Meeting the Challenges of Biosimilar Medicines

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As science and innovation progress they will require Parliamentarians to examine the changes and opportunities they bring to the NHS. The advent of biotechnology-derived medicines is an example of this progress which brings with it new challenges, in particular those of biosimilar medicines (also known as biosimilars).

Biotech medicines are a ground-breaking development in the treatment of a number of diseases, including cancer, osteoporosis and arthritis. Today there are around 230 biotech medicines available, benefiting over 325 million people worldwide. Some of these innovator biotech medicines are reaching patent expiry, and follow-on, or biosimilar, products are appearing on the market. Unlike generic copies of traditional medicines, these follow-on products cannot be identical to originator products – at most, they are "similar". This may have serious consequences for patient safety through unforeseen adverse drug reactions. Additionally, biosimilar medicines rely on extrapolated data from originator treatments and do not yet have the same robust data of the originator products. This raises concerns as to whether they behave in the same way as the originator products and therefore how they should fit into the current prescribing mechanisms in the UK or if new regulation is required to safeguard patient safety. Biosimilar medicines therefore pose a number of challenges to the NHS and to the health policies in all of the devolved regions of the UK.

The EU and the European Medicines Agency (EMEA) has already started to address the challenge of biosimilars by establishing a new pathway for the appraisal of these biosimilar drugs. They recommend that prescribing decisions should only be made by fully qualified healthcare professionals. In addition, several European countries have since gone further and introduced regulations to ban the automatic substitution of the often cheaper biosimilar treatments. The European Commission director responsible for pharmaceutical policy has written to the heads of national regulatory agencies, outlining a need to improve the pharmacovigilance systems in the countries in order to ensure that the arrival of biosimilar erythropoiesis stimulating agents (ESA or EPOs) will not cause any problems – such as incorrect attribution of adverse events. The Commission also emphasises the need for the prescribing doctor to know which product has been given to which patient.

The UK has yet to decide how to respond to this challenge. Whilst biosimilars open up alternative treatment options that may save the

Case Study – G-CSF and Febrile Neutropenia

Biosimilars are gradually entering the market place in the UK. One that is expected to become available in the coming months in the UK is Granulocyte-Colony Stimulating Factor (G-CSF). This is a growth factor that stimulates the bone marrow to produce white blood cells. G-CSF is used to prevent a low count of a certain type of white blood cell during treatment for chemotherapy. This low white cell count is known as Febrile Neutropenia, or FN.

There are currently a couple of daily G-CSF products that have different biological characteristics and are currently licensed for use in Europe, including in the UK. Comparative studies have demonstrated differences between these two products with regard to their pharmacological properties and clinical outcomes. These two products are not considered to be interchangeable.

Since there will be limited clinical experience with the use of biosimilars when they are first licensed, it is important that healthcare professionals are fully informed about the possible risks of substitution. Automatic substitution, in the same way that is currently seen with generic treatments, may lead to the administration of multiple products. In this scenario it would not be possible to link an adverse reaction, or indeed particularly successful treatment, to a specific product. Furthermore, the identification of biopharmaceutical products might not be possible if multiple products share one International Non-proprietary Name (INN).

In knowing how a biosimilar will work, data extrapolation can be useful and has a rational basis; however, if this is the only way by which indications for a product are approved, this should be well known to all healthcare practitioners and to patients. A particular concern with data extrapolation arises in G-CSF biosimilars, since efficacy and risks may differ in patient populations depending on age, on disease (malignant or non-malignant) and immunosuppression.

NHS money on its drugs bill, it is important that Government, healthcare professionals and patients are aware of the possible associated risks that these treatments may bring with them. It was with these concerns in mind that I accepted an invitation from Dr Brian Iddon MP (Bolton South East) to address the Parliamentary Review on Biosimilars, held in November 2007 and supported by the biotech company, Amgen.

At the Review, which heard evidence from a number of other industry experts, the panel agreed on a number of actions that should be taken forward across all of the devolved health regions in recognition of the increasing number of biosimilar medicines that will become available to the NHS in the coming months and years.

The first recommendation agreed was that biosimilar prescribing procedures should be amended as a matter of urgency. It is common practice to substitute existing generic medicines without discussion with the prescribing clinician. This is because traditional small molecule generic medicines have an identical chemical structure to the innovator, such as aspirin. However, the "similar" nature of biosimilars should now make this an obsolete practice for this particular group of treatments. Much of the clinical concern revolves around both patient safety and treatment efficacy.

The key to ensuring patient safety is an immediate ban on the automatic substitution of biosimilars, which should themselves be prescribed by brand name alone to avoid confusion and inadvertent substitution. With healthcare becoming increasingly personalised, as advocated in the Darzi review, it will be important that people are kept on treatments known to be effective for them. Where a patient has been receptive to a biomedical treatment they should be maintained on that particular treatment and not moved to a biosimilar, which, while designed to treat the same condition, may do so in a slightly different manner.

At the Parliamentary Review into Biosimilars it was explained how the British National Formulary (BNF) would be able to alert healthcare professionals to the complications related to biosimilars. The review panel agreed that the BNF should be responsible for highlighting the difference between biosimilars and the originator products. In addition the panel called for all biosimilar medicines to be marked with black triangle symbols by the MHRA until the available scientific data can provide certainty about the possible implications of biosimilars.

Pharmacovigilance and reporting mechanisms of adverse reactions to medicines is an integral component in improving our knowledge of biosimilars. In the UK this is administered through the yellow card scheme. Concerns were raised that this system may need to be strengthened to deal with the added pharmacovigilance requirements that are necessary with biosimilars. This information needs to be shared between doctors and across the EU. It is important that patients are aware of adverse reactions and what should be reported, together with the possible risks of biosimilars in the first place. Any successful programme to ensure patient safety will educate all healthcare professionals, including doctors, nurses and pharmacists. A crucial part of this education will be to ensure that prescribers are aware that biosimilar data are usually extrapolated from data of the originator product.

The decision to start treatment with biosimilars, as with any potential treatment, should be openly discussed by the prescriber and the patient. Should they chose to prescribe a biosimilar, there should be clear information on Patient Information Leaflets to inform patients about potential adverse reactions to biosimilars that may not occur in the originator product. To assist in this process of discussion with patients, we believe it would be useful for the Government to launch an awareness campaign to educate the public about biosimilars and the importance of reporting any adverse reactions to biosimilars, regardless of their severity, to enable an accurate picture of the efficacy and safety of each biosimilar.

Biotechnology-derived products are at the cutting edge of modern medicine and as their patents expire we enter a new phase which brings new challenges for policy makers. However, biological therapies are complex medications, and variation in both the drug component and the delivery methodology (for example the solution it is delivered in) may lead to unexpected consequences. Therefore, until we have better information with which to answer the questions they pose, we would be wrong to risk patient safety by failing to impose the rigorous safety standards and precautions we have come to expect, as these treatments are gradually introduced to the UK market. Other countries, including France and Spain, have put restrictions on the automatic substitution of biosimilars. To ensure patient safety remains our highest concern, the UK should not hesitate to follow suit.

Biography: Dr Richard Fluck

Dr Richard Fluck is a consultant renal physician and clinical lead for renal services at Derby Hospitals NHS Foundation Trust. He trained at Trinity Hall, Cambridge and the London Hospital before carrying out research at St Bartholomew's Hospital, before moving to the Medical Unit at the Royal London Hospital as a Lecturer. He was appointed to his current position in 1996. Over the last 10 years Derby Renal Services has grown from a single-handed practice to an active research and training centre. In addition to local duties, he has been a member of the Renal Association executive, Council member of the British Renal Society, programme chair for the BRS annual conference, member of the Renal Registry committee and most recently national lead for DOPPS. He has been national lead for renal associated infection and vascular access issues and has worked with the HPA and DH on renal associated infections. He has lectured widely on infection, vascular access and patient safety in renal disease. He and his team won the 2007 Hospital Doctor Renal Team of the Year award.