Position Statement

Use of analogue insulins (for review in 2013)

February 2012  Page 1 of 5

Insulin analogues were developed in an attempt to overcome the problems associated with human insulin, ie slow and prolonged absorption of meal-time insulin, and unduly short absorption of basal insulin, both often rather unpredictably, and thus leading to hyper- and hypo-glycaemia (Holt, 2009).

Analogues have been available for use by people with diabetes since the introduction of the first rapid-acting analogue, insulin lispro, in the mid 1990s. Since then, two additional rapid-acting analogues (insulin aspart and insulin glulisine) and two long-acting analogues (insulin detemir and insulin glargine) have entered the clinical arena. Rapid-acting analogues (lispro and aspart) are also available in premixed insulin preparations, and other analogues are in an advanced state of development.

Since their introduction, analogues have become increasingly popular for use in clinical practice despite their considerably higher cost. Questions have been raised as to whether their benefits outweigh these higher costs. Although costs are of increasing importance within the current climate in the NHS, we are concerned that cost should not become the only criteria on which prescribing decisions are made although it has to be a consideration.

We would support The National Institute of Health and Clinical Excellence (NICE) conclusions that insulin analogues should be available to people with diabetes, (NICE CG15 2004, NICE CG66 2008, NICE CG87 2009), albeit with restrictions, especially for those with Type 2 diabetes. For people starting insulin, human insulins are recommended as first line treatment, switching to analogues for optimal control as recommended by NICE (for a summary of those recommendations, see Appendix A). Those already on analogue insulins should not have their treatment changed if already well controlled.

Diabetes UK has reviewed the evidence relating to the use of insulin analogues in both Type 1 and Type 2 diabetes. While there is limited evidence that insulin analogues improve HbA1c, there is good evidence that some rapid acting analogues reduce postprandial glucose levels, while long acting analogues may improve fasting glucose levels, leading to reduced hypoglycaemia (especially nocturnal), and less weight gain, particularly in people with Type 2 diabetes.

- Fear of hypoglycaemia is a determinant of treatment concordance (Gough 2006), so any reduction in episodes of hypoglycaemia is likely to improve concordance and therefore diabetes management, reducing the chances of developing the long term complications of diabetes.

- Fear of hypoglycaemia has marked effects on health-related quality of life (Currie et al 2006, Vexiau et al 2008)

- The wider impact of mild hypoglycaemia should also not be underestimated, as it has a measurable impact on productivity and costs for both employers and employees
• Weight management is the primary nutritional strategy in managing glucose control in people with Type 2 diabetes who are overweight or obese (Dyson et al 2011) so insulins that effectively control blood glucose but with lesser weight gain should be considered

• Post-prandial glucose level is a direct and independent risk factor for cardiovascular disease and a reduction in post-prandial levels is important for people with diabetes, who are already at increased risk of CVD (IDF Guideline Group, 2007)

While clinical trails provide the best quality of data for assessing a drug’s efficacy, certain limitations to the literature reviewed must be taken into consideration. Most trials into insulin analogues were not designed to demonstrate superiority in blood glucose management, merely equivalence (Plank 2005, Sheldon 2009) although a trial published by Hermansen (2004) showed slight superiority. Some trials had HbA1c as a secondary endpoint. There are also difficulties in interpreting the data, as terms such as severe hypoglycaemia are open to bias-prone definitions (Horvath 2007). Finally, trial populations tend to be more motivated and different results may be found in clinical practice (Holt 2009).

What Diabetes UK recommends:

Diabetes UK recommends that all insulin analogues should be available to people with diabetes in the same way as human or animal insulin. The decision of which insulin is most appropriate should be made in consultation between the person with diabetes and their healthcare team and should follow NICE guidance. ie human insulins should, in general, be tried as first line treatment, with analogues being introduced if optimal control cannot be attained.

This position statement relates to the use of analogue insulins when commencing insulin therapy rather than changes in prescribing policy of those already well controlled on analogue insulins. Diabetes UK recommends that people who are already established on analogue insulin and well controlled should continue with their treatment.

Diabetes UK would like to see pharmaceutical companies addressing the issue of cost to ensure that new and novel therapies are affordable in the current climate and are supported by robust evidence of superiority to established therapies.
Appendix 1
Summary of NICE Guidance

Type 1: NICE CG15 (2004)
Adults with Type 1 diabetes should have access to the types (preparation and species) of insulin they find allow them optimal well-being.
Cultural preferences need to be discussed and respected in agreeing the insulin regimen for a person with Type 1 diabetes.
Multiple insulin injection regimens, in adults who prefer them, should be used as part of an integrated package of which education, food and skills training should be integral parts.
Appropriate self-monitoring and education should be used as part of an integrated package to help achieve optimal diabetes outcomes.
Mealtime insulin injections should be provided by injection of unmodified (‘soluble’) insulin or rapid-acting insulin analogues before main meals.
Rapid-acting insulin analogues should be used as an alternative to mealtime unmodified insulin:
- where nocturnal or late inter-prandial hypoglycaemia is a problem
- in those in whom they allow equivalent blood glucose control without use of snacks between meals and this is needed or desired.
Basal insulin supply (including nocturnal insulin supply) should be provided by the use of isophane (NPH) insulin or long-acting insulin analogues (insulin glargine).
Isophane (NPH) insulin should be given at bedtime. If rapid-acting insulin analogues are given at mealtimes or the midday insulin dose is small or lacking, the need to give isophane (NPH) insulin twice daily (or more often) should be considered.
Long-acting insulin analogues (insulin glargine) should be used when:
- nocturnal hypoglycaemia is a problem on isophane (NPH) insulin
- morning hyperglycaemia on isophane (NPH) insulin results in difficult daytime blood glucose control
- rapid-acting insulin analogues are used for mealtime blood glucose control.
Twice-daily insulin regimens should be used by those adults who consider number of daily injections an important issue in quality of life: biphasic insulin preparations (pre-mixes) are often the preparations of choice in this circumstance
Biphasic rapid-acting insulin analogue pre-mixes may give an advantage to those prone to hypoglycaemia at night.

Type 2: NICE CG66 and 87 (2008/9)
Insulin therapy should be initiated from a choice of a number of insulin types and regimens.
Preferably begin with human NPH insulin, taken at bedtime or twice daily according to need.
Consider, as an alternative, using a long-acting insulin analogue (insulin glargine) for a person who falls into one of the following categories:
- 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 once daily basal insulin injections in combination with oral glucose-lowering medications.
Consider twice-daily biphasic human insulin (pre-mix) regimens in particular where HbA1c is elevated above 9.0 %. A once-daily regimen may be an option when initiating this therapy.
Consider pre-mixed preparations of insulin analogues rather than pre-mixed human insulin preparations when:
- immediate injection before a meal is preferred, or
- hypoglycaemia is a problem, or
- there are marked postprandial blood glucose excursions.
Offer a trial of insulin glargine if a person who has started with NPH insulin experiences significant nocturnal hypoglycaemia.
Monitor a person using a basal insulin regimen (NPH or a long-acting insulin analogue (insulin
glargine) for the need for mealtime insulin (or a pre-mixed insulin preparation)). If blood glucose control remains inadequate (not to agreed target levels without problematic hypoglycaemia), move to a more intensive, mealtime plus basal insulin regimen based on the option of human or analogue insulins.

Monitor a person using pre-mixed insulin once or twice daily for the need for a further preprandial injection or for an eventual change to a mealtime plus basal insulin regimen, based on human or analogue insulins, if blood glucose control remains inadequate.

**Children and Young People (NICE CG15 2004)**

Children and young people with type 1 diabetes should be offered the most appropriate insulin preparations (rapid-acting insulin analogues, short-acting insulins, intermediate-acting insulins, long-acting insulin analogues or biphasic insulins) according to their individual needs and the instructions in the patient information leaflet supplied with the product with the aim of obtaining an HbA1c level of less than 7.5% without frequent disabling hypoglycaemia and maximising quality of life.

Children and young people with type 1 diabetes using multiple daily insulin regimens should be informed that injection of rapid-acting insulin analogues before eating (rather than after eating) reduces postprandial blood glucose levels and thus helps to optimise blood glucose control. For pre-school children with type 1 diabetes it may be appropriate to use rapid-acting insulin analogues shortly after eating (rather than before eating) because food intake can be unpredictable.

Research is needed to evaluate the effectiveness of long-acting insulin analogues in children and young people with type 1 diabetes.
References:


International Diabetes Federation (2007). Guideline for the management of postmeal glucose

