NRAS position paper on biosimilar medicines – Revised June, 2016

Introduction

At a time when the burden of chronic diseases is increasing across the world, ensuring that patients can access safe, high quality, affordable and modern medicines, such as biological medicines, is vital to improving people's health.

Biological medicines ('biologics') are made from living organisms using biotechnology techniques. Since their introduction in the 1980s, biologics have revolutionised the treatment of many diseases and benefitted millions of people worldwide. They have been available for rheumatoid arthritis since the end of the 1990s.

Many original biologics are now reaching the end of their patents. This means other manufacturers are now permitted to produce similar versions of these medicines, called biosimilar medicines[1] ('biosimilars'). Due to the complex manufacturing process, biosimilars are not classed as 'generic' medicines, because they are not absolutely identical to the original medicine.

Since developing our original position paper back in the summer of 2014, we have revised some of our views in the light of the experience of the actual introduction of biosimilars and the fact that the safety and effectiveness data being reported from across Europe and the rest of the world is pretty much the same as for the original biologic products. Furthermore, the designation of a biologic drug as a "biosimilar" by a regulatory authority demands that extremely rigorous quality controls are met with respect to characterisation of the biosimilar in relation to the originator drug. This can give us a great deal of confidence as patients. These quality controls for the biosimilar are much more stringent than were required for originators back in the early days of biologic DMARDs. We also have to adapt to the reality of what is actually going on in the NHS and the need to make savings where this is possible, feasible and the responsible thing to do, provided that quality and safety of care are prioritised, rheumatology benefits from some of the funds saved and longitudinal safety data is collected via the British Society for Rheumatology Biologics Registers are collected.

However, particularly important from a patient perspective, is that it is vital that biosimilars are prescribed with care and thought and with proper consultation, care planning and shared decision making between the clinician and the patient.

As more biosimilars enter the UK market, especially those administered by sub-cutaneous route, the reality is likely to be that patients will be switched from a biologic on which they may stable and responding well, to a biosimilar. This can be alarming for patients unless handled properly and with

[1] IAPO International Alliance of Patient Organisations – biological and Biosimilar medicines – Fact sheet Introduction and Key Definitions http://www.patientsorganizations.org/showarticle.pl?id=1763&n=961

due opportunity for discussion and enabling the patient to ask any questions they may have about the safety and efficacy of the biosimilar being proposed. In this position paper we set out our recommendations for a national best practice approach to be taken.

Biosimilars approved for rheumatoid arthritis:

At the time of this revised position paper (March, 2016), the only currently approved biosimilar medicines for rheumatoid arthritis in the UK are based on Remicade (originator infliximab) and Enbrel (originator etanercept). In the case of infliximab, two biosimilars were filed under two separate names with the European Medicines Agency (Remsima and Inflectra), and were introduced to the UK in 2015 by two different companies.

When compared to Remicade, these biosimilars have demonstrated similar therapeutic efficacy and incidence of drug-related events, are well tolerated, and have a comparable record of safety. However, owing to the complexity of these drugs and their relative newness, we still believe that ongoing safety monitoring is vital.

Benepali has been granted marketing authorisation in the European Union (EU) for the treatment of adults with moderate to severe rheumatoid arthritis, psoriatic arthritis, non- radiographic spondyloarthritis and plaque psoriasis. Benepali is the first etanercept biosimilar referencing Enbrel to be approved in the EU, making it the first sub-cutaneous anti-TNF available here.

Concerns raised and/or addressed through stakeholder consultation:

Pharmacovigilance is a key concern. This is especially important in differentiating true biosimilar medicines that have been approved on the basis of an abbreviated development programme, from copy biologic medicines already available in some markets that have not been approved by the normal regulatory bodies at all.

Cost is also a concern. Availability of lower-priced biosimilar medicines is perceived to be changing the landscape of biologics in the pharmaceutical industry, and while this may increase pressure to prescribe the newer alternatives, eligibility criteria for treatment remains unchanged for the time being and the hope of wider access to treatment for patients remains unfulfilled since NICE turned down the BSR/NRAS appeal to widen the access to those with moderate to severe disease with poor prognostic markers. However, concerns originally raised about the cost of prescribing and the pressure to curtail drug expenditure with the use of cheaper biosimilar medicines without the necessary guidance being put in place regarding use of brand names, has been clarified and NICE clearly state that evidence summaries will use the **brand names of the medicines because substitutability and interchangeability cannot be assumed**. Evidence summaries do not make recommendations hence the decision regarding the choice of biosimilar or originator biologic for an individual patient rests with the responsible clinician **in consultation with the patient.**

NRAS position and recommendations:

Healthcare professionals

- A clear discussion and agreement between the consultant/prescriber and the patient should take place before switching to a biosimilar so that the patient can ask any questions and risks/benefits can be explored and explained
- Where a trust level decision is taken to switch 'all' or 'groups' of patients, it is possible that a group meeting of patients, with facility for individuals being able to ask a question in private if they wish, run by a consultant-led team could help to allay any anxieties or fears about switching which patients may have
- Healthcare professionals should prescribe all biologic and biosimilar medicines by brand name and not by International Non-proprietary Name (INN). This is in line with the intention of the European Union pharmacovigilance legislation to impose an obligation for healthcare professionals to prescribe biological medicines by brand name in order to facilitate compliance with the patient safety and pharmacovigilance identification and traceability requirements.[2]
- Substitution of a biosimilar product should only occur under the direct supervision and consent of the treating healthcare professional and with patient agreement in line with bullet one above
- Patients newly starting on biologic treatment may be started on a biosimilar with the approval of the physician and the consent of the patient in line with the starting of any new medication regimen

In a recent paper by Tina Hawkins and Paul Emery in the Pharmaceutical Journal (November 2015), the following recommendations were made in regard to 'introducing biosimilar medicines into practice' and we agree with this approach, although NRAS would further support the project team by including 2 patients:

"The formation of a local project team, which includes a senior physician, pharmacist lead, management sponsor, commissioning leads and staff delivering the service, is recommended to support the safe introduction of biosimilar medicines. Communication and collaboration is essential and at the start of the process. It is important to define appropriate measures that provide assurance of safe and successful implementation of biosimilars into prescribing practice.
These measures should include consultation with all stakeholders (including patients) who will be involved and affected by the switch. Appropriate information should be sent out to both clinicians and patients, explaining what biosimilars are and the rationale for switching. Centres that have already switched patients to biosimilar infliximab developed patient information leaflets which were sent out

[2] ABPI Position on Biosimilar medicines

to patients in advance of the switch. In addition a nurse specialist at these centres contacted patients by phone to explain the process and answer any questions. Clinical consensus on use and approval on the hospital formulary should be sought for each new biosimilar product. The formulary approval process should include recommendations on good prescribing practice of biosimilars to ensure the appropriate brand is prescribed for a patient. Hospitals that reconstitute a biosimilar product with their own preparative services will also need to ensure standard operating procedures are put in place to prevent the wrong brand of the medicine being aseptically prepared for a patient.
Considerable financial savings can be generated as a consequence of biosimilar prescribing. Prior to introduction of the biosimilar, information on the potential savings should be gathered and discussed with local commissioners in order to gain agreement on sharing financial rewards generated by the switch. Both University Hospital Southampton NHS Foundation Trust and University College London Hospitals NHS Foundation Trust have been able to develop and improve their services for inflammatory bowel disease patients as a consequence of commissioners sharing the financial rewards generated by the switch. Both hospitals used a clinical data collection template and patient questionnaire to provide a longitudinal data set before and after switching. Patients were also registered on the IBD biologic registry".

The full article is referenced in links at the end of this paper.

People with RA

- A clear discussion and agreement between the consultant/prescriber and the patient should take place before switching to a biosimilar so that the person with RA can ask any questions and discuss risks/benefits. This could be one to one or as part of a presentation to a group of patients by one of the members of the Multi-disciplinary team.
- People with RA should be fully aware of which medications they are being prescribed and if they are being prescribed a biosimilar medicine they should know how to report any adverse reaction to the MHRA
- People with RA should always check their prescription to ensure it is for the medication agreed with their physician and that the pharmacist has dispensed the one expected
- Patients should be made aware of what complaints process is available to them if they feel they are being switched onto a biosimilar medicine with insufficient information/discussion or shared decision making process as recommended elsewhere in this paper

Commissioners

- While some guidelines may be useful to be developed and shared to help commissioners in their use of biosimilars it would be best to avoid strict guidance that would not allow the prescribing physician to make case by case clinical decisions where appropriate
- The introduction of biosimilars onto the UK market makes the need for "shared care agreements" and integration of primary and secondary care even more vital to ensure secondary care healthcare professionals and the primary care healthcare professionals have clear oversight of the patient's medications and therapies and overall pathway of care
- Gain share from the savings from switching to biosimilars must benefit rheumatology and patients in an equitable way (ie it doesn't all go to the CCG or Trust for use in other therapeutic areas or for plugging deficits)
- Commissioners should note the recommendations in the healthcare professional section about 'introducing biosimilars into practice'

Pharmaceutical industry

- The pharmaceutical industry should promote better understanding of biosimilar medicines with all healthcare professionals, especially biologic therapy nurses to enhance their training in collaboration with the Royal College of Nursing, Department of Health and the MHRA
- All data relating to the development of biosimilar medicines should be made publically available to demonstrate the level of equivalence with the originator product
- Biosimilars should have distinct names allowing them to be easily identified and distinguished from the originator medicine so that patient, pharmacist and physician know exactly what medication the patient is receiving so as to ensure any improved efficacy, lack of efficacy or adverse effects are accurately reported
- Pharmaceutical industry needs to support financially the provision and training of staff, and the collecting and interpretation of data gathered by physicians, nurses, patients, trusts and NHS that will feed into the national registers (BSRBR)
- Collection of longitudinal safety data is, in our view, essential for cohorts of patients going onto biosimilar medicines in exactly the same way as has happened with the originator products

Healthcare bodies

- The British Society for Rheumatology Biologics' Register captures essential outcome data and it is important that RA patient outcomes of those people prescribed any biosimilar medicine is also captured in the same way as original biological medicines
- NICE have updated their guidance on use of biosimilars which can be viewed here: https://www.nice.org.uk/news/article/evaluating-biosimilar-medicines

NRAS

- Patients must be properly informed through robust shared decision making mechanisms about being switched – a round robin letter from Trust with inadequate information is not satisfactory or appropriate
- The manufacturers must agree to long term safety data collection through the BSR Biologics Registers
- Gain share from the savings from switching to biosimilars must benefit rheumatology and patients in an equitable way (ie it doesn't all go to the CCG or Trust for use in other therapeutic areas or for plugging deficits) it
- NRAS will continue to keep their lay and professional membership informed of developments in the use of biosimilar medicines for the treatment of RA (note article in NRAS member magazine end April, 2016)
- NRAS will aim to ensure that a best practice national approach is developed to 'switching' and shared with people with RA, healthcare professionals and those who commission care
- NRAS recommends that all manufacturers of biosimilars subscribe to the British Society for Rheumatology Biologics Registers so that pharmacovigilence protocols are on par with those of the biologics and longitudinal safety data is properly collected

Finally, we would like to raise awareness of our desire to see NICE revisit the outcome of the Final Appraisal Determination (FAD) of the Multiple Technology Appraisal of the biologics Review (ID 537). This FAD was appealed jointly by the BSR and NRAS and was unsuccessful. With the introduction of the first sub-cut Anti-TNF biosimilar (Benepali – Etanercept biosimilar introduced to the UK market in early 2016) the price of the originator product has been reduced and the health economic landscape has altered significantly.

Both we and the BSR would like to see NICE review the health economic model as we believe that calculated today, given the drop in pricing the ICERS would be well within the £30,000 limit.

Many studies and reports on biosimilars say "…availability of biosimilars for the treatment of rheumatological conditions should improve access via decreased medication costs, allowing more patients to be treated for the same health care dollar." This may well be the case in mainland Europe where access to biologics and biosimilars is more widespread due to less stringent accessibility criteria than we have here in the UK, but it is incorrect to say this applies in the UK because until NICE revise their guidance on this, no additional patients will have access to biosimilars. It's possible that procurement arrangements made locally may enable some Trusts to offer some patients a biosimilar at an earlier stage but this will vary and take us back to the bad old days of post code prescribing.

Further reading & resources on Biosimilars

NRAS Stakeholder Event April 2014 Report & filming of presentations "Uncharted Waters". Available at : www.nras.org.uk/biosimilars

ABPI position on biosimilar medicines. Available at:

http://www.abpi.org.uk/our-work/library/Documents/ABPI%20position%20on%20biosimilar%20medicines.pdf

EuropaBio Guide to biological medicines. Available at: http://www.europabio.org/sites/default/files/report/guide_to_biological_medicines_a_focus_on_biosimilar_medicines.pdf

European Medicines Agency Questions and answers on biosimilar medicines. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Medicine_QA/2009/12/WC500020062.pdf

MHRA Drug Safety Update. Available at: http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON084739

World Health Organisation 55th Consultation on International Non-proprietary Names for Pharmaceutical Substances Geneva, 16-18 October 2012. Executive Summary. Available at: http://www.who.int/medicines/services/inn/55th_Executive_Summary.pdf

IAPO International Alliance of Patient Organisations – briefing papers available at: http://www.patientsorganizations.org/showarticle.pl?id=1763

European Generic Medicines Association Biosimilars Handbook Second edition 2011 available at: http://www.egagenerics.com/index.php/biosimilar-medicines/introduction

European Commission – Consensus Information Paper 2013 http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/biosimilars_report_en.pdf

http://www.pharmaceutical-journal.com/learning/learning-article/biosimilar-medicines-in-rheumatology/20200018.article

This NRAS Position paper has been endorsed by NRAS Chief Medical Advisor, Professor Peter Taylor, Norman Collisson Professor of Musculoskeletal Sciences, Oxford University.