

Insulin Therapy in Type 2 Diabetes

Introduction

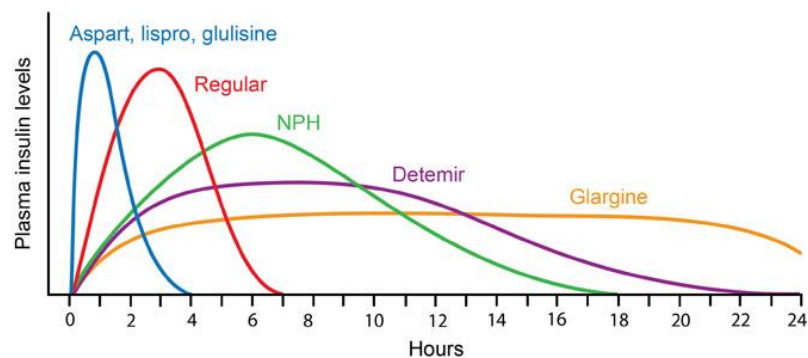
There are many different types of insulin (see Appendix H: Insulins), falling in to four main categories: rapid-, short-, intermediate- and long-acting. Extremely rapid-acting insulins are about to be marketed.

Rapid-acting analogue insulins (eg, Insulin lispro – Humalog®, NovoRapid®) are convenient because they can be administered with or even after food, with less need for snacks, better control of post-prandial glucose levels and less risk of hypoglycaemia.

Short-acting, non-analogue insulins (eg Actrapid®, Humulin® S) target post-prandial blood glucose rises, but some have to be given 2-30 mins before a meal and greater need for snacks and risk of hypoglycaemia.

Intermediate-acting insulins (eg Humulin® I, and Human Insulatard®) are given twice daily to target basal hyperglycaemia. Slower to reach a peak and longer-lasting.

Pharmacokinetic profiles of common insulin preparations

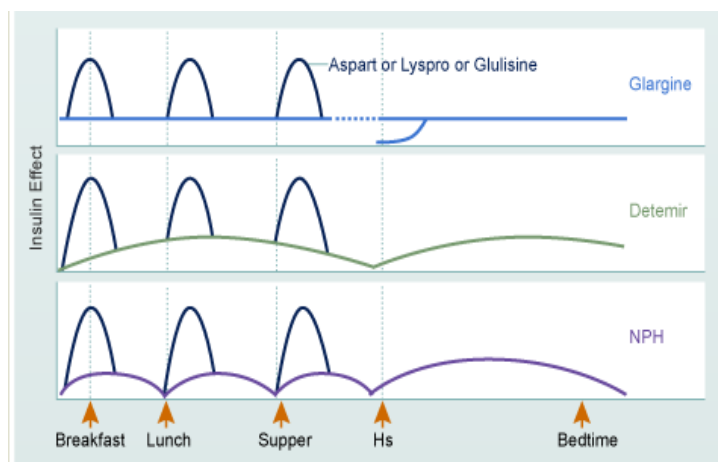


Long-acting insulin analogues and biosimilar (eg Insulin glargine – Abasaglar®, Lantus®, Toujeo®. Insulin detemir - Levemir® and insulin degludec -Tresiba®). More predictable and less risk of weight gain and hypoglycaemia. Can be given alone or in combination with rapid-acting analogues at mealtimes.

Mixtures (eg NovoMix® 30, Humalog® Mix 25 and 50, Humulin® M3). Combinations of short- and intermediate-acting insulin in ratio suggested by the number (eg NovoMix 30 = 30% short- and 70% intermediate acting insulin, the commonest ratio). Particularly effective in those with high HbA1c and lower BMI

Insulin regimens

Usual practice, if good diabetes control is not being achieved with oral therapy alone, is to add in an intermediate-acting, non-analogue insulin, usually in the evening, generally continuing metformin, but reviewing other drugs. As the regimen intensifies, rapid-acting analogue insulin is added prior to the main meal and then before the other meals. Pre-mixed (biphasic) preparations containing short-acting analogues, rather than human insulin, are alternatives if



the person prefers to inject immediately before eating, if hypoglycaemia is a problem or there is significant post-prandial hyperglycaemia. Some people also cope better with a simpler insulin regimen.

It almost goes without saying that insulin therapy should be initiated by a practitioner with the appropriate knowledge, competencies and experience to choose the most appropriate starting regime tailored to each patient.

Which basal insulin?

Abasaglar®, a biosimilar insulin which is identical to insulin glargine in its structure and properties, is significantly less expensive than other basal insulins. Alternatives are Lantus®, Levemir®, Toujeo® and Tresiba®. **Note:** Toujeo® is U300 strength and Tresiba® is available in both U100 and U200 strengths.

Insulin formulations

Most insulin in the UK is available in the U100 strength (100 units of insulin/ml). However, more concentrated insulins are now available that reduce the volume that patients taking a high dose of insulin must inject and, in some cases, prolong its effect. The National Patient Safety Agency (NPSA) advises that the word 'strength' should always be used when prescribing more concentrated insulin (eg *U200 **strength** Tresiba® insulin*).

Toujeo® insulin

U300 strength preparation of insulin glargine. Given via the Toujeo SolStar® pen with which the correct dose can be dialled up in units, but in a third of the volume of U100 strength Lantus® insulin. Each click of the pen delivers 1 unit and the maximum single dose is 80 units. When transferring from other intermediate- or long-acting insulins it is advisable to reduce the total dose by 20% and, when starting insulin-naïve patients, use an initial dose of 0.2 units per kg.

Tresiba® insulin

Insulin degludec (Tresiba®) is available in the traditional U100 strength insulin for people on smaller doses (up to 80 units) in a cartridge and a Flex Touch pen device. It also comes as a U200 strength insulin preparation in an insulin Flex Touch pen only. This device can be used to dial up to 160 units. Care must be taken because the packaging of the two strengths is very similar. Each click of the U200 strength pen device represents two units of insulin.

Other more concentrated insulin preparations

Insulin lispro (Humalog®) is available in two strengths, U100 and U200. U500 strength insulin (ie Humulin® R – five times stronger than U100 strength insulin) is sometimes used in people who are insulin-resistant and require larger doses of insulin (usually greater than 200-300 units daily). It must be obtained on a named patient basis and is not licensed in the UK. It is rarely used in Barnsley because of funding issues and concerns over safety.

WARNING

NEVER draw up insulin from from an insulin cartridge or pre-filled pen using a syringe.

Use of GLP1 analogues in combination with insulin

- Lixisenatide, liraglutide, exenatide and dulaglutide are all licensed for addition to patients currently receiving insulin.
- Patients being considered for this combination must fulfil the following criteria;
 - Significantly overweight (BMI >35 kg/m²) **and**
 - HbA1c > 75mmol/mol (9%) **and**
 - Currently using insulin
- Xultophy® (insulin degludec 100 units/ml + liraglutide 3.6 mg/ml) is a combined preparation. Start patients on tablets alone on 10 dose-steps daily and those

transferring from a basal insulin on 16 dose-steps daily, increasing to a maximum of 50 dose-steps daily in each case. The dose of any sulfonylurea should be reduced.

- These regimens must be initiated by a specialist, with on-going support from a consultant-led multi-disciplinary team.
- **Continue the GLP1 in combination with insulin only if the person has a reduction in HbA1c of ≥ 11 mmol/mol (1.0 %) ¹ and a 3% loss of initial bodyweight in 6 months.**

SGLT-2i plus insulin

NICE recommends that an SGLT-2i in combination with insulin with or without other anti-diabetic drugs is an option.

Insulin delivery devices

- Offer education to a person who requires insulin about using an injection device (usually a pen injector and cartridge or a disposable pen) that they and/or their carer find easy to use.
- Appropriate local arrangements should be in place for the disposal of sharps.
- Only insulin detemir (Levemir®) and Insulatard® can be used with the Innolet® device.
- If a person has a manual or visual disability and requires insulin, offer a device or adaptation that:
 - takes into account his or her individual needs
 - he or she can use successfully.

Insulin Passport

All patients prescribed insulin should carry an insulin passport. The insulin passport was introduced by the National Patient Safety Agency in 2011 to improve patient safety by empowering patients as they take an active role in their treatment with insulin.

(<http://www.nrls.npsa.nhs.uk/resources/?EntryId45=130397>)

A patient-held record (the Insulin Passport) documents the patient's current insulin products and enables a safety check for prescribing, dispensing and administration. The Insulin Passport complements existing systems for ensuring key information is accessed across healthcare sectors.

Prescribers are reminded to issue an insulin passport to patients currently prescribed insulin. In Primary Care insulin passports should be ordered through the Primary Care Support England Portal <http://pcse.england.nhs.uk/supplies/>

Registration to the portal is required to generate an order. Please note a "cost to the NHS" for each item is stated, however the practice do not have to pay anything. The cost information is simply there to remind people not to over order.

¹ A 0.5% difference in HbA1c is equivalent to a difference of about 5.5mmol/mol, and a 1% difference is equivalent to a difference of about 11mmol/mol. Note that these are rounded equivalents.

Summary of Insulin on Barnsley Joint Formulary

Insulin	Strength	Traffic light status
Rapid-acting insulin analogues		
Humalog® (Insulin lispro)	100u/ml	Green
	200u/ml	Green
Novorapid® (Insulin aspart)	100u/ml	Green
Short-acting non-analogue insulins		
Actrapid® (Insulin human)	100u/ml	Green
Humulin® S (Insulin human)	100u/ml	Green
Intermediate-acting insulins		
Humulin® I (Isophane. Human)	100u/ml	Green
Insulatard® (Isophane. Human)	100u/ml	Green
Long acting insulin analogues and biosimilar		
Abasaglar® (Insulin glargine. Biosimilar)	100u/ml	Green
Lantus® (Insulin glargine)	100u/ml	Green
Levemir® (Insulin detemir)	100u/ml	Green
Toujeo® (Insulin glargine)	300u/ml	Amber G
Tresiba® (Insulin degludec)	100u/ml	Amber G
	200u/ml	Amber G
Biphasic Insulins		
Novomix® 30 (Biphasic insulin aspart)	100u/ml	Green
Humalog® Mix25 (Biphasic insulin lispro)	100u/ml	Green
Humalog® Mix50 (Biphasic Insulin lispro)	100u/ml	Green
Humulin® M3 (Biphasic isophane insulin)	100u/ml	Green