

Managing Type 2 Diabetes

Diabetes Specialist Nurses
2016

NICE guidelines

NICE ng28(2015). Type 2 diabetes In adults:
Management

<http://www.nice.org.uk/guidance/ng28>

Individualised targets (NICE 2015)

HbA_{1c} may be > 48mmol/mol (6.5%) if risk of hypoglycaemia is of a concern.

- Encourage maintenance of individual target unless the resulting side effects (including hypoglycaemia) or their efforts to achieve this impair quality of life
- Offer therapy (lifestyle and medication) to help achieve and maintain the HbA_{1c} target level
- Inform the person with a higher HbA_{1c} that any reduction in HbA_{1c} towards the agreed target is advantageous in reducing risk of micro and macro complications
- Avoid pursuing highly intensive management to levels of <48mmol/mol(6.5%), especially the elderly or frail.

Algorithm for blood glucose lowering therapy in adults with type 2 diabetes

<http://www.nice.org.uk/guidance/ng28/resources/algorithm-for-blood-glucose-lowering-therapy-in-adults-with-type-2-diabetes-2185604173>



Bristol
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Health

Treating the glucose with oral medication

Increase insulin sensitivity

Weight loss
Exercise
Metformin

Approaches

Always diet and lifestyle

Helping you to live life well

Initial Drug Treatment Monotherapy

Metformin

- Reduces hepatic glucose production and increases insulin sensitivity.
- Does not stimulate insulin production
- 1st line treatment unless rescue therapy required.

Side Effects

- Gastric side effects - Step up metformin therapy gradually over weeks to minimise risk of gastro-intestinal side effects. (MR preparation)
- Rash
- Lactic Acidosis
- Decreased Vitamin B12 absorption

Cautions

- Significant altered LFT(ALT \geq 3x upper limit of normal range)
- Malabsorption problems – side effects
- Significant chronic pulmonary disease

- Stop Metformin if the **eGFR is below 30 ml/minute.**
- Caution for those at risk of a sudden deterioration in kidney function and risk of eGFR falling below 45ml/minute.
- Consider modified – release Metformin if GI side effects.

Metformin contraindicated or not tolerated

- A) Dipeptidyl Peptidase – 4 (DPP4)
- B) Pioglitazone
- C) Sulphonylurea

Rescue therapy

- Symptomatic Hyperglycaemia at any phase of treatment – consider Insulin or Sulphonylurea, review treatment once blood glucose control has been achieved.

Treating the glucose

Increase insulin sensitivity

Weight loss
Exercise
Metformin

Enhance Endogenous Insulin Secretion

Approaches

DPP4 Inhibitors

Always diet and lifestyle

First Intensification Dual Therapy

Treatment with 2 non –insulin
blood glucose lowering therapies

DPP-4 Inhibitors (Gliptins)

- DPP4 Inhibits dipeptidylpeptidase – 4 enzyme from breaking down GLP1 (glucagon like peptide -1) which acts on the presence of food in the gut.
- This in turn increases insulin secretion and reduces hepatic glucose secretions

Side Effects

- URTI symptoms
- GI symptoms – delayed gastric emptying
- Possible increase risk Pancreatitis/Pancreatic CA – especially with known history
- Peripheral oedema
- Contra-indication/caution – Previous pancreatitis/ gallstones/ excessive alcohol
- ?? Increased risk Heart Failure in existing Heart or Kidney disease (FDA April 2016)

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Pioglitazone

- Pioglitazone reverses insulin resistance by causing changes at point of insulin resistance in the muscle and fat cells, increasing peripheral glucose uptake
- Reduces hepatic glucose output

Side effects

- Weight gain
- Oedema
- Gastric side effects
- Impotence

Cautions

- Do not commence or continue a thiazolidinedione (pioglitazone) in people who have heart failure, or who are at higher risk of fracture.
- Heart failure or IHD
- Microscopic or uninvestgated macroscopic Haematuria
- Previous or active bladder cancer
- Hepatic impairment

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Sulphonylureas

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Sulphonylureas

Insulin secretagogues

- Sulphonylureas stimulates insulin secretion through the beta cell sulphonylurea receptor, and possibly through a direct effect on intracellular calcium transport.

Side Effects

- Hypoglycaemia – DVLA guidelines
- Gastric side effects
- Rash

Cautions

- T1DM
 - Pancreatic CA/Pancreatitis without specialist guidance
 - Elderly
 - Glibenclamide
 - In conjunction with other hyperglycaemic agents
 - Reducing renal function
-

Second Intensification Triple Therapy

1) Metformin, DPP-4 and Sulphonylurea

2) Metformin, Pioglitazone and Sulphonylurea or Insulin

- If triple therapy with Metformin and 2 other oral drugs not effective, tolerated or CI – consider adding GLP-1 with Metformin and SU if...

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Sulphonylureas
GLP-1 receptor Agonists
DPP4 Inhibitors

Increase Glucose Excretion

Always diet and lifestyle

GLP1's

- BMI $>35\text{kg/m}^2$
- BMI $< 35\text{kg/m}^2$ and whom insulin therapy would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.
- Should be discontinued if not achieving desired results (reduction in HbA1c of at least 11mmols/mol and 3% weight loss at 6 months)
- GLP1 in combination with Insulin should be offered with specialist care advice and ongoing support.

Glucagon Like Peptide 1 agonist

- GLP-1 agonists
 - Increases glucose dependant insulin secretion
 - Supresses inappropriately elevated glucagon secretion
 - Slows gastric emptying
 - Promotes feelings of satiety – crosses blood brain barrier

GLP1's

- Are all injectables
- Can cause significant weight loss due to feeling of satiety
- Do not cause hypoglycaemia unless used in conjunction with other blood glucose lowering medications
- Can cause gastrointestinal disturbances
- Caution in renal impairment
- Should not be used if risks of pancreatitis or previous pancreatitis

GLP1's

- Lixisenatide – 1st line – works on post prandial blood glucose – take with main meal of the day
- Liraglutide – works on fasting blood glucose – take same time each day – not food related
- Exenatide – works on post prandial blood glucose – take before breakfast and EM
- Bydureon – SR Exenatide – weekly – works on fasting levels – new pen device
- Dulaglutide (Lilly) – Weekly, can be used with Insulin

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SGLT2 Inhibition

Sodium – Glucose Co-transporter 2 (SGLT2)

- Treatment with combinations of medicines including SGLT2's may be appropriate for some people with Type 2 Diabetes at first or second intensification

Sodium – Glucose Cotransporter 2 Inhibitors (SGLT2)

- SGLT2 or Gliflozins
 - Blocks glucose reabsorption in the kidneys by reversibly inhibiting sodium glucose co-transporter 2 thereby causing increased glycosuria
 - Initial trials show reduction in HbA1c 5-10mmols/mol
 - Approx 2.5kg weight loss
 - Once daily medications

Side Effects/Cautions

- Glycosuria
- UTI's
- Genital infection/Candida
- Hypoglycaemia with insulin's or SU
- Constipation

Possible risk of DKA

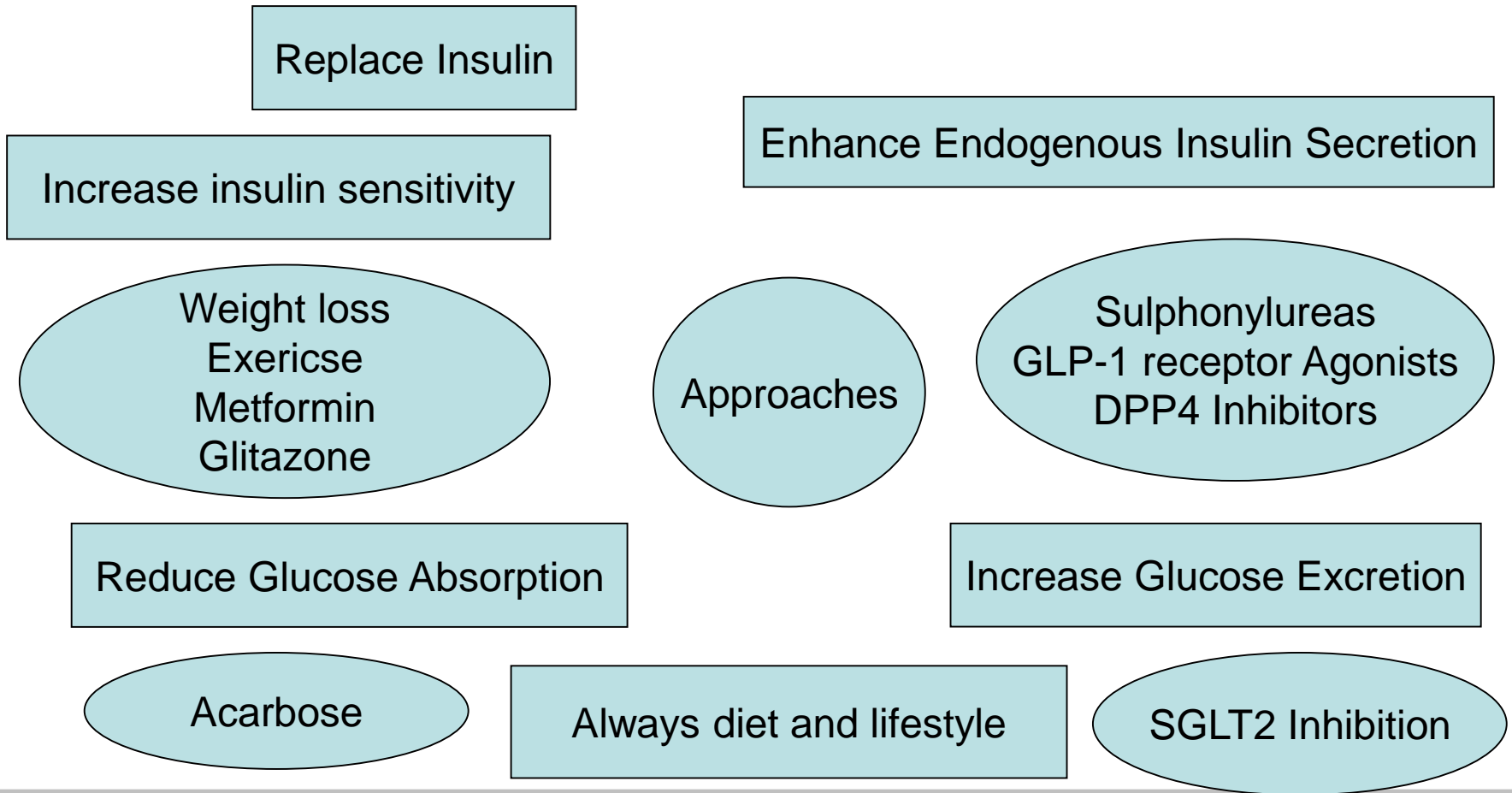
When treating patients who are taking an SGLT2 inhibitor:

1. Test for ketones in patients with symptoms of diabetic ketoacidosis (DKA)
2. Inform patients of the symptoms and signs of DKA (eg nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness) and test for raised ketones in patients with these signs and symptoms.
3. SGLT2 inhibitors are not approved for treatment of type 1 diabetes

Cautions

- Renal function
- T1DM
- Volume depletion – Contra-indicated with loop diuretics
- Hypotension – especially with existing CVD
- Elderly
- Not with Pioglitazone (??bladder cancer) – Dapagliflozin only (SPC)

Treating the glucose



Case Study 1

56 yr Female

T2DM 10yrs

BMI 36

Hba1c 68mmol/mol

eGFR 80

What treatment next?

Metformin 500mg 2 bd

Gliclazide 80mg 2 BD

Case Study 2

82 yr Male

T2DM 5yrs

BMI 29

HbA1c 65mmol/mol

eGFR 60

- Next steps?

Metformin 500mg 2 bd

Case Study 3

60yr Female

BMI 40

T2DM 2yrs

eGFR >90

Hba1c 72mmol/mol

Metformin 500mg 2bd

Gliclazide 80mg 1 bd

- What next?

Insulin Therapy in Diabetes

Debbie Hodge/Nicki Mead
Community DSNs

Insulin Therapy

- First discovered in 1921 by Banting and colleagues
- First used as a treatment in 1922
- Required several injections a day – as had a short duration period
- Given through re-useable glass syringes with large and often blunt needles



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Helping you to live life well

Insulin in Type 1 diabetes

- Usually multiple daily injection (MDI)
- Often analogue insulins
- Adjustment often based on carbohydrate counting and ratios
- Insulin requirement usually approximately $\frac{1}{2}$ -1unit per kg in weight
- Split approximately 50% basal/50% bolus

Why use Insulin in Type 2?

- UKPDS – Type 2 is a progressive disorder¹
- Beta cell function may be reduced by 50% at diagnosis. Decline continues regardless of therapy²
- 80% of people with Type 2 are obese with a BMI greater than 30Kg/m²

- 1 UKPDS (49). JAMA (1999). 281(21): 2005-12
- 2 Williams G & Pickup JC. (2004). Handbook of Diabetes, 3rd Ed. Pp 63 & 59

National Service Framework for Diabetes 2001

- Effective management of the condition increases life expectancy and reduces the risk of complications
- Improving BG control reduces the risk of developing microvascular complications
- Improving BG control may reduce the risk of developing cardiovascular disease³
- DH. (2001). NSF for Diabetes: Standards. Pages 6 and 26.

Who would you consider for Insulin?

- Those with Type 2 who have poor control despite being on maximum oral or injectable treatment and improved lifestyle
- Those with Type 2 where other diabetes treatments are contraindicated i.e. renal impairment
- Those with Type 2 unable to tolerate other diabetes treatments due to side effects

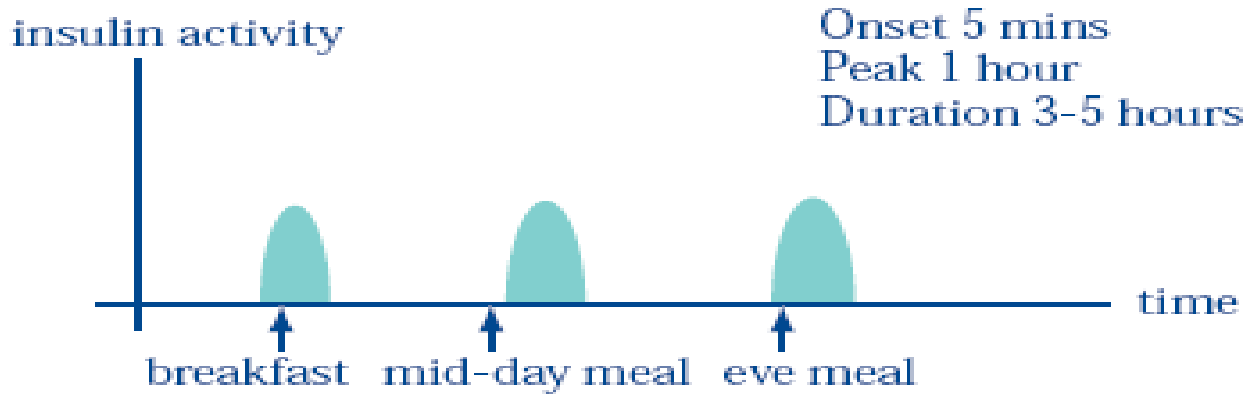
Who would you consider for Insulin? (2)

- Gestational diabetes
- Those with Type 2 after an acute MI
- Some people with Type 2 with acute illness or infection
- Those with Type 2 who go on to oral steroids and the OHA's are not managing blood glucose control

What are the different types of insulin

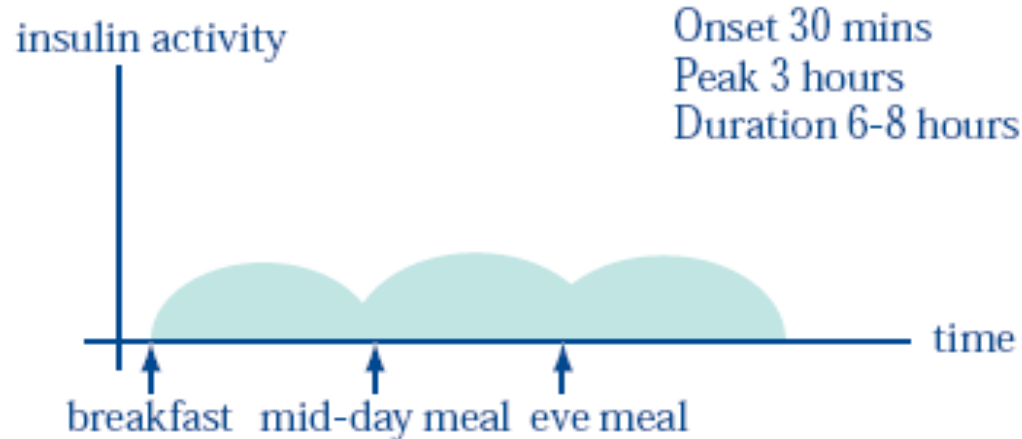
- Rapid Acting
- Short Acting
- Intermediate Acting
- Long Acting
- Mixed Insulin

Rapid Acting Insulin



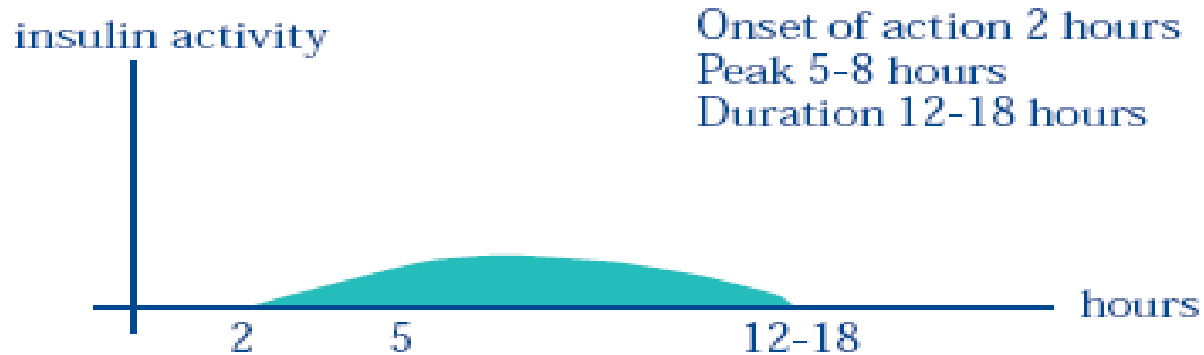
- Onset 5 - 15 minutes
- Peak 1-2 hours
- Duration 3-5 hours
- Can be injected immediately before meals or up to 15 minutes after
- Used pre-meals with intermediate or long acting background insulin
- (basal bolus therapy)

Short Acting Insulin



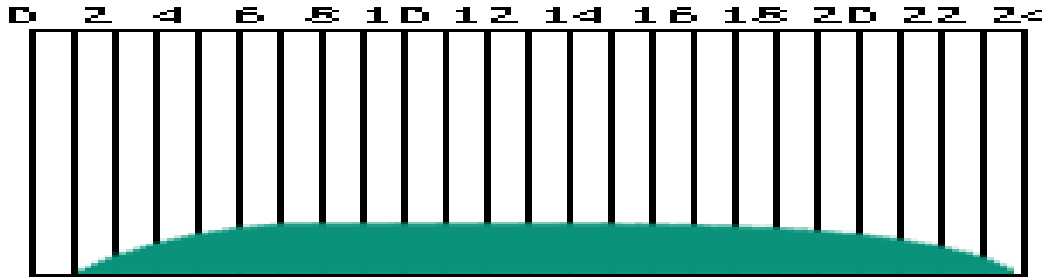
- Onset 30 - 45 minutes
- Peaks 2 - 4 hours
- Duration 6 - 8 hours
- Often used pre meals combined with intermediate or long acting
- background insulin (basal bolus) or in a ‘free-mix’

Intermediate Acting Insulin



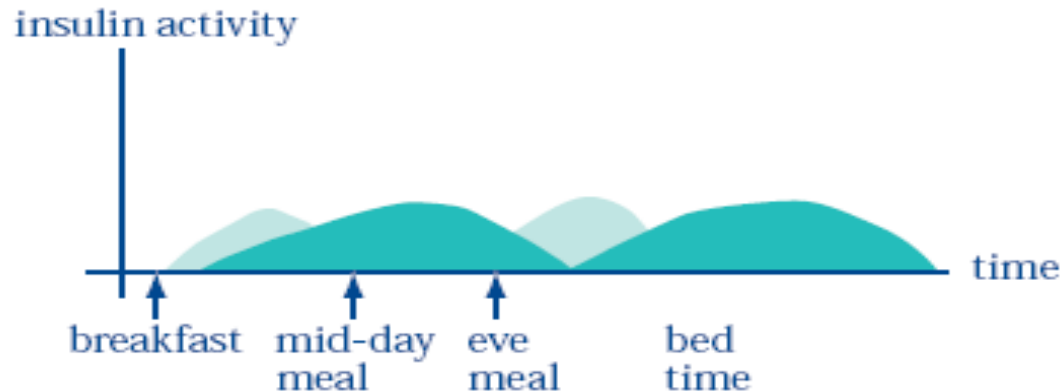
- Onset 2 - 4 hours
- Peak 4 - 8
- Duration 10 - 16 hours
- Can be used daily/ twice daily on its own or in combination with
- analogue or short acting insulin

Long Acting Analogues



- Onset 2 hours
- Peak none
- Duration 18 - 24 hours once daily or once/twice daily
- Less variation in absorption than NPH
- Level profile with no peaks

Mixed Insulin



- Premixed short acting and intermediate insulin e.g. Humulin M3 or Insuman Combi 50
- Or analogue insulin combined with intermediate acting insulin e.g. Humalog Mix 25 or NovoMix 30
- Generally used twice daily
- Suits people with regular lifestyle pattern
- Mixtures - not re-suspending alters mix

Insulin in combination therapy

- Metformin (with any insulin) – helps to minimise weight gain
- Gliclazide – will need to be gradually decreased once insulin started and in the majority of cases will be discontinued
- Glitazones – although Pioglitazone licensed with insulin usually discontinued

Insulin in combination therapy

- Gliptins – licensed to be used as triple therapy with insulin and metformin but can be stopped depending on control achieved
- GLP-1 agonists:-
 - Licensed with basal insulin only
- SGLT2 – licensed for use with insulin

Insulin in combination therapy

All combinations need to be reconsidered and stopped if not having desired effect apart from Metformin

What we know

- There are different types of insulin
- There are different people with variable lifestyles i.e work shift patterns, irregular eating patterns etc
- Some may have special needs i.e. visual problems, dexterity problems etc
- Some may have other concerns i.e. job loss, weight an issue and number of injections per day etc

What we know

- Insulin initiation is NOT a science but an art – working with what you know about the persons lifestyle their blood glucose readings and very importantly - what they want
- It's about individualised care

Common Pitfalls

- Injection sites
- Needle length
- Time of insulin administration
- Storage
- Under/Over titration
- Omitting insulin due to blood glucose results



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New Insulins

- A Biosimilar Insulin is defined as a copy of a biological molecule that is already approved. <http://www.medscape.com/viewarticle/831441>
- Biosimilar rather than a generic version can't be said to be identical to the original. This is because tiny changes in the structure of the product and in the manufacturing process can change the way the drug works.
- ABASAGLAR (Insulin Glargine by Lilly) – 1st Biosimilar Insulin to market

High Strength Insulins

Insulin Glargine

- Lantus 100units/mL
- Abasaglar 100units/mL
- Toujeo U300 300units/mL

Degludec

- Tresiba 100/200units/mL

Case Study 4

- 56 yr Male
- BMI 27
- T2DM 5yrs
- HbA1c 60mmol/mol Next steps?
- Renal – >90

- Metformin 500mg bd
- Gliclazide 80mg 2 bd
- Saxagliptin 5mg od

Case Study 5

- 68 yr male
- BMI 29
- T2DM 15yrs
- Hba1c 75mmol/mol
- eGFR 73
- Metformin 1g bd
- Gliclazide 160mg bd
- Lixisenatide 20mcg od
- What next?

References

1. UKPDS (49). JAMA (1999). 281(21): 2005-12
2. Williams G & Pickup JC. (2004). Handbook of Diabetes, 3rd Ed. Pp 63 & 59
3. DH. (2001). NSF for Diabetes: Standards. Pages 6 and 26.