NICE advice

Diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar)

Evidence summary
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Key points from the evidence

Summary

In 2 randomised controlled trials (RCTs) insulin glargine biosimilar (Abasaglar) was as effective as insulin glargine (Lantus) at reducing HbA1c levels in people with type 1 and type 2 diabetes. The safety profile of Abasaglar is comparable to that of Lantus.

Regulatory status: Insulin glargine biosimilar 100 units/ml (Abasaglar) received a European marketing authorisation in September 2014 and was launched in the UK in September 2015. It is the first biosimilar insulin glargine to be launched in the UK and as part of the licensing process, has been shown not to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy.

Effectiveness	Safety
• Insulin glargine biosimilar 100 units/ml (Abasaglar) once daily was non-inferior to insulin glargine 100 units/ml (Lantus) in people with type 1 diabetes (treatment difference 0.11% points [1.18 mmol/mol] p>0.05) for change in HbA1c from baseline (1 open-label RCT, n=535, 24 weeks). • Insulin glargine biosimilar 100 units/ml (Abasaglar) once daily was non-inferior to insulin glargine 100 units/ml (Lantus) in people with type 2 diabetes (treatment difference 0.05% points [0.57 mmol/mol] p>0.05) for change in HbA1c from baseline (1 double-blind RCT, n=756, 24 weeks).	• The safety profile of Abasaglar is comparable to that of Lantus and as expected for an insulin product. No additional safety signals were detected with regard to hypoglycaemia, allergic reactions or injection site reactions and the immunogenicity profiles are comparable (European public assessment report [EPAR]). • The Abasaglar summary of product characteristics lists the same contraindications, cautions and undesirable effects as for Lantus and lists hypoglycaemia as a very common adverse reaction.

Patient factors	Resource implications
• Abasaglar is given once daily by subcutaneous injection, and is available as 100 units/ml in cartridges or as a pre-filled pen. • Across the 2 RCTs similar numbers of people withdrew because of adverse events with Abasaglar compared with Lantus (1% compared with 2% in people with type 1 diabetes and 2% compared with 3% in people with type 2 diabetes). • Abasaglar is a new insulin product and people with diabetes need to understand the differences between Abasaglar and several other new insulin products that have recently become available to minimise the risk of medication error. • All biological medicines, including biosimilar medicines, should be prescribed by brand name so that products cannot be automatically substituted at the point of dispensing. • The choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.	• The cost of Abasaglar cartridges 100 units/ml, 5×3 ml for the pen or Abasaglar pre-filled pen 100 units/ml, 5×3 ml is £35.28 (excluding VAT; prices taken from MIMS, November 2015). This is 15% less than the cost of Lantus. • Comparable costs for other standard-strength basal insulins range from £17.50 to £72.00 for 5x3 ml cartridges or pre-filled pens (excluding VAT; prices taken from MIMS, November 2015). • The cost of Abasaglar and other basal insulins will depend on the preparation chosen and the insulin dosage used.

Introduction and current guidance

Diabetes mellitus is a group of metabolic disorders in which blood glucose is persistently raised. Type 1 diabetes is a long-term hormonal deficiency disorder treated with insulin replacement therapy. This is supported by active management of other cardiovascular risk factors, such as raised blood pressure and disturbed blood lipid levels. Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in high blood glucose levels. It is commonly associated with obesity, physical inactivity, raised blood

pressure, disturbed blood lipid levels and a tendency to develop atherosclerosis, and therefore is recognised to be associated with an increased cardiovascular risk. NICE has published guidance on the management of type 1 and type 2 diabetes in adults with recommendations on insulin therapy and an individualised approach to diabetes care. A biosimilar medicine (or biosimilar) is a biological medicine that is developed to be highly similar to an existing biological medicine (the reference medicine). The active substance of a biosimilar and its reference medicine is essentially the same biological substance but, just like the reference medicine, the biosimilar has a degree of natural variability. When approved, this variability and any differences between the biosimilar and its reference medicine will have been shown not to affect safety or effectiveness. In the development of a biosimilar, there is no requirement to demonstrate clinical benefit to patients *per se* as this has been shown for the reference medicine. Instead, biosimilars undergo a comprehensive regulatory process which demands extensive comparability studies that demonstrate similarity to the reference medicine. Biosimilars have the potential to offer the NHS considerable cost savings. However the choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.

Full text of introduction and current guidance.

Product overview

Insulin glargine biosimilar (Abasaglar) is licensed for the treatment of diabetes mellitus in adults, young people and children over 2 years. Abasaglar is a basal insulin for once daily use and is bioequivalent to insulin glargine (Lantus). Abasaglar is available as cartridges of 100 units/ml for use in the reusable pen or as a pre-filled Abasaglar pen 100 units/ml. It should be noted that the Abasaglar device is not the same as that of the originator (Lantus). Abasaglar cartridges cannot be used in the re-useable pen devices produced for Lantus.

Full text of product overview.

Evidence review

This evidence summary is based on the 2 phase III studies of insulin glargine biosimilar (Abasaglar) in people with type 1 and type 2 diabetes (ELEMENT 1 [Blevins et al. 2015] and ELEMENT 2 [Rostenstock et al. 2015], respectively). The objective of these randomised controlled trials (RCTs) was to compare the efficacy (in terms of HbA1c reduction) and safety of the biosimilar Abasaglar) and the reference medicine Lantus in people with type 1 and type 2 diabetes.

- In ELEMENT 1 in people with type 1diabetes (n=535) and ELEMENT 2 in people with type 2 diabetes (n=756), once-daily Abasaglar was non-inferior to once-daily Lantus (primary end point) and Lantus was non-inferior to Abasaglar (secondary end point), demonstrating equivalent efficacy of both medicines. A similar reduction in HbA1c from baseline to 24 weeks was seen in both treatment groups, with a difference between groups of 0.11% (1.20 mmol/mol), 95% confidence intervals (CI) −0.00 to 0.22 (−0.00 to 2.40 mmol/mol) in ELEMENT 1 and 0.05% (0.60 mmol/mol), 95% CI −0.07 to 0.18 (−0.80 to 1.90 mmol/mol) in ELEMENT 2. The treatment difference was below the pre-specified non-inferiority margins of 0.4% and 0.3% in both studies. The study in people with type 1 diabetes, ELEMENT 1, was continued to 52 weeks and non-inferiority of Abasaglar to Lantus was confirmed at this further time point.

- There were also no statistically significant treatment differences in either study for secondary outcomes such as the proportion of participants meeting HbA1c targets or the mean change in body weight between people using insulin glargine biosimilar (Abasaglar) and those using insulin glargine (Lantus).

- In both ELEMENT 1 and ELEMENT 2, the number of participants with any adverse event, any serious adverse event or withdrawing because of an adverse event was similar in the Abasaglar and Lantus groups ($p>0.05$ for all treatment differences).

- In both studies there was no treatment difference between Abasaglar and Lantus for the most frequently reported adverse events. In people with type 1 diabetes (ELEMENT 1) these were nasopharyngitis (16.4%), upper respiratory tract infection (8.0%) and diarrhoea (4.1%),whereas the incidence in people with type 2 diabetes (ELEMENT 2) was 5.7%, 4.5% and 3.0% respectively. Hypoglycaemia was reported in 4.7% of people with type 1 diabetes in ELEMENT 1. The majority of adverse events were mild to moderate in severity.

- In ELEMENT 1 and ELEMENT 2, total mean hypoglycaemia rates (events per person per year), as well as rates of nocturnal or severe hypoglycaemia, were not statistically significantly different between Abasaglar and Lantus in either study. As would be expected the total incidence of hypoglycaemic episodes was greater in people with type 1 diabetes than in people with type 2 diabetes, where 60% of participants were insulin naive at entry into the study.

- There are no published clinical studies comparing Abasaglar with Lantus in children and young people. However, the summary of product characteristics includes reference to paediatric studies with Lantus.

- Medication errors are an important risk with insulin glargine biosimilar (Abasaglar) 100 units/ml. The MHRA Drug safety update advises that healthcare professionals and people with

diabetes should understand the differences between Abasaglar and several other new insulin products that have recently become available.

- The European public assessment report (EPAR) states that both studies provided data on patients switching from Lantus to Abasaglar at the same dose regimen, and no difference in dose changes after titration to tighten blood glucose control was reported between the 2 treatment arms.

Full text of evidence review.

Context

Basal insulin supply for people with type 1 and type 2 diabetes can be provided by:

- NPH (isophane) insulin (for example, Insulatard, Humulin I or Insuman Basal) or
- long-acting insulin analogues: insulin glargine (Abasaglar, Lantus or high-strength Toujeo), insulin detemir (Levemir) or insulin degludec (Tresiba).

Biosimilar and reference biological medicines that have the same international non-proprietary name (INN) are not presumed to be identical in the same way as generic non-biological medicines. The MHRA recommend that it is good practice to prescribe all biological medicines, including biosimilars, by brand name to prevent automatic substitution at the point of dispensing (Drug Safety Update 2008). Also see the NHS England publication, What is a biosimilar medicine? for more information.

NICE guidance on the management of type 1 and type 2 diabetes in adults recommends once daily insulin glargine can be considered for some people in certain situations (see the type 1 diabetes and the type 2 diabetes guidelines for more information).

The manufacturer estimates that the annual average cost of Abasaglar 100 units/ml once daily is £214.44 per person with type 1 diabetes and £278.77 per person with type 2 diabetes. This is based on estimated average daily doses of 25 units per day in type 1 diabetes and 40 units per day in type 2 diabetes.

Full text of context.

Estimated impact for the NHS

Biosimilar medicines have the potential to offer the NHS considerable cost savings, especially as they are often used to treat long-term conditions. Abasaglar is a biosimilar insulin glargine of standard strength 100 units/ml. It has a list price 15% lower than Lantus, however the cost of Abasaglar and other basal insulins will depend on the preparation chosen and the insulin dosage used. The European Medicines Agency (EMA) has approved Abasaglar based on extensive comparability studies that demonstrate similarity to Lantus. Abasaglar is licensed for the same indication as Lantus (treatment for adults, young people and children aged 2 years and above with diabetes mellitus) and the summary of product characteristics includes the same contraindications and warnings. See also the NHS publication 'Answers to commonly asked questions about biosimilar versions of insulin glargine' for more information. In the 2 phase III clinical studies (which included people with type 1 and type 2 diabetes) there was a subgroup that was switched from Lantus to Abasaglar at the same dose regimen and no difference in dose changes after titration to tighten glucose blood control was reported between the 2 treatment arms. However, in a Drug safety update the MHRA advised that some dose adjustment may be needed for some patients.

Full text of estimated impact for the NHS.

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance.**

Full evidence summary

Introduction and current guidance

Diabetes mellitus is a group of metabolic disorders in which blood glucose is persistently raised. Type 1 diabetes is a long-term hormonal deficiency disorder treated with insulin replacement therapy. This is supported by active management of other cardiovascular risk factors, such as raised blood pressure and disturbed blood lipid levels. Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in high blood glucose levels. It is commonly associated with obesity, physical inactivity, raised blood pressure, disturbed blood lipid levels and a tendency to develop atherosclerosis, and therefore is recognised to be associated with an increased cardiovascular risk. Type 1 and type 2 diabetes are

different conditions with very different physiological profiles. However, people with either condition are at increased risk of developing microvascular and macrovascular complications, including renal disease, neuropathy, retinopathy, cardiovascular and cerebrovascular disease.

Type 1 diabetes

In people with type 1 diabetes insulin replacement therapy is necessary to ensure circulating glucose levels are kept as near normal as possible, reducing tissue damage. The updated NICE guideline on type 1 diabetes in adults: diagnosis and management recommends adults with type 1 diabetes should be supported to aim for a target HbA1c level of 48 mmol/mol (6.5%) or lower, to minimise the risk of long-term vascular complications. HbA1c targets should be individualised taking into account factors such as the person's daily activities, aspirations, likelihood of complications, comorbidities, occupation and history of hypoglycaemia, and should not be accompanied by problematic hypoglycaemia.

Multiple daily injection basal–bolus insulin regimens are recommended as the insulin injection regimen of choice for all adults with type 1 diabetes. Twice-daily insulin detemir is recommended as the preferred basal insulin therapy. An existing insulin regimen being used by the person can be considered as an alternative if that is achieving their agreed targets. Once-daily insulin glargine or insulin detemir can also be considered if twice-daily basal insulin injections are not acceptable, as can once-daily insulin glargine if insulin detemir is not tolerated. Other basal insulin regimens should only be considered if these regimens do not deliver agreed targets. When choosing an alternative insulin regimen, the person's preferences and acquisition cost should be taken in to account. See the guideline for more information.

Type 2 diabetes

The updated NICE guideline on type 2 diabetes in adults: management recommends adopting an individualised approach to diabetes care that takes into account personal preferences, comorbidities, risks from polypharmacy, and the ability to benefit from long-term interventions because of reduced life expectancy. NICE recommends that adults with type 2 diabetes managed either by lifestyle and diet, or by lifestyle and diet combined with a single drug not associated with hypoglycaemia, should be supported to aim for an HbA1c level of 48 mmol/mol (6.5%). Adults on a drug associated with hypoglycaemia, should be supported to aim for an HbA1c level of 53 mmol/mol (7.0%). NICE recommends if HbA1c levels are not adequately controlled by a single drug and rise to 58 mmol/mol (7.5%) or higher, advice about diet, lifestyle and adherence to drug treatment should be reinforced, the person supported to aim for an HbA1c level of 53 mmol/mol (7.0%) and drug treatment intensified. The target HbA1c level can be relaxed on a case-by-case basis, with particular consideration for people who are older or frail, those with a reduced life expectancy,

those for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, and those for whom intensive management would not be appropriate, such as people with significant comorbidities.

In people with type 2 diabetes insulin therapy is a treatment option when intensification is required to improve long-term management of blood glucose levels, reducing tissue damage. When insulin therapy is necessary (see the NICE guideline, for details), it should be started from a choice of a number of insulin types and regimens. NPH insulin injected once or twice daily according to need is the preferred basal insulin. Insulin detemir or insulin glargine can be considered as an alternative for some people in certain situations (see the guideline for details).

The NICE pathway on diabetes brings together all related NICE guidance and associated products on the condition in a set of interactive topic-based diagrams.

Biosimilars

A biosimilar medicine (or biosimilar) is a biological medicine that is developed to be highly similar to an existing biological medicine (the reference medicine) in physicochemical and biological terms. Biosimilar medicines introduced into the UK market are approved by the European Medicines Agency (EMA). The EMA has produced a document covering a series of questions and answers on biosimilar medicines. Biological medicines such as monoclonal antibodies, growth hormone and insulin are produced in or derived from living systems. The size and complexity of biological medicines, as well as the way they are produced, may result in a degree of natural variability in molecules of the same active substance, particularly in different batches of the medicine. The active substance of a biosimilar and its reference medicine is essentially the same biological substance but, just like the reference medicine, the biosimilar has a degree of natural variability. When approved, this variability and any differences between the biosimilar and its reference medicine will have been shown not to affect safety or effectiveness and therefore not to have any clinically meaningful differences from each other in terms of quality, safety and efficacy. See the NHS England publication, What is a biosimilar medicine? for more details.

In the development of a biosimilar, there is no requirement to demonstrate clinical benefit to patients *per se* as this has been shown for the reference medicine. Instead, biosimilars undergo a comprehensive regulatory process which demands extensive comparability studies that demonstrate similarity to the reference medicine. This comparability exercise is similar to that carried out for originator medicines when any modification is made, for example when there is a change in manufacturing process. The benefits and risks are then inferred from the comparability of the biosimilar medicine to the reference medicine in terms of quality, efficacy and safety.

Biosimilar medicines are usually licensed for all the indications in the licence of the originator biological medicine, but this requires appropriate scientific justification on the basis of demonstrated or extrapolated equivalence. They are generally used at the same dose and route of administration as the biological reference medicine and have the same contraindications and warnings.

In the UK, the MHRA recommends that all biological medicines, including biosimilar medicines, are prescribed by brand name (Drug Safety Update February 2008). Because biosimilar and reference biological medicines that have the same international non-proprietary name (INN) are not presumed to be identical in the same way as generic non-biological medicines, brand name prescribing ensures that the intended product is received by the patient. It ensures that products cannot be automatically substituted at the point of dispensing. The choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.

Pharmacovigilance is important for biosimilar medicines and every biosimilar authorised by the EMA will have a risk management plan in place (details of which will be in the European Public Assessment Report). Based on similarity being demonstrated with the reference medicine, the biosimilar can also refer to the safety experience gained with the reference medicine. As with all new medicines, biosimilars have a 'black triangle' in the first years after approval and any suspected adverse drug reactions should be reported through the Yellow Card Scheme (see Drug Safety Update, June 2009, on the black triangle scheme for more information). Patient registers are used to monitor for emerging safety and efficacy issues with biological medicines and the MHRA supports the recording of brand names and batch numbers for traceability when reporting suspected adverse drug reactions (Drug Safety Update, November 2012).

Biosimilars have the potential to offer the NHS considerable cost savings, especially as biological medicines are often expensive and are often used to treat long-term conditions. Further information on biosimilars is available in the NICE adoption resource introducing biosimilar versions of infliximab: Inflectra and Remsima, which has been produced to help manage the introduction of biosimilar medicines into care pathways safely and effectively.

Product overview

Drug action

Insulin glargine is a human insulin analogue for basal insulin use. Abasaglar is an insulin glargine biosimilar product containing 100 units/ml solution for injection in a cartridge and a pre-filled pen (Abasaglar summary of product characteristics).

Insulin glargine 100 units/ml (Abasaglar) has been shown to be bioequivalent to insulin glargine 100 units/ml (Lantus). The European public assessment report (EPAR) for Abasaglar, states that the pharmacokinetic and pharmacodynamic equivalence of Abasaglar and Lantus has been established based on an extensive comparability exercise performed in 5 studies, which tested several dose levels and were conducted in healthy volunteers as well as people with type 1 diabetes. Abasaglar is the first biosimilar insulin glargine to be launched in the UK and as part of the licencing process, has been shown not to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy.

Licensed therapeutic indication

Insulin glargine biosimilar (Abasaglar) is licensed for the same indication as insulin glargine (Lantus). It is licensed for the treatment of diabetes mellitus in adults, young people and children aged 2 years and above. The dose regimen (dose and timing) should be individually adjusted. In people with type 2 diabetes, it can also be given together with oral antidiabetic medicinal products.

Course and cost

Insulin glargine biosimilar (Abasaglar) has the same posology and method of administration as insulin glargine (Lantus). It is licensed for once-daily administration at any time but at the same time each day. It is administered subcutaneously by injection.

As with Lantus, the summary of product characteristics states that when changing from a treatment regimen with an intermediate or long-acting insulin to a regimen with Abasaglar, a change of the dose of the basal insulin may be required and the concomitant antidiabetic treatment may need to be adjusted (dose and timing of additional regular insulins or fast-acting insulin analogues or the dose of oral antidiabetic medicinal products). Transferring a person to another type or brand of insulin should be done under strict medical supervision. Changes in strength, brand (manufacturer), type (such as regular, NPH, Lente, long-acting), origin (animal, human, human insulin analogue) or method of manufacture, may result in the need for a change in dose (Abasaglar summary of product characteristics).

Abasaglar is available as cartridges of 100 units/ml for use in a reusable pen or as a pre-filled pen 100 units/ml. Both products cost £35.28 per pack of 5×3 ml (excluding VAT; price taken from MIMS, November 2015). It should be noted that the Abasaglar device is not the same as that of the originator (Lantus). Abasaglar cartridges cannot be used in the re-useable pen devices produced for Lantus.

Evidence review

The biosimilar development pathway for Abasaglar involved an extensive comparability exercise with the reference medicine (Lantus) in order to ensure a close resemblance in terms of physical chemistry, biological characteristics, safety and efficacy. This followed a stepwise approach with demonstration of quality comparability, non-clinical comparability and clinical comparability (EPAR for Abasaglar).

This evidence summary focuses on the clinical comparability of the biosimilar and the reference medicine and is based on the 2 phase III studies of insulin glargine biosimilar (Abasaglar) in people with type 1 and type 2 diabetes (ELEMENT 1 [Blevins et al. 2015] and ELEMENT 2 [Rostenstock et al. 2015] respectively). The objective of these studies was to compare the efficacy (in terms of HbA1c reduction) and safety of the biosimilar Abasaglar and the reference medicine Lantus in people with type 1 and type 2 diabetes. Information from the EPAR for Abasaglar has been used to clarify and supplement data from the 2 published studies included in this evidence summary.

ELEMENT 1 was in people with type 1 diabetes who were using basal and bolus insulin. In ELEMENT 2, people with type 2 diabetes were either insulin naive or were previously on basal insulin glargine and were using oral antidiabetic medicines. The trial designs were very similar and they are discussed together.

ELEMENT 1 (Blevins et al. 2015) and ELEMENT 2 (Rostenstock et al. 2015)

- Design: Both were multicentre (59 sites in ELEMENT 1 and 88 sites in ELEMENT 2), parallel-group randomised controlled trials (RCT). ELEMENT 1 was open-label, whereas ELEMENT 2 was double-blind. The studies were multinational, with ELEMENT 1 conducted in 9 countries in North America, Europe and Japan whereas ELEMENT 2 was conducted in 13 countries, recruiting from additional countries across America, Europe and Asia. There was a 24-week main study treatment period in both studies. Following this, ELEMENT 1 also included a further 28-week comparative safety extension period. In both studies randomisation was centralised and stratified by country, HbA1c level <8.5% (<69.4 mmol/mol) and ≥8.5% (≥69.4 mmol/mol) and time of basal insulin injection (daytime, evening or bedtime).

In ELEMENT 2 participants were also stratified for randomisation by sulfonylurea use (yes or no).

- Population: ELEMENT 1 enrolled 535 adults (mean age 41 years) with type 1 diabetes who had been using basal insulin (NPH, insulin glargine or detemir) and mealtime insulin (human regular insulin, insulin analogue lispro, aspart or glulisine) for at least 1 year and had an HbA1c level less than or equal to 11.0% (≤96.7 mmol/mol) and had a body mass index (BMI) of less than or equal to 35 kg/m^2. People using other insulin glargine biosimilar, recent twice daily insulin glargine, or continuous insulin infusion, oral antidiabetic medicines, total daily insulin dose of 1.5 units/kg or more, or 1 or more episode of severe hypoglycaemia or emergency hospital attendance or admission for poor glucose control in the last 6 months were excluded. At baseline, the mean duration of diabetes was 16.5 years, mean HbA1c was 7.8% (61.5 mmol/mol), mean body mass index was 25.5 kg/m^2 and mean basal insulin was 0.32 units/kg/day (24 units/day). ELEMENT 2 enrolled 756 adults (mean age 59 years) with type 2 diabetes who had been receiving 2 or more oral antidiabetic medicines at stable doses for at least 12 weeks prior to screening (with or without concomitant insulin glargine use), had HbA1c levels between 7.0% (53.0 mmol/mol) and 11.0% (96.7 mmol/mol) if insulin naive or less than or equal to 11.0% (96.7 mmol/mol) if previously on insulin glargine, and had a BMI of less than or equal to 45 kg/m^2. People using any insulin other than glargine in the previous 30 days (90 days for insulin glargine biosimilar), history of or a requirement for bolus insulin therapy to achieve target control, a total daily insulin dose of 1.5 units/kg or more or more than 1 episode of severe hypoglycaemia in the last 6 months were excluded. At baseline, the mean duration of diabetes was 11.5 years, mean HbA1c was 8.3% (67.2 mmol/mol), and mean body mass index was 32.0 kg/m^2; 60.5% of participants were insulin naive and 83.5% of participants were using sulfonylureas.

- Intervention and comparison: In both ELEMENT 1 and ELEMENT 2 participants were randomised 1:1 to once daily injections of insulin glargine biosimilar 100 units/ml (Abasaglar) or insulin glargine 100 units/ml (Lantus) once daily for 24 weeks. In ELEMENT 1 study treatment was open-label, in order to provide efficacy and safety data using the planned pre-filled pen device, and both treatment groups also used mealtime insulin lispro during the treatment period. Basal insulin dose was primarily adjusted by the investigator during phone and office visits, aiming for morning fasting plasma glucose (FPG) of less than or equal to 6.0 mmol/litre, HbA1c less than 7.0% (53.0 mmol/mol) and pre-prandial capillary blood glucoses 3.9-7.2 mmol/litre while minimising or avoiding hypoglycaemia. Mealtime insulin doses were administered 3 times daily, at doses equivalent to participants' pre-study mealtime insulin. After 24 weeks an extension period was included (for a 52-week safety endpoint) and participants continued to receive their assigned treatment for a further 28 weeks. In ELEMENT 2 participants who were randomised to study treatment were provided with

covered study insulin vials to maintain blinding. People who were insulin naive prior to enrolment were started on 10 units per day whereas people who were already using insulin glargine were randomised to study treatment at a dose equivalent to their pre-study dose. Dose titration was participant led by adding 1 unit per day until FPG levels of less than or equal to 5.6 mmol/litre were reached. In both ELEMENT 1 and ELEMENT 2 insulin dose adjustments were only made after week 12 in the case of safety concerns such as hypoglycaemia, at the discretion of the investigator.

- Outcome: The primary end point in both ELEMENT 1 and ELEMENT 2 was HbA1c change from baseline to 24 weeks in the modified intention to treat (ITT) population (all randomised participants who received at least 1 dose of study insulin). This was analysed using an analysis of covariance (ANCOVA) model using the last observation carried forward (LOCF) method to handle missing data. Both RCTs were designed to demonstrate non-inferiority of Abasaglar compared with Lantus (with a non-inferiority margin of <0.4% [4.4 mmol/mol], and <0.3% [3.3 mmol/mol] if the 0.4% non-inferiority margin was met, for the upper bound of the 95% CI). Analysis was also undertaken for the per-protocol (PP) population. The PP population included all ITT participants who had no violations of inclusion or exclusion criteria, had not discontinued from the study prior to 24 weeks, had not been off study medication for more than 10 consecutive days during the treatment period, and had not received chronic (lasting longer than 14 days) systemic glucocorticoid therapy. The key secondary end point was to compare Lantus with Abasaglar at the non-inferiority margin of <0.4% (4.4 mmol/mol). If Abasaglar was declared non-inferior to Lantus in the primary treatment comparison and Lantus was declared non-inferior to Abasaglar in the secondary treatment comparison, then Abasaglar was considered to have equivalent efficacy to Lantus. Other secondary end points included percentage of participants with HbA1c <7.0% (53 mmol/mol) or ≤6.5% (48 mmol/mol) and rate of hypoglycaemia expressed as events per person per year. Safety assessments included the occurrence of adverse events in the safety population (as per the modified ITT population), including allergic reactions and injection site adverse events. Severe hypoglycaemia (requiring assistance) was categorised as a serious adverse event.

Table 1 Summary of ELEMENT 1 (Blevins et al. 2015) and ELEMENT 2 (Rostenstock et al. 2015)

	Study	Insulin glargine biosimilar (Abasaglar)	Insulin glargine (Lantus)	Analysis
Randomised	ELEMENT 1	n=269	n=267	
	ELEMENT 2	n=379	n=380	

Efficacy[a]	ELEMENT 1	n=268	n=267	
	ELEMENT 2	n=376	n=380	
Primary outcome: LS mean change±SD in HbA1c from baseline to week 24[b]	ELEMENT 1	−0.35±0.05% p<0.001 Endpoint: 7.42±0.05% (58±1.00 mmol/mol) from baseline of 7.75±1.13% (61±12.00 mmol/mol)	−0.46±0.05% p<0.001 Endpoint: 7.31±0.05% (56±1.00 mmol/mol) from baseline of 7.79±1.03% (62±11.00 mmol/mol)	LS mean difference0.11% 95% CI −0.00 to 0.22 (1.20 mmol/mol, 95% CI −0.10 to 2.40) Non-inferiority criteria met[c]
	ELEMENT 2	−1.29±0.06% p<0.001 Endpoint: 7.04±0.06% (53±1.00 mmol/mol) from baseline of 8.34±1.09% (68±12.00 mmol/mol)	−1.34±0.06% p<0.001 Endpoint: 6.99±0.06% (53±1.00 mmol/mol) from baseline of 8.31±1.06% (67±12.00 mmol/mol)	LS mean difference0.05% 95% CI −0.07 to 0.18 (0.60 mmol/mol, 95% CI −0.80 to 1.90) Non-inferiority criteria met[c]
Selected secondary outcomes:				

LS mean change ±SD in HbA1c from baseline to week 52[b]	ELEMENT 1	0.26±0.06% Endpoint: 7.52±0.06% (59±1.00 mmol/mol) from baseline of 7.75±1.13% (61±12.00 mmol/mol)	0.28±0.06% Endpoint: 7.50±0.06% (58±1.00 mmol/mol) from baseline of 7.79±1.03% (62±11.00 mmol/mol)	LS mean difference 0.02% 95% CI 0.10 to 0.14 0.20 mmol/mol, 95% CI −1.10 to 1.50) No statistically significant difference between groups (p>0.05)
	ELEMENT 2	Not applicable; 24-week study		
People with HbA1c of less than 7.0% (53 mmol/mol) at week 24[b]	ELEMENT 1	35% (92/268)	32% (86/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	49% (180/376)	53% (197/380)	No statistically significant difference between groups p>0.05
People with HbA1c of less than 6.5% (48 mmol/mol) at week 24[b]	ELEMENT 1	20% (54/268)	18% (49/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	27% (99/376)	30% (114/380)	No statistically significant difference between groups p>0.05

LS mean change ±SD in body weight from baseline to week 24[b]	ELEMENT 1	0.36±0.20 kg from baseline of 76 kg±17 kg	0.12±0.20 kg from baseline of 75 kg±15 kg	No statistically significant difference between groups p>0.05
	ELEMENT 2	1.8±0.30 kg from baseline of 90 kg ±20 kg	2.0±0.30 kg from baseline of 90 kg ±19 kg	No statistically significant difference between groups p>0.05
Safety[d]	ELEMENT 1	n=268	n=267	
	ELEMENT 2	n=376	n=380	
Participants reporting serious adverse events	ELEMENT 1	8% (20/268)	9% (24/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	4% (15/376)	5% (18/380)	No statistically significant difference between groups p>0.05
Participants discontinuing due to adverse events	ELEMENT 1	1% (2/268)	2% (6/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	2% (6/376)	3% (11/380)	No statistically significant difference between groups p>0.05

Adverse events	ELEMENT 1	62% (167/268)	62% (166/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	52% (196/376)	48% (184/380)	No statistically significant difference between groups p>0.05
Mean total hypoglycaemia rate ±SD (events per person per year)[e] at 24 weeks	ELEMENT 1	86.50±77.30	89.20±80.10	No statistically significant difference between groups p>0.05
	ELEMENT 2	21.30±24.40	22.30±28.20	No statistically significant difference between groups p>0.05
Mean rate of nocturnal hypoglycaemia[f] ±SD (events per person per year) at 24 weeks	ELEMENT 1	18.30±23.60	18.40±21.50	No statistically significant difference between groups p>0.05
	ELEMENT 2	7.60±11.80	8.10±14.60	No statistically significant difference between groups p>0.05
Mean rate of severe hypoglycaemia[g] ±SD (events per person per year) at 24 weeks	ELEMENT 1	0.06±0.52	0.09±0.50	No statistically significant difference between groups p>0.05

	ELEMENT 2	0.04±0.66	0.01±0.16	No statistically significant difference between groups p>0.05
Participants reporting injection site adverse events	ELEMENT 1	3% (7/268)	1% (3/267)	No statistically significant difference between groups p>0.05
	ELEMENT 2	4% (13/376)	3% (11/380)	No statistically significant difference between groups p>0.05

Abbreviations: CI, confidence interval; LS, least square, SD, standard deviation, p, p value.

[a] Modified intention-to-treat population: all participants who received at least 1 dose of study treatment.

[b] ANCOVA analysis with last observation carried forward.

[c] No statistically significant difference between groups (p>0.05); non-inferiority criteria met (non-inferiority margin of <0.4% [4.4 mmol/mol] and <0.3% [3.3 mmol/mol] for the upper limit of the 95% CI).

[d] All participants who received at least 1 dose of study treatment.

[e] Hypoglycaemia defined by blood glucose of 3.9 mmol/l or less (with or without symptoms) or by signs or symptoms associated with hypoglycaemia. The overall rate at 24 weeks accounts for all events reported during the 24-week treatment period.

[f] Nocturnal hypoglycaemia defined as any hypoglycaemic event that occurred between bedtime and waking. The overall rate at 24 weeks accounts for all events reported during the 24-week treatment period.

[g] Severe hypoglycaemia defined as a hypoglycaemic event requiring assistance of another person to actively administer treatment or other resuscitative actions. The overall rate at 24 weeks accounts for all events reported during the 24week treatment period.

Clinical effectiveness

The 2 phase III studies conducted in people with type 1 and type 2 diabetes (ELEMENT 1 and ELEMENT 2 respectively), demonstrated that insulin glargine biosimilar (Abasaglar) was non-inferior to insulin glargine (Lantus) in achieving HbA1c reduction at week 24 (the primary end point) and that Lantus was non-inferior to Abasaglar (secondary end point). This demonstrated equivalent efficacy of both medicines. In both studies the treatment differences for change in HbA1c from baseline were not statistically significantly different ($p>0.05$) and met the 0.4% and 0.3% margin for non-inferiority (see table 1 above). A similar reduction in HbA1c from baseline to 24 weeks was seen in both treatment groups, with a difference between groups of 0.11% (1.20 mmol/mol), 95% CI −0.00 to 0.22 (−0.10 to 2.40 mmol/mol) in ELEMENT 1 and 0.05% (0.60 mmol/mol), 95% CI −0.07 to 0.18 (−0.80 to 1.90 mmol/mol) in ELEMENT 2.

The European public assessment report (EPAR) states that non-inferiority of Abasaglar compared with Lantus for the primary HbA1c end point was demonstrated in both ELEMENT 1 and ELEMENT 2 using datasets for the modified-ITT and the PP populations. Results in both clinical trials showed an upper limit of the 95% CI being less than 0.25%, which is less than the pre-specified 0.3% non-inferiority margin required. There were also no statistically significant treatment differences in either study for secondary outcomes such as the proportion of participants meeting HbA1c targets or the mean change in body weight from baseline to week 24 between people using insulin glargine biosimilar (Abasaglar) and those using insulin glargine (Lantus). See table 1 above for further information.

According to the EPAR, the results of the secondary end points were consistent with the results for the primary end point and although some treatment differences were identified in both studies, these were not statistically significant or considered clinically relevant. The study in type 1 diabetes (ELEMENT 1) was continued up to 52 weeks and non-inferiority of Abasaglar to Lantus was also confirmed at this further time point (see table 1).

Safety and tolerability

In phase III clinical studies, the safety population for insulin glargine biosimilar (Abasaglar) consisted of 644 people with type 1 and type 2 diabetes; 69% of whom were exposed to the study treatment for at least 6 months. The EPAR reports that the safety profile of Abasaglar is comparable to that of Lantus and in line with that expected from an insulin product. No additional safety signals were detected for Abasaglar with regard to hypoglycaemia, allergic reactions or injection site reactions. The summary of product characteristics for Abasaglar lists the same contraindications, cautions and undesirable effects as for Lantus. The most frequent adverse reaction is hypoglycaemia.

In the phase III studies, ELEMENT 1 and ELEMENT 2, there were no statistically significant differences between treatment groups in the reported incidences of adverse events and serious adverse events (see table 1). In people with type 1 diabetes (ELEMENT 1) the most frequently reported adverse events for both Abasaglar and Lantus were nasopharyngitis (16.4%), upper respiratory tract infection (8.0%) and diarrhoea (4.1%), whereas in people with type 2 diabetes (ELEMENT 2) the corresponding incidences were 5.7%, 4.5% and 3.0% respectively. Hypoglycaemia was reported in 4.7% of people with type 1 diabetes in ELEMENT 1. The investigators in both studies reported that in both treatment groups, the majority of adverse events were mild to moderate in severity.

The total mean hypoglycaemia rates (events per person per year), as well as rates of nocturnal or severe hypoglycaemia were not statistically significantly different between Abasaglar and Lantus in either study (see table 1 for details). As would be expected the total incidence of hypoglycaemic episodes was greater in people with type 1 diabetes than in people with type 2 diabetes, where 60% of participants were insulin naive at entry into the study.

The incidence of allergic reactions was also similar in both treatment groups (8% for Abasaglar and 4% for Lantus in ELEMENT 1 and 6% compared with 7% respectively in ELEMENT 2, $p>0.05$ for all treatment comparisons). Self-reported injection site reactions were 3% with Abasaglar and 1% with Lantus in ELEMENT 1 and 4% compared with 3% respectively in ELEMENT 2, $p>0.05$ for treatment comparison). The EPAR states that the number of allergic events and injection site-related abnormalities appeared similar between the 2 insulins and were considered acceptable.

The immunogenicity profiles of Abasaglar and Lantus were comparable up to the 52-week end point. In ELEMENT 1 a total of 212 participants (39.8%) had detectable antibodies to insulin at 52 weeks and in ELEMENT 2, 96 participants (13.2%) had detectable antibodies to insulin at 24 weeks, with no statistically significant difference between treatment groups. The EPAR reports that there was no evidence that these antibodies had any impact on efficacy and safety outcomes (HbA1c, weight, insulin dose, hypoglycaemic episodes, allergic or injection site reactions).

In both ELEMENT 1 and ELEMENT 2 similar numbers of people withdrew because of adverse events in both treatment groups (see table 1 above). Across both RCTs there were a total of 3 deaths (1 person with type 1 diabetes in ELEMENT 1 and 1 person with type 2 diabetes in ELEMENT 2 who were on Lantus and 1 person with type 2 diabetes in ELEMENT 2 who was on Abasaglar). In each study the investigators reported that these deaths were not thought to be treatment related.

An important risk with insulin glargine biosimilar (Abasaglar) 100 units/ml is to ensure that healthcare professionals and people with diabetes understand the differences between Abasaglar and several other new insulin products that have recently become available. These need to be used correctly to minimise the risk of medication errors such as the wrong insulin dose being administered (MHRA. Drug safety update. April 2015).

Evidence strengths and limitations

In the development of a biosimilar medicine, there is no requirement to demonstrate benefit to patients *per se* as this has been shown for the reference medicine. The benefits and risks are inferred from the similarity of the test medicine to the reference medicine in terms of quality, efficacy and safety.

The findings from ELEMENT 1 and ELEMENT 2 confirm earlier pharmacokinetic and pharmacodynamic studies that insulin glargine biosimilar (Abasaglar) is comparable to the reference medicine (Lantus). Both studies provided data on switching from Lantus to Abasaglar at the same dose regimen in people with type 1 and type 2 diabetes, and no difference in dose changes after titration to tighten blood glucose control was reported between the 2 treatment arms. The EPAR states that ELEMENT 1 and ELEMENT 2 were appropriately designed studies to determine the non-inferiority of insulin glargine biosimilar (Abasaglar) to insulin glargine (Lantus).

The use of the ANCOVA method of analysis in the 2 clinical trials discussed in this evidence summary ensured that the results were adjusted for variables including concomitant treatment and baseline HbA1c. The investigators used the last observation carried forward (LOCF) approach to take account of missing data, which can affect the results. In this approach, the last available result for an individual is carried forward and analysed as though it were the result at the study end, regardless of when that person left the trial. According to the investigators in both studies further sensitivity analyses provided reassurance that the handling of the missing data did not affect conclusions regarding efficacy and confirmed the robustness of the results.

In both studies, participant demographics and disease characteristics for both treatment groups were well balanced, except for in ELEMENT 1 more people entered the study with HbA1c levels less than 7.0% (53.0 mmol/mol) in the Abasaglar group than in the Lantus group (27% and 18% respectively). However, the average baseline HbA1c levels were still around 7.8% (62 mmol/mol) in each treatment group. Based on the data provided, non-inferiority of Abasaglar to Lantus was demonstrated in both studies using modified ITT and PP datasets, providing reassurance of the validity of the non-inferiority results.

In ELEMENT 1 the authors state that an open-label design was chosen in order to provide efficacy and safety data using the planned pre-filled pen device for insulin administration. Double-blinding was not appropriate as it would have involved a double-dummy design, requiring further daily injections for participants in a relatively long duration study. The lack of blinding, may account for differences in insulin dose and HbA1c levels between the 2 treatment groups during the 12-week dose titration period. Investigators were aware of the treatment received by each participant, which according to the authors, may have contributed to the more aggressive dose titration from baseline to 18 weeks in the Lantus group because of greater investigator familiarity and confidence in titration with Lantus than with Abasaglar. Insulin doses between treatments were more similar during the course of the study after the titration period and there were no statistically significant treatment differences in HbA1c (or in insulin dose) at the 24-week (primary) and 52-week endpoints. The authors note that in the double-blind study in people with type 2 diabetes, no between-treatment differences in insulin dose titration or HbA1c were reported.

The primary end point of ELEMENT 1 and ELEMENT 2 was an HbA1c end point at 24 weeks. In ELEMENT 1 there was an additional analysis at 52 weeks. There are very limited patient-oriented outcome data on macrovascular or microvascular outcomes with Abasaglar, or on the long-term safety of this particular formulation. However, the Abasaglar summary of product characteristics includes reference to long-term studies with Lantus such as the Early Treatment Diabetic Retinopathy Study (ETDRS) and the Outcome Reduction with Initial Glargine Intervention (ORIGIN) trial.

The European Medicines Agency (EMA) has approved Abasaglar for treatment of diabetes mellitus in adults, young people and children aged 2 years and above. There are no published clinical studies comparing Abasaglar with Lantus in children and young people. However, the summary of product characteristics includes reference to paediatric studies with Lantus.

Context

Alternative treatments

Basal insulin supply for people with type 1 or type 2 diabetes can be provided by:

- NPH (isophane) insulin (for example, Insulatard, Humulin I or Insuman Basal) or
- long-acting insulin analogues: insulin glargine (Lantus, the biosimilar Abasaglar or high-strength Toujeo), insulin detemir (Levemir) or insulin degludec (Tresiba).

Biosimilar and reference biological medicines that have the same international non-proprietary name (INN) are not presumed to be identical in the same way as generic non-biological medicines. The MHRA recommend that it is good practice to prescribe all biological medicines, including biosimilars, by brand name to prevent automatic substitution at the point of dispensing (Drug Safety Update February 2008).

Costs of alternative treatments

	5×3 ml cartridge[a]	5×3 ml pre-filled pen[a]
Insulatard NPH (isophane) insulin 100 units/ml solution	£22.90	£20.40
Humulin I NPH (isophane) insulin 100 units/ml solution	£19.08	£21.70
Insuman Basal NPH (isophane) insulin 100 units/ml solution	£17.50	£19.80
Lantus insulin glargine 100 units/ml solution	£41.50	£41.50
Abasaglar biosimilar insulin glargine 100 units/ml solution	£35.28	£35.28
Toujeo high-strength insulin glargine 300 units/ml	-	3×1.5 ml pre-filled pen, £33.13
Levemir insulin detemir 100 units/ml solution	£42.00	£42.00 or £44.85
Tresiba insulin degludec 100 units/ml solution	£72.00	£72.00
Tresiba insulin degludec 200 units/ml solution	-	3×3 ml pre-filled pen, £86.40
[a]Costs are excluding VAT; taken from MIMS (November 2015).		

The cost of Abasaglar and other basal insulins will depend on the preparation chosen and the insulin dosage used. The list price of Abasaglar is about 15% lower than Lantus. The manufacturer estimates that the annual average cost of Abasaglar 100 units/ml once daily is £214.44 per person with type 1 diabetes and £278.77 per person with type 2 diabetes. This is based on estimated average daily doses of 25 units per day in type 1 diabetes and 40 units per day in type 2 diabetes.

Estimated impact for the NHS

Likely place in therapy

Biosimilar medicines have the potential to offer the NHS considerable cost savings, especially as they are often used to treat long-term conditions. Abasaglar is a biosimilar insulin glargine of standard strength 100 units/ml. It has a list price 15% lower than Lantus.

The EMA has approved Abasaglar based on extensive comparability studies that demonstrate similarity to Lantus. These include several pharmacokinetic and pharmacodynamic studies and 2 clinical studies with HbA1c end points in 535 people with type 1 diabetes and 756 people with type 2 diabetes. Abasaglar is licensed for the same indication as Lantus (treatment of diabetes mellitus in adults, young people and children aged 2 years and above) and the summary of product characteristics includes the same contraindications and warnings. See also the NHS publication 'Answers to commonly asked questions about biosimilar versions of insulin glargine' for more information. In the 2 phase III clinical studies (which included people with type 1 and type 2 diabetes) there was a subgroup that was switched from Lantus to Abasaglar at the same dose regimen and no difference in dose changes after titration to tighten glucose blood control was reported between the 2 treatment arms. However, in a Drug safety update the MHRA advised that some dose adjustment may be needed for some patients.

Before starting treatment with any high strength, fixed combination or biosimilar insulin product, the MHRA advise health professionals to:

- consult the summary of product characteristics and any educational material
- ensure that patients read and understand the patient leaflet and any patient education material
- ensure that patients receive appropriate training on the correct use of the product
- give patients a patient booklet and Insulin Passport (or safety card)

- warn patients only to use insulin as they have been trained because using it any other way may result in a dangerous overdose or underdose
- monitor glucose levels closely after starting a new treatment and in the following weeks. Doses and timing of concurrent rapid-acting or short-acting insulin products and other antidiabetic treatments may need adjustment.

The choice of whether a patient receives a biosimilar or originator biological medicine rests with the responsible clinician in consultation with the patient.

The NICE guideline on type 1 diabetes in adults: diagnosis and management recommends multiple daily injection basal–bolus insulin regimens as the insulin injection regimen of choice for all adults with type 1 diabetes. Once-daily insulin glargine can be considered if twice daily insulin detemir, the preferred basal insulin therapy, is not tolerated. Other basal insulin regimens should only be considered if these regimens do not deliver agreed targets or a person is using an existing insulin regimen which is achieving agreed targets. When choosing an alternative insulin regimen, the person's preferences and acquisition cost should be taken in to account.

In people with type 2 diabetes insulin therapy is a treatment option when intensification is required to improve long-term management of blood glucose levels, reducing tissue damage. When insulin therapy is necessary (see the NICE guideline for details), it should be started from a choice of a number of insulin types and regimens. NPH insulin injected once or twice daily according to need is the preferred basal insulin. Insulin detemir or insulin glargine can be considered as an alternative for some people in certain situations (see the guideline for details).

Estimated usage

The NHS prescription cost analysis for England 2014 reports that approximately 1.4 million community prescriptions for Lantus were dispensed in 2014 at a cost of approximately £79 million (net ingredient cost).

The manufacturer estimates that Abasaglar is expected to only be prescribed to a percentage of annual new initiators to long-acting insulin analogues. These are people with type 1 or type 2 diabetes who are insulin naive or require an intensification of treatment as a result of inadequate glycaemic control. Based on prevalence, incidence and mortality data, the manufacturer estimates that approximately 39,503 people are eligible for treatment with Abasaglar in England and Wales over 5 years. Of these new initiators, the manufacturer estimates that Abasaglar is expected to have a 4% market share in year 1, rising to 18% by year 5. This estimate equates to approximately

23,220 people who are likely to be prescribed Abasaglar in England and Wales over 5 years. (Personal communication Eli Lilly and Company Ltd. June 2015.)

Relevance to NICE guidance programmes

NICE has issued guidelines on the diagnosis and management of type 1 diabetes in adults and the management of type 2 diabetes.

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Development of this evidence summary

The integrated process statement sets out the process NICE uses to select topics for the evidence summaries: new medicines and how the summaries are developed, quality assured and approved for publication. NICE's position statement on evaluating biosimilar medicines was published in January 2015 and describes how NICE will consider producing an evidence summary: new medicine for biosimilar medicines in some circumstances.

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Declarations of interest

Dr TA Chowdhury and K Wind have no interests to declare.

J Wright attended an Advisory Board, funded by Merck Sharp and Dohme Ltd, in November 2014 to discuss implications of biosimilar infliximab in clinical practice.

About this evidence summary

'Evidence summaries: new medicines' provide summaries of key evidence for selected new medicines, or for existing medicines with new indications or formulations, that are considered to be of significance to the NHS. The strengths and weaknesses of the relevant evidence are critically reviewed within this summary to provide useful information for those working on the managed entry of new medicines for the NHS, **but this summary is not NICE guidance.**

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