

FINAL REPORT



Biologics **AND** Biosimilars

ADVOCACY WORKSHOP ON PATIENT SAFETY

Copenhagen, Denmark



I N T R O D U C T I O N

Biosimilar medicines are being prescribed to more and more patients across Europe. But access to, and use of, these new medicines differs greatly by European country. A recent workshop hosted by the Global Alliance for Patient Access (GAfPA) allowed patient advocates from across Europe's Nordic region to explore these challenges, consider biosimilar policies, and discuss a topic of growing international interest: switching from a biologic to a biosimilar medicine.

The workshop, held on October 5-6, 2016 in Copenhagen, drew seven different patient advocacy groups from Denmark, Sweden and Iceland. Representatives came from the Nordic Rheuma Council, the Swedish Rheumatology Association, the Danish Crohn's and Colitis Association, the Danish Hidradenitis Suppurativa Association and the Danish Psoriasis Organisation, as well as the Icelandic League Against Rheumatism, and the Icelandic Crohn's and Colitis Organisation.

The workshop provided participants a greater understanding of the current landscape for biologic and biosimilar medicines in Europe. It also sought to empower patient advocates with effective tools to inform policymakers about patients' concerns in their own Nordic countries. Participants shared their patient stories and experiences with biologics and biosimilar medicines, agreed on key issues, and formulated how best to support each other at a national, Nordic, and EU level.

KEY CONCERNS AROUND BIOLOGICS AND BIOSIMILARS

As biologic and biosimilar medicines become more common across the Nordic region and the rest of Europe, patients' knowledge of these medicines is slowly increasing. But it is GAfPA's position – as well as the sentiment expressed by the patient advocates in attendance – that more education and awareness is needed. The workshop included discussion of their key concerns surrounding biologic and biosimilar medicines, such as **non-medical switching, indication extrapolation, tracking and tracing of biologic and biosimilar medicines, and the meaning of informed consent.**



BACKGROUND

What are biologic medicines?

- Biological medicines revolutionized healthcare in the 1980s and have transformed treatment for a number of diseases and conditions, including: cancer, diabetes, blood conditions, rheumatoid arthritis, multiple sclerosis, psoriasis, Crohn's disease and autoimmune disorders.
- Biological medicines are in use by **more than 350 million patients** worldwide.
- Biological medicines are developed from or in living organisms. Unlike conventional (small molecule) medicines that are made by following chemical formulas, **biologics are very large, complex molecules.**

What are biosimilar medicines?

- Biosimilar medications are products that are **'highly similar' to – but not exact copies of** – a biological medicine (which is often known as the 'reference' or 'originator' medicine).
- Biosimilar medications may have meaningful differences from the original biologic.
- Biosimilar medications therefore must prove to be clinically comparable in terms of safety and efficiency.¹

CONCERNS AROUND PATIENT SAFETY

SWITCHING FROM ONE MEDICINE TO ANOTHER

- **Medical Switching** - a clinical decision by the physician to change a patient's medication because there is a problem experienced by the patient - perhaps because the first one no longer works or because of **side effects**.
- **Non-medical Switching** - a decision to change a patient's medication for reasons unrelated to efficacy or side effects - **usually to save money**. These cost-cutting changes are not directed by the patient's physician. They are often directed by pharmacy managers, healthcare systems, and insurance companies.

For patients who are currently stable and responding well to their current treatment, non-medical switching can be disruptive and upsetting. It may also be less effective or worse, provoke a harmful immune response. Therefore, non-medical switching can be very counterproductive in the long-run, leading to higher costs.

At present, limited evidence is available regarding the practice of non-medical switching between biologics and biosimilars. Many physicians agree, however, that switching from an original biologic to a biosimilar, or vice versa, should always include both patient and physician consent.^{ii,iii} This is echoed by the European Medicines Agency (EMA) which states, **'for questions related to switching from one biological medicine to another, patients should speak to their doctor and pharmacist.'**



INDICATION EXTRAPOLATION

Of interest to the participants, the topic of indication extrapolation was discussed, in which a biosimilar may be approved for use for a medical condition in which it has not been tested. Group members expressed concern at this practice and offered concern that their members were likely unaware that they could be treated with a medicine not thoroughly tested in their medical condition.

THE PHYSICIAN'S PERSPECTIVE

The Nordic workshop included a presentation from neurologist **David Charles, M.D., GAfPA Chairman**. Dr Charles spoke about the differences between biologic and biosimilar medicines, explaining the complex manufacturing process involved. He emphasised the intricate nature of these medicines and the diligence required within the manufacturing and administration process, without which, patients are at risk of an adverse reaction lack of efficacy.

Dr Charles was clear that he fully supports the development of biosimilar medicines and identified some benefits including: increased competition, lower costs, and additional options for patients and physicians.

Dr Charles underlined the public policy issues concerning biosimilars and the importance of ensuring patient safety through **rigorous tracking, tracing, and pharmacovigilance (see Q&A)**. The key areas Dr Charles identified as essential to ensuring patient safety are:

- Naming of biologics,
- Clinical trials for each indication, and
- Transparent labelling and prescribing information.

The group discussion demonstrated gaps in patient groups' knowledge of these areas, which Dr Charles sought to address with detailed explanation of the need for biosimilars to carry distinct non-proprietary names and for medicines to be dispensed 'as written' by the prescribing physician when medically indicated. Dr Charles explained the potential risk of adverse reactions presented by not adhering to the highest standards in naming biologics and the essential need for transparent prescribing information.

NOR-SWITCH

The Nordic groups then discussed the implications of the recently published NOR-SWITCH study. NOR-SWITCH is a randomized, double blind clinical trial of patients with six inflammatory diseases being switched from the original biologic, Remicade® to the biosimilar, Remsima®. Funded by the Norwegian government, it explores if the new biosimilar is medically inferior to the original biologic.

The concern is that some policymakers may use the recent data as a justification for switching patients stable on an original biologic to a biosimilar. The need for lowering costs should not lead policymakers to exaggerate NOR-SWITCH findings and apply them inappropriately to other biologics or disease states not evaluated in this study.

Three key areas in which NOR-SWITCH does not provide data are:

- Switching of any biosimilar not evaluated in the study
- Multiple switches over the course of an illness
- Switching in any disease state not evaluated in the study

Participants discussed their concerns around switching patients currently stable on an original biologic and the inappropriate application of NOR-SWITCH results by pharmacists and policymakers to justify switching other biologics in disease states not studied. They also made clear that patients and physicians should always get a say in their treatment not be forced to switch if they are stable on their current biologic medicine.



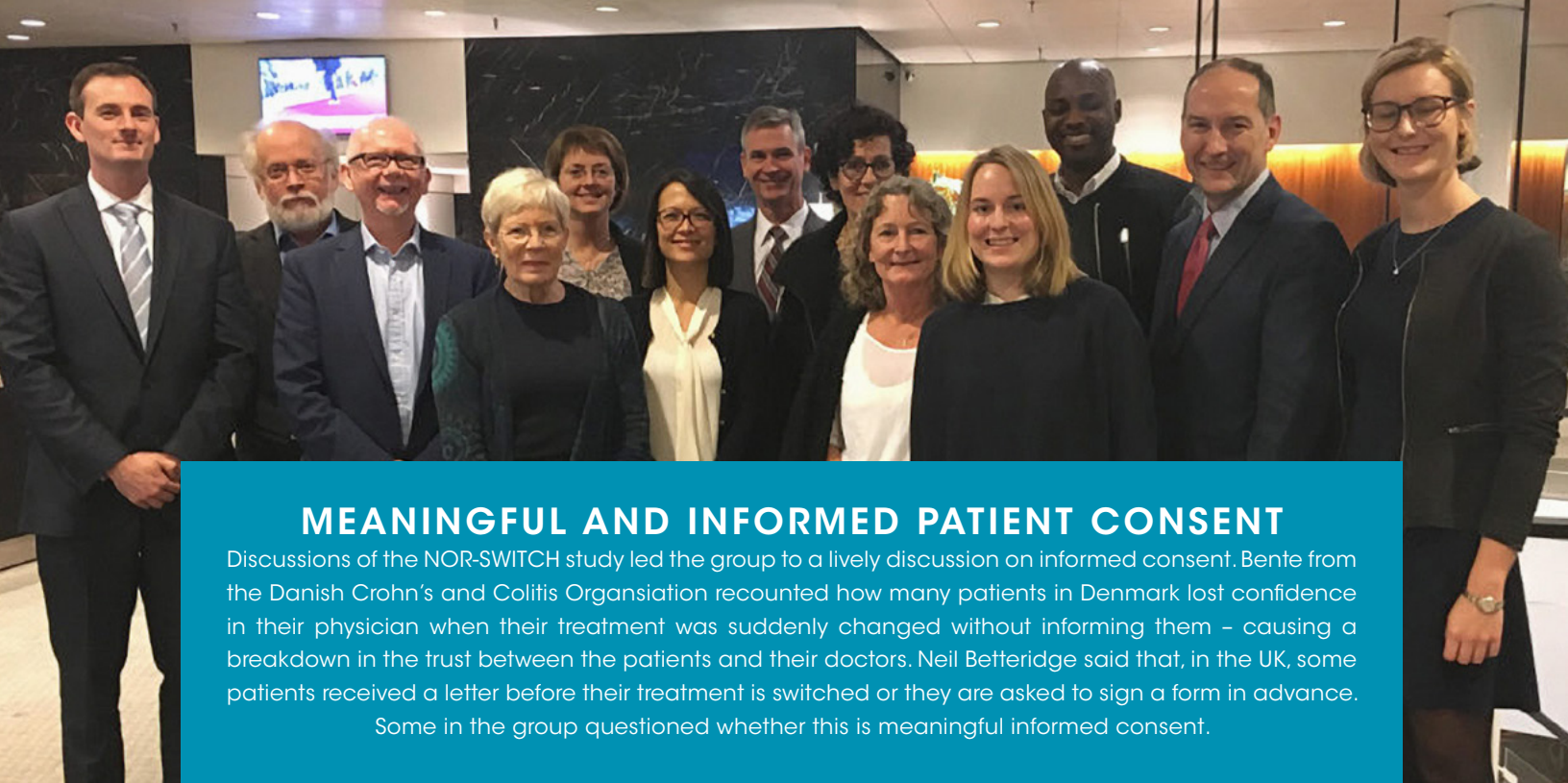
PATIENT PERSPECTIVES

Nordic delegates discussed the differing levels of access to both biologic and biosimilar medicines in their countries, with several representatives from Iceland explaining that patients with long term conditions are initially treated with steroids before being allowed to receive biologics. This 'step therapy' or 'fail first' approach was a cause for concern amongst all delegates, who believe that patients are being pushed into enduring prolonged suffering because of the cost concerns.

Representatives gave first-hand experiences involving biologics and biosimilars in their countries. Bente Buus Nielsen from the Danish Crohn's and Colitis Association, recounted the experience of nearly 3,000 Crohn's and colitis patients who were switched from their original biologic to a biosimilar overnight. Many of these patients were not told about the switch, and some who asked about it found that their physician had not noted the change of medication in their notes. Therefore, when they subsequently tried to report adverse reactions, they were recorded under the name of the original biologic and not the biosimilar they actually received. Bente told the group that, despite EMA guidance that biologic medicines should be recorded by brand and batch number, this was happening in only 2% of cases in Denmark.

Bente's organization mobilised patients through social media to inquire about adverse reactions to the biosimilar. Some 150 patients replied indicating they had suffered a range of reactions, from side effects to exacerbations of their disease. Some patients were therefore switched back to their original biologic medicine. Following a successful campaign, Bente's patient group has now succeeded in changing the policy in Denmark, so that decisions about switching are made on a case-by-case basis.





MEANINGFUL AND INFORMED PATIENT CONSENT

Discussions of the NOR-SWITCH study led the group to a lively discussion on informed consent. Bente from the Danish Crohn's and Colitis Organisation recounted how many patients in Denmark lost confidence in their physician when their treatment was suddenly changed without informing them – causing a breakdown in the trust between the patients and their doctors. Neil Betteridge said that, in the UK, some patients received a letter before their treatment is switched or they are asked to sign a form in advance. Some in the group questioned whether this is meaningful informed consent.

ENGAGING WITH EU POLICY MEMBERS

COMMON AREAS OF CONCERN WERE:

- **NON-MEDICAL SWITCHING** – that patients may be switched for cost concerns only
- **TRACEABILITY** – that it is of paramount importance to be able to trace back an administered medicine in case there are adverse effects or lack of efficacy
- **INDICATION EXTRAPOLATION** – prescribing biosimilars for illness in which they have not been studied
- **INFORMED CONSENT** – ensuring that patients are always fully informed and give consent for any treatment or medication switch

PARTICIPANTS CAME TO THESE CONCLUSIONS:

- There is a **need for strong collaboration amongst the patient community in the Nordic region:** some delegates represented disease groups with very limited resources and low visibility. To maximise patient advocacy, all disease groups should gather around common objectives to have more impact and higher visibility with policy makers.
- There is a clear **need for the informed participation of patients** in decision-making.
- Referring to the issue of **switching**, it is **essential to communicate with all relevant stakeholders** (dispensing pharmacist, prescribing physician, and patient) in order to optimize treatment outcome. The patient advocates who attended the Nordic workshop agreed to continue the conversation around biologics and biosimilars in the Nordic region and that intend to collaborate further.

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GAfPA will continue to work with the Nordic patient groups to raise awareness around the important issues of patient safety and accurate information, as well as educating and empowering patient groups. A number of future activities are currently in planning.



EU POLICY AND REGULATORY ENVIRONMENT

Why are biosimilars coming onto the market?

Companies that make an originator or reference biologic medicines can pursue and receive a patent and a period of protection during which they alone can make and sell the product. As patents expire, other companies may seek to create a similar biologic medication. The first biosimilars received authorisation from the European Commission in 2006. Currently, 21 biosimilars are in use across Europe.^{iv}

How biosimilars are approved?

Biosimilars, like all biological medicines, must be approved centrally at the European Union (EU) level. Marketing authorisations are granted by the European Medicines Agency (EMA), which carries out a robust comparison to make sure that the biosimilar medicine does not differ greatly in terms of quality, safety, and efficacy from the originator biologic medicine.^v

Policy in different EU countries

In Europe, the EMA does not determine if a biosimilar is interchangeable with an original biologic and therefore leaves such decisions to each individual country. At present, policy decisions taken on the use of biosimilar medicines differs greatly between the 28 EU countries.

TRACKING AND TRACING

Switching between biologic and biosimilar medicines raises another important safety concern – that of the traceability of a prescribed medication. Traceability is the ability to **track and trace** medicines, including biosimilars, from the patient back to the manufacturer.^{vi} This is important because adverse reactions may not be detected during clinical trials. Therefore, once the medicines are available to patients, drug regulatory authorities need to track and assess all unexpected reactions to ensure the long-term safety of a medicine. This monitoring process is known as **pharmacovigilance**.^{vii} Patient advocates at the Nordic workshop were in agreement that it is important to be able to trace back a biologic or biosimilar in case there were adverse effects.

ENSURING PHARMACOVIGILANCE

EU legislation on pharmacovigilance has identified biologics and biosimilars as priorities for additional monitoring.^{viii} Medicines under additional monitoring have a black inverted triangle (▼) in their labelling. This triangle highlights that it is a new medication and encourages both physicians and patients to report adverse drug reactions (ADR).^{ix} Under EU pharmacovigilance law, anyone reporting a suspected adverse drug reaction is asked to provide the brand name and specific batch number of the biologic medicine to ensure traceability.^x



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The Global Alliance for Patient Access (GAfPA) is a network of physicians and patient advocates with the shared mission of promoting health policy that ensures patient access to appropriate clinical care and approved therapies. GAfPA accomplishes this mission through educating physicians and patients on health policy issues and developing education material and advocacy initiatives to promote informed policymaking.

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