Barking, Havering and Redbridge University Hospitals NHS Trust

INSULIN INITIATION AND INTENSIFICATION PATHWAY FOR TYPE 2 DIABETES MELLITUS

Number:	Version No: 1
Approved by (name): Medicines Optimisation Group	Date:
On behalf of (Committee/Group) : Medicines Optimisation Group	
Approved by BHR CCGs Area Prescribing sub-Committees: September 2019	
Name & Title of originator/author: Dr Edel Casey, Consultant Endocrinologist; Sanjay Patel QIPP Pharmacist and Dinesh Gupta, Assistant Chief Pharmacist	
Date issued: April 2019	Review Date: April 2019
Template V3 Issued May 2016	

This document will be available (state where): Trust intranet
Individual responsible for this document, including ensuring it is reviewed and updated by date given above, is: Dr Edel Casey
Previous version is archived (state where): N/A

Insulin Initiation and intensification pathway

When to start Insulin:

When other measures no longer achieve adequate blood glucose control to HbA1c <59mmol/mol (7.5 %) or other higher level agreed with the individual, discuss the benefits and risks of insulin therapy. Start insulin therapy if the patient agrees.[1]

Strong indications for insulin therapy include: [2]

- symptoms of hyperglycaemia such as polyuria, thirst, recurrent fungal infections (especially genital thrush) or bacterial infections (especially urine infections)
- pregnancy or planning pregnancy
- oral hypoglycaemic treatments not tolerated/contra-indicated
- weight loss without dieting in someone of low or normal weight

Possible indications for insulin therapy include:

- unsatisfactory glycaemic control even with the maximum tolerated dose of oral hypoglycaemic agents (OHAs) (HbA1c higher than 59mmol/mol, self blood glucose monitoring results higher than 7mmols before meals or 9mmols two hours after meals)
- personal preference
- painful neuropathy
- foot ulceration and infection

When starting insulin therapy, use a structured programme employing active insulin dose titration that encompasses: [1]

- structured education
- continuing telephone support
- frequent self-monitoring
- dose titration to target
- dietary understanding
- management of hypoglycaemia
- management of acute changes in plasma glucose control
- support from an appropriately trained and experienced healthcare professional.
- Ensure appropriate local arrangements are in place for the disposal of sharps.
- 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. If a person has a manual or visual disability and requires insulin, offer an appropriate device or adaptation that can be used successfully
- Issue insulin passport (where available)

Insulin Therapy for Type 2 Diabetes Mellitus

Step 1. Insulin Initiation

Option 1

If HbA1c is ≥ 59mmol/mol to < 69mmol/mol

NPH Insulin - Begin with basal NPH insulin 10 units ONCE DAILY. Alternatively use a smaller dose BD and adjust according to need.

- Insulatard – Onset of action is within 1.5 hours, reaches a maximum effect within 4-12 hours and the entire duration of action is approximately 24 hours.[3]
- Humulin I – Onset of action is within 1-3 hours, reaches a maximum effect within 4-6 hours and the entire duration of action is approximately 22 hours.
- Insuman Basal – Onset of action is within 60 minutes, the phase of maximum action is between 3 and 4 hours after injection and the duration of action is 11 to 20 hours.[3]

Option 2

If HbA1c is ≥ 59 to < 69mmol/mol

Long-acting insulin analogue-preferably 10 units ONCE DAILY at the same time each day to be considered for the following patients (NICE criteria):

- Those who require assistance from a carer or healthcare professional to administer their insulin injections
- Those whose lifestyle is significantly restricted by recurrent symptomatic hypoglycaemic episodes
- Those who would otherwise need twice daily basal insulin injections in combination with oral glucose-lowering medication

1st line – Abasaglar or Semglee (biosimiliar insulin glargine-prescribe by brand name)[9]
Start with 10 units ONCE DAILY

If contra-indicated then

2nd Line - Levemir (Detemir)
Start with 10units ONCE DAILY

Tresiba (Degludec)[4]*
Start with 10units ONCE DAILY

*Should only be considered when ONCE DAILY use of glargine/detemir is insufficient and TWICE DAILY use of human insulin or detemir is being considered, in particular patients suffering nocturnal hypoglycaemia or where issues with third party administration of twice daily injections.

Conversion table
% to mmol/mol
6.5% = HbA1c 48mmol/mol
7.5% = HbA1c 59mmol/mol
8.5% = HbA1c 69mmol/mol

Important considerations at all stages of insulin therapy:

- Reassess psychological issues and any lifestyle changes (diet & exercise). Reassess medication if BMI is ≥ 35 (patient is likely to be insulin resistant). Refer to Diabetes Team
- Give/obtain appropriate support, discuss and agree treatment change to insulin
- **Prescribe insulin by brand name only**
- **Include dose information on all insulin prescriptions**
- Adjust dose daily using self-monitoring blood glucose titration chart to achieve target fasting blood glucose (4.0-7.0mmol/ L) weekly or twice weekly. Postprandial (1-2 hours after meals) aim up to 8.0-9.0mmol/L[5]
- Continue treatment with Metformin **(please ensure creatinine < 150umol/l and eGFR > 30 ml/minute/1.73m2)[5]**
- Glitazones (if wish to continue, please discuss risks with patient and Diabetes Team) ***Note:*** Risk of heart failure, weight gain, fluid retention, anaemia, risk of bladder cancer (check urine for blood at least twice yearly, if positive, stop Glitazones, rule out infection and consider referral to urologist.)
- Review or substitute other medications (GLP1, Gliptins, SGLT2) and/or interventions as appropriate i.e. Refer to obesity clinic. Be aware of the risk of euglycaemic DKA if starting an SGLT-2i.
- Review the use of sulphonylurea if hypoglycaemia occurs: preferably discontinue use or reduce dose.

Step 2. Insulin Intensification

Intensifying insulin OR for patient with HbA1c ≥ 69mmol/mol

Basal bolus regime[5]: basal insulin** 6-8 units nocte with short or rapid acting insulin's with breakfast, lunch and evening meal e.g. 2-4 units THREE TIMES A DAY

Short Acting Insulin (soluble Insulin): Onset of action 30-60mins, peak levels at 2-4 hours, duration 5-8 hours. Actrapid, Humulin S, Insuman Rapid

Rapid Acting Insulin (Analogue): Onset of action 15 minutes, peak levels at 3-5 hours, duration of action 3-5 hours. Novorapid (Aspart) Apidra (Glulisine) Humalog (Lispro)

** Basal Insulin: NPH human or if NICE criteria met long acting insulin analogue

Bisphasic (Pre-mixed) insulin e.g. initial dose 8 units TWICE DAILY[5] (if applicable stop basal insulin). ONCE DAILY regimen may be an option when initiating this therapy.

Human: (NPH:Isophane+soluble): onset 30-60 mins, peak variable, duration of action 10-16 hours. Humulin M3, Insuman Comb15,25,50

Analogue: Onset 5-15mins,peak variable, duration of action 10-16 hours. Novomix 30 (Aspart), Humalog (Lispro) mix 25,50

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Intensifying Insulin

Intensification of insulin therapy can cause weight gain which may be avoidable.

Note:

1. Insulin doses are for guidance only and should be adjusted as per patient's requirements.
2. If patients insulin requirement is >1 unit / kg please refer to secondary care – possible insulin resistance and worsening metabolic syndrome
3. NICE recommends beginning with human NPH insulin.
4. Patients on animal (pork, bovine) insulin – if well controlled may continue.
5. Please be aware that some human insulins may not be available in pen or cartridge form.
6. If any concerns please refer to GPwSI / DSN or secondary care

Important considerations at all stages of insulin therapy:

- Reassess psychological issues and any lifestyle changes (diet & exercise). Reassess medication if BMI is ≥ 35 (patient is likely to be insulin resistant). Refer to Diabetes Team
- Give/obtain appropriate support, discuss and agree treatment change to insulin
- **Prescribe insulin by brand name only**
- **Include dose information on all insulin prescriptions**
- Adjust dose daily using self-monitoring blood glucose titration chart to achieve target fasting blood glucose (4.0-7.0mmol/ L) weekly or twice weekly. Postprandial (1-2 hours after meals) aim up to 8.0-9.0mmol/L[5]
- Continue treatment with Metformin **(please ensure creatinine < 150umol/l and eGFR > 30 ml/minute/1.73m2)[5]**
- Glitazones (if wish to continue, please discuss risks with patient and Diabetes Team) ***Note:*** Risk of heart failure, weight gain, fluid retention, anaemia, risk of bladder cancer (check urine for blood at least twice yearly, if positive, stop Glitazones, rule out infection and assess referral to urologist.)
- Review or substitute other medications (GLP1, Gliptins, SGLT2) and/or interventions as appropriate i.e. Refer to obesity clinic. Be aware of the risk of euglycaemic DKA if starting an SGLT-2i.
- Review the use of sulphonylurea if hypoglycaemia occurs: preferably discontinue use or reduce dose.

Step 3. Referral to Secondary Care

Further intensifying insulin OR for patient with HbA1c ≥ 69mmol/mol

- Patient requires single dose of insulin > 60 units OR total daily dose > 200 units
- Patient BMI>35

Initiation by <u>Hospital Consultant Only</u> and to be continued in primary care.

- Xultophy (combination of insulin degludec and liraglutide)[6]
- Tresiba (Insulin degludec 200 units/ml) [4]
- Toujeo (Insulin glargine 300units/ml)[7]
- Exenatide (used in combination with Insulin)[1]
- Dulaglutide (used in combination with or without Insulin)[8]

Key to abbreviations used:

BMI – Body Mass Index
DSN – Diabetes Specialist Nurse
GPwSI – General Practitioner with Specialist Interest
NPH – Neutral protamine Hagedorn (intermediate acting insulin)
DKA – Diabetic ketoacidosis
SGLT2i– Sodium Glucose Co-transporter 2 inhibitor e.g. dapagliflozin
GLP 1 – Glucagon-like Peptide-1 receptor agonists e.g. exenatide

References:

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