MTRAC
Midlands Therapeutics Review and Advisory Committee

Considerations for Commissioners
Biosimilar insulin glargine *(Abasaglar®▼)*

For the treatment of type 1 and type 2 diabetes

Commissioning considerations:

When making a decision about the use of this new biosimilar insulin glargine, commissioners may wish to consider the following:

- That people are receiving appropriate treatment with a long-acting insulin analogue according to the current NICE guidance and that adequate arrangements are in place for regular monitoring and review of patients' diabetes medications. The National Diabetes audit (2012/13) reported that 80% of people with Type 1 diabetes and 93% of people with Type 2 diabetes had an annual check for the effectiveness of diabetes treatment.
- It may be appropriate to initiate Abasaglar® treatment in new patients, or patients assessed to need a medication change, in the first instance until clinical experience of the treatment and its delivery device has been gained.
- Draft MHRA guidance suggests that prescribers ensure that patients read and understand the patient information leaflet, receive appropriate training on correct use, are given a patient booklet and insulin passport and should be warned only to use insulins as they have been trained.
- NICE's biosimilars position statement, states that NICE guidance on a product also applies to relevant licensed biosimilar products which subsequently appear on the market.
- That the yearly cost of Abasaglar® is about 15% lower than Lantus®; at £343 per patient per year, compared with £403 per patient per year for Lantus® (assuming 40 units per day for each treatment).

Strength of the evidence

To gain licence approval from the European Commission the manufacturer had to demonstrate that Abasaglar had similar physicochemical and biological characteristics, similar pharmacodynamics and pharmacokinetics, and a similar safety and efficacy profile to that of the reference product, Lantus®.[1] The committee considered that the evidence from the two phase 3 randomised controlled trials (RCTs) adequately demonstrated the non-inferiority of Abasaglar® to Lantus® in both safety and efficacy.

Description of technology

Abasaglar is a biosimilar form of insulin glargine that has the same primary amino acid sequence as the original insulin glargine product (Lantus) and the same pharmaceutical form and strength. Comparability testing has shown that Abasaglar has a comparable pharmacological and toxicological profile to Lantus.[1]

Abasaglar (100 U/mL) is licensed for the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above.[2] It should be administered once daily at any time, but at the same time each day. In patients with type 2 diabetes mellitus, Abasaglar can also be given together with orally active antidiabetic medicinal products. Full details are given in the Summary of Product Characteristics for Abasaglar.[2]

Background

Diabetes mellitus is a common chronic disease, associated with markedly increased morbidity and mortality. It is estimated that in the UK, more than 1 in 16 people has diagnosed or undiagnosed diabetes, and that there are 3.9 million people living with the disease.[3] This number is estimated to rise to 5 million people by 2025.[3] Diabetes is associated with serious long-term microvascular (nephropathy, retinopathy, and neuropathy) and macrovascular complications (coronary heart disease, stroke, and peripheral vascular disease).[4] About 90% of people with diabetes mellitus have type 2 diabetes.[3] The total cost (direct care and indirect costs) associated with diabetes in the UK currently stands at £23.7 billion and is predicted to rise to £39.8 billion by 2035/6.[3]

Adults with type 1 diabetes must inject insulin several times daily, using a combination of long-acting and short acting insulins to replace the normal pattern of insulin production from the pancreas.

Dietary and lifestyle modifications form the mainstays of therapy for type 2 diabetes, but most patients will eventually need an antidiabetic drug and/or insulin. Drug treatments currently available include sulphonylureas, metformin, pioglitazone, acarbose, prandial glucose regulators (repaglinide and nateglinide), DPP-4 inhibitors or 'gliptins', GLP-1 analogues (exenatide, liraglutide, dulaglutide and lixisenatide), SGLT2 inhibitors (dapagliflozin, canagliflozin, and empagliflozin) and insulin.

Clinical evidence for efficacy and safety

Two phase 3, non-inferiority trials have evaluated the clinical efficacy of biosimilar insulin glargine: ELEMENT 1 and 2.[5,6]

ELEMENT 1[5] was a 52-week open-label, non-inferiority RCT that randomised 535 adults with type 1 diabetes to Abasaglar or Lantus. Eligible participants had been using once daily insulin (NPH, Lantus or detemir) combined with mealtime insulin for at least 3 months, had a glycosylated haemoglobin (HbA_{1c}) level ≤ 11.0% (97 mmol/mol) and a body mass index (BMI) ≤ 35 kg/m^2. The trial used a treat-to-target approach, starting with the participants own pre-study insulin dose levels and adjusting the dose to meet targets including HbA_{1c} < 7% (53 mmol/mol), and fasting plasma glucose ≤ 108 mg/dL [6.0 mmol/L], without incurring hypoglycaemia.

ELEMENT 2[6] was a 24-week, double-blind, non-inferiority RCT that evaluated Abasaglar *vs*. Lantus in 756 adults with type 2 diabetes who had received at least 2 oral antidiabetic drugs (OADs) at stable dose for at least 12 weeks. Some of the participants had also been treated with Lantus before trial entry. Participants had to have an HbA_{1c} ≥ 7.0% (53 mmol/mol) and ≤ 11.0% (97 mmol/mol) if previously on Lantus and a BMI ≤ 45 kg/m^2. For participants previously treated with Lantus, pre-trial doses were used. Insulin naïve patients had a starting dose of 10 U once daily. This trial also used a treat to target approach with all participants aiming to maintain a fasting blood glucose (FBG) level ≤100 mg/dL (5.6 mmol/L) while avoiding hypoglycaemia.

The primary outcome measure in both trials was the change in HbA_{1c} from baseline to week 24. Provided the upper limit of the 95% confidence interval for the difference in HbA_{1c} change between treatments was less than 0.3%, the products were considered to be non-inferior. Secondary outcomes included the percentage of participants achieving <7.0% after 24 weeks or 52 weeks and levels of hypoglycaemia.

Results

Change in HbA_{1c}: In the ELEMENT 1 trial[5], HbA_{1c} decreased by 0.35% and 0.46% (4-5 mmol/mol) for Abasaglar and Lantus, respectively from a baseline of 7.7% or 61 mmol/mol when used in combination with mealtime insulin lispro. In the ELEMENT 2 trial, HbA_{1c} decreased by 1.29% and 1.34% (14-15 mmol/mol) for Abasaglar and Lantus, respectively from a baseline of 8.3% or 67 mmol/mol when used in combination with OADs. For both trials, the conditions for non-inferiority were met for Abasaglar *vs.* Lantus. In the ELEMENT 1 trial the mean treatment difference was 0.020% (95% CI: -0.099% to 0.140%) or 0.2 mmol/mol (95% CI −1.1 to 1.5) after 52 weeks' treatment, and in the ELEMENT 2 trial the mean treatment difference was 0.052% (95% CI: -0.070% to 0.175%) or 0.6 mmol/mol (95% CI −0.8 to 1.9) after 24 weeks' treatment.

The percentage of participants achieving HbA_{1c} <7.0% after 24 weeks' treatment was 35% and 32% in the ELEMENT 1 trial, and 49% and 53% in the ELEMENT 2 trial for Abasaglar and Lantus, respectively.

Hypoglycaemia: There was no significant difference between treatment groups for the total incidence of hypoglycaemia in either trial or incidence of nocturnal hypoglycaemia in the ELEMENT 2 trial.[6]

Weight gain in the trials was similar between groups in both trials, and there was no significant difference between Abasaglar and Lantus.

Adverse events

Safety data, which included 52-week data from the study in adults with type 1 diabetes, found that overall the adverse event profile and immunogenicity profile (i.e. detectable antibodies to insulin) was similar for Abasaglar and Lantus. The most frequently reported adverse events in both trials were nasopharyngitis, upper respiratory tract infection, hypoglycaemia and diarrhoea. No major safety findings or signals were identified in the clinical programme.

Considerations for cost impact

- From 2013/14 QOF data there were 2,814,004 patients in England with diabetes mellitus recorded in QOF disease registers (average prevalence 6.21%) in adults over 17. In the Midlands and East of England Commissioning region there were 890,000 patients with diabetes mellitus recorded, of which 185,808 are from subscriber CCGs (average prevalence 7.44%).[7]
- Using September 2015 prices, the cost of Abasaglar is 15% lower than that of Lantus.

References

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