

Starting Injectable Treatments in Adults with Type 2 Diabetes

4th Edition

CLINICAL PROFESSIONAL RESOURCE



This publication is
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Publication

This is an RCN clinical professional resource.

Description

This guidance has been developed as a resource for nurses and clinical staff working in general practice and community settings to effectively care for people living with Type 2 diabetes, who are starting or using injectable treatments.

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The Nine Quality Standards

This publication has met the nine quality standards of the quality framework for RCN professional publications. For more information, or to request further details on how the nine quality standards have been met in relation to this professional publication, please contact publications.feedback@rcn.org.uk

Evaluation

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Introduction and using this guide

The complications of diabetes are wide reaching and include stroke, renal failure, ischaemic heart disease, blindness and amputation. Evidence shows that intensifying treatment and ensuring good glycaemic control early on during the disease process improves health outcomes and reduces complications over the longer term (UKPDS 1998) and hence early detection, screening and prevention are essential. One in six of all people in hospital have diabetes and hence often need a longer stay in hospital, are more likely to be readmitted and have a higher risk of mortality.

The *Five Year Forward View* (NHS England, 2014) the *General Practice Forward View* (NHS England, 2016)) and more recently the *NHS Long Term Plan* (2019) represented a step change in the level of investment and support for general practice and, particularly, at scale working. Practices can still maintain their unique identity and relationship with their own patients; and at the same time through at-scale working will be able to offer more to their local population, by delivering integrated services between health and care providers, including community health services, social care and voluntary organisations.

Traditionally, injectable therapy in Type 2 diabetes has been managed by specialist diabetes services. However, the growing shift of responsibility for routine diabetes management to primary and community care – reinforced by these publications – means there is now an expectation that nurses in primary and community care are much more involved in the initiation of injectable therapies in people with Type 2 diabetes.

This publication was written by members of the RCN Diabetes Nursing Forum Committee, all of whom have many years of expertise in the specialist management of diabetes in all care settings.

Intended as a resource for clinicians working in general practice and community settings, this guide includes an overview of the underlying principles for starting injectable therapies, along with some practical tips on diabetes education, adjustment of doses, how these therapies work and some case studies. In turn it is hoped that this guidance could help develop clinical skill, confidence and competency that the nurse could benchmark alongside such documents as *An integrated career and competency framework for diabetes nursing 5th Edition* (TREND-UK, 2019a).

1. How injectable therapies work

Insulin and metabolic process

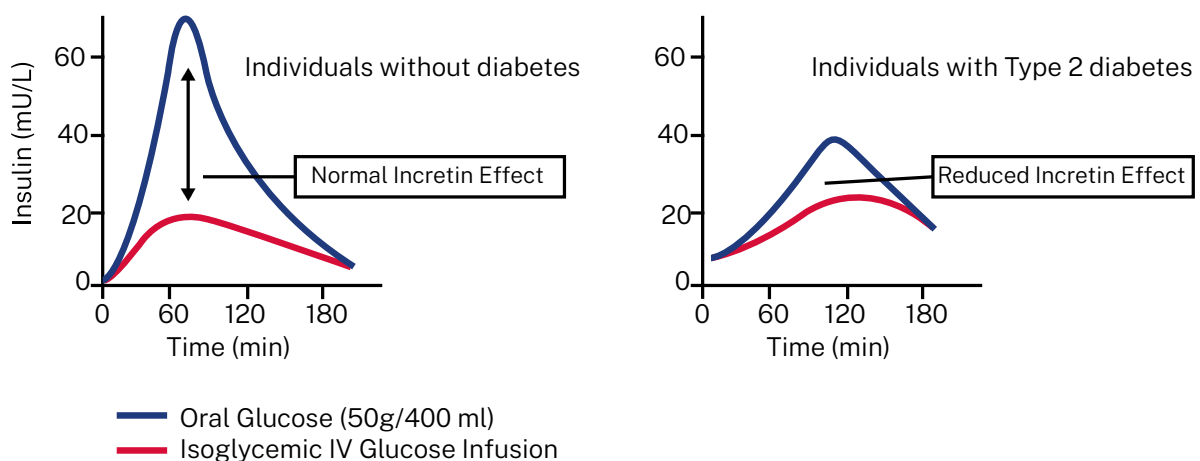
The most vital role of insulin in the human body is its interaction with glucose to allow the body cells to use glucose as energy. The pancreatic beta cells produce more insulin in response to a spike in blood glucose levels; for example, after eating a meal with carbohydrates. This is because the insulin acts as a “key” to open the cells in the body and allows the glucose to be used as energy. In the absence of insulin, the body is not able to utilise the glucose as energy in the cells. As a result, the glucose remains in the bloodstream and can cause chronic hyperglycaemia.

In individuals who do not have diabetes, approximately 50% of the total daily insulin is secreted during basal periods, suppressing lipolysis, proteolysis and glycogenolysis. The remainder of insulin secretion is postprandial. In response to a meal, there is a rapid and sizable release of preformed insulin from storage granules within the beta cell. This “first phase” of insulin secretion promotes peripheral utilization of the prandial nutrient load, suppresses hepatic glucose production, and limits postprandial glucose elevation. First-phase insulin secretion begins within two minutes of nutrient ingestion and continues for 10 to 15 minutes. The second phase of prandial insulin secretion follows, and is sustained until normoglycaemia is restored.

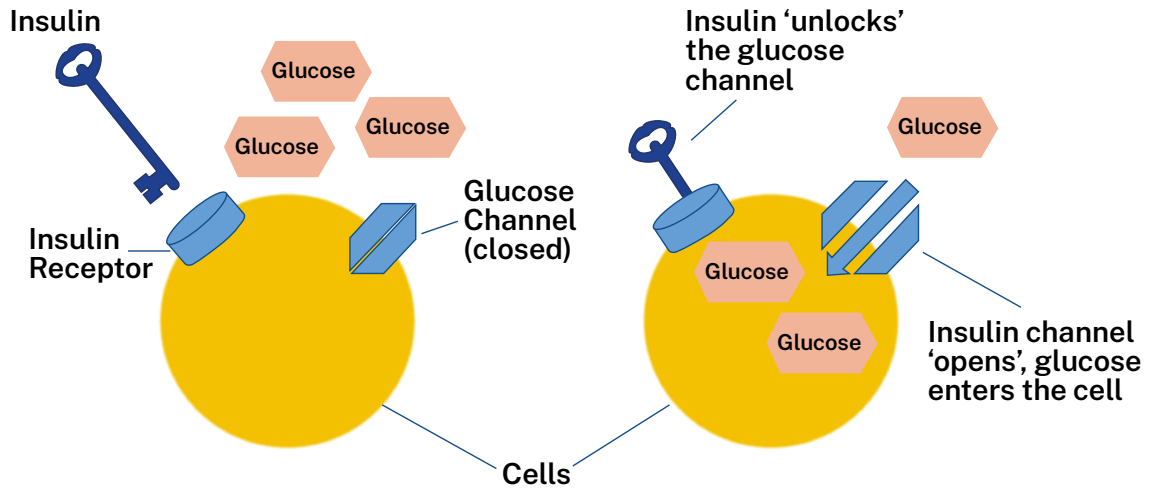
The incretin effect

The incretin effect describes the phenomenon whereby oral glucose elicits higher insulin secretory responses than intravenous glucose, despite inducing similar levels of glycaemia in healthy individuals. This effect, which is uniformly defective in patients with Type 2 diabetes, is mediated by the gut-derived incretin hormones; glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). The importance of the incretin effect for the maintenance of glucose homeostasis is clearly established, and incretin-based therapies are among the most promising new therapies for Type 2 diabetes.

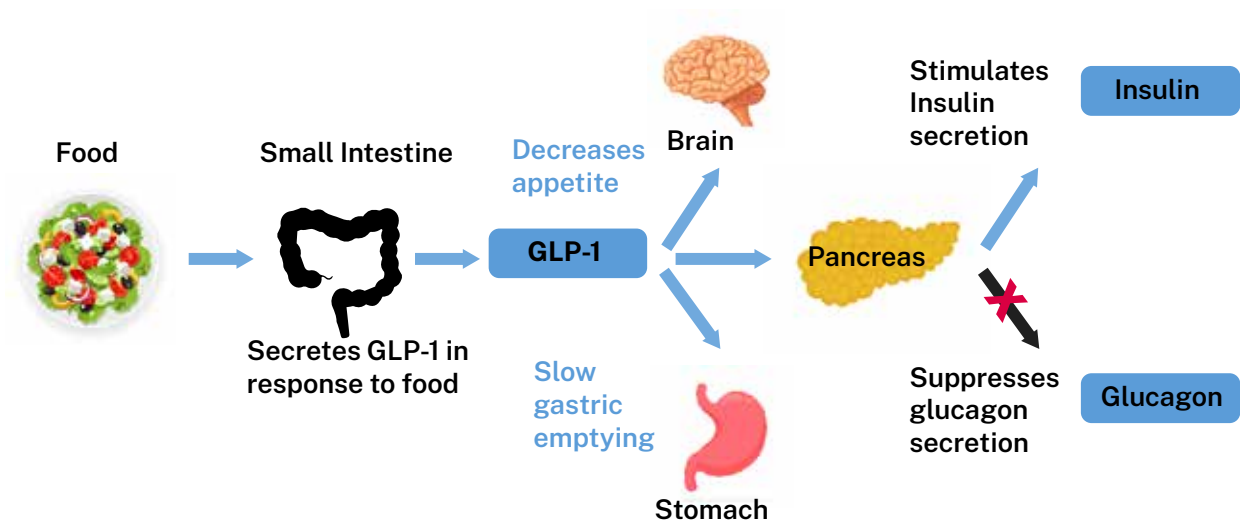
Diabetes and the incretin effect



How insulin works



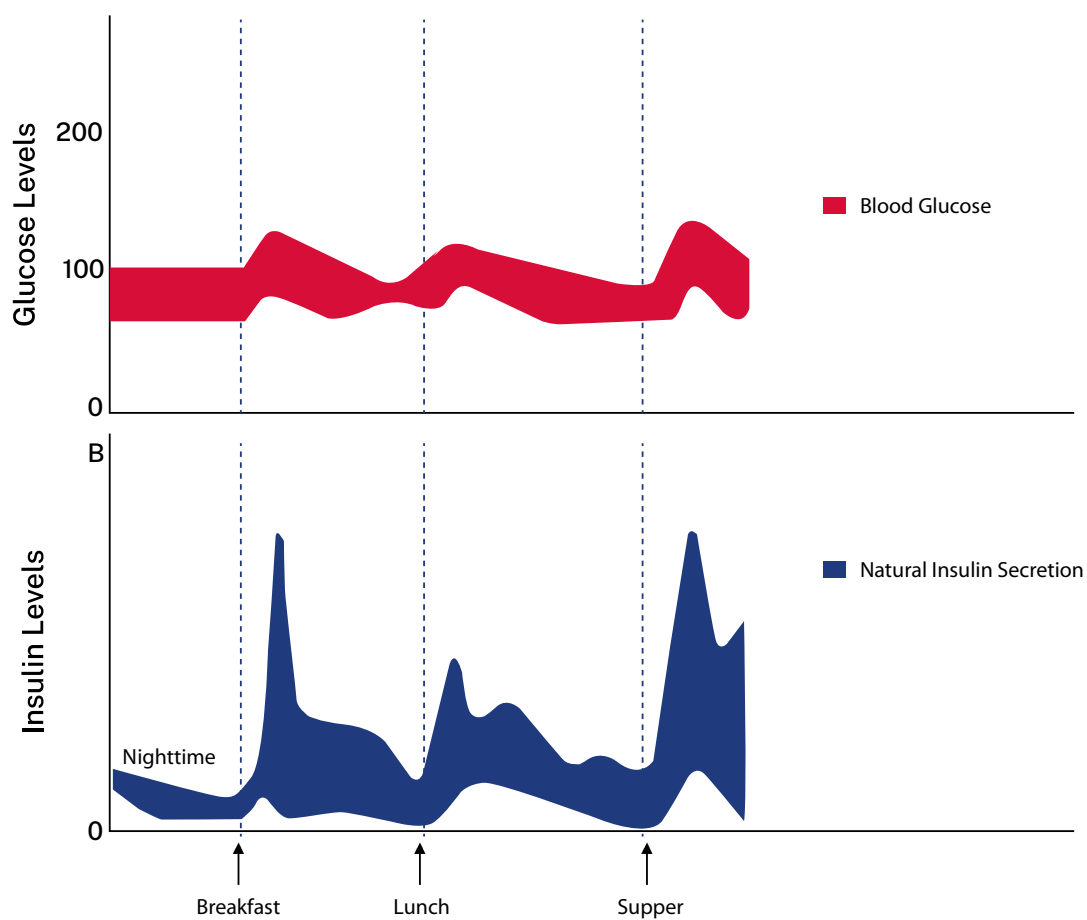
GLP-1 therapy mechanism of action



Insulin production without diabetes

To keep the blood glucose in a narrow range throughout the day, there is a low steady secretion of insulin overnight, fasting and between meals with spikes of insulin at mealtimes. Adapted: (Jacobs, 1997)

Normal (individual without diabetes) Blood Glucose and Insulin Levels over 24 Hours



Manufactured insulin and GLP-1 Therapy

Manufactured insulin and GLP-1 therapy aims to mimic these natural patterns. GLP-1 analogues (incretin mimetics) work by increasing the level of hormones called Incretins. These hormones help the body produce more insulin only when needed and reduce the amount of glucose released by the liver when it is not required. GLP-1 also delay gastric emptying, promoting satiety.

GLP-1 preparations available in the UK are produced by the following companies: Sanofi, Lilly, Novo Nordisk and AstraZeneca.

Manufactured GLP-1s that are currently available: Dulaglutide (Trulicity), Exenatide (Byetta), Exenatide Extended Release (Bydureon), Liraglutide (Victoza), Lixisenatide (Lyxumia) and Semaglutide (Ozempic).

UK insulin manufacturers are: Sanofi, Lilly, Novo Nordisk, Wockhardt and Mylan. Manufactured insulin can be either human insulin analogue, human insulin or animal in origin, and fall into six main categories.

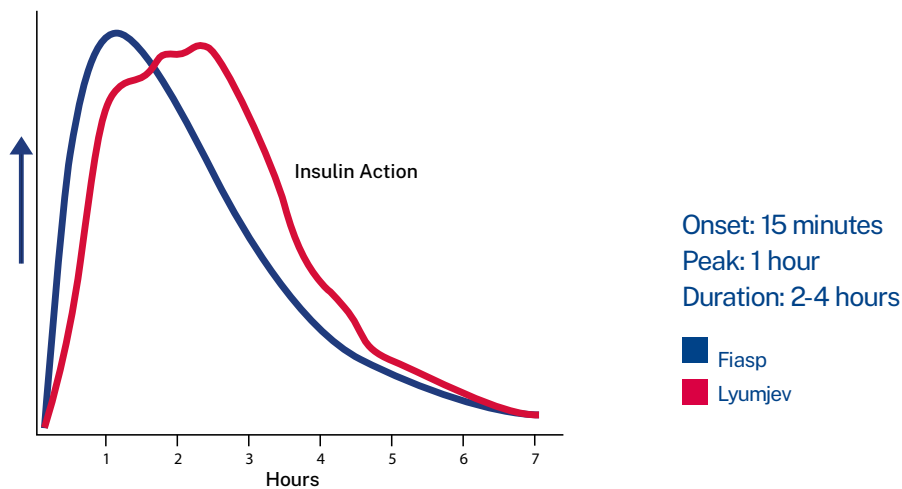
- **Ultra rapid-acting** - to cover post meal glucose rise - inject with food.
- **Rapid-acting** – to cover post meal glucose rise – inject with food. Can be administered after food if there are uncertainties about the amount of carbohydrate that will be consumed.
- **Short-acting** – covers post meal rise in glucose. Caution as duration can overlap with next meal and increase hypo risk (see below).
- **Intermediate-acting** (also called Isophane insulin or Neutral Protamine Hagedorn (NPH) – use for an insulin start or where once daily dosing would be beneficial e.g., community nurse or carer administration.
- **Fixed mixtures** (of rapid/short-acting and intermediate-acting insulin) ideal to cover post-meal rise. For people who require prandial cover but only wish to inject twice a day and no more. Appropriate if patient has regular meal pattern/lifestyle.
- **Long-acting** – once daily dosing. Can be useful when risk of hypoglycaemia needs reducing (flatter profile – see below) or if weight gain needs to be minimised.
- **Ultra-long** – once daily dosing. Can be useful when timing of insulin injection is not reliable every 24 hrs. Can also reduce the risk of hypoglycaemia for patients for whom this is problematic.

Time action profiles of manufactured insulin

The following diagrams illustrate how the different types of insulin work. Up-to-date charts showing the characteristics of all manufactured insulin preparations available in the UK are published regularly in the British National Formulary (BNF, 2019) and MIMS (MIMS, 2019).

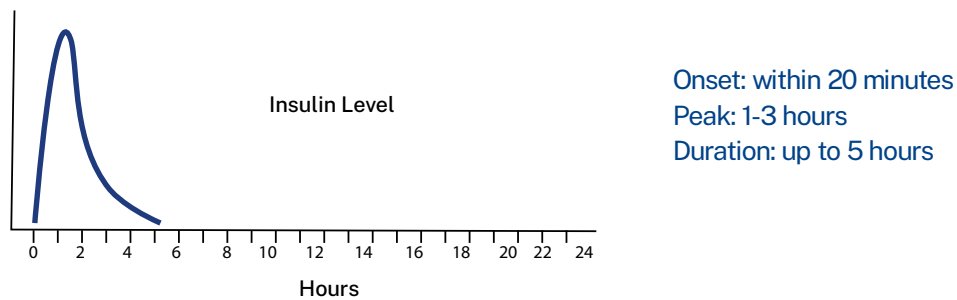
Ultra-Rapid acting meal - time insulin

Product names include Fiasp and Lyumjev.



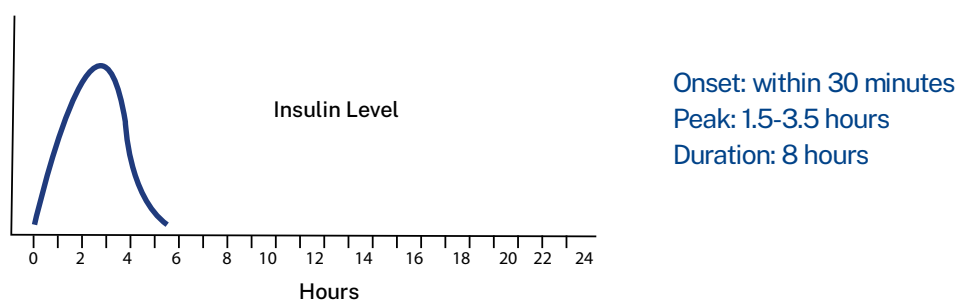
Rapid-acting meal-time insulin (analogues)

Product names include Humalog, Novorapid and Apidra.



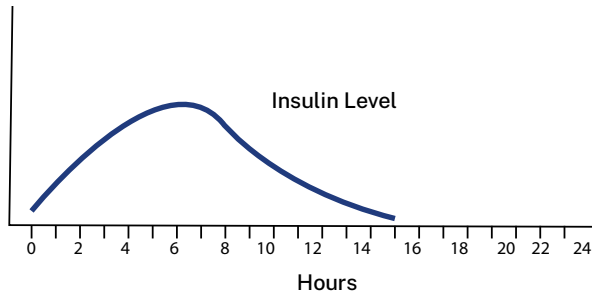
Short-acting meal-time insulin (human)

Product names include Actrapid, Humulin S and Insuman Rapid.



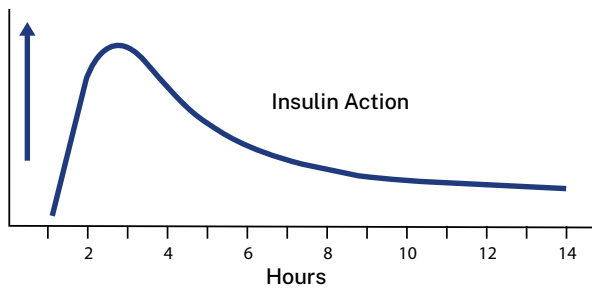
Intermediate-acting insulin (human)

Product names include Insulatard, Humulin I and Insuman Basal



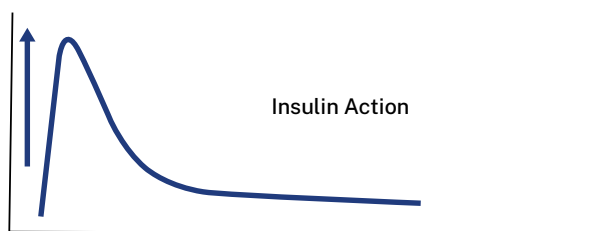
Fixed Mixtures:

Pre-mixed Human: Humulin M3, Insuman Comb 15/25/50



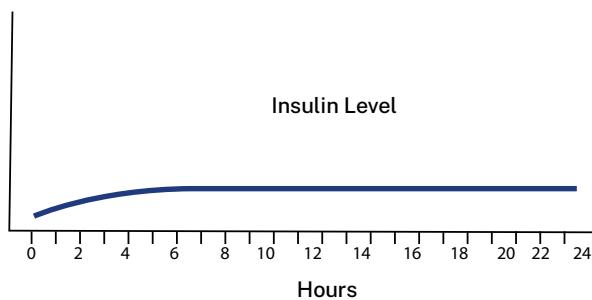
Onset: within 30 mins
Peak: 2-4 hours
Duration: up to 14 hours

Pre-mixed Analogue: Novomix 30, Humalog Mix 25/Mix 50

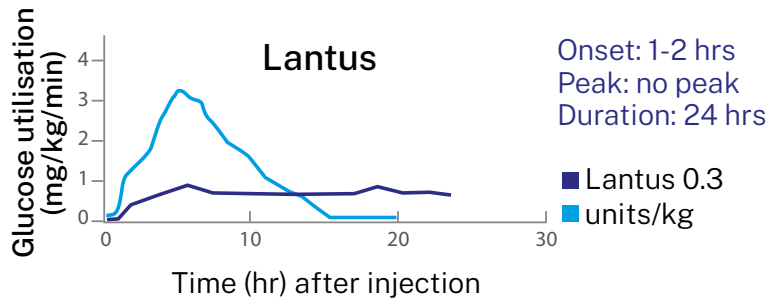


Onset: Less than 15 mins,
Peak: 50-90 mins
Duration: up to 14 hours

Long-acting insulin (analogues): Levemir, Lantus, Abasaglar, Semglee Levemir:

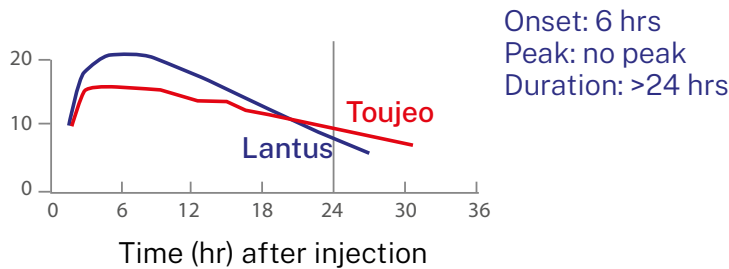


Lantus/Abasaglar/Semglee (comparison with Intermediate/NPH)

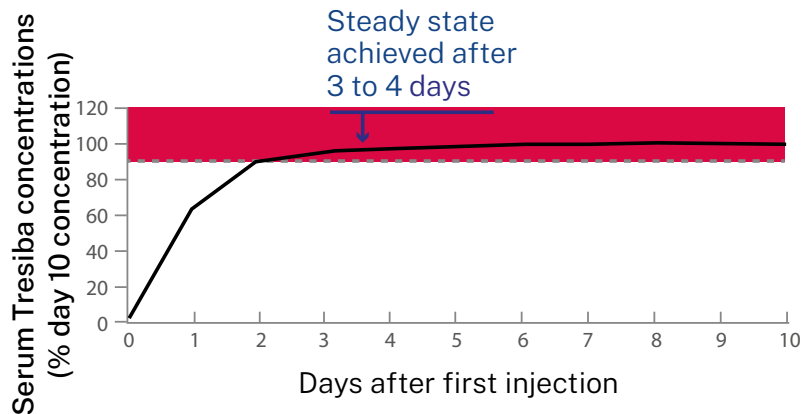


Ultra-long-acting insulin

Toujeo (u300) and Tresiba (U100 OR U200) are currently the only products in this category.



Tresiba: Duration up to 42 hours (Steady state means the time it takes to build the insulin concentration in the blood to be therapeutic).



2. Indications for injectable therapy

Glucagon-Like Peptide 1 (GLP-1) therapy – who may benefit?

NICE recommends (2022) that GLP-1 therapy should be considered if triple therapy with metformin and two other oral drugs is not effective, not tolerated or contraindicated.

NICE (2022) GLP-1 Indications

- A BMI of 35 kg/m² or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity.
- Or have a BMI lower than 35 kg/m² and for whom insulin therapy would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

GLP-1s have the benefit of not causing hypoglycaemia unless they are used in conjunction with a drug that can cause this independently for example sulfonylureas.

Recent evidence from cardiovascular outcome trials (Bethel et al, 2018) suggests that some GLP-1s can improve cardiovascular outcomes and therefore should be used at an earlier stage (Davies et al, 2018). Please refer to your local guideline for further advice.

Which patient groups are not suitable for GLP-1 therapy?

- People with Type 1 diabetes - can be used off licence in certain individuals with an elevated BMI.
- Acute pancreatitis.
- Severe GI disease.
- Pregnant or nursing mothers.
- End stage renal failure (Chronic Kidney Disease Stage 5; eGFR less than 15 ml/min).
- History of alcoholism.
- Low BMI.

Insulin therapy – who may benefit?

Insulin is a polypeptide hormone secreted by pancreatic beta cells. Insulin increases glucose uptake by adipose tissue and muscles, and suppresses the hepatic glucose release.

The pancreas works increasingly harder to produce more insulin as resistance increases over time. Eventually the pancreatic cells effectively 'wear out'; resulting in the need to add insulin when other oral medications are less effective in maintaining blood glucose levels and HbA1c. Potentially anyone with Type 2 diabetes stands to benefit from insulin treatment.

Insulin is likely to be required in up to 50 per cent of patients with Type 2 diabetes. It may be a temporary or permanent treatment choice.

Insulin is being used increasingly as a temporary treatment for patients with:

- severe hyperglycaemic symptoms
- infection causing hyperglycaemia not controlled on oral therapy
- after myocardial infarction or other vascular episode (CABG, peripheral bypass, CVA)
- patients on steroids
- acutely unwell patients pre and post-surgery.

It is important to record why insulin was started and to reassess whether insulin is still needed.

Insulin should be considered as a 'permanent' treatment for:

- when dual therapy has not continued to control HbA1c to below the person's individually agreed threshold, also consider insulin-based therapy (with or without other drugs)(NICE, 2022)
- people with suboptimal glycaemic control (58–75mmol/mol) who are at high risk of complications through young age or who have established microvascular or macrovascular complications (NICE, 2017; Davies et al, 2018)

Other indications for insulin therapy may include:

- personal preference
- painful neuropathy
- foot ulceration and infection
- pancreatitis
- enteral feeding
- ketosis prone diabetes
- pregnancy or planning pregnancy
- recurrent fungal or bacterial infections
- people who cannot tolerate oral hypoglycaemic drugs.

Which patient groups are not suitable for insulin therapy?

It is not always obvious who will do well and who won't. Age in itself is not a bar to insulin. Indeed, elderly patients often derive substantial symptomatic benefit and manage injections without difficulty. A 'trial' of insulin is appropriate for some people.

- The success of the intervention must be examined at regular intervals.
- If there is no benefit from insulin or there are side-effects e.g. significant hypoglycaemia, marked weight gain, it could be stopped.
- People who have Type 2 diabetes and who are frail will not always benefit from a low HbA1c target (for example less than 53mmol/mol). Aiming for a target such as this may place frail patients at risk of hypoglycaemia and subsequent falls/hospital admission. Targets should be adjusted accordingly.
- People with other physical or mental health problems living with minimum or no support.
- People who are not concordant with oral hypoglycaemic agents (OHAs) will not suddenly start taking injectable therapy. The underlying reasons for non-concordance should be discussed with the patient first before further intensification of treatment. Consider slow release versions of OHAs that can be taken once daily that may improve the situation.
- Individuals with alcoholism who are actively drinking alcohol (hypo risk) and those who are self-harming.

Is my patient likely to benefit from insulin?

Likely to benefit	May not benefit
Marked symptoms	No symptoms
Slim and losing weight	Overweight and gaining
Well-motivated	Poorly motivated
Careful with diet	Not careful with diet
Established complications and/or long-life expectancy	No complications and limited life expectancy
	Socially isolated

Starting insulin treatment

As part of patient education, insulin therapy should be discussed as a treatment option from diagnosis onwards. The emphasis should be placed on the pancreas that is not able to cope with demand and not that the individual has failed. Insulin treatment should not be used as a threat to improve diabetes management.

When people don't want insulin therapy

Bear in mind that there will be some situations or factors that may put people off starting insulin therapy.

- **Driving** – People using insulin therapy are required by law to inform the DVLA and their car insurance company. Accessing the DVLA website for all the legalities is required. There is also a patient information leaflet entitled *Diabetes: Safe driving & the DVLA* from TREND UK (2019) that is available. Please see reference section for more detail.
- **Employment** – It is unlawful for an employer to operate a blanket ban on recruitment of people with diabetes. Some jobs involving safety-critical work will have legitimate health requirements that may exclude some people with certain medical conditions, including diabetes. Following extensive campaigning by Diabetes UK, the blanket bans have been lifted in the emergency services for people with Type 1 diabetes and people with Type 2 diabetes who use insulin. Decisions made on someone's suitability for employment in these services should be made by a process of individual assessment. Recruitment and retention of people with diabetes in the police, fire and ambulance services should now be subject to individual medical assessment. However the UK armed forces are exempt from the Equality Act and can operate a blanket ban on the recruitment of people with diabetes (Diabetes UK, 2019a).
- **Emotional health** – people with diabetes can have many complex emotional problems that they may need help with, for example, fear of hypos, facing life with diabetes, and communication. Diabetes UK (2019) states 'Psychological barriers to insulin use are the negative thoughts or feelings that people with diabetes may have about starting, using or intensifying insulin.' Of those people with Type 2 diabetes for whom insulin is clinically indicated, around one in four report being 'not at all willing' to start insulin. The guide for health professionals offers strategies and tools to help with the recognition and conversation of many of these issues.
- **Misconceptions** – some people may have heard "stories" about insulin that may be untrue or outdated, for example they know of people who got worse after insulin was initiated, they think they won't be allowed to drive or travel, or that insulin will make them collapse.
- **Live for today** – some people may prefer to live with the increased risk of complications, particularly if they do not have any symptoms. They should be in a position to make an informed choice.
- **Fear of weight gain** – often justifiable, so it may be worth exploring ways to improve lifestyle treatments (diet and exercise) or consider other therapies.
- **Physical barriers** – concern may be around dexterity or visual problems. It is worth demonstrating different types of devices to help with this.

3. Choosing the right injectable therapy

Who makes the decision about starting injectable therapies?

Your role is to explain the options and present all the 'pros and cons'. The final decision must be made by the person themselves. To carry out your role, you will need to understand:

- indications for GLP-1 analogue therapy for Type 2 diabetes
- what is a GLP-1 analogue
- GLP-1 analogue treatment options
- how GLP-1 works
- the GLP-1 analogue delivery devices
- the principles of normal insulin production
- the types of insulin available
- why insulin is needed
- how insulin works
- common insulin regimens
- the benefits and disadvantages of the various delivery devices.

When starting insulin therapy in adults with Type 2 diabetes, continue to offer metformin for people without contraindications or intolerance and review the continued need for other blood glucose lowering therapies (NICE, 2017).

There could be some advantages to combining insulin/GLP-1 with oral hypoglycaemic agents (OHA). These include:

- less risk of weight gain
- less risk of hypoglycaemia
- a simpler treatment regimen
- better glycaemic control while insulin/GLP-1 are being introduced and the dosage adjusted
- cardiovascular benefits (Davies et al., 2018).

The criteria for continuing and withdrawing OHAs when insulin is introduced are clearly stated in the NICE (2017) guidance. These should be utilised alongside this document to aid clinically appropriate decision making.

GLP-1 treatment options

There are six injectable GLP-1 analogues currently available and used as a treatment option for people with Type 2 diabetes.

Name	Dose
Dulaglutide (Trulicity)	0.75mg once weekly/1.5mg once weekly
Exenatide (Byetta)	5mcg twice daily/10mcg twice daily
Exenatide Extended Release (Bydureon)	2mg once weekly
Liraglutide (Victoza)	0.6mg initially can be increased up to 1.2/1.8mg once daily
Lixisenatide (Lyxumia)	50mcg /100mcg
Semaglutide (Ozempic)	0.25mg weekly for 4 weeks and then increase to 0.5mg once weekly. It can be increased to 1mg once weekly thereafter if further glycaemic control is needed. Semaglutide is also available in an oral formulation (Rybelsus)

Which insulin regimen?

There are many different insulin regimens available. These are used to suit varying requirements/individual needs of the person living with diabetes. There is no one right choice and one regimen may not necessarily continue. If unsuitable, the regimen requires to be changed.

Insulin preparations

Insulin preparations can be broadly categorised into the following groups based on their time-action profiles (see page 9) (the duration of action of each particular type of insulin could vary from one patient to another, therefore needs should be assessed individually).

- Ultra-rapid acting insulins.
- Rapid-acting insulins.
- Short-acting insulin.
- Intermediate-acting insulins.
- Fixed mixtures.
- Long-acting insulin.
- Ultra-long acting insulin.
- Insulin and GLP-1 combination; (Xultophy®).

Usual strength insulin 100 units/ml

All insulin is available in a concentration/strength of 100 units/ml. This should be the most commonly prescribed insulin strength and always used for new insulin starts.

Higher strength insulin

Some manufacturers have developed insulin with a higher strength formulation for example, 200 units/ml and 300 units/ml. These offer the same insulin action but in less volume and can be very useful for patients on doses greater than 40 units to help with insulin absorption and lower the risk of lipohypertrophy.

These insulins only are available in pre-filled pens to ensure that the correct dose: volume concentration is given. The patient still dials to the same dose but a different volume is given. Higher strength insulin that is available:

Insulin preparation/ Time action group (see page 9)	Insulin name	Strength available	Volume injected
Ultra rapid-acting	Lyumjev	200 units/ml	This is double the concentration of 100 units/ml. Therefore half the volume is injected
Rapid-acting	Humalog	200 units/ml	This is double the concentration of 100 units/ml. Therefore half the volume is injected
Ultra-long acting	Tresiba	200 units/ml	This is double the concentration of 100 units/ml. Therefore half the volume is injected
Ultra-long acting	Toujeo (insulin Glargine)	300 units /ml	This is three times the concentration of 100 units/ml. Therefore one third of the volume is given

These high strength insulins will be primarily initiated by specialist services, but General Practice will be required to provide prescriptions for them. Always ensure that anyone prescribed these higher concentration insulins has been given the following advice:

- ✓ always check the name and strength of insulin that they have been given before they leave the pharmacy
- ✓ always carry their insulin passport or insulin safety card with them
- ✗ never use a syringe to withdraw the insulin from the pre-filled pen device.

Recommended insulin regimens

Multiple daily injection basal bolus insulin regimens

This regimen is closer to the way the pancreas naturally produces insulin. The person administers basal insulin once/twice daily at the same time each day with bolus injections of rapid-acting insulin before mealtimes. This regimen gives greater flexibility to tailor insulin therapy with the carbohydrate load of each meal.

Once daily (basal) insulin regimens

This group of insulins have many names and can be referred to as NPH or Isophane or basal or background. These are intermediate and long-acting insulins (see page 9) for example, Humulin I, Insuman basal, Insulatard, Levemir, Glargine, Abasaglar, Semglee. NICE (2022) states that Isophane (NPH) insulins should be offered as first line. Levemir or Glargine can be used as an alternative if hypoglycaemia is experienced with Isophane insulin and the patient is unable to reach their target HbA1c. Isophane insulin can be injected once or twice daily, according to individual requirements.

We would not advise the use of ultra-long acting insulins for example, Toujeo or Tresiba for new insulin starts.

Twice daily regimen

Human Isophane insulin in combination with short-acting insulin are administered either separately or as pre-mixed (biphasic) human insulin preparation.

Pre-mixed (biphasic) preparations that include a rapid-acting human analogue insulin (rather than short-acting human soluble insulin) are preferable for patients who prefer injecting insulin before a meal and have a regular meal pattern. If their meals are irregular pre-mixed will cause hypoglycaemia and they would be better on a basal bolus regimen.

There are a number of pre-mixed insulin preparations available (See chapter 1 on page 5).

4. A step-by-step guide to starting injectable therapies

This section provides a practical guide to starting insulin, from choosing the most appropriate course of treatment to managing supplies of medication and equipment.

Prepare yourself

Don't jump in with both feet, identify your own barriers:

- time
- skills
- knowledge
- support
- lack of preparation
- keeping up to date.

Check the *Integrated career and competency framework for diabetes nursing* (TREND-UK, 5th edition, 2019) to identify the competences required for starting insulin. Make sure you understand exactly what's involved.

Is this within the scope of your professional practice? If not, seek help and supervision. Spend time with a diabetes specialist nurse and observe some insulin and GLP-1 starts.

We would recommend that relevant e-learning modules on the safe use of insulin and Cambridge Diabetes Education Programme (CDEP) are completed (Diabetes on the Net, 2019; CDEP, 2019).

The Nursing & Midwifery Council (NMC) *Standards for medicines management* (2007) (and underpinning NMC Circulars 16/2008 and 05/2009) were withdrawn on 28 January 2019 because the NMC felt it was not within their remit as a regulator to provide clinical practice guidance on this topic. Therefore we would recommend that you are familiar with guidance from the Royal Pharmaceutical Society (2019) for accurate information on the safe and effective handling, management and administration of medicines.

Areas to discuss with your patient

- Is there a clear need for injectable therapy?
- Does the person fully understand and agree with the need for injectable therapy?
- Do you understand what barriers the person may have?
- Feelings of failure – for example, 'no matter what I do it doesn't improve'.
- Perception that the disease is becoming worse for example, 'My diabetes is bad'.
- Occupational reasons.
- Fear of injecting or painful injections.
- Fear of injecting in public.
- Fear of hypoglycaemia.

- Fear of weight gain.
- Complexity of regimens.
- Restrictions on daily living.
- Pre-conceived ideas.

If they are still reluctant to start an injectable therapy, suggest a three-month trial period; experience shows that very few people want to stop a treatment once they have started but the idea of using it 'for life' can be daunting.

If they refuse outright, you must respect their choice. It may be worth encouraging them to talk to someone who has already started insulin or GLP-1 and is doing well.

Have you done a practice injection? Many people think they will have to use a large needle, and inject into a vein. It's important to allay their fears, and show them how easy and painless injecting can be. They will then be able to concentrate on the rest of the discussion.

Ensure that your documentation includes any refusal/delay for treatment.

Dealing with practice injections

Talk to the person about undertaking a 'practice' injection and reassure that it is not as bad as they expect. Understand that with Type 2 diabetes the person may have preconceived ideas of what injecting is like as a family member or friend may have used insulin in the past.

Ask the person if they would be willing to simply insert a needle for a 'dry run'. It can be reassuring for people to try this soon after diagnosis, long before injectable treatment is actually required.

Note: A practice injection is purely for the patient to feel the insertion of the needle and how to handle an insulin/GLP-1 pen. The saline fluid contained in the pen device should never be injected into the person. The pen device should be disposed of after the demonstration to avoid cross-patient contamination.

First appointment, first injection

As a general guide, you should allow between 30 and 60 minutes for the first appointment. The amount of time you need will depend on the complexity of the chosen regimen and the individual person's capabilities, for example, culture, language, mental capacity, health beliefs.

You will need to cover the following points:

- agree a date and time for the first injection – some may wish to postpone it, for example, until after a holiday, or after Ramadan
- agree a place – injectable therapy starts can take place in an outpatient clinic, on a hospital ward, at a GP surgery, or in the person's home; you can start people individually, or in groups.

- encourage them to bring a partner or friend – two heads are better than one when it comes to remembering what to do when alone at home; most people will manage their injections themselves but some will need support from a partner, carer or district nurse
- discuss whether or not they plan to carry on taking OHA
- practice nurses can provide further support about dietary intake and how carbohydrate can affect the glucose levels. Referral to a diabetes specialist dietitian can be useful to increase that knowledge further with advice on portion control and avoiding large variations on a daily basis to improve glucose levels.

Follow-up appointments

Ideally, the first injection should be near the beginning of the week so the person is fairly confident before the weekend. This is because only emergency cover is available in most areas at weekends. Appropriate support for the person with diabetes will be difficult to find.

Telephone them the day after their first injection, and see them as often as necessary, gradually spacing out the appointments as their confidence grows.

Choosing a delivery device

Injection devices for GLP-1

All GLP-1 therapies are dispensed in disposable devices:

- once and twice daily preparations are in disposable pen devices which contain two to four weeks treatment
- Trulicity once weekly preparation is in a single use pen device
- Ozempic once weekly preparation is in a disposable device that lasts for four injections (one month)
- the once weekly preparation of Exenatide (Bydureon) needs to be reconstituted prior to administration and it is therefore essential that this process is clearly explained to the patient. Demonstration packs are available from the manufacturers to facilitate this process.

Insulin injectable devices

There are two main types of injection devices on the market. Some ‘pens’ come pre-loaded with insulin and are known as ‘pre-filled’ pens. They cannot be re-used once they are empty of insulin and the whole pen is disposed in a sharps bin. Others use cartridges of insulin that are inserted into a re-usable device. Pre-filled injection devices can be easier to use. All cartridge pens are available on prescription. Refer to the most current edition of the BNF or online electronic compendium (EMC).

Give people the chance to try out different devices and involve them in the final decision. You must take into account the person's manual dexterity – how heavy is the pen and how easy it is to push in the insulin or GLP – and the size of dose they are likely to need. Some devices will deliver a bigger maximum dose than others.

If the person is visually impaired, you should also consider:

- whether the pen has an audible click on dialling
- the size of the numbers on the dial
- whether appropriate magnifiers are available.

People with a fear of needles may prefer to use needles such as the auto shield safety needle, where the needle is not exposed during the injection.

Needle length

Trend UK recommend (2018) that needles longer than 4mm can contribute to problems with insulin delivery, leading to glycaemic variations which may contribute to unexplained hypoglycaemia and/or above target HbA1c.

Teaching injection technique

TREND UK Injection Technique (2018) recommends the following steps:

- observe the person assemble the pen, attach the needle, dial the dose, perform a test/air shot and give the injection themselves
- an 'air shot' will make sure the plunger is connecting and expel air from the pen. You may need to guide them – but don't do it for them. Use the product information leaflet which comes with the pen device as a tool to guide the teaching process. And ensure the needle is viable. (Trulicity does not need an 'air shot'. GLP-1s only need priming once)
- if using cloudy insulin, invert or rotate (rock n roll) the pen at least 10 times to mix the insulin
- show the patient how to check expiry dates before administration
- inject into clean skin with clean hands. Alcohol wipes are not recommended. Alcohol is an astringent and can make the injection more painful, as well as hardening the skin
- choose injection sites – to raise a skin fold or not to raise a skin fold? Insulin should be injected into subcutaneous fat, not muscle. To avoid intramuscular injection, slim people, or those using injection sites without much subcutaneous fat should use a lifted skin fold. (FIT, 2016)
- inject the insulin slowly, once the plunger is fully depressed, leave the needle in the skin for 10 seconds (FIT, 2016).

Occasionally, there may be bleeding after the needle is withdrawn. Reassure the person, and advise them to apply gentle pressure for a couple of minutes to minimise bruising. They should not rub the area, as deep massage for several minutes may increase the rate of insulin absorption.

Choosing an injection site

There are a number of alternatives:

- **abdomen** – fastest absorption, usually plenty of subcutaneous fat, making it easy and a good option for fast-acting insulin. Can be the site with the most consistent rate of absorption and it is less affected by physical activity
- **thighs** – slower absorption, best with intermediate acting insulin or the evening dose of a twice-daily insulin regimen; very little subcutaneous fat laterally
- **back of arms** – medium to fast absorption, make sure there is sufficient fat and use short needles
- **buttocks** – slowest absorption, use for intermediate or long-acting insulins; plenty of subcutaneous fat.

The above information applies only to human insulin, the absorption of analogue insulin is not affected by the injection site used (FIT, 2016).

Rotating injection sites

Repeatedly injecting into the same small area will cause lumps (lipohypertrophy) which hinder insulin absorption resulting in unstable blood glucose levels, and can be unsightly. Alternate between the left and right side on a weekly basis, and rotate sites within the same area. Each injection should be at least a finger's breadth away from the last one. Check for lumps on a regular basis. If lipohypertrophy is found, that area should not be used for injection until it has become soft again. This may take weeks or even months, depending on the severity of the lipohypertrophy (FIT 2016).

Injection technique

All GLP-1 analogues are injected into the subcutaneous fat layer in the same way as insulin is administered. See the injection technique section on page 23.

Hypoglycaemic risk

GLP-1 treatment does not induce hypoglycaemia, but when used in combination with sulfonylurea therapy the risk of hypoglycaemia secondary to sulfonylurea treatment will be increased. The essential education (which is covered in section 6 – Stage 1 – on page 31) should therefore be covered for patients commencing GLP-1 therapy in combination with a sulfonylurea.

Side effects

The common side effects of GLP-1 therapy are nausea which should resolve after 7-10 days. If there is vomiting, stop and review treatment with a GP. Side effects can be minimised by starting at the lowest dose recommended and titrating the dose after four weeks and injecting immediately prior to food. Patients using the once weekly preparation of Bydureon may complain of pea size lumps at the site of their injection; these lumps should resolve spontaneously after approximately six weeks.

Insulin doses, storage and checklists

Getting the insulin dose right

In general most doses are calculated on a weight basis using 0.3-0.5 units per kg of body weight. However, once-daily insulin regimens can start with 10 units once a day and twice-daily insulin regimens start with 10-12 units twice daily, depending upon the person's weight. Starting low and giving clear insulin titration guidance over the following months will build the person's confidence and your own.

You should aim for a gradual improvement in blood glucose levels. Sudden normalisation of long-standing high blood glucose can sometimes cause rapid progression of diabetic retinopathy, insulin neuritis or 'pseudo hypos' (hypo symptoms at normal glucose levels).

Storage of insulin

Insulin pens can be kept at room temperature for 28 days and then should be discarded. Spare insulin pens/cartridges should be stored in the fridge.

Insulin mixing

All cloudy insulin needs to be gently mixed prior to administration (gently roll the insulin pen between your hands for around 10 seconds).

5. Adjusting the dose

GLP-1

There are a number of preparations available and the individual formulation and dosing may affect efficacy. Refer to section 3 for types and dosing (page 16).

NICE (2017) recommends that this treatment is only continued if after six months the HbA1c has reduced by 11mmol/mol and a weight loss of 3% is achieved.

Insulin dose adjustment – some basic principles

What can raise blood glucose values?

Illness, emotional stress, inactivity, dietary indiscretion, medications for example, steroids.

What can lower blood glucose values?

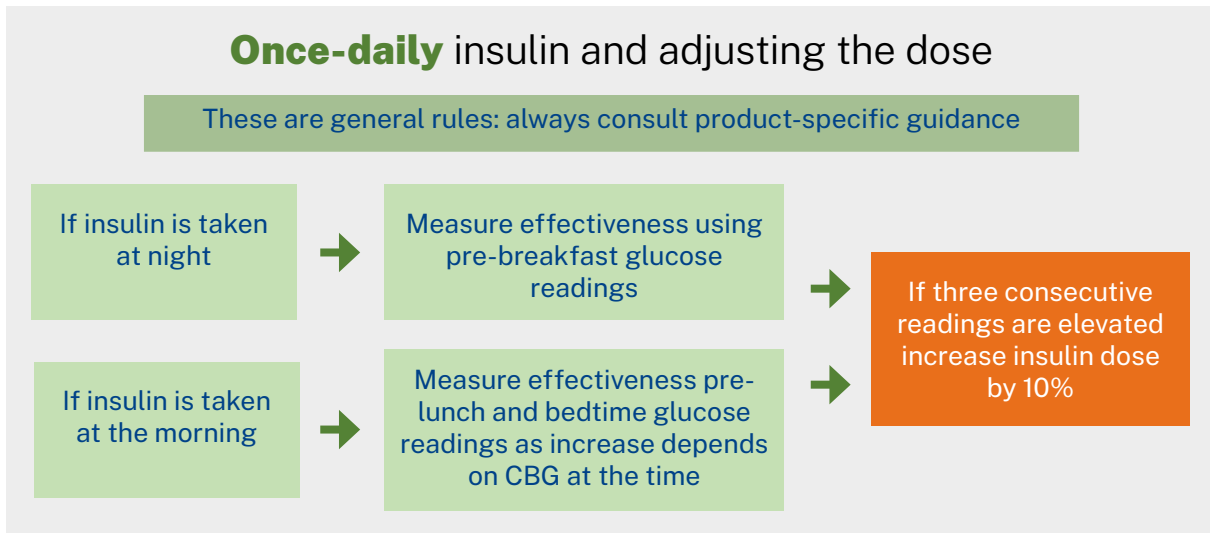
More activity than usual, missed or inadequate carbohydrate, alcohol and illness.

- Individual blood glucose target ranges should be individualised and agreed with the person.
- Don't adjust the dose in response to a single high/low result, look for patterns. Use the person's blood glucose monitoring diary to get the overall picture. The individual columns will show what's happening at different times of the day. You should also check the comments column: is there a connection between blood glucose levels and the person's comments?
- Ask the person what they think of the results, and what action they think is needed. This will help them build up the confidence to adjust their own insulin doses.
- Generally, insulin doses are increased in 10% increments.
- Preventing hypoglycaemia should always take precedence over correcting hyperglycaemia.
- Where hypoglycaemia has been a problem, insulin doses should be reduced by at least 20%.

Adjusting once-daily insulin

- Pre-breakfast (fasting) blood glucose levels give a good indication of the effectiveness of these insulins.
- Intermediate-acting insulins – are usually given on an evening/bedtime and predominately targets blood glucose control overnight.
- Long-acting/Ultra-long insulin – as intermediate but any dose change can take up to three days to reflect in fasting/pre-breakfast glucose results.

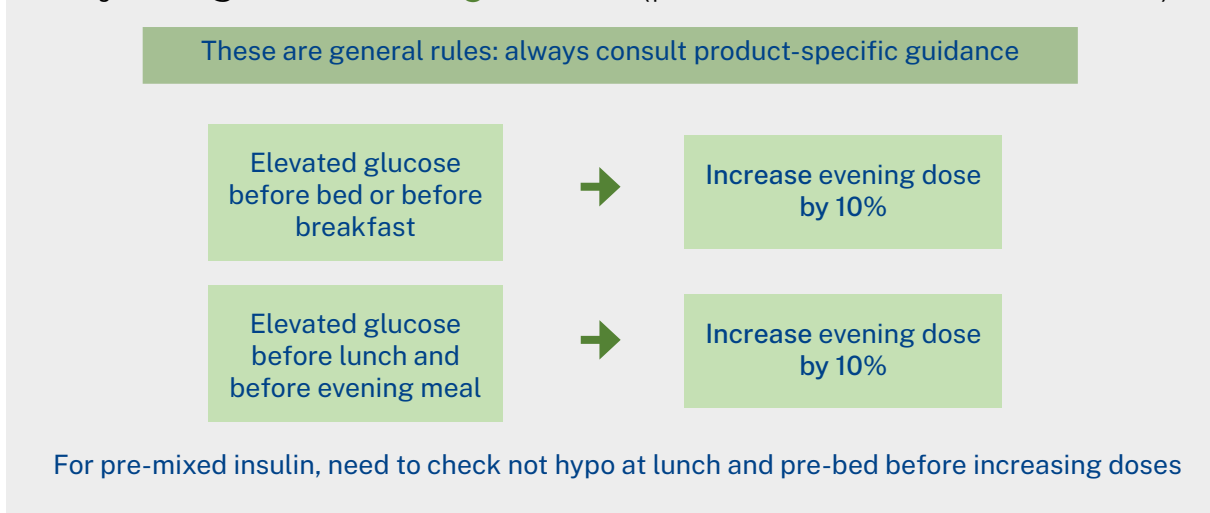
Insulin Adjustment



If Fasting Blood Glucose are within target range but HBA1c is above target range:

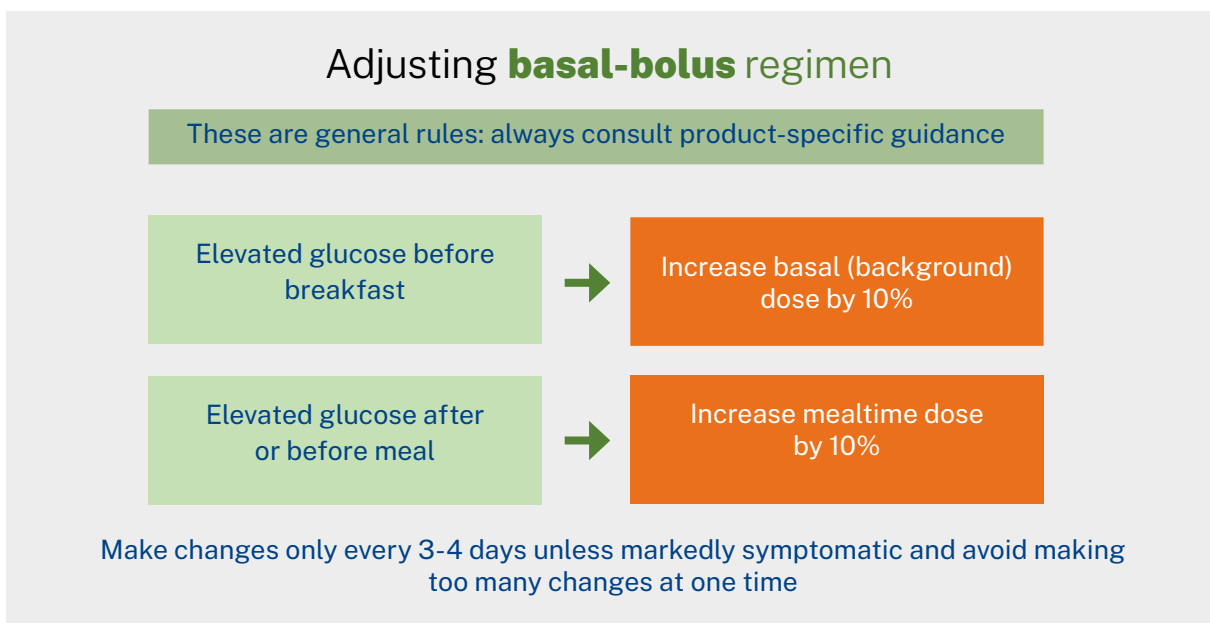
- monitor blood glucose readings before breakfast, lunch, evening meal and supper
- consider changing insulin regimen
- consider adding in additional OHAs or GLP-1 therapy to target insulin resistance
- if these rises cannot be adequately controlled, consider adding rapid insulin to their regimen
- consider referral to Community Diabetes Specialist Nurse, GP and/or dietitian.

Adjusting **twice-daily** insulin (pre-mixed or intermediate)



Adjusting multiple injection therapy (Basal Bolus)

- People who add rapid-acting meal-time insulin to their once-daily insulin regimen can continue their current dose of long-acting insulin, and simply include a dose of rapid-acting insulin before each main meal.
- For those choosing a multiple injection regimen from the start of insulin treatment, try starting with one-third of the daily total insulin dose as long-acting insulin. Divide the remaining two-thirds of the rapid-acting insulin between the three main meals.



No glycaemic effect

- check insulin usage matches the prescribed dose
- check injection technique
- check injection device/insulin storage
- confirm patient has not stopped metformin at time of insulin initiation (if so review)
- consider alternative more aggressive titration regimen (doubled steps)
- review goals and motivation
- consider alternative insulin regimen.

Dose adjustment in practice

This is Mr J's diary. He is taking 22 units of Humulin M3 in the morning and 18 units in the evening. He feels tired. What would you advise?

Mr J's diary

Date	Breakfast	Lunch	Evening meal	Bed	Comment
May 1	12.4		14.3		
2	14.6	14.3			
3			11.7		
4				15.7	
5	13.0				
6		15.1			

Suggested advice: Increase both insulin doses by 10% and review weekly.

Mrs R has been on insulin for 18 years. She takes 64 units of Humulin M3 in the morning and 48 units in the evening.

She is feeling poorly and thinks it might be her diabetes. What advice would you give her?

Mrs R's diary

Date	Breakfast	Lunch	Evening meal	Bed	Comment
Jan 11	12.9				
12					
13					
14					
15	13.8				
16					
17				7.1	
18					

Suggested advice: increase the number of tests to get a clearer picture of Mrs R's blood glucose profile. She may need to see her GP in the meantime if she continues to feel unwell.

Jane has lost weight recently and started taking regular exercise. She takes 40 units of Humulin M3 in the morning and 36 units in the evening. Would you change anything?

Jane's chart

Date	Breakfast	Lunch	Evening meal	Bed	Comment
May 7	4.4				
8		3.3	14.6		Hypo lunch
9			7.1		
10				4.7	
11	3.2				
12		4.1			
13			4.3		
14				8.2	
15	4.0				
16		4.9			
17			hypo		
18				3.7	
19	5.1				

Suggested advice: reduce both doses by 20%. Jane is currently likely to be feeling tired and possibly worried about hypos. Her diabetes control is too tight. You should reiterate the principles of hypo prevention and management. In the light of recent changes to her lifestyle, Jane may also want to consider a different insulin regimen.

6. Essential education

Most people starting injectable therapy should be aiming for self-management. Understanding their condition and taking responsibility for their own treatment helps people maintain their independence. It also minimises the impact of their condition on their everyday life and equips them to deal with any problems or complications that may arise. Effective education is therefore essential.

There is a lot of information for the person to remember and retain. It is best to break down essential education into five manageable stages:

Stage 1	Preparing patients for starting injectable therapy.
Stage 2	On the day of starting injectable therapy.
Stage 3	Topics that need to be covered at the next appointment and within the first few weeks of starting injectable therapy.
Stage 4	Topics to be covered once the person is feeling more confident.
Stage 5	Ongoing annual review 'checklist'.

The subjects to be covered at each stage are outlined below. If you feel you are not qualified to teach any of these topics, ask your local diabetes specialist team for advice or consider referring your patient on.

Stage 1 – preparing patients for starting injectable therapy

- **Type/action/side effects** of injectable therapy to gain consent and patient engagement.
- **Doses and timing** – written instruction including name of injectable treatment, dose and timing/s. Including any changes to other oral medication that may be required (see section 5 on page 26).
- **Injection technique**, including rotating sites and disposing of sharps (see section 4 on page 20).
- **Blood glucose monitoring** – timing and frequency of tests and interpreting the results. Insulin dietary advice – avoid missing meals.
- **GLP-1 dietary advice** – appetite will get smaller; so, prepare patient for leaving food on the plate and not finishing the meal, eat more slowly allowing for signs of satiety (fullness in stomach) to become stronger. If feeling nauseous; rice cakes, flat diet lemonade, ginger tea can help.
- **Exercise** – insulin will be absorbed faster by an exercising muscle. Advise the person not to inject into their arm if they're about to do the ironing, or into the thigh if planning to walk the dog or go shopping.
- **Driving** – it is the person's responsibility to inform the DVLA and their car insurance company if they start insulin treatment. If they are starting a GLP-1 they do not need to

inform the DVLA. Use the TREND UK leaflet; *Diabetes: safe Driving* (TREND UK 2019b).

Stage 2 – on the day of starting injectable therapy

As above plus:

- **insulin passport/ID** – give the person an insulin ID card/passport showing which insulin they are being treated with. All insulin manufacturers have credit card size ID for each insulin that is commercially available. Please contact your local representative. You can also issue the leaflet *The safe use of insulin and you* (NHS England, 2017)
- **follow up and contact numbers** – arrange a further appointment and provide both a routine contact and a helpline run by the insulin or GLP 1 manufacturer
- **insulin storage** – insulins have varying shelf life at room temperature; refer to Summary of Medical Product Characteristics. Refrigerated stock will last until expiry date
- **GLP-1 storage** – each can be stored at a temperature less than 30⁰ Celsius for between 2-6 weeks. But please refer to relevant manufacturer’s instructions. Refrigerated stock will last until expiry date
- **cold insulin** may take longer to absorb, and cause stinging. Give the insulin at least 30 minutes at room temperature before injecting
- **injecting through clothing** – is not advised. In addition, with the use of shorter needles, injecting through clothes may result in a subdermal rather than a subcutaneous injection. Injecting through the clothes affects the lubrication of the needle and makes it difficult to check for bleeding.

Manufacturers recommend that needles should be used once only. People with diabetes should be informed that after use:

- the needle will no longer be sterile
- insulin may block the needle
- the needle may be blunt or damaged – and that damaged needles can bend or break
- extremes of temperature can cause insulin to leak from the needle if it is not removed from the pen; this could change the relative concentrations of short or intermediate-acting insulin in a mixture
- that air may enter the device through the needle, which can lower the dose
- the possibility of hypoglycaemia – signs and symptoms, treatment and prevention (see below) if starting insulin or if the GLP-1 is in combination with with sulfonylurea tablets. Please refer to section 9 on page 40)
- local arrangements for sharps disposal.

Stage 3 – the first few weeks

- **Stage 1 revision:** revise and check that the information you covered in Stage 1 is still being used by the patient and they have retained that knowledge.
- **Invite questions and queries.**
- **Check confidence levels and how they are feeling about injecting.** Shared decision making and increasing person involvement in decision making will increase patient adherence and concordance with their medication regimen (NICE Pathways 2019).
- **Ask about hypos** – if they've had a hypo, try to work out how it could have been prevented, and what they can do differently in the future. How did they treat the hypo? If they haven't had any hypos, check they have remembered how what to do and what they have bought as preparation.
- **Blood glucose monitoring** – interpreting the results with the person will enable further education on how the injectable treatment is working for them. Use the person's own experiences to demonstrate the effects of food, exercise and treatment on blood glucose levels. Adjusting the dose (see section 5 on page 26) – discuss blood glucose levels and teach dose titration.

Food and alcohol

Alcohol – explain that alcohol increases the risk of delayed hypoglycaemia, and that they should therefore eat while drinking alcohol. Extra insulin is not required to cover this food.

Insulin treatment - carbohydrates – will need to be assessed on an individual basis in accordance with which injectable therapy is being taken. Broadly regular portions and intake of long-acting carbohydrates will help stabilise blood glucose levels. Patients may need to be reminded which food is in this group, as well as differences in portion sizes will give irregular glucose results and make dose adjustments difficult.

Eating out – advise the person on adjusting doses or altering the timing of their injections for special occasions.

GLP-1 advice – reassure the person that their appetite will reduce and to go for smaller portions. They should also take their time in eating their meal. Satiety (feeling full) may well be a new or stronger feeling that the person with diabetes must to learn to adjust to. Advice to stop eating if they feel full is encouraged as overeating may cause vomiting.

Sick day rules – discuss how illness can affect the blood glucose levels and usually makes them rise. Advise on checking blood glucose levels at least four times daily (at mealtimes even if they are not eating and at bedtime) and if they find they are constantly higher than usual provide them with your local guidelines for urgent contact details.

GLP-1 and acute abdominal pain develops – advise that the injections should stop immediately, and the person should seek urgent medical attention.

GLP-1 and vomiting – patients should stop this medication until they have recovered. Medication should only be re-commenced following review.

Insulin – advise that the dose may well need to increase

All adjustments are incremental and should be reduced gradually as the illness subsides. If blood glucose levels are dropping down to 4mmol/L or less, reduce the insulin dose by 10% (for example, if your dose is usually 20 units, reduce by 2 units, if it is usually 40 units, reduce by 4 units).

For oral diabetes medications

Advise the patient to continue to take their oral medications even if they are not eating.

However:

- if they are taking Metformin or an SGLT2 inhibitor and have vomiting or have diarrhoea, they should stop this medication temporarily until they have recovered
- if they take a sulfonylurea; this should be continued. The dose may need to be increased.

Meal replacements:

- Fruit juice 100 ml
- Milk 200 ml
- Plain vanilla ice-cream 1 large scoop
- Tomato soup 200 gram (half a large tin)
- Low fat yoghurt 150 gram (1 small pot)
- Two rich tea or malted milk biscuits
- 100–150mls water or sugar free fluid hourly.

For further information please use TREND UK (2018) patient information leaflet *Type 2 Diabetes: What to do when you are ill*.

Stage 4 – Further topics to be covered once the person is feeling more confident and ready to take on more information

Religious and cultural considerations

Although people with diabetes are exempt from religious fasts, some will prefer to observe them. Ultimately, it is a personal choice whether to fast. Depending on the time of year for Ramadan the fasts can be 10–21 hours long, lasting for 29–30 days. People who are fasting all day and eating in the evening will need specific advice on how to manage their insulin therapy during this time as long fasts put them at higher risk of hypoglycaemia and dehydration. Preparation should be encouraged before Ramadan with an appointment to make sure that they are able to look after themselves properly. Failing to do so is contrary to the Qur'an, which clearly states that you must not act in a way that harms your body. Although if they are in any doubt, they should discuss this with their Imam.

Ramadan: Main points to consider and discuss with the patient in preparation (Diabetes UK, 2017)

Insulin: requirements will be less insulin before the start of the fast	
Rapid acting insulin needs to be omitted during fasting	Such as Humalog, Novorapid, Apidra, Fiasp
Pre-mixed insulin is not recommended during fasting e.g. Novomix 30, Humalog Mix 25	Consider a medium/long acting insulin instead such as Levemir
GLP-1s: once weekly, once daily, there isn't any need for change dosing	Twice daily is not recommended such as Byetta
Before starting the fast, patients should include more slowly absorbed food (low GI), such as basmati rice and dhal, in their meal, along with fruit and vegetables	
Blood glucose levels should be checked more often	
When the fast is broken recommend only small quantities of food, and avoid only eating sweet or fatty foods	
Recommend trying to eat just before sunrise, when the next day's fast is commenced	
At the end of each fasting day drink plenty of sugar-free and decaffeinated fluids to avoid being dehydrated	

Stage 5 – ongoing annual review

- Contraception and pregnancy, where appropriate.
- Progression of the condition – people with Type 2 diabetes can expect a slow decline in glycaemic control over time and will therefore need to keep reviewing their treatment regimen.
- Have the injection sites been checked for signs of lipohypertrophy?
- Is the correct injection technique being used?

Identifying the causes of hypoglycaemia

- Medication, and are they taking it as prescribed? Does their sulfonylurea dose need reducing or stopping?
- Did the person take their insulin at the appropriate time?
- Are they missing meals?
- Are they changing the quality/quantity of food they eat – for example, in order to lose weight – without changing their insulin dose or in response to the GLP-1 impact on their appetite?
- Are hypos occurring on particular days of the week, for example, at weekends?
- Was alcohol a contributory factor?
- Was exercise a contributory factor?
- Was the hypo related to pre- or post-menstrual changes in blood glucose levels?
- Is the person taking a hot bath or shower before their insulin injection? If using pre-mixed or intermediate insulin, are they mixing it properly by rolling the pen 10 times in the palm of the hands and inverting it at least 10 times?

Supporting and assessing concordance

People with diabetes do not always take their medicines exactly as prescribed and healthcare professionals are often unaware of how patients take their medicines. The purpose of assessing adherence is not to monitor patients but rather to find out whether patients need more information and support.

Recognise that non-concordance is common and that most people are non-concordant sometimes. Routinely assess concordance in a non-judgemental way whenever you prescribe, dispense and review medicines.

Consider assessing non-concordance by asking the person if they have missed any doses of medicine recently. Make it easier for them to report non-concordance by:

- asking the question in a way that does not apportion blame
- explaining why you are asking the question
- mentioning a specific time period such as ‘in the past week’
- asking about medicine-taking behaviours such as reducing the dose, stopping and starting medicines
- consider using records of prescription re-ordering, pharmacy patient medication records and return of unused medicines to identify potential non-concordance and people needing additional support.

Interventions to increase concordance

People with diabetes may need support to help them make the most effective use of their medicines. This support may take the form of further information and discussion, or involve practical changes to the type of medicine or the regimen. Any interventions to support adherence should be considered on a case-by-case basis and should address the concerns and needs of individual patients.

Find out what form of support the person would prefer to increase their adherence to medicines. Together, you can consider options for support.

Be aware that although concordance can be improved, no specific intervention can be recommended for all people. Tailor any intervention to increase adherence to the specific difficulties with adherence the patient is experiencing.

If a person is not taking their medicines, discuss with them whether this is because of beliefs and concerns or problems about the medicines (intentional non-adherence) or because of practical problems (unintentional non-adherence). Address any beliefs and concerns that patients have that result in reduced adherence.

NICE (2019) suggests interventions that might include:

- suggesting that the person records their medication-taking
- encouraging them to monitor their condition
- simplifying the dosing regimen.

Side effects can be a problem for some people. If this is the case you should:

- discuss the benefits, side effects and long-term effects with the patient to allow them to make an informed choice
- consider adjusting the dosage
- consider switching to another medicine with a different risk of side effects
- consider what other strategies might be used (for example, timing of medicines).

Also refer to *Diabetes & Emotional Health: A practical guide for healthcare professionals supporting adults with Type 1 and Type 2 diabetes* (Diabetes UK, 2019).

7. Case studies

Case study 1: Mr W

Mr W has been living with Type 2 diabetes over 10 years. He was referred by his GP for insulin initiation. The referral stated that Mr W “has a strong aversion to starting insulin”.

Mr W was tired and taking little exercise. His diet needed improvement. His HbA1c was 124mmol/mol, and the results of his home glucose blood tests were consistently between 17 and 28mmol/l. He was on maximum tolerated doses of Metformin, Gliclazide and Sitagliptin.

Mr W said that he dreaded starting insulin. The nurse discussed his concerns, fears and perceptions before discussing insulin initiation. The nurse showed him different insulin devices and demonstrated how to administer an insulin injection. Mr W was encouraged to do a ‘dry’ injection. Mr W was amazed – not only did it not hurt, but he could hardly feel it at all.

Mr W only consented to start a mix of long/intermediate acting insulin and also mealtime insulin in combination with Metformin and Gliclazide. Sitagliptin was discontinued.

Case study 2: Miss R

Miss R, 66, has had Type 2 diabetes for six years. Her BMI is 30. She has Coronary Heart Disease and renal failure. Her HbA1c is 69mmol/mol and eGFR is 45mL/min. She takes 160mg of Gliclazide twice daily, Metformin 1g daily. Miss R eats two main meals (breakfast and dinner). Her blood glucose levels are between 9-11mmol/l before breakfast and 10-12mmol/l before evening meal before starting SGLT-2 (Dapagliflozin 10mg once a day) treatment.

After discussion, Miss R chose to administer Liraglutide (Victoza) 0.6mg once per day for a week and then increased this to 1.2mg daily thereafter. Her blood glucose levels have improved. Her weight has reduced by 3kg since she had started SGLT-2 (Dapagliflozin 10mg once a day), three months ago. She has also attended a diabetes structured education programme and has reduced her daily carbohydrate intake. She has had no ‘hypos’ and her HbA1c is 52mmol/mol.

8. Other problems that may occur

Needle phobia

BD Auto Shield Duo™ and the Novofine Autocover™ safety needles are suitable for patients who do not want to see the needles. They can be used with any pen device and are available on prescription in accordance with local guidance. Also refer to *Diabetes & Emotional Health: A practical guide for healthcare professionals supporting adults with Type 1 and Type 2 diabetes* (Diabetes UK, 2019).

Insulin allergy

Occasionally people may have a localised allergic reaction to injected insulin. The usual cause is sensitivity to a particular preservative. Different insulin manufacturers use different preservatives, so the problem can usually be solved by switching products. Ask your local specialist team for advice.

Insulin neuritis

‘You told me insulin would make me feel better, but the pains in my legs are unbearable. I feel worse than before.’

Rapid improvement of glycaemic control following the initiation of insulin can trigger acute symptomatic neuropathy. Usually this will only be a temporary problem and will resolve with time of improved glycaemic control.

Altered vision

Changes in blood glucose can lead to altered vision. Again, this should only be temporary. You should advise people against changing their glasses until their blood glucose levels have settled down.

Steroid-induced hyperglycaemia

Insulin doses will usually need to be significantly increased during steroid treatment. Likewise, to avoid hypoglycaemia when steroid treatment is discontinued insulin doses should be reduced. Refer to TREND leaflet *Type 2 diabetes & Steroid tablets* (TREND-UK, 2019c)

9. Management of hypoglycaemia

The symptoms of hypoglycaemia

Hypoglycaemia is the main potential side effect of insulin therapy or a GLP-1 in combination with a sulfonylurea and it is essential that the person starting insulin and if necessary, their carer, know what symptoms to expect, how to reduce the risks of hypos and how to treat them.

Hypoglycaemia occurs when blood glucose levels fall below 4mmol/l.

Symptoms can vary between individuals, but early signs and symptoms may include:

- sweating, becoming pale, feeling anxious, trembling and shaking, palpitations, irritability, hunger and tingling lips.

If the early signs are missed or not recognised, then the symptoms can worsen and include:

- poor concentration, poor co-ordination, slurred speech, confusion, aggressive behaviour, double vision, weak legs, drowsiness and loss of consciousness and seizures.

Verbal information is not enough

Providing verbal information is not enough. Ask the person to repeat key facts and instructions back to you to check their understanding. Re-enforce the message and allow the patient to read written material in their own time. Understanding hypoglycaemia and knowing how to deal with it is essential to the patient's safety. You will need to check and repeat the information at future appointments. Please also re-enforce verbal communication with the leaflet for patients: *Why do I sometimes feel shaky, dizzy, and sweaty?* (TREND UK, 2018).

Treating hypoglycaemia

Treat mild hypoglycaemia with:

- 15-20g of fast-acting carbohydrate; for example, five gluco-tabs, six dextrose tablets, 200ml (small carton) of fresh orange juice or fizzy drink (not the diet version), 4 jelly babies.

One of those treatments should cause the blood glucose level to rise rapidly. The person should be advised to wait ten minutes for this to happen, wash their hands (as have handled sugary products and subsequent results would be falsely high) and check their glucose level. If still below 4mmol/l repeat with the treatment again.

Advise the person with diabetes, when they feel better they should follow up with some longer-acting carbohydrate – for example, a sandwich, two plain biscuits, banana or a meal containing carbohydrate such as bread, potatoes or pasta (if it is due).

Treatment Cautions with all Lucozade[®] & Ribena[®] products. They now contain approximately 50% less glucose. All flavours have significantly less glucose-based carbohydrates and mean that much more is needed than previously advised. Health care professionals and their patients need to check the nutritional information label located on the back of the pack to ensure that the correct volume is used to treat a hypo as much more is now needed because the sugar concentration is so much less.

LUCOZADE ENERGY IS CHANGING

Lucozade Energy's formula is changing from April 2017. This applies to all flavours.

Check nutritional label for information.





NUTRITIONAL INFORMATION

Typical values	100ml	380ml
Energy kJ/kcal	158/37	600/141
Carbohydrate, g	8.9	33.8
of which sugars, g	4.5	17.1
salt, g	0.08	0.31

Contains negligible amounts of - Fat, saturates and Protein.

Contains 8.9g glucose based carbohydrate per 100ml and 33.8g per 380ml bottle.

Reference in take of an average adult (8400KL/2000kcal)

Please note that Ribena (Squash and Ready to Drink) and Orangina will also be reducing in sugar during 2017. Please check nutritional label for information.

LUCOZADE ENERGY and the Arc Device are a registered trade mark of Lucozade Ribena Suntory LTD

All new Ribena Blackcurrant will now contain sugars naturally occurring from the juice, a reduced level of added sugar (sucrose), and the sweeteners Acesulfame K and Sucralose.

Current product label			New product label		
NUTRITION INFORMATION			NUTRITION INFORMATION		
Typical values after dilution 1 part with 4 parts water			Typical values after dilution 1 part with 4 parts water		
	100ml	250ml		100ml	250ml
Energy, kJ/kcal	183/43	458/108	Energy, kJ/kcal	89/21	223/53
Carbohydrate, g	11	27	Carbohydrate, g	4.7	11.9
of which sugars, g	10	26	of which sugars, g	4.6	11.5
Salt, g		0.01	Salt, g	<0.06	0.15

Ribena Blackcurrant Ready to Drink will also change from 10g sugars per 100ml to 4.6g sugars per 100ml.

Chocolate is not recommended because of its high fat content which slows down the absorption of the glucose contained in it; leading to symptoms lasting longer and over treatment. All new Ribena Blackcurrant will now contain sugars naturally occurring from the juice, a reduced level of added sugar (sucrose), and the sweeteners Acesulfame K and Sucralose.

10. Holidays and travel

Main points for both insulin and GLP-1s

Air travel should not pose significant problems for people using injectable treatments to control their diabetes. Pre-planning is important and discussion of the travel itinerary, four to six weeks in advance, with the relevant health professional/GP/treating specialist team is recommended.

Travel letter and ID

When travelling with injectable treatments people must take with them supporting documentation from a relevant qualified medical professional for airport security to advise that they have diabetes and need to carry injectable treatments with them, including needles and monitoring kit with them in their hand luggage. Medications of this type packed into the hold baggage will be exposed to very low temperatures, which will degrade the insulin, in addition there is also the potential that luggage may be lost en-route. It is also useful if the patient takes a recent prescription with them as well. (An example letter can be found in appendix 1 on page 47).

What should they pack?

It is essential that they carry adequate equipment (glucose meters, lancets, batteries). Diabetes UK (2019b) recommends that twice the quantity of medical supplies normally used should be packed.

The Civil Aviation Authority (2019) states that: “Passengers may carry essential liquid medicines such as insulin for the period of their trip. These are permitted in larger quantities above the 100ml limit for liquids but will be subject to authentication. Passengers must have obtained the prior agreement of the airline with which they are travelling and with their departure airport.”

It is useful to have simple carbohydrates to treat hypoglycaemia including glucose tablets or sweets. It may also be useful to pack longer lasting carbohydrates such as snack bars or biscuits in case of delayed meals. Advise to carry some extra snacks in case of delays or airline meal inadequate/not liked. Advise against ordering ‘diabetic’ meals, which often don’t have enough carbohydrate.

What should they do on board?

Cabin crew may request medication be handed over for storage during the flight. Keep diabetes medication and equipment in the same bag to avoid anything being mislaid or lost.

There is anecdotal evidence to suggest that blood glucose meters can underestimate glucose whilst flying (meaning that the actual glucose will be higher than the glucose meter is displaying). The person should test as appropriate but if symptoms of hypoglycaemia are present then the person should be advised to just treat the hypo. If they over treated, then a short period of slightly high glucose levels will not cause harm.

Avoid excess caffeine and alcohol as these can affect diabetes control including your warning of hypoglycaemia.

Time zones and insulin

In general, if the time zone change is less than four hours, major changes will not be needed to injections. For long haul destinations where time zones may become an issue, advise on an appointment to discuss the person's travel plans in detail. It is important to prepare and discuss this. The patient will need to bring the details of their itinerary including flight details of both outwards and return journeys, including departure times, the length of the flight, stopovers and the local time of arrival.

General guidance points

- **If travelling North or South:** there is no need to change the timing of the insulin or other medications.
- **If travelling East to West:** the day is lengthened and will mean extra meal/s are eaten and therefore will need to cover with extra insulin (such as Humalog, Novo rapid). Injections taken further apart than usual are unlikely to cause problems. A short period of slightly high glucose levels will not cause harm.
- **If travelling West to East:** the day is shortened, and the amount of insulin and carbohydrate will need to be reduced. Injections taken too close together could lead to hypoglycaemia.
- **Twice daily regimens:** a greatly lengthened day may mean a small amount of rapid acting insulin with a meal is needed between the two main injections. A shortened day may mean a reduction in pre-flight insulin.
- **Rapid acting and long-acting regimens:** rapid-acting injections during the day, followed by a medium or long-acting injection in the evening gives a great deal of flexibility over the timing of injections and meal times, it can be easily adapted to time zone travel. The normal sleep cycle is broken by time zone travel. As a result, the medium or long-acting insulin is being taken more than once in every 24 hours and cause hypoglycaemia. It may be a more suitable option to leave out the medium or long-acting injection entirely and rely on rapid-acting injections before meals until back on a 24-hour clock in the country of arrival.

Other general points

Hot weather destinations

- Blood glucose levels can be affected by hot weather. In very hot climates, it is best to store insulin and GLP-1s in a fridge in their room or in a cool bag (providing it does not freeze). A variety of cool bags and storage containers are available, some have cooling gel activated by cold water for example, Frio®. If using a cool bag that uses plastic ice blocks, make sure that the insulin does not come into contact with the frozen plastic containers. If glucose levels are a lot higher consider whether the insulin could have been damaged by the heat.
- In hot countries, the biggest health threat is the sun, so advise patients to keep covered. Wear long sleeves, loose trousers, a wide-brimmed hat and sunglasses with a UV400 label. For areas of the body left exposed, including the backs of hands and feet, a high factor sunscreen of 30+ is recommended.
- Foot care: advise on taking particular care; especially if they have neuropathy. Walking bare foot on hot sand or pavements will be dangerous as they won't be aware their skin is burning. Advise on protection from the sun with socks or sunscreen and wear good-fitting sandals on the beach.
- Long periods of sunbathing on the beach can affect diabetes control, making blood glucose levels higher than normal.
- On the flipside, insulin will be absorbed more quickly from the injection site in hot weather and this increases the risk of hypos. Increased monitoring is recommended and making adjustments to their diet or insulin dose accordingly.
- Extremes of temperature can also affect the accuracy of the glucose meter – consider whether the meter could have been damaged by the heat.

Cold climates

- In cold weather, insulin is absorbed more slowly at first, but can then be absorbed suddenly when warmed up later in the day for example after ski-ing. This could cause a hypo as the body uses up more energy staying warm, eg, by shivering.
- Hypos are more dangerous in cold conditions - they interfere with the body's attempts to stay warm and increase the risk of hypothermia - so guarding against them is really important. As with hot climates, the glucose meter may not be accurate in cold conditions.
- If patients have poor circulation or neuropathy, it's particularly important to prevent frostbite as they won't feel the cold.
- It is recommended that the person with diabetes applies for the free UK Global Health Insurance Card (UK GHIC) or the European Health Insurance Card (EHIC) if travelling to the European Union, see here for information and application details: nhs.uk/using-the-nhs/healthcare-abroad/apply-for-a-free-uk-global-health-insurance-card-ghic/. It will ensure that the person living with diabetes has easy access to healthcare in that country.

- People with diabetes should buy travel insurance. Even if they hold the GHIC or EHIC, it's still advisable to buy travel insurance, as the card doesn't cover, for example, emergency repatriation, and not all countries give the level of cover of the NHS. The RCN travel health pages have further information [rcn.org.uk/clinical-topics/Public-health/Travel-health](https://www.rcn.org.uk/clinical-topics/Public-health/Travel-health)
- Find out where you can get supplies of insulin at the destination, in case of emergency. Advise that the name of the insulin may also be different in another country. Insulin manufacturers can be contacted before the trip to check the name and where to obtain supplies: Eli Lilly & Company, tel: 01256 315000, Novo Nordisk Ltd, tel: 0845 6005055, Sanofi-Aventis, tel: 01483 505515, Wockhardt Ltd, tel: 01978 661261

Food poisoning

Hot climates pose a greater risk of food poisoning, especially in countries where levels of sanitation are not as high as you're used to. Food cooked hot to order is the safest option – be wary of anything that may have been left standing or reheated. Watching where local people eat, or asking for recommendations, is a good way of finding the most reputable eating places.

Any concerns about the safety of the local tap water, stick to bottled or sterilised. Remember to also avoid ice in drinks, salads that may have been washed in tap water and fruit that can't be peeled.

Dealing with illness while abroad

Revise and advise sick day rules as in section 6 (page 31). Further information can be sought from the tourist office, embassy or high commission of the country they're visiting about getting medical treatment while they are there. Please advise the traveller that they should check their insurance policy, so they know what their insurers will pay for (Diabetes, 2019b).

11. Conclusion

As you will now understand this topic is wide and varied. Therefore, this guideline has sought to signpost the reader to leading expert advice and guidance in the multiple areas that surround using injectable treatments. Throughout this guide, we have encouraged readers to seek specialist advice at every opportunity, in order to ensure the highest possible standards of patient care, and for the reader to develop their own knowledge and competence.

People with diabetes should also be encouraged to take responsibility for their own care as far as possible. A good understanding of their own condition and how to treat it increases the chances of effective control of blood glucose levels, which will minimise the risk of complications. Educating people with diabetes, their carers, partners and families is therefore a vitally important part of the nurse's role.

We hope that reference to this booklet – in conjunction with local guidance and input from diabetes specialists – will lead to increased knowledge and expertise for both nurses and the people you treat for improved health and wellbeing for people with Type 2 diabetes requiring insulin treatment.

Appendix 1: Example of a travel letter

Mr XXXXX
Flat 47
XXXXX Road
London
XX20 8XX

Corporate LOGO
Corporate address
Telephone Number:
Email address:

date

Private and confidential

TO WHOM IT MAY CONCERN regarding XXXX XXXXX
DOB: XX/XX/XXXX
NHS number: XXX XXX XXXX

This is to confirm and certify that XXXX XXXXX has insulin treated diabetes/diabetes that requires treatment with injections.

Therefore, they must carry injectable treatment/insulin, pen needles, glucose monitor, finger pricker needles and other medical supplies with them in their hand luggage.

It must NOT be put in the hold of an aircraft with other main luggage as the insulin will become inactive in such low temperatures at altitude.

Please do not hesitate to contact me if you require any further information.

Yours sincerely,

Florence Nightingale
Super Nurse
XXXXX Diabetes Services

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