UKMi
MIDLANDS
January 2015

TRENT MEDICINES INFORMATION SERVICE
MEDICINES MANAGEMENT UPDATES

Biosimilars – new developments

Introduction

Biologic medicines are based on large molecules (proteins, antibodies or other similar molecules), that perform specific pharmacological or therapeutic actions. Examples include hormones (eg growth hormone), drugs used in inflammatory diseases (eg infliximab), therapies for cancer, (eg trastuzumab) and haematologic agents (eg filgrastim). This briefing is intended to provide more background for some new biologic medicines that will be coming to the market in the next few months, particularly infliximab.

What is a biosimilar?

A biosimilar is a biologic medicine that has been developed to have a very similar pharmacological effect to that of an original branded biologic products (or 'reference' product) and with the same dose regimen, but it does not have an identical chemical structure. Biosimilars are marketed after the patent for the branded product has expired. Although they might be regarded as 'generic' medicines, they are not chemically identical, so the process for approval of licences for marketing is not the same as it is for generic drugs.

How are biologic medicines produced?

Biologic products are produced in a variety of ways, often involving cell culture and recombinant DNA technology. The resulting genetically modified cells can produce the desired molecule in large quantities. These are highly technical processes that require very specific conditions, close monitoring and checks at all stages of manufacturing. Producing biologic products is more complex than production of relatively small molecules such as aspirin or penicillin.

Patent expiry and biologic medicines

Patents for biologic medicines are broadly similar to those for other pharmaceuticals. After a period of exclusivity, competing pharma companies are allowed to develop products with a similar therapeutic effect, but as noted above, for biosimilars these new medicines do not have identical chemical structures to the reference product. They therefore have different names even though they have the same therapeutic effect as the reference product.

How are biosimilars introduced and regulated?

Biosimilars undergo broadly the same process for approval by the European Medicines Agency (EMA) as other generic pharmaceuticals, although there are more stringent checks during the manufacturing process and clinical trials are required to demonstrate efficacy.

In clinical trials, more attention is paid to immunogenicity, development of antibodies to the new product, adverse reactions and safety. Once the new biosimilar has been tested in one or more indications, it is not considered necessary for trials to be done in every type of indication where that agent might be used, as its biological action is considered to be proven.

One important issue to note about biologics is that production methods change with time and there have often been changes to production processes of the originator products during their period of exclusivity. This has resulted in products that might be different from when they were first licensed, though their principal biological mechanism of action remains the same. This is known as 'iterative' change and each such change in manufacturing is agreed with regulatory authorities before implementation.

The possibility that some biosimilars might have an improved mechanism of action compared with the reference product has been suggested and this may become more apparent in the future.

Tel 0116 258 6491 Email medicines.info@uhl-tr.nhs.uk

What biosimilars are already in use and what others are coming soon?

A number of biosimilars have already appeared on the market, notably growth hormone (somatotropin) - there are now seven available, haematologicals such as granulocyte stimulating factors and erythropoietin, as well as a diverse range of monoclonal antibodies to treat inflammatory and malignant diseases.
In February 2015, biosimilars for infliximab are due to be launched, with the brand names Inflectra™ and Remsima™. These have been available in Eastern Europe since early in 2014.

How will biosimilar infliximab be introduced?

This will involve commissioners, clinicians, pharmacists, nursing staff and patients and may necessitate some changes in current practice. It is clearly important to be able to identify the particular biologic product an individual patient has been treated with. For this reason the MHRA has said that there should not be automatic substitution of biosimilar for the original or reference product, and brand name prescribing should apply.[1] This will enable appropriate reporting of safety issues, whether it involves the originator product or a biosimilar. As infliximab has often been prescribed by generic name until now, this will require more care in prescribing, dispensing and documentation. Recording of batch number is also appropriate to ensure accurate reporting of adverse events.[2]

Future guidance

NICE has recently issued a position statement on future guidance and has indicated that guidance and technology appraisals will include both originator and biosimilar brand names and that technology appraisals would apply to any biosimilars that appear after publication of guidance.[3]

Changes for Hospital Trusts and CCGs

Prescribing and administration of infliximab in hospitals

Prescribing – will need to be specify the brand of infliximab that will be used for each patient
Record keeping: clinical notes should identify brand administered and batch number to facilitate reporting of adverse events.
Formularies will need to identify the product that new patients should receive where appropriate.
Dispensing: pharmacists should dispense brand ordered and not substitute; there is likely to be a need for stockholding of more than one brand of infliximab.
Administration: if vial sharing is done, this will need to be streamlined according to brand used and patients on each brand will need to attend on the same date to facilitate vial sharing.
Communications with GPs should provide brand details of product used. Patients should be monitored with a particular emphasis on possible immune-related adverse events.
Adverse reactions (whether suspected or established) should be documented on yellow card reports to the MHRA, as previously.

Commissioning considerations/CCG perspectives

Cost savings as a result of using biosimilars are possible in the short term but uptake of biosimilars for infliximab is not likely to be immediate because existing patients will not change treatment from one brand to another. One county in the East Midlands has estimated that this change may initially only involve a single-figure number of patients in rheumatology, the speciality with the largest number of patients on biologics.
Reimbursement of Hospital Trusts for their costs by commissioners will be more complicated because of use of a mixture of originator and biosimilar products for each biologic entity, at least until biosimilars are more widely adopted. Prices may fall following introduction of biosimilars, it is unclear by how much.

References
1. MHRA. Biosimilar products. Drug safety update 2008;vol 1:7:8, accessed via http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON084739, accessed Jan 2015
2. EMEA guide on biosimilars for monoclonal antibodies, available at http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500128686.pdf, accessed Jan 2015
3. NICE position statement on biosimilars, at http://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/biosimilars-statement.pdf, accessed Jan 2015

Further reading:
Chaplin S. Biosimilars: what are they and why do we need to know? Prescriber 2014: 25: 40-42

Tel 0116 258 6491 Email medicines.info@uhl-tr.nhs.uk