Formulary Factsheet:
Insulin for Type 2 Diabetes

Background
The purpose of this fact sheet is to emphasise the importance of following NICE guidance with regard to the use of insulin in type 2 diabetes, and to support the implementation of local insulin initiation guidelines.

A recent study has shown that the annual cost of analogue insulin increased across the NHS from £18 million in 2000 (12% of total insulin cost) to £305 million in 2009 (85% of total insulin cost). If only 50% of analogue insulin dispensed in the UK between 2000 and 2009 had been for human insulin alternatives, the NHS would have saved an estimated £312 million.

What does NICE recommend?

Human NPH (isophane) insulin, used once or twice-daily according to need, is the preferred first choice insulin. It is preferred based on cost effectiveness and its well-recognised safety profile. Insulin analogues (glargine, detemir) should be considered only in specific circumstances, see below:

The Bottom Line
- For most people with type 2 diabetes, long-acting insulin analogues offer no significant advantage over human NPH (isophane) insulin and are much more expensive.
- In terms of HbA1c lowering, there is no difference between long-acting insulin analogues and human NPH insulin.
- Whilst <7 year data from the ORIGIN study looks positive, the longer-term safety of the long-acting insulin analogues, insulin glargine and insulin detemir, is not known. Robust evidence that they improve patient-orientated outcomes and are cost effective is not available at the current time.

When are analogue insulins appropriate?
The main benefits of the long acting insulin analogues relate to lower rates of hypoglycaemia, and once daily use. However, these potential benefits need to be balanced against their much higher costs and lack of long-term safety and outcome data. It is more cost-effective to target the use of long acting insulin analogues to those people with type 2 diabetes who would be most likely to benefit. NICE therefore recommends them as an option if:

- The patient needs assistance from a carer or health professional to inject insulin, and use of a long-acting insulin analogue would reduce the frequency of injections from twice to once daily OR
- The patient’s lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes OR
- The patient would otherwise need twice-daily NPH insulin injections in combination with oral glucose-lowering drugs OR
- The patient cannot use the device to inject NPH insulin
- Patient with significant renal/liver pathology due to increased risk of hypoglycaemia (eGFR<30 or established cirrhosis)

When is it appropriate to switch from analogue to NPH insulin?
By initiating new type-2 patients on NPH insulins first line rather than the analogues, and reviewing patients with sub-optimal (HbA1C>9%) control with a view to switching to NPH insulin, prescribers will regain experience with this type of insulin. Mass switching to NPH insulin is not recommended at present and switching should only be considered on an individual patient basis. Specialist input should be sought if required. Going forward however it may be that the 50% aspiration identified in the current Prescribing Strategy can be achieved through wider switching programmes. This will result in significant savings to the healthcare economy.

What are the safety issues? (inc. nocturnal hypoglycaemic attacks)
Compared with human NPH insulin, long acting insulin analogues result in a statistically significantly lower incidence of any hypoglycaemia and a statistically significantly lower incidence of nocturnal hypoglycaemia. However, there is no statistically significant reduction in the incidence of severe hypoglycaemia.
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**What NPH Isophane insulin could be prescribed?**

<table>
<thead>
<tr>
<th>Insulin</th>
<th>Prefilled devices</th>
<th>Cartridges</th>
<th>Syringes</th>
<th>Insulin Basal, Insulatard, and Humulin I all have a similar duration of action (8-12 hours)</th>
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</table>
| Insulatard    | 5x3ml **Insulatard Innolet** device £20.40 (1-50 units, 1 unit dial up) | 5x3ml Penfill cartridges £22.90  
- Novopen 3 £25.95  
  (1-35 units, 0.5 unit dial up)  
- Novopen 4 Blue or Silver £26.86  
  (1-60 units, 1 unit dial up)  
- Novopen Echo Blue or Red £26.86  
  (0.5-30 units, 0.5 unit dial up) | 10ml vial £7.48  |
| Humulin I     | 5x3ml **Humulin I Kwikpen** £21.70 (1-60 units, 1 unit dial up) | 5x3ml cartridges £19.08  
- Autopen Classic £16.25  
  (1-21 units, 1 unit dial up OR 2-42 units, 2 unit dial up)  
- Humapen Luxura/Memoir/Luxura HD £26.82  
  (1-60 units, 1 unit dial up OR 1-30 units, 0.5 unit dial up) | 10ml vial £15.68  |

**Switching to NPH insulin**

When switching a patient from a long acting analogue to an NPH insulin it would be advisable to reduce the number of daily units by 10% then adjust according to requirements. Although patient preference will guide the device of choice, Insulan Basal may be the most cost-effective option and is the first line formulary choice within the NPH insulin group. The Solostar Prefilled device is the same as the Lantus pre-filled pen which may make the transition easier for some patients. The local diabetic specialist nurses have the greatest experience with Insulan Basal and endorse its use first line if an NPH insulin is required.

**Biphasic insulins (Specialist input required)**

Biphasic insulins (e.g. Humulin M3, Insulan Combi etc) have a place in the management of patients who have difficulty with, or prefer not to use multiple injection regimens. They may also be useful in particular where HbA1c is elevated above 9%. Biphasic preparations of insulin analogues (e.g. Humalog Mix25) may be considered over pre-mixed human insulin preparations however when:

- Immediate injection before a meal is preferred, or
- Hypoglycaemia is a problem, or
- Blood glucose levels rise markedly after meals

**References**

1. Evaluation of the incremental cost to the National Health Service of prescribing analogue insulin, BMJ, Sept 11