DIABETES – INDICATIONS FOR INSULIN

The North West London health and care partnership

Introduce the likely need for insulin in the future early on as part of patient education

Emphasise that it is the pancreas that fails not the patient

Assess if greater compliance with oral agents and lifestyle changes could negate the need for insulin

ALWAYS	USUALLY	CONSIDER
Type 1 Diabetes	Type 2 Diabetes failure to reach glycaemic targets using diet and non insulin therapies	Symptomatic e.g. rapid weight loss, polyuria, nocturia
Not sure of whether the diagnosis is Type 1 Diabetes or Type 2	Type 2 Diabetes Pre and post surgery or following a MI	Women with Type 2 DM on oral agents hoping to conceive
Pregnant women with Type 2 DM	Chronic pancreatitis	Acute neuropathies i.e. femoral amytrophy
Gestational Diabetes Not controlled on diet or metformin	Type 2 Diabetes requiring enteral feeding	Ketosis prone Type 2 Diabetes
Post surgical pancreatectomy		Steroid induced Diabetes

WHICH INSULIN SHOULD BE USED INITIALLY FOR T2DM DIABETES (T2DM)

Animal insulin is no longer used for insulin starts

Begin with human NPH insulin injected at bed-time or twice daily according to need such as Insuman Basal, Humulin I or Insulatard . Can be given at breakfast when required e.g.: people on steriods.

Consider, as an alternative, using a long-acting insulin analogue such as Insulin Detemir, Insulin Glargine if:

- The person needs assistance from a carer or healthcare professional to inject insulin, and use of a long-acting insulin analogue (Insulin Detemir, Insulin Glargine) 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, or
- The person cannot use the device to inject NPH insulin

Consider twice daily pre - mixed (biphasic) human insulin (particularly if HbA1c ≥ **75 mmol/mol or 9%**)

Consider pre-mixed preparations that include short-acting insulin analogues, rather than pre-mixed preparations that include short acting human insulin preparations, if:

- A person prefers injecting insulin immediately before a meal, or
- Hypoglycaemia is a problem, or
- Blood glucose levels rise markedly after meals
- Consider initiation of **pre - mixed insulin** if the **A1c** is high particularly above **75 mmol/mol** or **9%**

This would however depend on the individual people preference and convenience.

Other factors to consider:

Lifestyle
- Meal times
- Employment

Potential risk of hypoglycaemia
- High alcohol intake
- Malnutrition
- Low BMI

Physical barriers
- Dexterity
- Vision

Emotional barriers
- Needle phobia

PEOPLE WITH TYPE 1 DIABETES (T1DM)

In Type 1 Diabetes Insulin needs to be started within 24 hours of diagnosis

If the patient is severely ketotic and or vomiting, pregnant, or a child, admission is required/ urgent referral / telephone contact to the specialist team or acute on call medical team is required

T: or hospital switchboard and ask to speak to a diabetologist or paediatrician or acute on call medical team

Out of hours may well be the on call medical team who deal with this

DIABETES – CHOICE OF INSULIN

The North West London health and care partnership

THERE ARE MANY TYPES OF INSULIN TO CHOOSE FROM: ALL OF TODAY'S INSULINS ARE MANUFACTURED USING RECOMBINANT DNA TECHNOLOGY

HUMAN INSULINS	ANALOGUE INSULINS
e.g. Insuman Rapid, Humulin S, Insulatard • Human insulins are produced by recombinant DNA technology and have the same amino acid sequence as endogenous human insulin • Time of action can be modified by the addition of protamine	**e.g. Novorapid, Glargine** • Insulin analogues are produced in the same way as human insulins, but the insulin is modified to produce a desired kinetic characteristic, such as an extended duration of action or faster absorption and onset of action. • They are more expensive • When bioequivalent insulins may become available, these may be more cost-effective

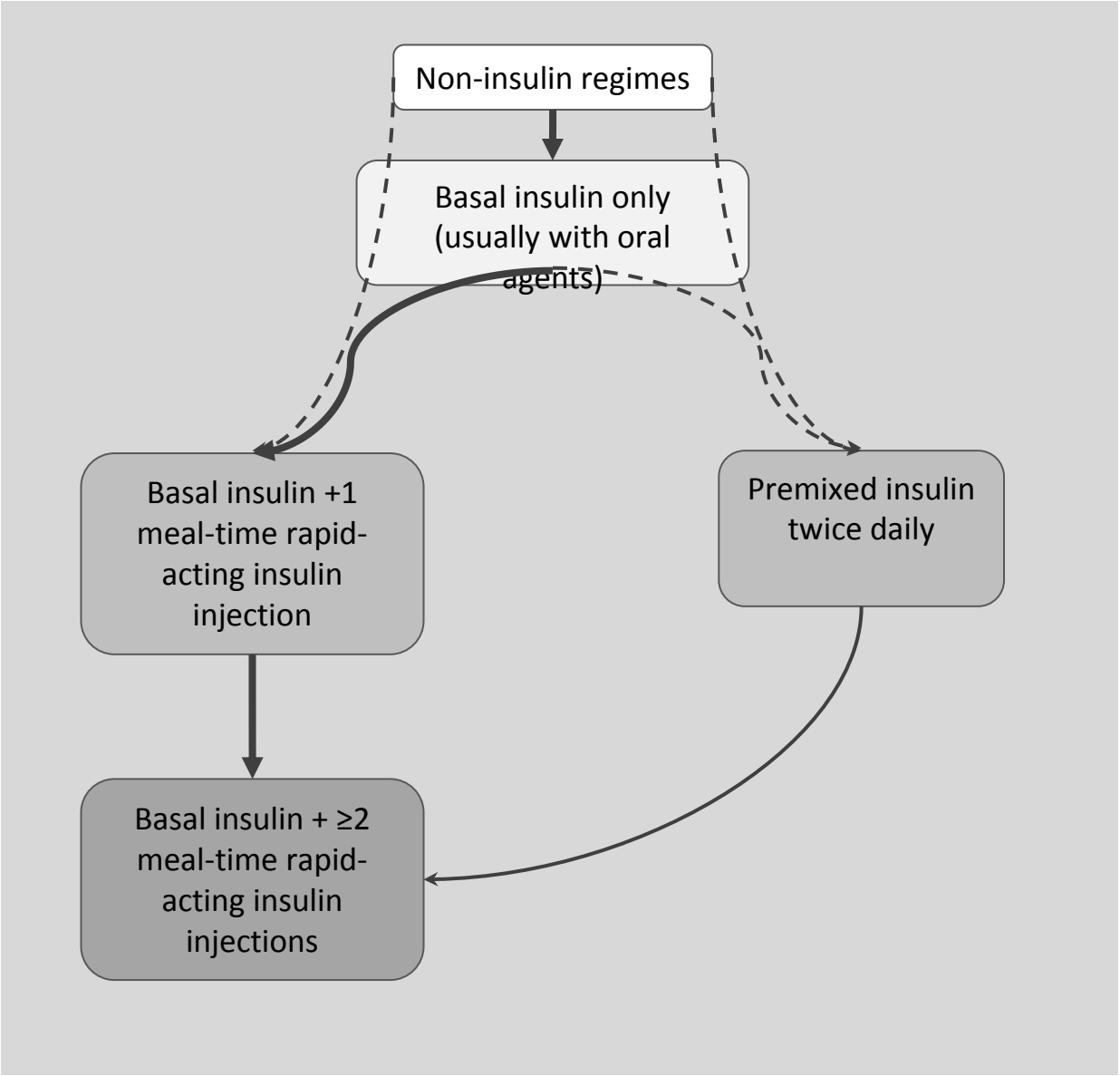
Human Insulins should be the initial choice of insulin for most people with Type 2 Diabetes as they are safe and considerably cheaper than the analogue insulins
Exceptions are:
- **Those at high risk of hypoglycaemia**
- **Low BMI, malnourished, frail and elderly, erratic eating patterns**

	RAPID ACTING	SHORT ACTING	INTERMEDIATE ACTING	LONG ACTING	MIXTURES RAPID + INTERMEDIATE ACTING	MIXTURES SHORT + INTERMEDIATE ACTING
Type	**Analogue**	**Human**	**Human**	**Analogue**	**Analogue**	**Human**
Onset of action	within 15 minutes	30 - 60 mins	1 - 2 hours	2 - 3 hours	Up to 15 mins	Up to 30 mins
Duration*	2-5 hours	up to 9 hours	11 - 24 hours	Up to 36 hours	Up to 24 hours	Up to 24 hours
Examples	Novorapid Humalog Apidra	Humulin S Insuman Rapid	Insulatard Humulin I Insuman Basal	Levemir (Determir) Abasaglar/Lantus/ Semglee (Glargine)	NovoMix 30 Humalog Mix 25 Humalog Mix 50	Humulin M3 Insuman Comb 15, 25, 50
Peak effect	0.5 - 1.5 hours	1 - 4 hours	3 - 12 hours	varies based on the dose	1 - 4 hours	2 - 8 hours

ORAL AND NON – INSULIN THERAPY	USE WITH INSULIN
Metformin	Normal and overweight people with Type 2 Diabetes can be continued on Metformin as there is evidence that this combination is insulin sparing and has other benefits including weight management glycaemic control and cardiovascular disease (CVD)
sulfonylureas (SU) *Glimepiride* *Gliclazide*	Continue with regular dose reviews if the individual is on a daily isophane or analogue insulin. Avoid concurrent use in people with severe renal impairment (<45mL/min/1.73m^2).
DPP-4 Inhibitors (DPP-4Is): *Alogliptin,* *Linagliptin,* *Saxagliptin,* *Sitagliptin,* *Vildagliptin*	May be used in combination with insulin. Risk of hypoglycaemia when used together, consider reducing dose of insulin.
Sodium glucose co-transporter 2 Inhibitors (SGLT-2) *Canagliflozin,* *Dapagliflozin,* *Empagliflozin* *Ertugliflozin*	May be used in combination with insulin or other antidiabetic drugs (if existing treatment fails to achieve adequate glycaemic control). Risk of hypoglycaemia when used together, consider reducing dose of insulin.
Pioglitazone	May be used in combination with insulin. If pioglitazone is used in combination with insulin people should be observed for signs and symptoms of heart failure, weight gain, and oedema. Risk of hypoglycaemia when used together, consider reducing dose of insulin.
Glucagon-like peptide-1 receptor agonists (GLP-1 Agonists) *Exenatide modified-release (once **weekly**)* *Exenatide standard-release (twice daily)* *Liraglutide (once daily)* *Lixisenatide (once daily)* *Dulaglutide (once **weekly**)* *Semaglutide (once **weekly** injection or once **daily** tablet)*	May be used in combination with insulin. In adults with type 2 diabetes, only offer a GLP-1 mimetic in combination with insulin with specialist care advice and ongoing support from a consultant-led multidisciplinary team.
Acarbose	Not recommended in combination with insulin. Risk of hypoglycaemia when used together, consider reducing dose of insulin. Risk of hypoglycaemia when used together, consider reducing dose of insulin.
Meglitinides: *Repaglinide*	Not recommended in combination with insulin.

Please see pages 34-37 and 60-61 for individual drug monographs

TYPE 2 DIABETES – SEQUENTIAL INSULIN STRATEGIES



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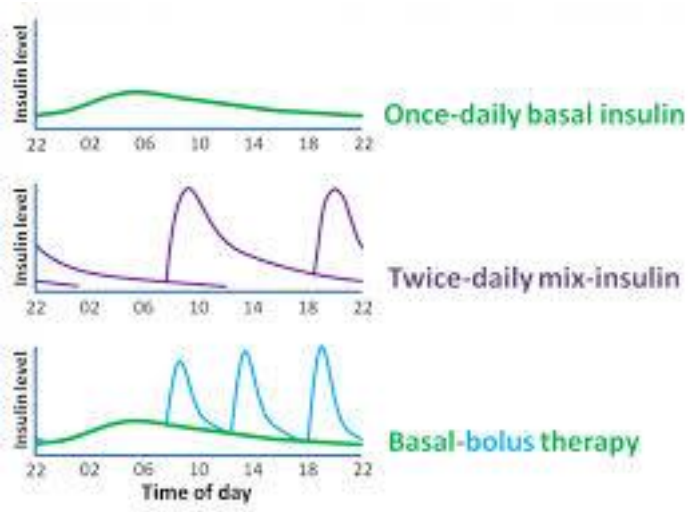
TYPE 2 DIABETES – BENEFITS OF INITIATING BASAL INSULIN

PROS
Just one injection a day
Easy for the patient to adjust the dose
Can stay on current oral agents to start with
Buys time and confidence until a twice or three or 4 times a day insulin regime is required



DIABETES –PROS/CONS OF TWICE DAILY HUMAN INSULIN MIXTURE

PROS

Provides both background and prandial cover with two injections a day

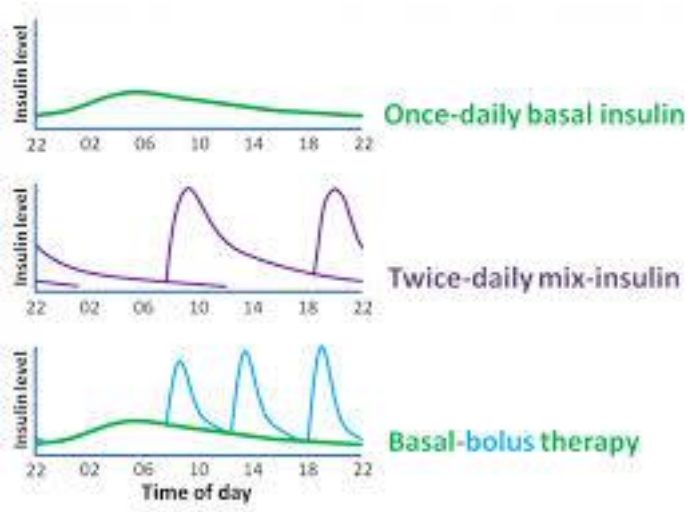
Unlike the analogue insulin mixtures provides sufficient background insulin to cover a light lunch

CONS

More difficult to titrate evening mixed insulin against pre-breakfast glucose due to risk of nocturnal hypoglycaemia

Requires people to have a regular meal pattern including breakfast and a main meal in the evening, rather than lunch time

Increased risk of hypoglycaemia if eat dinner very late at night or tendency to skip breakfast or lunch



DIABETES – STARTING A BASAL INSULIN

Tell the patient they are likely to need between 20-50 units of insulin and it is safe for them to increase the insulin.

Start with 10 units before bed of insulin if <100kg (or 20 units of insulin if >100kg)

For elderly frail patients where there is no requirement for tight control, morning NPH (human basal) insulin is safe as the peak will cover breakfast and a bit of lunch, and can be given by a morning carer who can ensure the patient has eaten. In the elderly it is quite likely that NPH will have a much longer duration of action as when the eGFR falls the half life of the insulin increases.

Increase by 2 units every 3rd day until before breakfast blood glucose is 8-10 mmol/l

Reduce the Sulphonylurea dose. Continue to increase by 2 units every 3rd day aiming for before breakfast blood glucoses of 6-8 mmol/l

STOP INCREASING if :

symptoms of hypoglycaemia at night - go back to previous dose

some readings are <5mmol/l

when insulin dose reaches 50 units - review with Diabetes team

DIABETES – REVIEWING A BASAL INSULIN REGIME

The North West London health and care partnership

Is the before breakfast blood glucose 5-8 mmol/l ? **If no:**

Continue to increase basal insulin by 2 units every 3rd day providing there is no nocturnal hypoglycaemia:

If HbA1c above agreed individual target at 3-4 months? –and the before breakfast blood glucose 5-8 mmol/l; examine post prandial blood glucose readings

If > 10mmol/l:

Switch to twice daily mixed insulin.

DIABETES – STARTING A TWICE DAILY HUMAN INSULIN MIXTURE

Tell the patient the insulin needs to be given 20-30 minutes before breakfast and dinner and stress the need to eat on time. Stop all sulphonylureas.

Start with 10 units BD if <100kg (or 20 units BD of insulin if >100kg mixed insulin) 20-30 minutes before breakfast and dinner

Start with the pre-dinner mixed insulin. Increase by 2 units every 3rd day until the 2 hour post-dinner glucose is <10 mmol/l and before breakfast blood glucose is 6-8 mmol/l

Then increase the pre-breakfast mixed insulin by 2 units every 3rd day until the 2 hour post-breakfast glucose is <10 mmol/l and before dinner glucose is 6-8 mmol/l

STOP INCREASING if:

symptoms of hypoglycaemia

pre-breakfast or dinner glucose <5mmol/l

when total insulin dose reaches 100 units and review with diabetic team

DIABETES – REVIEWING A TWICE DAILY HUMAN INSULIN MIXTURE

Is the pre-breakfast blood glucose 5-8 mmol/l and 2 hour post-meals blood glucoses if > 10mmol/l?

Continue to increase the evening mixed insulin by 2 units every 3rd day to target post-dinner and pre-breakfast values if no nocturnal hypoglycaemia:

Continue to increase the morning mixed insulin by 2 units every 3rd day to target post-breakfast and pre-dinner values if no day time hypoglycaemia:

If HbA1c above agreed individual target at 3-4 months and pre-meal glucose values in target and post prandial blood glucoses > 10mmol/l:

Review diet and consider switch to an Analogue Insulin Humalog Mix 50 BD or NovoMix 30

DIABETES – REUSABLE INSULIN PEN DEVICES

The North West London health and care partnership

DEVICE	AUTOPEN CLASSIC	AUTOPEN 24	NOVOPEN 4	NOVOPEN 5	NOVOPEN Echo	HUMAPEN SAVVIO	HUMAPEN LUXURA HD	ALLSTAR	ALLSTAR Pro	JUNIORSTAR
Dosing	1 unit (1-21) 2 units (2-42)	1 unit (1-21) 2 units (2-42)	1 unit (1-60)	1 unit (1-60)	½ unit (0.5-30)	1 unit (1-60)	½ unit (1-30)	1 unit (1-80)	1 unit (1-80)	½ unit (1-30)
General features	Plastic		Metal Blue or chrome	Metal Blue or chrome	Metal Blue or red	Metal Audible click Multiple colours	Metal Green Audible click	Purple or Teal	Blue or Silver	Blue, red or silver
Special uses	Release button on side makes it easier for some to handle Spring loaded release button ensures that force required to push the insulin is significantly less than for other insulin pens.			Memory function on pen end indicates timing and units of last dose	Memory Function - Records dose and time since last injection for extra reassurance		Half unit doses so suitable for children or those with low insulin requirements			Allows for half-unit dose increments which helps to provide flexibility especially in young people.
Insulin compatibility	**Lilly** Humulin Humalog Abasaglar **Wockhardt**	**Sanofi** Insuman Lantus Apidra	**Novo Nordisk** Insulatard Novorapid Novomix Levemir	**Novo Nordisk** Insulatard Novorapid Novomix Levemir	**Novo Nordisk** Insulatard Novorapid Novomix Levemir	**Lilly** Humulin Humalog Abasaglar	**Lilly** Humulin Humalog	**Sanofi** Insuman Lantus Apidra	**Sanofi** Insuman Lantus Apidra	**Sanofi** Insuman Lantus Apidra
Device										

DIABETES –DISPOSABLE INSULIN PEN DEVICES

DEVICE	SOLOSTAR	FLEXPEN	FLEXTOUCH	INNOLET	KWIKPEN	SEMGLEE
Dosing	1 unit (1-80)	1 unit (1-60)	1 unit (1-80)	1 unit (1-50)	1 unit (1-60)	1 unit (1-80)
General features	Apidra and Lantus versions of this pen have different colours (blue for Apidra, grey for Lantus) and textures to help users distinguish between the types of insulin. Insuman is a white pen. Green label for basal and blue for comb.	Pen is blue, with labels of different colours for various types of insulin.		An easy-to-use doser with a large, ergonomic dial	Buff colour for human insulin, blue for analogue. Humalog Junior Kwikpen can be differentiated by a orange and white label.	A light blue pen with white label.
Special uses			Reduced manual dexterity (due to push button not having to extend)	Poor eyesight Reduced manual dexterity (usually due to different joint related conditions)		
Insulin compatibility	**Sanofi** Apidra Lantus Insuman Basal Insuman Comb Insulin Lispro	**Novo Nordisk** NovoRapid Novomix Levemir	**Novo Nordisk** NovoRapid	**Novo Nordisk** Insulatard Levemir	**Lilly** Humulin Humalog Humalog Junior Abasaglar	**Mylan** Semglee
Device