Type 2 Diabetes Insulin Titration Guidelines
For Primary Care

Scope and Purpose

These guidelines are intended for primary care clinicians to facilitate the management of patients with Type 2 diabetes who are already established on insulin therapy, where the target HbA1c has not been met, or where self-measured capillary glucose is persistently outside of the target parameters for the individual. Please see below for guidance on individualised HbA1C targets and target fasting blood glucose levels.

Before adjusting therapy consider the following principals:

- **Are you confident** in adjusting Insulin doses? If unsure, ask a colleague with confidence in undertaking insulin dose adjustments
- **Is the patient unwell?** Consider infections, ketoacidosis, hyperosmolar states, sudden unexpected changes in insulin requirements e.g.: weight loss, abdominal pain, jaundice (consider pancreatic causes). **Remember foot infections need prompt referral**. Consider other drugs too e.g., metformin and SGLT2-i -see Sick day rules
- **Consider hypoglycaemia** including loss of awareness, especially night-time. This needs to be screened for and documented and where appropriate dose adjustments made
- **Injection technique**- does the patient rotate injection sites and could there be variable absorption of insulin e.g.: lipohypertrophy?
- **Patient factors**- any changes of diet, exercise, alcohol, self-neglect or mental health problems or medication e.g.: steroids?
- **Do not** adjust Insulin dose on a single glucose measurement, consider at least 72 hours' worth of readings, or preferably 1-2 weeks of readings. Check when the readings are being taken. **Remember: hypoglycaemia may be a risk even with an elevated Hba1c**
- Encourage lifestyle, weight loss and exercise at every opportunity where appropriate including NHS digital weight management or Low calorie diet replacement
- **Encourage patients to self-titrate** their insulin where appropriate
- **Check compliance** with injectable and oral medication
- Regularly check DVLA requirements. Check that the patient monitors capillary glucose within a 2-hr window prior to driving & ensures blood glucose is "5 to drive". Check patient has adequate awareness of hypoglycaemia for driving safely.
- Discuss any plans for pregnancy in women of childbearing age and refer for specialist preconception support if considering pregnancy (NICE advice here).

Useful weblinks and documents are available here:

- Assessment of ketoacidosis
- Examples of injection site rotation
- HbA1c targets
- Treatment of hypoglycaemia
- DVLA Guidelines on insulin
- Problematic hypos including Gold score
- Sick day rules
- Overview | Type 2 diabetes in adults: management | Guidance | NICE

This guideline is NOT suitable for the following:

- **Pregnant women (should be under the care of specialist teams)- see NICE preconception and pregnancy**
- **People with frequent unexplained hypos particularly needing help from third party and/or unexplained nocturnal hypos- seek specialist advice**
- **People with CKD 4/5 or patients on dialysis**
- **People on >1unit/kg body weight total daily dose insulin or basal bolus regimes**

The authors cannot accept responsibility for unexpected or idiosyncratic reactions to insulin dosing. This is a general guide only. If in doubt use the safest dose of insulin, avoiding extremes of glucose levels whilst specialist advice is sought

Insulin Dose Adjustment

Ascertain whether the patient is on a long/ intermediate acting basal insulin regime or a mixed insulin regime, then use the appropriate sheet to help you advise regarding insulin dose adjustments. Click on the links in the table.

Types of insulin and their mode of action can be found here

Type of insulin	Common clinical indication	Clinician advice sheet
Once daily intermediate acting taken in the evening e.g.**Humulin I, Insuman Basal or Insulatard**	A common initial regimen for patients with type 2 diabetes	Regime 1 Click here
Once daily intermediate acting taken in the morning e.g.: **Humulin I, Insuman Basal or Insulatard**	Useful for patients on steroids, requiring community nursing support or overnight hypos with evening intermediate insulin	Regime 2 Click here
Twice daily intermediate acting insulin e.g.: **Humulin I, Insuman Basal or Insulatard**	Used when glucose levels are above target at points when once daily intermediate insulin gives insufficient control	Regime 3 Click here
Once daily long-acting insulin analogues e.g.: **Abasaglar, Lantus, Levemir, Semglee**	Usual second line insulin if issues with overnight hypoglycaemia on once daily intermediate acting insulin or as an alternative to twice daily intermediate insulin	Regime 4 Click here
Once daily 'ultra-long' acting analogue e.g.: **Toujeo u300, Tresiba u100 or u200**	Confers flexibility with timing of dose (see SPC). Higher concentration insulin is also useful for patients on high doses of basal insulin	Regime 5 Click here
TWICE daily mixed insulin e.g.: **Humulin M3, Novomix 30, Humalog Mix 25, Humalog Mix 50, Insuman Comb 25 or Comb 50**	May be utilised in patients with consistent meals and a regular lifestyle who require some fast-acting insulin	Regime 6 Click here

Information leaflets to support patients with insulin dose adjustments are available here: Diabetes Care for You (sussexcommunity.nhs.uk)

Regime 1: ONCE daily 'intermediate acting' insulin
Taken in the EVENING (before evening meal or bed)

Humulin I or Insulatard or Insuman Basal

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before breakfast for at least 3 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked intermittently i.e. at least twice weekly before other main meals and before bed, to help judge overall daily glucose levels

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before breakfast, increase the current dose of insulin by **10% every 3 days** (5-7 days if eGFR<30) until blood glucose levels **are 5-7mmol/l before breakfast** (and no lower than 4mmol/l at any other time)**. Use individual targets if moderate or severe frailty-** *guide here*
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing & consider dose decrease

DECREASE DOSE

- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a 'one off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by 10% every 24 hours – until hypos stop.
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the insulin dose has been titrated up to 1 unit per kg bodyweight and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Regime 2: ONCE daily 'intermediate acting' insulin
Taken in the **MORNING** (before breakfast)

Humulin I or Insulatard or Insuman Basal

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before evening meal for at least 3 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked intermittently i.e. at least twice weekly before other main meals and before bed, to help judge overall daily glucose levels

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before evening meal, increase the current dose of insulin by **10% every 3 days** (5-7 days if eGFR<30) until blood glucose levels **are 5-7mmol/l before evening meal** (and no lower than 4mmol/l at any other time). **Use individual targets if moderate or severe frailty** - *guide here*
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing & consider dose decrease

DECREASE DOSE

- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a 'one off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by 10% every 24 hours – until hypos stop.
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the insulin dose has been titrated up to 1 unit per kilogram bodyweight and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Regime 3: TWICE daily 'intermediate acting' insulin
Taken before breakfast and before evening meal

Humulin I or Insulatard or Insuman Basal

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before breakfast and evening meal for at least 3 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked intermittently i.e. at least twice weekly before other main meals and before bed, to help judge overall daily glucose levels

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before breakfast, increase the evening dose of insulin by **10% every 3 days** (5-7 days if eGFR<30) until blood glucose levels **are 5-7mmol/l before breakfast and no lower than this at bedtime**
- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before evening meal, increase the morning dose of insulin by **10% every 3 days** until blood glucose levels **are 5-7mmol/l before evening meal (and no lower than 4mmol/l at lunch time)**
- Use individualised targets if moderate or severe frailty- ***guide here***
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing & consider dose decrease.

DECREASE DOSE

- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a 'one off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by 10% every 24 hours – until hypos stop.
- If hypos occur during the **day** up to evening meal reduce the **morning** dose of insulin. If hypos occur **after evening meal or overnight** reduce the **evening** dose
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the total daily insulin dose has been titrated up to 1 unit per kg bodyweight in a single dose and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team

Regime 4: ONCE daily long acting analogue insulin
Taken at any point of the day – as long as the same time each day (usually morning or evening)

Abasaglar, Lantus, Levemir, Semglee

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before breakfast for at least 3 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked intermittently i.e. at least twice weekly before other main meals and before bed, to help judge overall daily glucose levels

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before breakfast, increase the current dose of insulin by **10% every 3 days** (5-7 days if eGFR<30) until blood glucose levels **are 5-7mmol/l before breakfast** (and no lower than 4mmol/l at any other time). **Use individual targets if moderate or severe frailty**- *guide here*
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing & consider dose decrease.

DECREASE DOSE

- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a 'one off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by 10% every 24 hours – until hypos stop.
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team if available.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the insulin dose has been titrated up to 1 unit per kilogram bodyweight and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Regime 5: ONCE daily 'ultra-long-acting analogue'.
Taken at any point of the day (usually morning or evening) at approximately the same time each day

Toujeo u300 strength. Tresiba u100 or u200 strength

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before breakfast for 3-5 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked intermittently i.e. at least twice weekly before other main meals and before bed, to help judge overall daily glucose levels

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before breakfast, increase the current dose of insulin by **10% every 5 days** (**7 days if eGFR<30mL/min**) until blood glucose levels **are 5-7mmol/l before breakfast** and no lower than 4 mmol/l at any other time.
- **Use individual targets if moderate or severe frailty**- *guide here*
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing & consider dose decrease.

DECREASE DOSE

- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a one 'off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by **20% every 48 hours** – until hypos stop.
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team if available.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the insulin dose has been titrated up to 1 unit per kilogram bodyweight and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Regime 6: TWICE daily mixed insulin.
Taken before breakfast and before evening meal

Humulin M3, Novomix 30, Humalog Mix 25, Humalog Mix 50, Insuman Comb 25 or Comb 50

Monitor blood glucose levels

- **Do not** adjust insulin dose on a single glucose measurement
- Monitor blood glucose before breakfast and evening meal for at least 3 days (preferably 1-2 weeks) before making adjustments
- Blood glucose levels should also be checked **regularly i.e. at least 3 times a week** before lunch & before bed to help judge the effect of the 'fast' acting portion of the mixed insulin - & that glucose is not dropping at these times

Remember to look at frailty targets before adjustment

Adjust Dose

INCREASE DOSE

- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before bed and before breakfast, increase the evening dose of insulin by **10% every 3 days** (5 days if eGFR<30) until blood glucose levels **are 5-7mmol/l before breakfast** (and no lower than this before bed)
- If blood glucose levels are consistently **higher than 7mmol/l** (or individually agreed target) before lunch and evening meal, increase the morning dose of insulin by **10% every 3** days (5 days if eGFR<30) until blood glucose levels are **5-7mmol/l before evening meal** (and no lower than 4mmol/l before lunch)
- Use individualised targets if moderate or severe frailty- *guide here*
- When the target glucose is reached, you can stop increasing
- IMPORTANT: if the patient has any levels below 4mmol/l (hypoglycaemia – 'hypos') during these stages of insulin increase, then stop increasing and consider dose decrease.

DECREASE DOSE

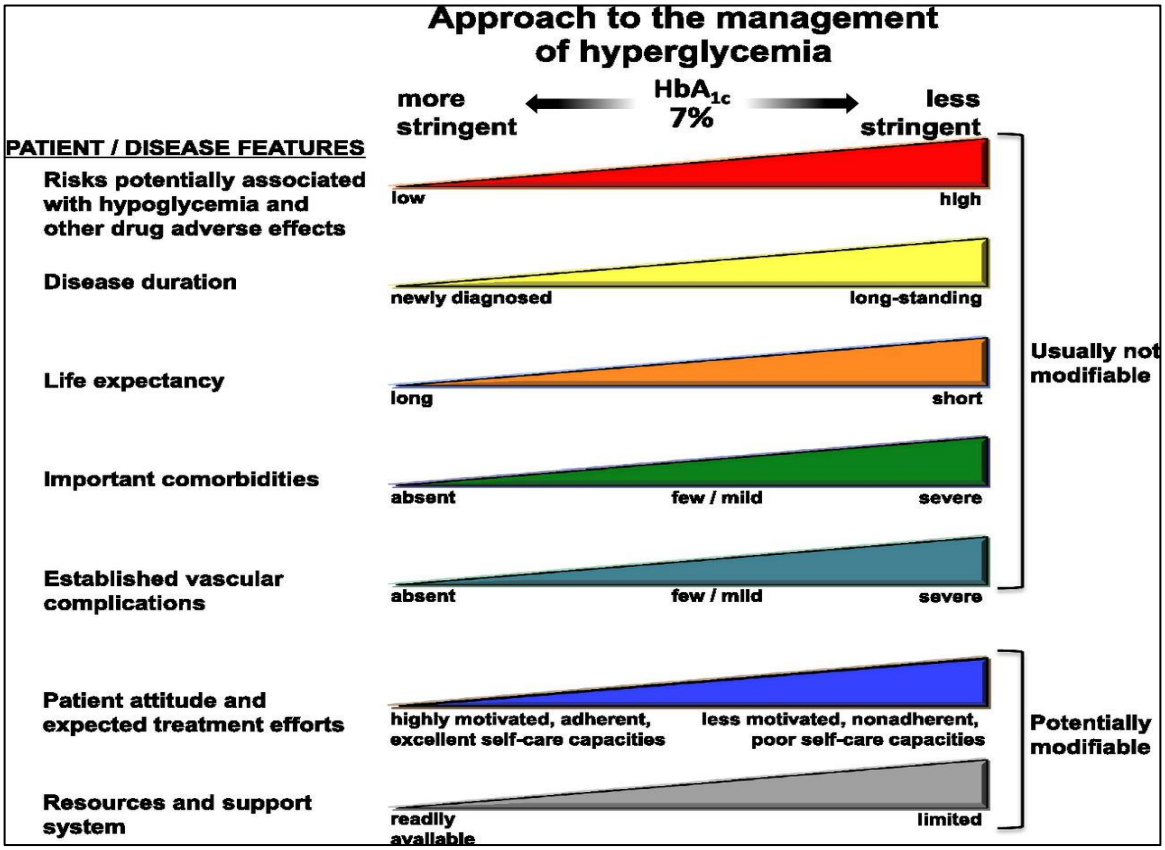
- If blood glucose levels are lower than 4mmol/l (hypoglycaemia), you need to treat the low glucose (see 'How to treat a hypo' page).
- Be aware of possibility of night-time hypos and severe hypos- may need specialist assessment
- Remember hypos may be caused by a change in food or activity levels - as well as by having too much insulin or glucose lowering medicine.
- If a 'one off' low glucose level occurs, monitor glucose levels and review after 3 days.
- If the blood glucose levels below 4mmol/l continue, reduce the insulin dose by 10% every 24 hours – until hypos stop.
- If hypos occur during the day up to evening meal reduce the morning dose of insulin. If hypos occur after evening meal or overnight reduce the evening dose
- If low glucose levels continue, please discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team if available.

Check HbA1c 3 months after stable insulin dose and 6 monthly thereafter. If above target, consider further adjustments or alteration in regimen

If you have any other concerns whilst increasing insulin or if the total daily insulin dose has been titrated up to 1 unit per kilogram bodyweight and the patient is still not to target - discuss with a colleague, GPwSI, diabetes specialist pharmacist or local specialist diabetes team.

Guidance on setting HbA1c targets (Haemoglobin A1c)

Factors to consider when setting an HbA1c target between the clinician and patient
The diagram below is a depiction of the elements of decision making used to determine appropriate efforts to achieve glycaemic targets. Greater concerns about a particular domain are represented by increasing height of the ramp. Thus characteristics /predicaments towards the left justify more stringent efforts to lower HbA1c, whereas those towards the right are compatible with less stringent efforts. Where possible such decisions should be made in conjunction with the patient, reflecting his or her preferences, needs and values.



This “scale” is not designed to be applied rigidly but to be used as a broad construct to help guide clinical judgement.

Targets
When setting a target HbA1c level, NICE recommends to:

- Involve patients with type 2 diabetes in the decision regarding individual HbA1c targets. Encourage them to achieve and maintain their targets unless any resulting adverse effects or their efforts to achieve their target impair their quality of life. Record the target HbA1c in the patient’s record and care plan.
- Consider relaxing target HbA1c level on a case-by-case basis, with particular consideration for patients who are older or frail.
- Inform a person with a higher HbA1c that any reduction in HbA1c towards the agreed target is advantageous to future health.
- If adults achieve a HbA1c level below target and if you are certain that the patient is not experiencing hypoglycaemia, encourage them to maintain it.
- Avoid pursuing highly intensive management to levels below 42mmol/mol (6.0%).

Patient decision aids can help adults with type 2 diabetes think about their options for controlling their blood glucose to try to reduce the long-term risks of diabetes. NICE have published a NICE patient decision aid which can be found under Tools and resources | Type 2 diabetes in adults: management | Guidance | NICE

Individualised care

Adopt an individualised approach to diabetes care that is tailored to the needs and circumstances of adults with type 2 diabetes, taking into account their personal preferences. An example of individualised treatment options is to consider the ABCD approach-

- **A**ge – less stringent HbA1c targets with decreasing life expectancy.
- **B**ody weight. Be aware of which drugs affect body weight – weight neutral – metformin and DPP4i (gliptins), weight gain – insulins, pioglitazone, sulphonylureas, weight loss – SGLT I and GLP1 RAs.
- **C**omplications – co-incident complications will impact drug selection e.g. patient with eGFR< 30ml/min/1.73m2 should avoid metformin.
- **D**uration – disease duration is a consideration when setting HbA1c levels. The shorter the disease duration the greater the cardiovascular protection offered by strict glycaemic control. Once disease duration is 10-12 years the beneficial effects of strict glycaemic control may be lost or reversed.

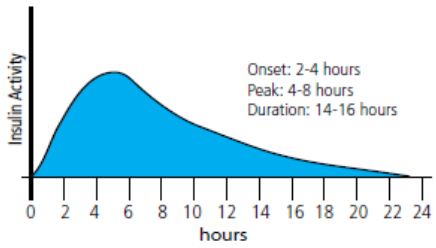
Reassess the person's needs and circumstances at each review and consider discontinuing any medicines that are not effective- for example, those agents that have failed to achieve expected HbA1c targets at 3-6 months.

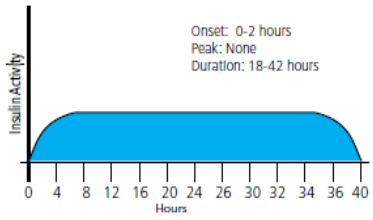
The table below is based on targets suggested by the American Diabetes Association and the American Geriatrics Society, the 2021 statement on type 2 diabetes and frailty and QoF

Health status	Treatment goals	Recommended Interventions	Target HbA1c (adapted from ADA)	QOF Target threshold	Suggested fasting capillary glucose range as guide- adapt depending on co-morbidities
Healthy or mild frailty • Life expectancy >10 years • Functional and independent	• Maintain functional status, independence and QOL • Prevent or delay macro/microvascular complications	• Tight glycaemic control • Resistance exercise and nutritional intervention • Statins where tolerated	≤58 mmol/mol	≤58 mmol/mol	5-7mmol/l
Moderate Frailty • Several co-morbidities (>2) • Limited functional ability, reduced life expectancy • Mild to moderate cognitive impairment	• Limit progression of microvascular complications • Avoid metabolic emergencies such as hypos	• Glycaemic control • Assess and reduce cognitive decline • Statins where tolerated	≤64 mmol/mol Review sulphonylureas and insulin. Avoid hypoglycaemia	≤75 mmol/mol	6-10mmol/l
Severe Frailty • End-stage chronic disease • In long-term care/ limited functional ability • Moderate to severe cognitive impairment • Markedly reduced life expectancy	• Improved QOL by reducing symptoms or hospitalisations • Maintain functional status, prevent lower limb dysfunction	• Less aggressive glycaemic control but be aware that hyperglycaemia can increase infections, thirst and dehydration • Consider stopping statin	≤70 mmol/mol Review sulphonylureas and insulin. Avoid hypoglycaemia	≤75 mmol/mol	7-12mmol/l
End of life and palliative care	• Symptom control avoid metabolic emergencies	• De-escalate treatment where appropriate to reduce medication burden	No Target Avoid symptomatic hyperglycaemia. De-escalate treatment	No target	Avoid hypos, low threshold for stopping insulin unless very symptomatic osmotic symptoms from raised glucose

A useful resource on diabetes management in end-of-life care can be found here

Actions of insulins
Intermediate and long acting

Intermediate-acting insulin action e.g. NPH, Insulatard, Humulin I, Insuman Basal		
	*Background insulin- normally given before breakfast/before bed or both* Intermediate-acting insulin usually starts working within 2-4 hours after injection, peaks somewhere between 4 and 8 hours and remains working for approximately 16 hours. Occasionally this insulin is given twice daily. NPH insulin should be considered **first line** for type 2 diabetes. Consider starting both NPH and rapid-acting insulin (particularly if the person's HbA1c is 75 mmol/mol [9.0%] or higher), administered either separately **or** as a pre-mixed (biphasic) human insulin preparation. This insulin is cloudy and requires re-suspending before use.	
Insulatard- (first line) Vial, cartridge, prefilled InnoLet 	Humulin I- (first line) Vial, cartridge, prefilled pen 	Insuman Basal Vial, cartridge, prefilled pen 

Long-acting Insulin Action e.g. Lantus, Levemir, Tresiba, Toujeo, Semglee			
	*Background insulin- normally given before breakfast/before bed or both* This type of insulin starts working within 2 hours and provides a continuous level of insulin activity for up to 18-42 hours depending on the product. Long acing insulins may be considered as an alternative to NPH if: the person needs assistance to inject insulin, and use of an analogue would reduce the frequency of injections from twice to once daily; **or** the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes; **or** the person would otherwise need twice daily NPH insulin injections in combination with oral glucose lowering drugs. This insulin is clear.		
Insulin glargine (Lantus) Vial, cartridge, prefilled pen 	Insulin detemir (Levemir) Cartridge, prefilled pen 	Insulin degludec (Tresiba)- Cartridge, prefilled pen *Note only higher strength 200units/mL is formulary*  Action can for up to 42hrs *Caution- higher strength; always check the strength*	Insulin glargine (Toujeo) Prefilled pen *Note 300units/mL*  *High dose insulin, be sure to choose correct insulin when prescribing*

Premixed Insulins

Consider transferring to twice daily pre-mixed insulin (depending on competency in primary care) if:

- The person prefers to inject immediately before a meal
- Blood glucose levels rise markedly after meals

The particular choice of which pre-mixed insulin is used may be influenced by:

- Choice of insulin injection device
- Perceived convenience for individuals
- Potential for weight gain and risk of hypoglycaemia

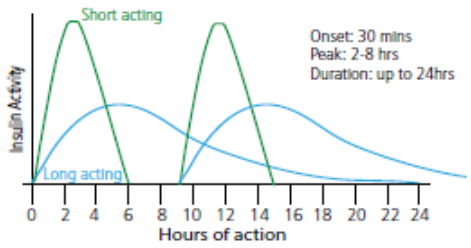
Advantages:

- Relatively easy to teach and simple for the patient to understand
- Has potential for better postprandial glucose control
- Is more effective in lowering HbA1c than basal alone

Disadvantages:

- Less flexibility (unable to adjust the short or basal component of insulin independently)
- Patients may not achieve optimal glycaemic control
- Time delay of injection with conventional mixture

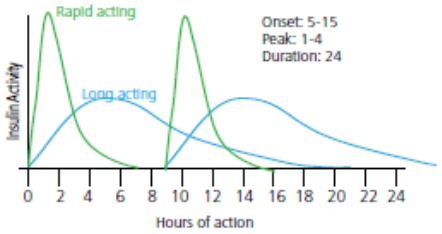
Pre-Mixed Human Insulins- Humulin M3, Insuman Comb 25, Comb 50



Mealtime and background insulin- normally given 30 minutes before breakfast and evening meal
Conventional short-acting and isophane insulin.

This insulin is cloudy and requires re-suspending before use.

Pre-Mixed analogues- NovoMix 30, Humalog Mix 25, Humalog Mix 50

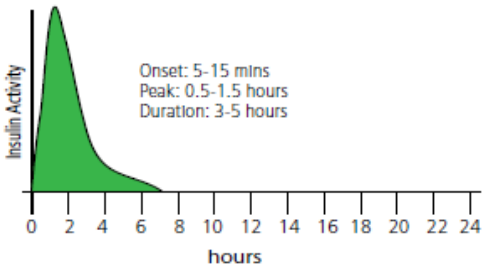


Mealtime and background insulin- normally given with breakfast and evening meal (can be three times a day)
These preparations are available with a percentage of rapid/fast-acting insulin which may have advantages in terms of patient convenience (no need to wait before eating) and control of post-meal glucose. However, use is limited for those patients who have regular and consistent diets.

This insulin is cloudy and requires re-suspending before use.

NovoMix 30	Humalog Mix 25	Humalog Mix 50
Cartridge, prefilled pen	Cartridge, prefilled pen	Cartridge, prefilled pen
		
30% rapid-acting insulin	25% rapid-acting insulin *Caution- administration errors*	50% rapid-acting insulin *Caution- administration errors*

Some patients with Type 2 diabetes will have short acting 'bolus' insulins. These are included here for reference

<table>
<tr><td colspan="3">Rapid-acting insulins e.g. NovoRapid, Humalog, Apidra</td></tr>
<tr><td> 
</td><td colspan="2">Mealtime insulin- normally given with meals
Rapid-acting insulin begins working in the body within 5-15 minutes. This type of insulin should be taken 15-20 minutes before eating. It peaks between 30 and 90 minutes and its duration of action is typically between 3 and 5 hours. Doses may need reducing 1 hour before planned exercise and subsequent doses reduced within a 24hr period.

This insulin is clear.</td></tr>
<tr><td>Insulin aspart- Novorapid
Vial, cartridge, prefilled pen
 
Insulin aspart with additional excipients enabing faster onset of action
Fiasp- take with meals (ultra-rapid acting)</td><td>Insulin lispro- Humalog 200 units/ml
Vial, cartridge, prefilled pen
 
</td><td>Insulin gluisine- Apidra
Vial, cartridge, prefilled pen
 
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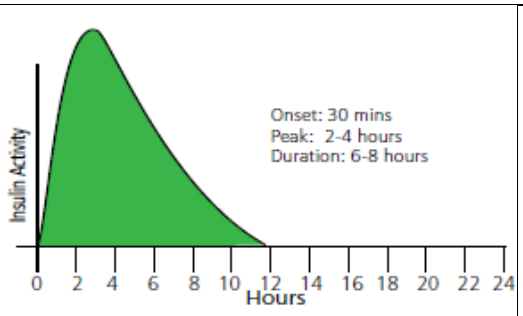
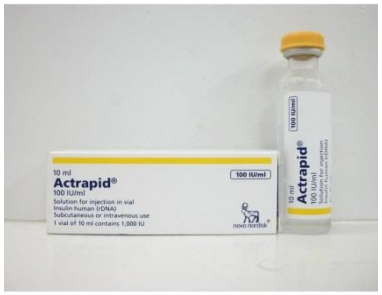
</table>

<table>
<tr><td colspan="3">Short-acting insulin e.g. Soluble Human Insulin: Actrapid, Humulin S, Insuman Rapid</td></tr>
<tr><td> 
</td><td colspan="2">Mealtime insulin- normally given 30 minutes before meals
Short-acting insulin begins working in the body between 30 and 60 minutes after injection. It peaks between 2 and 4 hours, and its duration is typically 6-8 hours. Short-acting insulin may need to be injected several times during the day. Patients may be at risk of hypos late in the morning or early hours of the night (e.g. 2am) depending on the timing of the dose.

This insulin is clear.</td></tr>
<tr><td>Actrapid
Vial
 
</td><td>Humulin S
Vial, cartridge
 
</td><td>Insuman Rapid
cartridge, prefilled pen
 
</td></tr>
</table>

Biosimilar insulins

Biosimilar insulin is a biological copy of an original insulin and there is increasing interest in developing and using them. Biosimilar insulins are cheaper than original products, so they present the NHS with opportunities around availability and cost of care

Biosimilar insulin by definition must have no clinically meaningful differences from the originator medicine in terms of quality, safety and efficacy.

Are biosimilars really the same?

The characteristics of biological medicines cannot be reproduced exactly; there will be an inherent degree of variability among biological medicines, and minor differences can occur from batch to batch. Despite this minor variability, strict controls are in place to ensure that the differences fall within the acceptable range and do not affect safety or efficacy. However, with regards to insulin, automatic switching from the reference medicine to a biosimilar medication is not recommended without clinical indication.

Some examples

Trade name	Drug name	Characteristics
Abasaglar 100 units/ml Semglee 100 units/ml	Insulin glargine	Long-acting analogue insulin
Insulin Lispro Sanofi 100 units/ml	Insulin lispro	Rapid-acting insulin analogue
Trurapi 100units/ml	Insulin aspart	Rapid-acting insulin analogue

Appendix 1: Table detailing authorship, contributors and reviewers of the guideline

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