HSE Guidance for Biological and Biosimilar Medicines use in Acute Hospitals

Introduction

This guidance provides information on the prescribing, procurement and educational resources for biological medicines and their approved biosimilars available for use in Health Service Executives (HSE) acute & non-acute hospitals, including both Voluntary and Statutory hospitals.

Biological medicines have greatly advanced the treatment of a wide range of acute and chronic conditions and their beneficial impact is as diverse as the product types themselves, which include vaccines, growth factors, immune modulators, monoclonal antibodies and products derived from donated blood and plasma[1]. Biological medicines are currently the largest area of spend in the HSE medicines budget.

The introduction of biosimilars has resulted in greater choice of biological medicines for patients and prescribers. The use of biosimilar medicines worldwide and in Irish clinical practice is well established with the number of biosimilars in use increasing year on year. To date, the European Medicines Agency (EMA) have approved over 80 biosimilar medicines[2]. Their availability brings competition to the pharmaceutical market and this presents an opportunity for significant improvement in value for patients and healthcare providers. The introduction of biosimilar medicines benefits all stakeholders as it allows for more patients to have access to a broader range of treatments and there is potential for healthcare providers to reinvest savings to further develop health services.

Background

The adoption of biosimilar medicines is identified by the Organisation of Economic Co-operation and Development (OECD) and the EU as a key strategy to reduce wasteful spending in the health service[3]. This remains a priority to improve cost-efficiencies in acute hospitals and a number of government and HSE-led initiatives are in place to support this:

- The Framework Agreement on Supply and Pricing of Medicines[4,5] entered into by Department of Health with Irish Pharmaceutical Healthcare Association (IPHA) and Medicines for Ireland (MFI) companies contains specific measures to provide cost efficiencies to the HSE when a biosimilar medicine is available in Ireland. The relevant clauses in the industry agreements require the reference medicine to reduce its price on the launch of biosimilar medicine.
- The Strategy for Procurement of Medicines in Acute and non-Acute Hospitals outlines procurement supports available to hospitals for the compliant procurement of medicines[6]. The National Pharmaceutical Procurement Support Team (NPPST) are available to support hospitals to realise the potential benefits of hospital supplied biosimilar medicines wherever possible in undertaking structured procurement processes.
- The Department of Health (DoH) Productivity and Savings Taskforce was established in January 2024. The Taskforce Action Plan sets out a range of productivity measures that aim to maximise access to health services for patients.
- The HSE Acute Hospitals Drug Management Programme (HSE-AHDMP) have implemented measures to achieve best value for HSE hospitals including medicines optimisation initiatives around prescribing, procurement, and education. The majority of biological medicine prescribing is within secondary care and biological medicines feature in the top spend of hospital drug expenditure reports in Ireland. The HSE-AHDMP:
    - Ensure clinical guidelines are updated to include biosimilar products
    - Support structured procurement exercises for biologics and biosimilar medicines

- Chair the Integrated Medicines Optimisation Pharmacist and Pharmacy Technicians (IMOPPT) initiative[7]

- The HSE Medicines Management Programme (HSE-MMP) Best-Value Biological (BVB) medicines process represents an innovative approach to ensuring that the efficiencies that the availability of biosimilar medicines present are realised:
  - The process for assessment and selection of BVB medicines is outlined in the Framework Agreement on the Supply and Pricing of Medicines (Schedule 2) and the Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines (Schedule 1).
  - The HSE-MMP is responsible for the identification of BVB medicines and for the co-ordination and implementation of measures to support prescribing and utilisation of the recommended BVB medicines.
  - In 2019, the HSE-MMP successfully implemented a BVB initiative for the anti-TNFα agents adalimumab and etanercept[8,9], which are prescribed in hospitals and supplied under the High Tech Arrangement in the community. A suite of information resources are available Here to support prescribing and utilisation of the BVB medicines.
  - A number of measures were introduced to support prescribing of the recommended BVB medicines for adalimumab and etanercept, including:
    - In 2019, the HSE introduced a gain share initiative to support prescribers in implementation of the BVB medicine recommendations.
    - Since February 2020, it is HSE policy that reimbursement of adalimumab and etanercept under the High Tech Arrangement is only supported for the BVB medicines in adult patients commencing such therapy, i.e. adult patients who are being initiated on adalimumab or etanercept (i.e. new patients to such therapy) should be prescribed a BVB medicine[10].
  - The HSE-MMP continues to undertake evaluations to identify, evaluate and recommend BVB medicines where savings can be made within the Irish Healthcare system[11] and support uptake of the recommended BVB medicines.

Contents and Scope

Section 1: Prescribing – interchangeability, switching, and substitution
Section 2: Procurement
Section 3: Resources and incentives to facilitate uptake of biologic medicines which offer the best value
Section 4: Education

This guidance document is only applicable for those biological medicines with at least one biosimilar alternative available that are prescribed, supplied and administered in the hospital setting. The recommendations in each section apply as follows:

- **Section 1:** The prescribing recommendations include general principles that apply to all biological medicines with a biosimilar alternative available that are prescribed, supplied and administered in the hospital setting. The HSE-MMP lead on BVB medicine processes for patent-expired biological medicines on the High Tech Arrangement/Community Drug Schemes.
- **Section 2:** Procurement recommendations apply to hospital-supplied biological medicines with a biosimilar available only.
- **Sections 3 and 4**: The sections on resources and incentives, and education apply to all biological medicines (both community and hospital-supplied).

Section 1: Prescribing – interchangeability, switching, and substitution

Prescribers of biological medicines may need to engage in a process of informed consent consultation with the patient as part of the treatment plan review to consider a biosimilar. This is applicable to treatment-naïve patients and those already being treated with a reference product or other biosimilar. For a biological medicine with a biosimilar available for the same licensed indication, the medicine offering better value should be prescribed, provided that this is the most clinically appropriate biological medicine for the patient.

The EMA define interchangeability as "*the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect*[12]". This can apply to replacing a reference medicine with a biosimilar (or vice versa) or replacing one biosimilar with another. Biologic interchangeability allows clinicians to prescribe a reference or biosimilar medicine with the aim of achieving the same therapeutic effect. Biosimilars must demonstrate, as part of their approval process, that there are no clinically meaningful differences between it and the reference medicine.

Interchangeability can be implemented in one of two ways:

- **Switching** is when the replacement is prescriber led and
- **Automatic substitution** is when the replacement occurs at the pharmacy level without the prescriber being contacted. In Ireland, substitution of a biological medicine at the pharmacy level, without consulting the prescriber, is not permitted under the Health (Pricing and Supply of Medical Goods) Act 2013[13,14].

Decisions to switch a patient's biologic medicine should be done so in line with local hospital procedures and policies. The processes for switching from the reference product to a biosimilar (or vice versa) should be well defined and align to local hospital policy. The EMA and Heads of Medicines Agencies (HMA) joint statement on interchangeability of biosimilar medicines states that considering the scientific evidence and practical clinical experience from the last 15 years, they support that medicines approved as biosimilars in the EU are interchangeable with their reference medicine or other biosimilar medicines of the reference medicine.

"*Switching between biological medicinal products manufactured and commercialised by different companies has become common in clinical practice, and interchangeability of EU-licensed biosimilars has been confirmed*.[12]"

This approach will increase access to biological medicines for patients[12]. Biosimilars approved in the EU have demonstrated comparable immunogenicity to the reference product and theoretical concerns around increased immunogenicity do not appear robust[12,15].

A significant body of high quality clinical evidence, including phase 3 equivalence trials supports switching of reference medicines to biosimilars. The NOR-SWITCH[16] trial studied a single switch from reference infliximab (Remicade®) to the biosimilar infliximab CT-P13 (Inflectra®, Remsima®) in inflammatory arthritides, inflammatory bowel disease, and psoriasis. The results of the study demonstrated non-inferiority of the biosimilars compared with the originator in terms of safety, efficacy and immunogenicity. Similar data exist for etanercept and adalimumab[17] and these data are supportive of the framework and scientific principles applied by the EMA in biosimilar development

to ensure no significant difference between reference medicines and their biosimilars. Switching to biosimilars has become routine clinical practice in Irish healthcare settings.

The evidence base in relation to multiple switches is evolving; it will continue to be an area of focus in future versions of this guidance document as the evidence base grows. Efforts should be made to publish case studies in order to contribute to evidence base.

Recommendations:
(NOTE: The following recommendations only apply to biological medicines with at least one biosimilar available that are prescribed, supplied and administered in the hospital setting.)

1. For a biological medicine with a biosimilar available for the same licensed indication, the medicine offering the better value should be prescribed (provided that this is the most clinically appropriate biological medicine for the patient)
    i. All treatment-naïve patients should be initiated on the better-value medicine [whether biosimilar or reference medicine].
    ii. All non-treatment-naïve patients currently on treatment with the reference medicine should be considered for a switch to a biosimilar if the biosimilar is better value compared to the originator or reference medicine.
    iii. All non-treatment-naïve patients on a significant (not necessitated by surgery, intercurrent illness, etc) break in treatment should be restarted on the better-value medicine [whether biosimilar or reference medicine] if further treatment is indicated. (The Summary of Product Characteristics should be referred to for precautions required with restarting treatment with biological medicines after a treatment break).
    iv. Switching by a Registered Nurse Prescriber [RNP] is recommended only if it is agreed as part of local governance arrangements.
    v. Automatic substitution at pharmacy level [without consulting the prescriber] is not recommended and not supported in Irish Legislation.
    vi. The evidence base in relation to multiple switches is evolving; it will continue to be an area of focus in future versions of this guidance document as the evidence base grows. Efforts should be made to publish case studies in order to contribute to evidence base.
    vii. When prescribing biological medicines, the brand name must be included on the prescription [e.g. Flixabi®, Inflectra®, Remicade® or Remsima® rather than infliximab] to avoid accidental substitution and to ensure traceability **(EMA recommendation).** The International Non-proprietary Name (INN) should also be included but is not a mandatory requirement. The patient (or their carer) must be made aware of the brand of biological medicine prescribed to avoid accidental substitution.
    viii. The patient (or their carer) must be counselled on the new device, if appropriate, with a focus on any different administration or storage requirements.
2. There are no specific safety requirements for biosimilars; monitoring requirements are the same as for the reference medicine. **(EMA recommendation)**.
3. All biological medicines [biosimilars and reference medicines] authorised by the European Commission after 01 January 2011 are "black triangle" medicines for a period of time; any suspected adverse drug reactions should be reported to the HPRA with the brand name and batch number of the medicine. **(EMA recommendation)**.
4. Clinical trial medicines supplied by the hospital should, if possible, and where appropriate, use the best value biologic [whether biosimilar or reference medicine], unless not permitted under the clinical trial agreement. If not permitted under the clinical trial agreement, the required biologic would need to be purchased locally so that this is not an impediment to opening the clinical trial. This does not apply if the medicine is supplied by the Contract Research Organisation (CRO).

Section 2: Procurement

Procurement of medicines in the HSE, or entities funded by it, is a public contract and is subject to EU legislation [18] and the HSE's National Financial Regulation Procurement Process (NFR B1).[19] The HSE have published the *Strategy for Procurement of Medicines in Acute & and Non-Acute Hospitals*[6]. This strategy aims to support medication tendering processes through a National Dynamic Purchasing System (DPS), as a preferred model to facilitate compliant procurement of medicines by HSE-funded hospitals. The National Pharmaceutical Procurement Support Team (NPPST) are available to support hospitals to realise the potential benefits of biosimilar products wherever possible in undertaking structured procurement processes.

The real-world evidence to date in Ireland has shown that a successful procurement exercise is pharmacy-led with input from clinicians, procurement and finance colleagues. The involvement of these stakeholders in awarding contracts will ensure the best outcomes are achieved. The evidence in recent years is that best value is realised when three or more products are in the market, one of which may be the reference medicine. The biosimilar marketing authorisation holders (MAH) competing with the reference medicine MAH in structured procurement exercises have offered lower prices, in excess of industry agreements (IPHA and MFI), to achieve cost efficiencies and supply chain sustainability for the healthcare system. Cost savings realised from the competitive procurement process is cited by hospitals as providing the motivation to undertake these complex procurement initiatives. Procurement can be undertaken at a single hospital level or aggregated at a regional or national level. Concessions offered by manufacturers are often volume based meaning aggregated tenders are more likely to result in lower prices for the payer. To sustain clinical stakeholder engagement, the benefits should be seen as wider than the immediate financial benefit and more directly benefiting patient care.

Recommendations:

1. Biological medicines for use in HSE hospitals should be procured in compliance with the EU Procurement Directive 2014/24/EU and the HSE's National Financial Regulation Procurement Process (NFR B1)
2. The NPPST are available to support with the tendering process for hospital supplied biological medicines. Information, and contact details can be found https://www.hse.ie/eng/about/who/national-drugs-management-programme/publications/
3. The tendering process should involve input from all key stakeholders
4. Hospitals should undertake a structured procurement exercise for hospital-supplied biological medicines where there is at least one biosimilar available; competitive tenders with high volume are likely to deliver maximum value
5. The value achieved should be used to maximise access to health services for patients.

Section 3: Resources and incentives to facilitate uptake of biologic medicines which offer the best value

A priority for the HSE is removing disincentives to prescribing biosimilar products.

Positive incentives, for example gainshare, have shown to improve uptake of biosimilars in clinical practice. Implementation of any form of incentives requires monitoring and reporting of prescribing and dispensing data. This would be facilitated by the HSE-AHDMP for hospital-supplied biological medicines and by the HSE-MMP, in collaboration with the Primary Care Reimbursement Service (PCRS), for community-supplied biological medicines. Prescribing trends may be assessed and reported back through National Clinical Programmes to drive clinician confidence in switching biological medicines. Reports can also be shared locally in the context of regional and national trends to monitor performance.

Recommendations for incentives to facilitate uptake of biologic medicines which offer the best value

1. Disincentives to prescribing best value biological medicine should be removed.
2. Any positive incentives should be monitored closely and reported back to prescribers on a regular basis.

Section 4: Education

Education of stakeholders is essential to improve the understanding of biological medicines and ensuring there is equal confidence in biosimilars and reference medicines among prescribers and patients. In addition to this document, a number of national guidelines have been published in recent years with the aim of improving understanding and uptake of biosimilar medicines.

Links to educational resources:

- The HSE Medicines Management Programme have produced a range of resources to support the prescribing and implementation of the Best-Value Biological Medicines available from: https://www.hse.ie/eng/about/who/cspd/medicines-management/best-value-medicines/
- EMA published information guides for Healthcare Professionals and patients: https://www.ema.europa.eu/en/human-regulatory/overview/biosimilar-medicines-overview
- HPRA published information guides for Healthcare Professionals and patients:
    - https://www.hpra.ie/homepage/medicines/special-topics/biosimilar-medicines
    - Guide to Biosimilars for Healthcare Professionals http://www.hpra.ie/homepage/about-us/publications-forms/guidance-documents/item?id=e6d50326-9782-6eee-9b55-ff00008c97d0&t=/docs/default-source/publications-forms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-and-patients-v2
- The Irish Platform for Patient Organisations, Science & Industry (IPPOSI) provide online educational material about biological medicines (including biosimilars) aimed at patients: https://www.ipposi.ie/our-work/policy/biologics-biosimilars/
- European Generic Medicines Association - biosimilars handbook https://www.medicinesforeurope.com/wp-content/uploads/2016/03/EGA_BIOSIMILARS_handbook_en.pdf
- Irish Institute of Pharmacy, Biosimilars: Supporting Your Patients (2023). Courses and Events | IIoP Portal

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Appendix I - Members of the National Steering Committee for Biosimilars in Acute Hospitals:

Chair of the Committee: Professor David Kane Rheumatology Clinical Lead & Consultant Rheumatologist, Tallaght University Hospital
Co-chair: Rhona O'Neill Chief II Pharmacist Acute Hospital Drug Management Programme
Dermatology Clinical Lead: Dr Anne Marie Tobin – National Clinical Lead & Consultant Dermatologist, Tallaght University Hospital
Gastroenterology Representative: Prof Glen Doherty, St Vincent's University Hospital
Oncology Clinical Representative: Margaret Triggs, Chief II Pharmacist NCCP
Ms Fionnuala King, Acute Hospital Drugs Management Programme Clinical Lead
Mr Bernard Duggan, Chief I Pharmacist, Medicines Management Programme
Hospital Pharmacist – Mr Ciaran Halleran - Chief Pharmacist, Mercy University Hospital
Hospital Pharmacist – Mr Paul Tighe Chief Pharmacist, St Vincent's University Hospital
Procurement – Ms Maeve Hynes, Chief II Pharmacist (Clinical Lead National Pharmaceutical Procurement Support Team)