

## **NRAS position paper on biosimilar medicines – Revised December, 2017**

### **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.

Some of the original biologics are already off patent and others are reaching the end of their patents in 2017/18 and beyond. This means other manufacturers are now permitted to produce similar versions of these medicines, called biosimilar medicines<sup>1</sup> ('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 are collected via the British Society for Rheumatology Biologics Registers.

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 the sub-cutaneous route, the reality is that patients are being switched from a biologic on which they may stable and

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<sup>1</sup> 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>

responding well, to a biosimilar. This can be worrying for patients unless handled properly and with 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.

### **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 changing the landscape of biologics in the pharmaceutical industry, and while this may increase pressure to prescribe the newer, less costly 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 less expensive 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 is the ideal way to approach switching to a biosimilar so that the patient can ask any questions and risks/benefits can be explored and explained. A best practice example (slide deck) of how Southampton are informing patients in routine clinic visits well in advance of a new biosimilar entering the UK market is attached to this position statement.
- ✚ 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 nurse specialise 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.<sup>2</sup>

- ✚ 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. Hospital pharmacy should not substitute a drug without the knowledge and consent of the treating physician and patient
- ✚ 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
- ✚ Strong safeguards are required to ensure that patients who have responded well to existing medicine who are switched for non-clinical reasons are closely monitored to ensure continuing efficacy and safety (as would be expected in the majority of such cases). However, if patients fail to maintain the efficacy achieved on a reference product then they should be able to consult with their rheumatology team and switch from the prescribed biosimilar to an alternative therapy. There is a wide range of effective therapies and the health care team should discuss whether it would be most appropriate to switch back to the originator biologic or an alternative therapy.
- ✚ Patients who are unwilling to switch for reasons important to the patient should not be forced, against their will, to switch. (This kind of scenario should be rare if patients are given sufficient information delivered in the right way and receive the necessary support to make informed decisions)
- ✚ There are current discussions within the healthcare system about a future scenario where patients could be switched from biosimilar to biosimilar (interchangeability). There is, as far as NRAS is currently aware, no evidence to support this practice and NRAS has concerns over patient safety and immunogenicity issues were this to become reality.
- ✚ It is a good idea to ensure that patients who are anxious or concerned are sign-posted to NRAS for appropriate emotional support. We have a national helpline and a telephone peer support service which can be helpful.

### **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 on a one-to-one basis or as part of a presentation to a group of patients by one of the members of the Multi-disciplinary team
- ✚ If informed by letter, which seems to be the most common way to inform patients of an intention to switch, adequate, correct information about the new drug and the reason for

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<sup>2</sup> ABPI Position on Biosimilar medicines

switching must be included and a telephone number given where the patient can ring for additional information and advice

- ✚ 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 their healthcare team for onward reporting 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
- ✚ Strong safeguards are required to ensure that patients who have responded well to an existing medicine who are switched for non-clinical reasons are closely monitored to ensure efficacy and safety. If patients fail to maintain the efficacy achieved on a reference product, then they should have the option of either reverting to the original medication or, if there are medical reasons to do otherwise, be offered an alternative treatment.
- ✚ 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/Health Boards**

- ✚ 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 Biosimilar Commissioning Framework was published by NHSE in September, 2017 and states clearly that “treatment decisions should always be made firstly on the basis of clinical judgement for individual patients and secondly on the basis of the overall value proposition offered by individual medicines”. However, it is important for NRAS to point out to commissioners that the reality of what is happening on the ground is that clinicians are being directed to switch patients on existing original biologics as soon as its biosimilar/s come onto the market firstly on grounds of cost saving. NRAS understands the imperative to save money wherever possible in today’s NHS and supports the principle of switching, but where a patient is not doing so well on an originator product, the likelihood of their doing well on that originator’s biosimilar is significantly less, and it may be more appropriate to switch that patient to a treatment with a different mechanism of action, which may be another originator product for which there may be no biosimilar as yet. Clinicians must remain in the driving seat when it comes to prescribing the right drug at the right time for the right patient.
- ✚ 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 that both secondary and the primary care healthcare professionals have clear oversight of the patient’s medications and therapies and overall pathway of care

- ✚ Where there is opportunity for “gain share” from the savings from switching to biosimilars, the funds realised 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). The only way that patient outcomes might be improved by savings from switching programmes is for the department doing the work of the switching and incurring those costs, to receive some of the gain share to improve service provision – for example taking on additional nursing resource
- ✚ Commissioners should note the recommendations in the healthcare professional section about ‘introducing biosimilars into practice’
- ✚ There are current discussions within the healthcare system about a future scenario where patients could be switched from biosimilar to biosimilar (interchangeability). There is, as far as NRAS is currently aware, no evidence to support this practice and NRAS has concerns over patient safety and immunogenicity issues were this to become reality.

### **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 publicly available to demonstrate the level of equivalence with the originator product
- ✚ Biosimilars should have distinct brand 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
- ✚ We would recommend and encourage the Pharmaceutical industry to support the collecting of data gathered by physicians, nurses, patients, trusts and NHS to feed into the national registers (BSRBR)
- ✚ There are current discussions within the healthcare system about a future scenario where patients could be switched from biosimilar to biosimilar (interchangeability). There is, as far as NRAS is currently aware, no evidence to support this practice and NRAS has concerns over patient safety and immunogenicity issues were this to become reality.
- ✚ 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 – in line with recommendations elsewhere in this document
- ✚ We will do all we can to encourage manufacturers to agree to long term safety data collection through the BSR Biologics Registers
- ✚ Gain share from the savings from switching to biosimilars (for as long as they exist) 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)
- ✚ NRAS will continue to keep their lay and professional membership informed of developments in the use of biosimilar medicines for the treatment of RA through our website, relevant publications and social media
- ✚ As a member of the NHSE National Programme Board for biosimilars, NRAS will represent the best interests of patients and aim to ensure that a best practice national approach to 'switching' is adopted 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 pharmacovigilance protocols are on a par with those of the original 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. This will change further when Humira (adalimumab) biosimilar/s come to market in 2018.

Both we and the BSR would like to see NICE review the health economic model as we believe that if recalculated today, given the drop in pricing by the introduction of biosimilars, 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 in rheumatology 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 we are not aware of this happening anywhere in England, as yet.

#### **Further reading & resources on Biosimilars**

**NRAS Stakeholder Event April 2014 Report & filming of presentations “Uncharted Waters”.** Available at : [www.nras.org.uk/biosimilars](http://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](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](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](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://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 Collison Professor of Musculoskeletal Sciences, Oxford University.**