with diabetes and HCPs in medical institutions and long-term care facilities is a primary consideration regarding injection technique.
- NSI are frequent yet largely preventable among HCPs. Consideration must also be given to the safe disposal of all injection and infusion devices to prevent injury to healthcare workers.
- Cross-contamination among people with diabetes is also preventable by the appropriate use and disposal of injection or infusion devices. Institutions are encouraged to develop a 'safety first culture' through staff education and increased awareness of best practice.
- Procedures on what to do in the event of a NSI must be clearly communicated. Formal protocols with named clinical care contacts must be available in all areas where sharps are used.[2]

SECTION 7

Key Points

1. Sharps items should be disposed in a proper way to prevent NSI and the transmission of blood-borne pathogens to third party.
2. Any healthcare setting which uses injectable pens should follow one-patient/one-pen policy.
3. Proper disposal technique should be demonstrated at the initiation of injection therapy and reinforced at subsequent visits.
4. Minimize the risk of NSI by using shorter needles or the proper technique of lifting the skin fold when injecting.
5. Use of Personal Protective Equipment is required when handling of individuals with diabetes who are seropositive for HIV, HBV and HCV.
6. Formal protocol in dealing with a NSI injury should be clearly communicated.

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SPECIAL CONSIDERATIONS IN INJECTABLE THERAPY

People with diabetes who are on injectable medications may experience some important issues that may affect the medication absorption and also their daily function. HCPs should educate all people with diabetes who are prescribed with insulin treatment on the symptoms and early management of hypoglycaemia. Other injection issues such as pain, bruising, bleeding and lipodystrophy need to be explored and assessed.

8.1 Hypoglycaemia

Hypoglycaemia is defined by either one of the following two conditions:[1]

- Low plasma glucose level (<4.0 mmol/L).
- Development of autonomic or neuroglycopenic symptoms (Refer to Table 8) in people with diabetes treated with insulin or OAD agents which are reversed by caloric intake.

Table 8: Symptoms of Hypoglycaemia

Autonomic	Neuroglycopenic
Trembling	Difficulty concentrating
Palpitation	Confusion
Sweating	Weakness
Anxiety	Drowsiness
Hunger	Vision changes
Nausea	Difficulty speaking
Tingling	Headache
	Dizziness

SECTION 8

8.1.1 Severity of hypoglycaemia

- The severity of hypoglycaemia can be defined by its clinical manifestations:
  - **Mild** – Autonomic symptoms present and the individual is able to self-treat.
  - **Moderate** – Autonomical and neuroglycopenic symptoms present and the individual is able to self-treat.
  - **Severe** – Unconsciousness may occur. Plasma glucose is typically <2.8 mmol/L and the individual requires the assistance of another person.

- Risk factors for hypoglycaemia in people with T2DM are:
  - Advancing age
  - Severe cognitive impairment
  - Poor health knowledge
  - Increased HbA1c
  - Hypoglycaemia unawareness
  - Long-standing insulin therapy
  - Renal impairment
  - Neuropathy

- Prevention of hypoglycaemia requires risk factor reduction and individualised treatment regimens.
- Improved education and recognition could prevent and reduce the frequency of hypoglycaemic events.

8.2 Bleeding and Bruising

- Local bruising, bleeding or pain will occasionally occur at the injection site.
- This does not appear to be associated with specific needle length or site but more likely to be affected by injection technique.[3,7]
- People with diabetes should be reassured that local bleeding and bruising do not have adverse clinical consequences on the absorption of insulin or overall diabetes management.[7]
- People with diabetes on anticoagulant therapy may experience bruises after insulin injection and are advised to apply direct pressure to the injection site once the needle is removed.[7]

8.3 Painful Injection

- Tips for making injections less painful:
  - Keeping injectable therapy that is in use at room temperature.
  - Using needles of shorter length and smaller diameter.[5]
  - Using a new needle at each injection.
  - Insert the needle in a quick smooth movement into the skin.
  - Inject slowly and ensure that the plunger (syringe) or thumb button (pen) has been fully depressed.
  - Remove at same angle and keep hand steady.
  - If bruising occurs repeatedly, revising the injection technique with the person with diabetes (or the caregivers) is recommended.
  - Sites with bleeding and bruising should be avoided until fully recovered.
  - Reassure the person with diabetes that bleeding and bruising do not have adverse effects on the absorption of insulin or overall diabetes management.
  - To prevent bleeding and bruising, avoid injecting into visible blood vessels and hair roots.

8.4 Hypersensitivity Reaction

- Localized skin reaction such as rash or itch around the injection area may indicate that the person with diabetes is allergic to a certain type of insulin.
- Filling up an adverse drug reaction form will help the pharmacist to investigate further to determine the probability of the allergic reaction.
- People with diabetes who develop hypersensitivity reaction may be admitted to the hospital and restarted on insulin at a lower dose before gradually increasing the dose (desensitization).

8.5 Lipohypertrophy

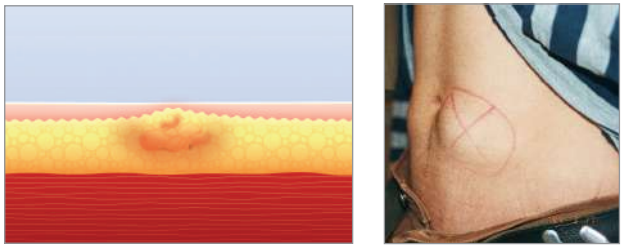
Lipohypertrophy is the most common lipodystrophy found at injection sites.[6,7] Lipohypertrophic areas may be visible or palpable, and identified as thickened or rubbery lesions that may feel hard when palpated with the finger tip.[2,8,9,10] Lipohypertrophy is formed when injections of insulin or other injectable therapy are repeatedly given in the same localised area. Microtrauma caused by the injection, combined with the effect of insulin on the repairing cells, causes fatty lumps to build up at the trauma site, causing lipo formation over time. This can be exacerbated if needles are reused.

SECTION 8

8.5.1 Detection of Lipohypertrophy

- The lesions may vary in size; some are visually apparent, while others require palpation for detection.[11]
- Lipohypertrophic areas can also be identified by pinching the skin: while healthy skin can be pinched together tightly, this cannot be done on lipohypertrophic areas (Refer to Diagram 5).

Diagram 5: Lipohypertrophy

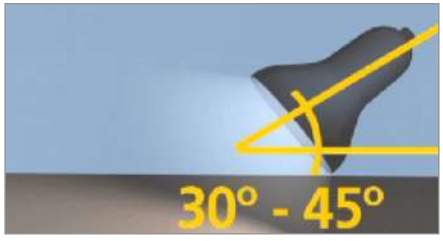


- Due to the irregular absorption of insulin injected into the lipohypertrophic lesion, lipohypertrophy can lead to unexplained hyperglycaemia, glycaemic variation and larger-than-required doses of insulin.

8.5.1.1 Assessment of Lipohyperthrophy

- Creating an optimal environment for lipohypertrophy detection:
  - The room must be warm to prevent chilling, shivering and muscle tension.
  - Use directional task lighting if possible. Light should be oblique at 30°–45° to the skin surface, preferably not overhead (Refer to Diagram 6).

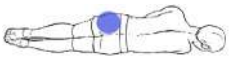
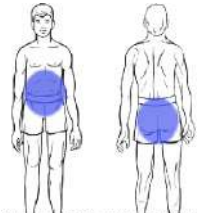
Diagram 6: Direction of Lighting for Assessment of Lipohypertrophy



8.5.1.2 Preparing for Clinical Examination

- Refer to Table 9 for steps of clinical examination of lipohypertrophy.

Table 9: Preparation for Clinical Examination of Lipohypertrophy

• Position the individual lying down on his back with only his underclothes on, then examine his abdomen, arms and thigh injection zones.	
• Ask the individual to lie on alternate sides and flex his knees towards the chest to examine the buttock area.	
• If without an examination bed, get the individual to sit upright in a chair with his hands resting on the lap and with his legs at right angles to the floor to examine the arms and thigh. For abdomen, get the individual in the standing position with his arms and hands by his sides.	 

8.5.1.3 Visual Examination of the Injection Site

- Visually examine the injection sites using angled lamp. Lipohypertrophy usually manifests as a raised or mound-like convex area, sitting above the surrounding skin surface.
- Occasionally, lipohypertrophic areas can manifest as shiny or hyper-pigmented zones, especially in darker skins. You may also notice some hair loss.
- Mark the areas if lipohypertrophic are detected.
- Bring clinical examination gel close to body temperature and apply into the area liberally. Palpate with your fingertips using a light massage motion, making forward thrust and circular sweeps.
- Use a skin-safe marker pen to draw a line around the lipohypertrophic areas.

8.5.1.4 After Examination Care

- Teach people with diabetes to conduct self-examination for lipohypertrophy at regular intervals. The use of hand or body lotion may help to locate lipohypertrophy more easily.
- Lipohypertrophic areas must not be injected.
- When injecting into a healthy area, monitor blood glucose levels closely and reduce the dose of insulin accordingly.

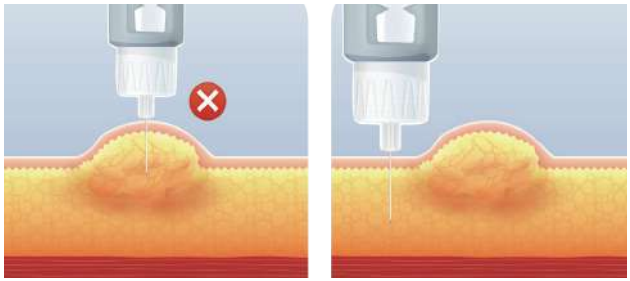
8.5.2 Lipohypertrophy Prevention

- Teach people with diabetes to rotate injections sites (Refer to Section 5 Injection Sites) using the zone system and to never reuse needles.

8.5.3 Effects of Lipohypertrophy

- Insulin is a growth factor and plays a role in the development of lipohypertrophy.[2,4,12] Injecting or infusing medication into a lipohypertrophic site may decrease or cause variability in the rate of insulin absorption resulting in variable glycaemic response and the development of disfiguring anatomical lesions.[4]
- Some people with diabetes may repeatedly choose lipohypertrophic sites for injections or infusions, as these areas have limited nerve innervations and thereby render the injections to be relatively painless (Refer to Diagram 7).[13,14,15]
- Majority of lipohypertrophy in people with diabetes are due to a lack in injection site rotation.[16]

Diagram 7: Incorrect Injection Site – Lipohypertrophy



- Higher HbA1c levels have been reported in people with diabetes who administer injections into lipohypertrophic sites. Pen devices and syringes (all needle lengths and gauges) and insulin pump cannulae have all been reported to be associated with lipohypertrophy.[3,4]
- Switching injections from lipohypertrophic to normal tissues often requires a decrease in the dose of insulin injected. The amount of insulin reduction varies from one individual to another and should be guided by frequent blood glucose measurements. Reduction often exceeds 20% of their original dose.[17]

Key Points

1. People with diabetes on insulin injection need to be educated on the early recognition and management of hypoglycaemia.
2. Injection issues such as pain, bleeding and bruising need to be explored and the injection technique has to be corrected when necessary.
3. Education regarding lipohyperthrophy should be included during injectable therapy initiation and reinforced at subsequent visits. Sites should be examined by HCPs at least once per year or more frequently if lipohyperthrophy is already present.
4. People with diabetes should be taught to inspect their own injection sites and should be given training on sites rotation, proper injection technique as well as detection and prevention of lipohyperthrophy.
5. People with diabetes should be encouraged through education and guidance to avoid insulin injection into areas of lipohyperthrophy until the next examination by HCPs. The use of larger injection zones and new needles should be recommended.

SECTION 8

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SPECIAL POPULATIONS

Education and treatment approaches for injectable therapy in special populations with diabetes mellitus such as in pregnancy, the elderly, children and adolescents are challenged by physical changes such as changes in muscle mass and strength, skin integrity as well as the differences in cognitive functions.

9.1 Pregnancy

- There is limited research published on insulin injection during pregnancy. Recommendations are based on a study using routine foetal ultrasonography assessing the subcutaneous fat patterns of pregnant women between 16 to 38 weeks gestation and the expert opinion from practitioners.[1,2]
- Pregnant women with diabetes are most concerned about the effect of insulin injection or infusion on the foetus – this must be addressed to ensure medication adherence. Other safety issues like hypoglycaemia and technical use of insulin pens and blood glucose monitoring device should also be discussed.[3] They should be reassured that insulin is not only safe in pregnancy but contributes to foetal and maternal well-being.
- Insulin requirement will change as the pregnancy advances. There will be insulin dose adjustments to achieve the blood glucose target recommended in pregnancy.
- The abdomen is a safe site for insulin administration in pregnancy.[2,4] The thigh may be used as an alternative area.[5]
- It is important to reassure pregnant women that there is no indication to change the insulin injection site or technique in the first trimester of pregnancy.
- The lateral sides of the abdomen are the recommended zones for injections when the skin is taut over the central abdomen during the second and third trimesters while ensuring that the skin fold is properly raised (Refer to Diagram 8).
- The use of skin fold and shorter needles (4 mm, 5 mm) decreases the potential for intramuscular injection[6,7,8,9] due to the thinning in abdominal fat from uterine expansion. Avoid injections within 2–3 cm around the umbilicus[7,9] or areas of the abdomen with taut skin.

SECTION 9

Diagram 8: Recommended Injection Sites During the Second and Third Trimesters of Pregnancy

9.2 Elderly

- Education and treatment on insulin or non-insulin injection for the elderly are challenged by both psychological and physical impairments. Both issues involve loss of muscle mass and strength, decreased skin integrity, and changes in memory, sight and hearing.
- Impairment of counter-regulatory hormones in the elderly reduces the recognition of hypoglycaemia, creating a potential for falls and fractures.[10]
- Therefore, the treatment approach in elderly people with diabetes must be individualised, while integrating all aspects of the person's life including physical, social and spiritual issues.[11,12]
- Elderly people with diabetes need to be assessed individually using standardised tests for cognitive and functional abilities.[14]
- A structured diabetes management and injection technique plan should be written down, based on comprehensive physical and psychological assessments.[5,12, 13]
- Education of family members and friends is encouraged for support and safety. Family members are encouraged to be involved on a daily basis.[12,14]
- The recommended area for injections in elderly people with diabetes is on the abdomen. The use of 4 mm pen needles is encouraged to avoid the need for a skin lift.
- All training on injection therapy should include follow-up demonstrations.[13,15]

9.3 Paediatrics (Children and Adolescents)

- Many children and adolescents are emaciated at the time of diagnosis. Furthermore, lean and slim children especially teenage boys have minimal subcutaneous fat tissues.
- All these factors are very challenging in ensuring that the appropriate insulin injection and correct dose are administered. Proper injection techniques are key to achieve optimal blood glucose control.
- HCPs should perform an individualised assessment to determine the amount of subcutaneous fat thickness at each injection site. This will guide the choice of needle length and administration technique.[16]
- Insulin pens are the injection device of choice as they fit shorter needle lengths (4, 5 or 6 mm); 4 mm needles are the safest needle length currently available.[17] A 4 mm needle can be inserted at a 90° angle without a skin fold in most children above 6 years old and adolescents.[18] However, children aged 2 to 6 years may need a skin lift to avoid an intramuscular injection with the 4 mm needle.
- If the children are lean, a 5 or 6 mm needle may require a 45° angle for injection with a skin lift.[18,19,,20]

Key Points

1. The abdomen is the preferred site of injection in pregnancy; injections around the umbilicus or areas of the abdomen with taut skin should be avoided.
2. A structured management plan is desirable and should be based on a comprehensive assessment of physical, cognitive and functional changes in elderly people with diabetes mellitus.
3. Assessment of subcutaneous fat thickness in children is important to determine the choice of needle length and administration technique.
4. Involvement and education of parents, family members or friends are encouraged for support and safety in children and elderly people with diabetes mellitus.
5. All training on injection therapy should include follow-up demonstrations.

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PSYCHOSOCIAL CHALLENGES OF INJECTION

Injection and insulin therapy are associated with numerous negative perceptions and side effects.[4,22,24] More than one-fourth of individuals with diabetes may refuse insulin therapy after prescription[19] or delay the initiation of insulin treatment and titration due to psychological factors.[15] This phenomenon is called psychological insulin resistance (PIR).

10.1 Psychosocial Challenges Among Adults

Managing diabetes in adults may be challenging in certain cases because of PIR that could be due to several factors.

- Very few adults have true needle phobia but many have anxiety about injecting, especially at the beginning of therapy.[18,21]
- Loss of quality of life: less flexible in performing daily activities, difficulty in injecting the right amount and at the right time daily.[21]
- Social stigma: embarrass to inject in public.[5]
- Social economic status: cost of medicine and injection equipment.[5]
- Misconceptions on insulin therapy[21]:
  - Insulin initiation means their condition as 'more ill' or a 'last resort' of treatment.
  - Insulin causes serious health problems.

Practical Tips

- Assess an individual's attitudes towards insulin and his or her expectations about insulin therapy.[8]
- Prepare all individuals with T2DM early after diagnosis that they will likely require injectable therapy in the future to treat their diabetes.[17]
- Explain the progressive nature of diabetes and making clear that injectable therapy treatment is not a sign of patient failure.[17]
- Discuss the advantages and disadvantages of injectable therapy versus other therapy.[7,8]
- Provide information on insulin and the various formulations.[26]
- Discuss both short- and long-term advantages of achieving target glucose level. It is important to explain that finding the right combination of therapies, which may include the use of injectable therapy to achieve individualised glycaemic targets is the treatment goal.[3]
- Involve the individual in decision making (e.g. selecting needle sizes, injection frequency).[20]
- Use devices such as i-Port@ or insujek if needed.

- Feeling a sense of personal failure or self-blame.[21]
- Fear of side effects: hypoglycaemia, diabetic ketoacidosis, weight gain.[5]

10.2 Psychosocial Challenges Among Adolescents

Adolescents is defined as children of puberty to 18 years of age.[6] They may exhibit sub-optimal adherence to insulin injection schedule due to[9]:

- Peer pressure
- Forgetfulness
- Lack of seriousness about their condition/treatment
- Rebellion
- Pain and frustration
- Fear of weight gain (especially girls)

Practical Tips

- Encourage adoslescents to discuss their feelings about injection particularly their frustration and struggles.[6]
- Reassurance that no one manages diabetes perfectly all the time; slip-ups do occur (as long as they do not become routine) and are not signs of failure.[6]
- Explain the benefits of injectable therapy[7,8]:
  - Improve blood glucose control
  - Reduce long-term complications
- Apply Cognitive Behavioural Therapy[25]:
  - Relaxation training
  - Guided imagery
  - Graded exposure
  - Active behavioral rehearsal
  - Modelling and reinforcement
- Give them a sense of control (e.g. flexible injection schedule for weekends and holidays).[6]

10.3 Psychosocial Challenges Among Children

The age at which children can self-inject is related to development maturity rather than chronological age. Most children over the age of 10 can administer their own injections.[2] There are several concerns regarding injection among children.

- Needle fear is common in both children with diabetes and their parents. Younger children report more fear and pain.[10,12,23]
- Children have lower threshold of pain and do not bring it up spontaneously.[11]
- Intentional underdosing or overdosing of insulin is common in children (and adolescents) and can lead to severe diabetic ketoacidosis or hypoglycaemia.[4,22,24]

Practical Tips

- For parents or guardians:
  - Project a calm and compose attitude towards injections.[9]
  - Inform parents that their displayed distress and negative attitudes can influence their child's co-operation.[3]
  - Let parents experience an injection with a pen tip needle attached to an empty insulin pen device.[3]
  - Encourage parents to be involved in insulin administration if insulin dose manipulation is suspected or confirmed.[1]
- For children:
  - Show concern to the child by asking about pain and use positive words.[14]
  - Use diversion techniques or play therapy[3]:
    - Injecting into a soft toy animal
    - Watching a favorite show
    - Looking for hidden objects in picture books
    - Blowing bubbles
- If self-injecting, young children should share this responsibility with their parents and do so under supervision.
- If omission or overdosing is an ongoing problem, the parents should be instructed to take over the task of injecting insulin.

10.4 Psychosocial Challenges among HCPs

Despite ample evidence showing that relatively few people with T2DM achieve glycaemic control with oral therapy alone, physicians are still reluctant to initiate insulin injection.[8] The reluctance to add insulin injection may be due to[16]:

- having negative perceptions about injectable therapy
- lack of motivation and confidence
- concern about the lack of continuity of care for the people with diabetes
- lack of manpower and resources

SECTION 10

Practical Tips

- Reflect on own perceptions of injectable therapy. Avoid using any terms which might imply that such therapy is a sign of failure or a form of punishment.[9]
- Ask people with diabetes about their use of complementary therapies when initiating insulin.[16]
- Initiate insulin with a lower starting dose.[13]
- Customize a follow-up plan for people with diabetes to facilitate initiation and optimisation of insulin.[16]
- Address misconceptions by counselling people with diabetes about the natural progression of diabetes at the early stage of the illness.[16]
- Policymakers to design and implement training curriculum of HCPs.[16]

Key Points

1. PIR causes more than 25% of the individuals with diabetes to delay the initiation of insulin and non-insulin injectable therapy.
2. Different age groups of the diabetes population demonstrated different concerns about injectable therapy. In general, fear and anxieties about injectable therapy occur in all ages.
3. It is advisable to use appropriate approaches to manage an individual's psychological challenges. Spending some time in addressing these challenges can be worthwhile.
4. Some HCPs have reservations in initiating injectable therapy. This may be due to personal negative perceptions towards the therapy and safety issues in using insulin.

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CHECKLIST

Injection Technique Using Pen Devices	Yes / No	Follow-up
1. Hand wash		
2. Check insulin for discolouration and formation of clumps. Discard if these occur		
3. Resuspension of cloudy insulin, roll 10 times and tip up and down 10 cycles (only for cloudy insulin)		
4. Place a new needle onto pen device		
5. Prime the pen		
6. Dial the correct dose		
7. Inspect injection site. Injection should be given to a soft and clean site		
8. Insert pen needle into the skin at 90° angle, push down the dose button completely		
9. Count to 10 slowly before withdrawing the needle from the skin		
10. Recap pen needle using outer cap		
11. Remove the used pen needle and dispose safely		

CHECKLIST

Injection Technique Using Insulin Syringe	Yes / No	Follow-up
1. Hand wash		
2. Check insulin for discolouration and formation of clumps. Discard if these occur		
3. Resuspension of cloudy insulin, roll 10 times and tip up and down 10 cycles (only for cloudy insulin)		
4. Cleanse the insulin vial's lid with alcohol swab		
5. Remove plunger protector and uncap the needle of insulin syringe		
6. Draw air into the syringe by pulling back the plunger to the level equal to the prescribed dose (the air is equal to the units of insulin to be injected)		
7. Inject syringe into the insulin vial at 90° angle		
8. Push the air into the insulin vial		
9. With the needle still in the vial, turn the insulin vial and syringe upside down		
10. Slowly pull down the plunger to withdraw/aspirate insulin into the syringe up to a unit past the prescribed dose. Check for the presence of air bubbles and remove using appropriate techniques		
11. Pull the needle out of the insulin vial		
12. Inspect injection site. Injection should be given to a soft and clean site (alcohol swab is recommended in healthcare setting).		
13. Lift gently a skin fold using thumb and index fingers		
14. Insert needle into the skin at 45° angle for needle length >8 mm, push down the dose button completely		
15. Count to 10 slowly before withdrawing the needle from the skin		
16. Release lifted skin fold		
17. Dispose used syringe safely		

APPENDIX

GLP-1 RA

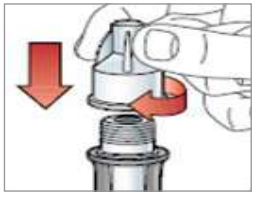
- Individuals who inject GLP-1 RA should follow the recommendations for insulin injection technique using pen devices with regard to needle length and site rotation.[1]
- GLP-1 RA may be injected at any of the usual injection sites as the pharmacokinetics do not appear to be site-specific.[2]
- The injection technique for Exenatide Immediate Release and Liraglutide are similar to insulin pen devices. However, priming is not required in both agents.
- The injection technique for Exenatide Extended Release involves three steps: [3]
  1. Prepare
  2. Mix
  3. Inject

1. Prepare

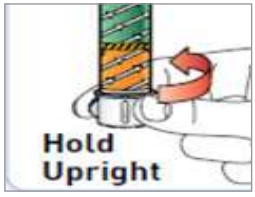
i) Remove one pen from the refrigerator. Wait for 15 minutes. Medicine that is at room temperature is easily mixed well.

ii) Attached the needle on the pen and do not remove the needle cover (Refer to Picture A).

iii) Combine the medicine by holding the pen in an upright position and slowly turning the knob. Stop until a 'click' sound is heard and the green label disappears (Refer to Picture B).



Picture A



Picture B

Picture C

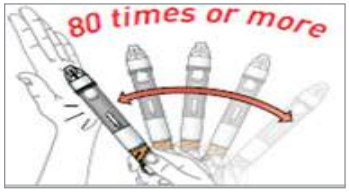
(Image source: AstraZeneca)

2. Mix

i) Hold the pen by the end at the orange label and tap the pen firmly against the palm of the hand to mix. Rotate the pen every 10 taps (Refer to Picture C).

ii) Hold the pen up to the light and look through both sides of the mixing window to make sure that the medicine is mixed well (Refer to Picture D).

*To get the full dose, the medicine must be mixed well. If not mixed well, tap longer and more firmly.



Picture C

Picture D

(Image source: AstraZeneca)

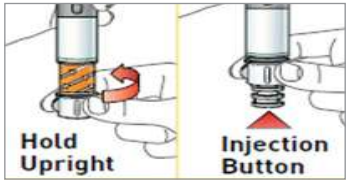
3. Inject

i) Twist the knob until the injection button is released (Refer to Picture E).

ii) Pull the needle cover off.

iii) Insert the needle into the skin.

iv) Press the injection button with the thumb until a 'click' sound is heard and hold for 10 seconds.



(Image source: AstraZeneca)

Picture E

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3. Bydureon Pen User Manual. AstraZeneca Pharmaceuticals LP; 2015.

GLOSSARY OF TERMS

Abbreviation	Terminology
BMI	Body mass index
GLP-1	Glucagon like peptide-1
GLP-1 RA	GLP-1 receptor agonist
HCP	Healthcare professional
HIV	Human immunodeficiency virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
NSI	Needle stick injuries
OAD	Oral anti-diabetic
PIR	Psychological insulin resistance
SMBG	Self-monitoring blood glucose
T1DM	Type 1 diabetes mellitus
T2DM	Type 2 diabetes mellitus

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