

Insulin Masterclass: Initiation and adjustment, CGM interpretation

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Disclaimer/disclosure



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- Lilly
- Novo Nordisk
- Sanofi
- Viatris

Content

- When and how to initiate
- Case studies: CGM and insulin adjustment



There are currently 27 different insulin preparations



Insulins and types

- Short or quick acting
- Premixed
- Intermediate or long acting
- Animal, Human, Analogue or Biosimilar

C,O

Keep It Simple Summary

	Quick/Fast	Mixed	Intermediate	Long	
	Also referred to as prandial or bolus insulin	Also referred to as Biphasic insulin (a mixture of quick/fast and intermediate insulin)	Also referred to as NPH (neutral protamine Hagedorn) background or basal insulin	Also referred to as background or basal insulin	
Human	Humulin [®] S Actrapid [®]	Humulin [®] M3	Humulin [®] I Insulatard [®]		
Analogue	Humalog [®] U100 Humalog [®] U200 NovoRapid [®] Apidra [®] Fiasp [®] Lyumjev U100 [®] Lyumjev U200 [®] Admelog [®] Trurapi [®]	Humalog [®] Mix25 Humalog [®] Mix50 NovoMix [®] 30		Lantus [®] Abasaglar [®] Semglee [®] Levemir[®] Tresiba [®] U100 Tresiba [®] U200 Toujeo [®]	
Animal	Hypurin [®] Porcine Neutral	Hypurin [®] Porcine 30/70	Hypurin [®] Porcine Isophane		

Insulin discontinuations from Novo Nordisk

Medicine	Presentations to be discontinued	Date of anticipated supply end	Presentations remaining available	
Levemir [®] (insulin detemir) ¹	Penfill® FlexPen®	December 2026	N/A	
Insulatard [®] (insulin isophane human) ²	Penfill®	March 2025	Vial	
NovoRapid [®] (insulin aspart) ³ FlexTouch [®]		March 2025	FlexPen [®] Penfill [®] PumpCart [®] Vial	

Insulin should be considered in type 2 diabetes when:

- Patient is on maximum tolerated oral antidiabetes agents (+/- GLP1-RA) and desired HbA1c is not achieved (>58mmol/mol)
- If experiencing osmotic symptoms related to poor glycaemic control & HbA1c is particularly high (and unlikely to reach desired target with the addition of other agents). Maybe temporarily used as a 'rescue therapy'
- Where HbA1c target is not achieved and other agents are contraindicated (e.g. eGFR <30).

Selecting an appropriate starting regimen

There is no evidence that starting a basal, a twice daily pre-mixed or a prandial regimen was definitively more effective, *however*.

- More effective blood glucose control was seen at 1 year when a twice daily premixed insulin or pre-prandial rapid-acting insulin were used first.
- Basal insulin regimen led to fewer hypoglycaemic episodes and less weight gain.
- Regardless of initial insulin regimen over 50% required the addition of a second insulin type.

These findings provide clear evidence in people with type 2 diabetes to support starting insulin therapy with a once a day basal insulin and then adding a mealtime insulin if glycaemic targets are not met.

The key is to make regular dose increases—some general rules

A basic principle in up titrating is to increase doses in 10% increments. However:

- If hypoglycaemia occurs reduce insulin dose by at least 20% and monitor
- Preventing hypos always takes priority over correcting hyperglycaemia
- Hypoglycaemia is potentially dangerous and can damage patient confidence

Royal College of Nursing. Starting insulin treatment in adults with type 2 diabetes. RCN guidance for nurses (2006) London. Royal College of Nursing

Insulin concentrations

The concentration of insulin is the number of units of insulin in 1 mL of fluid. All Insulin vials and most insulin pens commonly have a concentration of 100 units/mL.



However, some insulin products come in a higher concentration. 200 units/mL means that there are 200 units of insulin in 1 mL of fluid, 300 units/mL means that there are 300 units of insulin in 1 mL of fluid



There is currently one concentrated insulin available:

HUMULIN R U-500 vial, and there is a corresponding U-500 syringe. HUMULIN R U-500 is only ever prescribed by secondary care.

Higher concentration insulins

- There are many reasons why a health care provider chooses to prescribe a concentrated insulin, although the primary reason is often to decrease the volume given with an injection.
- The insulin pen device displays the number of *insulin units* to be delivered.
- Concentrated insulin should not be transferred to a different device (such as from an insulin pen to a syringe or pump), as this can result in over dosage and severe hypoglycemia.







Biosimilar Insulins

A "biosimilar" is a biological copy that is not identical, but demonstrates similarity to the original product, in terms of quality, efficacy and safety.



Admelog and Trurapi



DIN 0246989

Admelog* Asulin lispro injection Insuline lispro injectable **Dob units/unités/mt** Asulis Schiefer - Deur injection sous catanée-Asulis Sous Schiefer - Deur injection sous catanée-Asulis Asulis Asulis ar BRO and Jel Junios State Brossen South Mark J Attiliser seulement avec les stylos Injecteurs dissuline Alistar PRO and Jel Junios State Brossen South Mark J Attiliser seulement avec les stylos Injecteurs dissuline Alistar PRO and Jel Junios State Brossen South Mark J Attiliser seulement avec les stylos Injecteurs dissuline Alistar PRO and Jel Junios State Brossen South Mark J Attiliser seulement avec les stylos Injecteurs dissuline Alistar PRO and Jel Junios State Brossen South Mark J Attiliser South State Brossen State



Admelog ▼ 100 units/ml solution

- Admelog 100 units/ml solution for injection in vial
- Admelog 100 units/ml solution for injection in cartridge
- Admelog 100 units/ml solution for injection in a pre-filled pen

Trurapi▼ 100 units/ml solution

Trurapi^{*} 100 units/ml

lin ASPART

olution for injection

Trurapi 100 units/ml solution for injection in vial

Trurapi[®] 100 units/m

solution for injection

pre-filled pen

-0

- Trurapi 100 units/ml solution for injection in cartridge
- Trurapi100 units/ml solution for injection in a pre-filled pen

Why is this important?

Originator insulin	Cost (NHSBSA	Biosimilar insulin	Cost (NHSBSA	Potential cost	5	Originator insulin	Cost (NHSBSA	Biosimilar insulin	Cost (NHSBSA	Potential cost
(insulin aspart 100	dm+d April 2023)	(insulin aspart 100	dm+d April 2023)	saving		(insulin lispro 100	dm+d April 2023)	(insulin lispro 100	dm+d April 2023)	saving
units/ml) and		units/ml) and				units/ml) and		units/ml) and	······	
device(s)		device(s)				dovice/s)		device/s)		
NovoBanid®	£30.60	Trurani®	£21.42	£9.18		device(s)		device(s)		
Νονοιταρία	100.00	Парі	121.12	15.10	8	m	620.46		C22.10	67.26
5 x 3ml FlexPens		5 x 3ml SoloStar				Humalog®	129.40	Admelog®	£22.10	£7.30
		pens				5 x 2ml KwikDone		5 x 3ml SoloStar		
NovoRapid [®]	£32.13			£10.71		5 X SIIII KWIKPEIIS		5 x 5111 50105tai		
5 x 3ml ElexTouch								pens		
pens										
P					8	Humalog®	£28.31	Admelog®	£21.23	£7.08
NovoRapid [®]	£28.31	Trurapi®	£19.82	£8.49		Leaner B				
						5 x 3ml cartridges		5 x 3ml cartridges		
5 x 3ml cartridges		5 x 3ml cartridges								
NovoRapid®	£14.08	Trurapi®	£11.97	£2.11		Humalog [®]	£16.61	Admelog®	£14.12	£2.49
		5						1 Marie		
1 x 10ml vial		1 x 10ml vial				1 x 10ml vial		1 x 10ml vial		
Originator insulin	Cost (NHSBSA	Biosimilar insulin	Cost (NHSBSA	Potential cost						
(insulin glargine	dm+d April 2023)	(insulin glargine	dm+d April 2023)	saving						
100 units/ml) and		100 units/ml) and								
device(s)		device(s)					•			
Lantus®	£34.75	Semglee®	£29.99	£4.76						
5 x 3ml SoloStar		5 x 3ml prefilled					Dot	ontial	coving	D r
nens		nens					ΓU	CIIIAI	Saving	12
pens		pens								
or 5 x 3ml		Abasaglar [®]	£35.28	None						
cartridges		8 8								
		5 x 3ml KwikPens								
		or 5 x 3ml								
		cartridges								

Safe Use of Insulin and Insulin Safety Agenda



Module on all aspects of insulin safety, developed by the Primary Care Diabetes Society.

← All modules

FREE CPD MODULE

The six steps to insulin safety

UPDATED JUNE 2024: An essential module for all those prescribing, managing or administering insulin, with the overall aim of reducing insulin errors in clinical practice, particularly within the primary care setting.

Why, how you inject is as important as what you inject

- Re checking technique and sites used
- Inadvertent Intramuscular injection
- Lipohypertrophy
- Injections by a 3rd party
- Poor technique can lead to fluctuating glucose control



Continuous Glucose Monitoring

Understanding interstitial fluid measurement

- Continuous glucose monitoring systems measure glucose in the interstitial fluid
- Blood glucose and sensor glucose are closely related but not identical



Classic capillary blood glucose meter

CGM sensor

Understanding interstitial glucose measurement



the interstitial fluid may be **below** the blood glucose reading.

similar to blood glucose.

interstitial fluid may be higher than the blood glucose reading.

INTERNATIONAL CONSENSUS ON TIME IN RANGE

What is Time in Range?



Time in Range refers to the percentage of time that a person with diabetes spends within their Target Glucose Range, or above or below that target

Targets for adults, young people and children with type 1 or type 2 diabetes



* Readings >13.9 mmol/L are also included in the <25% target $\$ Readings <3.0 mmol/L are also included in the <4% target

Images are for illustrative purposes only. Not real patient data.

1. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care. (2019);42(8):1593-1603.

Targets for older people with type 1 or type 2 diabetes and those at high-risk from hypoglycaemia



* Readings >13.9 mmol/L are also included in the <50% target

Images are for illustrative purposes only. Not real patient data.

1. Battelino T, Danne T, Bergenstal RM, et al. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range. Diabetes Care. (2019);42(8):1593-1603.

Estimate of HbA1c for a given TIR level

Data from randomized clinical trials involving adults with Type 1 or Type 2 diabetes have shown that TIR is correlated with laboratory-measured HbA1c.

	ANALYSIS BY BECK ET AL ¹	ANALYSIS BY VIGERSKY ET AL ²
TIR	HbA1c CORRELATE % (mmol/mol)	HbA1c CORRELATE % (mmol/mol)
90 %	6.0 (42)	5.1 (32)
80 %	6.5 (48)	5.9 (41)
70 %	7.0 (53)	6.7 (50)
60 %	7.4 (57)	7.5 (58)
50 %	7.9 (63)	8.3 (67)
40 %	8.4 (68)	9.0 (75)
30 %	8.9 (74)	9.8 (84)
20 %	9.4 (79)	10.6 (92)

Every 5% (~1 hour 12 mins per day) increase in Time in Range is associated with clinically significant benefits³

Key insights

• There is an **inverse correlation** –as TIR increases, HbA1c decreases

%Time in Range 3.9-10 mmol/L (70-180 mg/dL)

THE RELATIONSHIP BETWEEN TIR AND HbA1c¹

 Although highly correlated, a wide range of HbA1c values can be associated with a specific TIR and vice versa

HbA1c (%)

* Correlations of %TIR with HbA1c for target glucose range 3.9-10 mmol/L (70-180 mg/dL). Analysis by Beck et al is based on data in T1D, analysis by Vigersky & McMahon includes data in T1D and T2D **1.** Beck RW, et al. J Diabetes Sci Technol. 2019; 13:614-626. **2.** Vigersky RA and McMahon C. Diabetes Technol Ther. 2018; 21:81–85. **3.** Battelino T, et al. Diabetes Care. (2019);42(8):1593-1603.

How glucose values appear after a scan



Trend arrow

The trend arrow shows the direction that glucose is heading, along with rate of change. Indicates how glucose is changing.

Current glucose reading

Based on the most recently updated glucose value (1 minute). Text-to-speech when enabled.

8 hour history

The graph is made up of 15-minute readings stored over the last 8 hours (15 minute).

Easily add notes

to record relevant events.



Images are for illustrative purposes only. Not real patient data.

The FreeStyle LibreLink app is only compatible with certain mobile devices and operating systems. Please check the website for more information about device compatibility before using the app. Use of FreeStyle LibreLink requires registration with LibreView.

FreeStyle Libre 2 plus

acts as a rt-CGM if used with smart phone





or Intermittently scanned Continuous Glucose Monitoring (isCGM) commonly known as Flash if using a reader

Addition of 3 optional alarms;

- low glucose alarm
- high glucose alarm
- signal loss

Dexcom one+

Real time Continuous Glucose Monitoring (rtCGM)

- The Dexcom ONE+ system features one-touch sensor applicator with a 30-minute warm up.
- There is no separate transmitter.
- 12-hour grace period before a sensor must be changed

Continually transmits glucose data without need for scanning device.

- Optional high and low glucose alerts
- Urgent low soon alarm

The AGP report – what are we looking for?

1. Glucose statistics and Targets

3. Ambulatory Glucose Profile (AGP)



Anatomy of the Ambulatory Glucose Profile (AGP)



Images are for illustrative purposes only. Not real patient data. **1.** Bergenstal RM, et al. Diabetes Technol Ther. 2013; 15: 198-211.

Firstly look for patterns of hypoglycaemia



What time of day is hypoglycaemia occurring?

is there any nocturnal hypoglycaemia?

Investigate causes of low glucose

Discuss with your patient what may be the cause:

- Medication/insulin dose
- Meal size/CHO content
- Fasting loss of appetite
- Alcohol consumption
- Exercise

Confirm with the daily glucose profiles

- Which days are hypos occurring?
- What is different about those days?

Images are for illustrative purposes only. Not real patient data.

*Guidelines recommend spending at least 70% of Time in Range (3.9 –10.0 mmol/L) for adults with Type 1 and Type 2 diabetes who are not pregnant, not older, or at risk. **1.** Battelino T, et al. Diabetes Care 2019; 42:1593-1603 doi:10.2337/dci19-0028.

Secondly look for patterns of hyperglycaemia

Is any of the IQR Band above the target range?

Images are for illustrative purposes only. Not real patient data.



What time of day is hyperglycaemia occurring?

Is it after meals/throughout the night/dawn phenomenon?

Investigate causes of high glucose

Discuss with your patient possible causes:

Food intake

Snacking

٠

Meal size and

Over-correcting

hypoglycaemia

Medication/insulin

- Timing and dose carbohydrate content
 - Missed insulin or diabetes medication

Lifestyle and behaviours

- **Illness/stress** ٠
- Activity/daily routine ٠

Confirm with the daily glucose profiles

- Is there a post-prandial spike?
- Does hyperglycaemia occur after hypoglycaemia?

Finally look for glucose variability

Look for a wider dark blue and grey outer band.



Images are for illustrative purposes only. Not real patient data.

What time of day are the bands widest?

Investigate causes of glucose variability

Talk to your patient and discuss what is changing from one day to the next around:

Insulin/oral medication

- Timing/dose
- Injection sites/technique

Food intake - erratic eating habits

- Missed meals
- Size/type of meals
- Snacking between meals

Lifestyle related

Activity/alcohol/sleep/stress/routine

Confirm with the daily glucose profiles

- Look for a good day and review what is happening on that day.
- How do week/work/active days differ from weekends?

When you see high or low glucose, use the shaded bands to guide you to the cause.

A narrow darker blue band indicates a trend that is happening consistently each day, so consider medication and mealtimes.

wider blue or outer grey band reflects glucose variation for distinct reasons on different days, focus on aspects of behaviour or lifestyle such as a missed insulin injection, periodic exercise, social events or illness.

In discussion with the individual, the daily logs can provide insights into possible times and activities that have contributed to the variability shown in the AGP.

Exploring exercise

exercise takes many forms, and the type and duration can have very different effects on glucose levels

explore exercise patterns

15

• explore regular exercise types

- explore how they deal with unplanned exercise and what form this took
- explore how effective previous attempts to manage exercise have been



Variability in blood glucose responses to different types of exercise

Riddell et.al (2017). Exercise management in type 1 diabetes: a consensus statement. Lancet Diabetes Endocrinol. 2017 May;5(5):377-390. doi: 10.1016/S2213-8587(17)30014-1.



exploring diet

- explore their understanding and ability to calculate carbohydrates
- explore the timing of insulin to meal
- explore their dose ratios
- explore their snacking habits and if doses are given at the time
- explore their hypo treatment
- is problem with just one meal or all meals?





Explore hypo treatment and reactions to high glucose readings



exploring insulin overlays: insulin use, stacking and benefits of insulin overlays to data on AGP





explore their awareness of insulin on board and insulin time profiles

Case Study



AMBULATORY GLUCOSE PROFILE (AGP)

AGP is a summary of glucose values from the report period, with median (50%) and other percentiles shown as if occurring in a single day.





clinical case

65yr lady with type 2 diabetes (2005)

Retinopathy since 2021 (R1M0 both eyes)

ACR 14.6mg/mmol (raised since 2021) eGFR 84ml/min

Hypertension (controlled on triple therapy)

most recent HbA1c 68mmol/mol

BMI 34kg/m2

Current concern – fear of hypos, erratic glucose levels

Current diabetes meds – Humalog Mix 25 insulin twice daily (40 units am and 44 units pm) Metformin 1g twice daily Dapagliflozin 10mgs daily



Visit 1

- Is there adequate data to review here?
- What do you consider her greatest

risk to be?

- a) Hyperglycaemia
- b) Hypoglycaemia
- c) Glucose Variability
- What advice around insulin (if any) would you offer?
- How would you use this data in her consultation?
- Is there anything else you'd like to know?

GLUCOSE STATISTICS AND	TARGETS	TIME IN RANGES			
15 May 2024 - 28 May 2024		14 Days			
Time sensor active:		99%		Very High >13.9 mmol/L	2% (29min)
Ranges And Targets For		Type 1 or Type 2 Diabetes	13.9		
Glucose Ranges Targets % of Readings (Time/Day) Target Range 3.9-10.0 mmol/L Greater than 70% (16h 48min)		Readings (Time/Day) 70% (16h 48min)		High 10.1 - 13.9 mmol/L	39% (9h 22min)
Below 3.9 mmol/L Less than 4% (58min)		(58min)	10.0		
Below 3.0 mmol/L Less than 1% (14min)		(14min)			
Above 10.0 mmol/L Less than 25% (6h)			Target Range	59%	
Above 13.9 mmol/L Less than 5% (1h 12min)			3.9 - 10.0 mmol/L	(14h 9min)	
Each 5% increase in time in range (3.9-10	0.0 mmol/L) is clinical	ly beneficial.			
Average Glucose		9.4 mmol/L	3.9	Low 3.0 - 3.8 mmol/L	0% (0min)
Glucose Management Indicator (GMI)		7.4% or 57 mmol/mol	3.0		0%
Glucose Variability 26.0%				<3.0 mmol/L	(Omin)
Defined as percent coefficient of variation	on (%CV); target ≤36	8%			

AMBULATORY GLUCOSE PROFILE (AGP)

10.0



Visit 2 -now on basal bolus

Abasaglar 56 units daily Humalog 6-8 units with meals

- Is there adequate data to review here?
- What do you consider her greatest risk to be?
 - a) Hyperglycaemia
 - b) Hypoglycaemia
 - c) Glucose Variability
- What advice around insulin (if any) would you offer?
- How would you use this data in her consultation?
- Is there anything else you'd like to know?

Key take home messages



Titrate to target without inducing hypoglycaemia

Injection technique and sites are equally as important as the regimen

Become familiar with AGP interpretation



Thank you.





