

# The role of newer insulins in diabetes: Summary

This *Bulletin* considers the evidence supporting the use of the newer insulins and their role in patients with type 1 and type 2 diabetes. In particular, the rapid-acting and long-acting insulin analogues are discussed, but some attention is also given to inhaled insulin.



## Rapid-acting insulin analogues

### Type 1 diabetes

- The rapid-acting insulin analogues do not appear to produce large benefits in glycosylated haemoglobin (HbA<sub>1C</sub>) control over short-acting soluble insulin in most patients with type 1 diabetes.
- There is some evidence that rapid-acting insulin analogues, particularly insulin lispro, are associated with a lower rate of nocturnal hypoglycaemia than soluble short-acting insulin in patients with type 1 diabetes. However, there is little evidence that they reduce episodes of overall or severe hypoglycaemia (the most important outcome).

### Type 2 diabetes

- For most patients with type 2 diabetes, the rapid-acting insulin analogues do not appear to result in significant reductions in HbA<sub>1C</sub> compared with short-acting soluble insulin.
- There is little evidence that the rapid-acting insulin analogues produce large reductions in episodes of severe, overall or nocturnal hypoglycaemia compared with short-acting soluble insulin in most patients with type 2 diabetes.

## Long-acting insulin analogues

### Type 1 diabetes

- For most patients with type 1 diabetes, insulin **glargine** used once daily does not seem to improve HbA<sub>1C</sub> compared with Neutral Protamine Hagedorn (NPH) insulin (isophane) used once or twice daily.
- For patients with type 1 diabetes, there appears to be some evidence that insulin **glargine** reduces hypoglycaemia, particularly hypoglycaemia at night. However, not all randomised controlled trials (RCTs) have shown a difference between insulin glargine and NPH in the incidence of hypoglycaemia.

- There is no strong evidence that insulin **detemir** provides better HbA<sub>1C</sub> control than NPH insulin in patients with type 1 diabetes. In addition, whilst some studies have shown benefits with insulin detemir on certain definitions of hypoglycaemia, particularly nocturnal hypoglycaemia, not all studies have shown a difference compared with NPH.

### Type 2 diabetes

- There is little evidence to suggest that insulin **glargine** used once daily reduces HbA<sub>1C</sub> compared with NPH insulin used once or twice daily in most patients with type 2 diabetes.
- In patients with type 2 diabetes, insulin **glargine** appears to reduce hypoglycaemia, particularly nocturnal, and symptomatic hypoglycaemia. However, there is little strong evidence that it reduces severe hypoglycaemia compared with NPH insulin.
- Insulin **detemir** does not appear to reduce HbA<sub>1C</sub> compared with NPH insulin in patients with type 2 diabetes. Whilst it might be associated with a lower incidence of nocturnal hypoglycaemia, this was not seen in all RCTs. In addition, there is little strong evidence that it reduces severe hypoglycaemia compared with NPH insulin.

## Inhaled insulin

There is currently little evidence that inhaled insulin has any clinical advantages over short-acting soluble subcutaneous insulin injections. It does not appear to improve HbA<sub>1C</sub> or reduce hypoglycaemia compared with short-acting soluble insulin injections used at mealtimes.

## Conclusion

Despite an increase in prescribing of the newer more expensive insulin

analogues, there is currently no strong evidence that they result in large improvements in HbA<sub>1C</sub> compared with older insulins. Several studies that compared rapid-acting insulin analogues with short-acting soluble insulin, and long-acting insulin analogues with NPH insulin, have suggested that insulin analogues reduce hypoglycaemia, particularly at night. However, studies could not be completely blinded, this has not been seen in all RCTs, and definitions of hypoglycaemia have often varied between trials, making assessment of these benefits difficult. Therefore, in the absence of long-term safety data over many years, it is reasonable not to support a widespread policy of using insulin analogues first-line in most patients. Nevertheless, they still have a valuable role in managing specific patients, particularly those whose glycaemic control is suboptimal with older insulins, especially if they have problematic hypoglycaemia.

Inhaled insulin does not appear to improve HbA<sub>1C</sub> or reduce hypoglycaemia compared with short-acting soluble insulin used at mealtimes. In addition, it does not completely eliminate the use of injections in most patients. Therefore, NICE have restricted its use to specialist diabetes centres, only in people with type 1 or type 2 diabetes who have poor control and either an injection phobia (meeting DSM-IV criteria) or severe persistent problems with injection sites.

Any decision to start a newer insulin needs to be balanced carefully against the lack of long-term safety data over many years and increased prescribing costs. In addition, people with control problems should be properly assessed for underlying causes before these newer, more expensive insulins are considered. This includes ensuring that they have been properly educated and understand how to manage their disease and treatment.