Why isn’t the NHS making the most of biosimilar insulin?

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With cheaper biosimilar insulins now reaching the UK market, there are opportunities for potential cost savings in diabetes management. However, uptake in the NHS has so far been low. In this article, Mark Greener explores the possible reasons for this.

The costs of managing diabetes are causing consternation from the groves of academe to the corridors of Westminster to the local primary care team desperately trying to balance a budget under ever-increasing pressure. After all, the direct costs of managing diabetes, according to Diabetes UK, reach some £10 billion a year. Some estimates suggest that the figure is even higher: a London School of Economics report estimated that the costs reached £13.8 billion in 2010. But Diabetes UK notes that both estimates are several years old and costs have almost certainly risen.

More recent figures from NHS Digital show that prescribing costs for diabetes in England now exceed £1 billion. In primary care, drugs used to treat diabetes account for 11.4% of total net ingredient costs (NIC) and 4.9% of all items prescribed. During the financial year 2017/18, 53.4 million items were prescribed for diabetes at a total NIC of £1,012.4 million. This represents an increase of 22.6 million prescription items and a rise of £421.7 million in NIC since 2007/08. And this doesn’t include drugs for complications, which account for 80% of the direct costs of type 2 diabetes.

Insulins alone cost £350.5 million in 2017/18. Industry group the British Biosimilars Association (BBA) says that insulin glargine costs the NHS an estimated £82 million a year. So, you might expect that cheaper biosimilar insulins (see Table 1) would find a ready market. But according to the BBA, uptake of biosimilar insulin in the UK is “stuck at around 5–6%”. So, what’s the problem?

Changing the market

Biopharmaceuticals are a diverse group of medicines encompassing monoclonal antibodies, growth factors, enzymes, receptor proteins and hormones, such as insulin. Biosimilars are not generics. Developing a conventional generic of a small, simple chemically synthesised drug – an antihypertensive, lipid-lowering agent or bronchodilator, for instance – is relatively cheap, quick and easy. Biopharmaceuticals are made by, or extracted from, living cells, which makes developing a biosimilar expensive, protracted and complex.
Type of insulin | Originator | Biosimilars | Company | Date of UK launch
--- | --- | --- | --- | ---
Insulin glargine | Lantus | Abasaglar | Eli Lilly | September 2015
Insulin lispro | Humalog | Insulin lispro | Sanofi | June 2018

Table 1. Biosimilar insulins currently available in the UK

So, the savings generated by using biosimilars are not on the same scale as generics, which typically attract a 90% discount. A position statement by the Association of British Clinical Diabetologists (ABCD) suggests that biosimilar insulin will be about 15% cheaper than the originator. The exact savings depend, of course, on local arrangements and the whether the originator price matches. “Biosimilars bring choice and competition to the market. It is very important that this is sustained long term,” says Carol Blount, NHS Partnerships Director at the BBA. “Without competition there is a real risk of prices going back up over time. There is, however, a significant opportunity in the biosimilar insulin market and we expect more products to be delivered in the next few years.”

Currently, three companies – Novo Nordisk, Eli Lilly and Sanofi – control 96% of the global insulin market. Some prescribers may lack confidence in biosimilar manufacturers if they do not have a track record in insulin development,” says Miles Fisher, Consultant Diabetologist, Glasgow Royal Infirmary. But the growing competition may challenge the current hegemony in the insulin market. “We need more companies in the insulin market to challenge the dominance of the ‘big three’,” says David Beran, Division of Tropical and Humanitarian Medicine, University of Geneva and Geneva University Hospitals.

Mutually reinforcing barriers
Several mutually reinforcing barriers seem to hinder uptake of biosimilar insulin in the UK. Firstly, there’s a sparse evidence base: relatively few studies compare biosimilar insulins with the originator. A meta-analysis of 11 studies compared biosimilars to insulin glargine and insulin lispro. Six studies found that pharmacokinetic, pharmacodynamic parameters or both were comparable between the biosimilar and originator. Five studies examined clinical efficacy, which again showed similar results. Adverse events, assessed in all studies, were also comparable. But there is clearly a need for more research.

Secondly, switching patients to an insulin biosimilar involves costs in addition to the price of the medicine, such as learning a new injection technique. The delivery device for Abasaglar differs from that used for Lantus, the originator insulin glargine. Abasaglar cartridges cannot be used in the re-usable Lantus pen. “These costs, which are factored into the overall value of the switch, are best controlled by standardising the approach, avoiding duplication and sharing best practice,” Ms Blount remarks. “This is one of the main lessons from earlier biosimilar introductions.”

“A trained healthcare professional should show patients the new device before switching, when the patient’s previous stocks of insulin run out,” Professor Fisher says. “There are no concerns about the insulin in the device – it’s equivalent. There is, however, a possibility that the new device will not be used properly or will malfunction, leading to inadequate doses and increases in blood glucose. For most patients and healthcare professionals, however, changing device should be easy. A minority will find the change confusing.”

In general, patients with stable HbA1c without unacceptable hypoglycaemia probably won’t switch. After all, an inpatient hospitalisation for severe hypoglycaemia in a person with type 2 diabetes in England taking insulin monotherapy involves a mean length of stay of 7.1 days at a mean cost of £1802 including excess bed days. “We do not believe that people already established on an insulin should have to switch to a biosimilar, especially if their control is already good,” says Douglas Twenefour, Deputy Head of Care at Diabetes UK.

Rather, most healthcare professionals will probably consider biosimilars for new patients or those who miss their treatment targets. “Abasaglar should only be initiated in patients new to insulin glargine or in those who require a review of their therapy due to poor control,” the ABCD guidelines state. Patients stable on Lantus, the originator, should not switch. The guidelines concede, however, that this advice “may well alter… once more clinical data are available, particularly from post-marketing and surveillance analysis”.

“The NHS needs to develop a national policy and guidance to ensure that best value is being delivered in insulin prescribing and setting out the need to change,” Ms Blount suggests. “We believe that industry could collaborate with NHS England to develop national guidance and processes to support switching, building on the 10 years of successful experience from introducing biosimilar medicines in the NHS.”

Into primary care
Most biosimilars in the UK are used, predominately, by specialist services in secondary care: adalimumab, etanercept, follitropin alfa and teriparatide, for instance. In contrast, Ms Blount points out, diverse healthcare professionals across primary and secondary care manage diabetes. “Better and proactive education for clinicians and patients about biosimilar insulins would deliver increased uptake and release savings for the NHS. However, the range of healthcare professionals involved in diabetes makes raising awareness and providing education more challenging for insulin compared with other biosimilars,” she says. “Patients and patient groups also need to be closely involved in education. We believe the decision must always be clinically led with the patient at the heart of the choice.”

The ABCD statement also highlights the “lack of knowledge” among healthcare professionals about the various
insulins and which delivery device is appropriate for which insulin. Biosimilar insulins further complicate the market, which, the statement warns, raises the prospect of prescription and dispensing errors. So, the ABCD say, it is “imperative” that all healthcare professionals are educated about safe insulin prescribing generally and biosimilar insulin in particular. For instance, healthcare professionals need training and guidance about which insulins can be used interchangeably and which need specific devices.\(^\text{4}\)

NHS workforce and capacity issues may also hinder uptake of biosimilar insulin. The ABCD guidelines state that only clinical teams with training, expertise and experience in treating diabetes should switch patients to a biosimilar insulin.\(^\text{4}\)

“Specialist diabetes nurses would need to explain the switch to patients, including potentially any differences in their injection device,” Ms Blount says. “As an industry, we wouldn’t want clinicians, nurses, patients and carers to have to learn different usage techniques when switching between medicines. Manufacturers can help provide training on the device and injection process.” Professor Fisher adds that “the time taken to put in place safeguards to allow safe switching either for individual patients or for groups of patients is a major issue”.

Against this background, the BBA called for “incentives to influence behaviour change of prescribers and reinvest the savings gained through biosimilar insulin at a local level”. However, Professor Fisher is sceptical that this will happen in practice. “Any savings will not automatically be re-invested in diabetes services as many Trusts, Health Boards and other organisations need to save money,” he says.

### Longer-term concerns

A chemically synthesised generic is interchangeable with the original brand. The active ingredient in generic captopril is chemically identical to that in Capoten, for example.\(^\text{3}\) But the same doesn’t necessarily apply to biosimilars. The specific manufacturing process can influence the biopharmaceutical’s characteristics, such as the protein’s three-dimensional structure and the carbohydrate side chains attached to the amino acid backbone.\(^\text{3,8}\)

Usually, these changes don’t make a clinical difference. However, in theory at least, the changes could result in differences in the way in which the originator and biosimilar stimulate the immune system (immunogenicity). “In practice, this is unlikely since any differences between the biosimilar and originator are of the same scale as the changes that the originator itself has gone through over time – for example, when making manufacturing process or production-site alterations,” says Ms Blount.

Any biological agent can induce antibody formation, for example. The ABCD notes that these antibodies can cause serious allergic reactions, local injection-site reactions and change the glucose-lowering effect or the insulin dose required.\(^\text{4}\) Five studies in the meta-analysis of biosimilar insulins assessed immunogenicity in patients with type 1 or type 2 diabetes. Immunogenicity seemed to be comparable between the biosimilar and originator during a follow up period that varied from 12 to 52 weeks.\(^\text{6}\) However, immunogenicity might emerge only when tens of thousands of patients are treated for longer.\(^\text{3}\) Robust post-marketing procedures are in place. However, Professor Fisher warns that “it is impossible to say whether the current pharmacovigilance procedures are adequate to detect rare safety signals, such as immunogenicity”.

These differences also mean that healthcare professionals should prescribe biosimilar and originator insulin by brand and specify the device to reduce the risk of accidental substitution, and include this information on the patient’s documentation, such as their insulin safety card or insulin passport.\(^\text{4}\) Healthcare professionals should also check the Summary of Product Characteristics: the biosimilar’s stability, shelf life and storage requirements may differ from the originator.\(^\text{4}\)

### Taking a global view

In the UK, we worry about the cost of treating diabetes. In many developing countries, people with diabetes worry about getting treatment at all. “In sub-Saharan Africa, the life expectancy of a child with type 1 diabetes could be as low as a year due to poor access to insulin,” remarks Dr Beran. “Currently, in Africa only one in seven people with type 2 diabetes who should be using insulin are doing so.”\(^\text{9}\)

Some people in developing countries find that insulin isn’t available. “In some countries, insulin is only available in hospitals in large urban areas,” Dr Beran says. “In other countries, there isn’t suffi-
cient insulin available overall. Supply systems and improved delivery of diabetes care need to be put in place to ensure that the insulin gets to individuals.”

But some patients are unable to afford insulin even if it’s available. “Most biosimilar insulin is analogue insulin, which is more expensive than human insulin and is not included on the World Health Organization Essential Medicine List. So, fundamentally, issues around the supply of insulin and provision of diabetes care will remain even if biosimilar insulins enter the market,” he explains.

“I hope, however, that biosimilars will reduce the price of human and analogue insulin by increasing competition. The price needs to come down for the health system and the individual.”

“Whether a patient uses an originator or a biosimilar should be a decision made by a person with diabetes in conjunction with their healthcare team,” Mr Twenefour concludes. “If a person with diabetes chooses to switch to a biosimilar, they should be encouraged and supported to monitor their blood glucose more closely to achieve good control. Biosimilar insulins are cheaper than originators, and so can present an opportunity to reduce cost, and improve access, in the UK and worldwide.”

References

Declaration of interests
Mark Greener is a full-time medical writer and, as such, regularly provides editorial and consultancy services to numerous pharmaceutical, biotechnology and device companies and their agencies. He has no shares or financial interests relevant to this article.

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