Best-Value Biological Medicines:

Tumour Necrosis Factor-α Inhibitors

Questions and Answers for Healthcare Professionals

1) What is a biological medicine?

A biological medicine is a medicine that contains an active substance made by a biological process or derived from a biological source.[1] Most biological medicines are produced from cell cultures of living organisms, such as mammalian cells, bacterial or yeast cells, which have been engineered to produce a specific therapeutic molecule or group of molecules, usually protein(s).[1] Biological medicines contain larger and more complex active substances than chemically synthesised small molecules and in general tend to be more targeted in their therapeutic activity.[1] The tumour necrosis factor-alpha (TNF-α) inhibitors are examples of biological medicines.

2) What is a biosimilar medicine?

A biosimilar medicine ('biosimilar') is a biological medicine that is highly similar to another biological medicine (called the reference biological medicine) that has already been authorised for use in the European Union (EU).[1] The European Medicines Agency (EMA) list the following specific features of biosimilar medicines:[2]

- They are highly similar to the reference biological medicine
- There are no clinically meaningful differences compared with the reference biological medicine
- The variability between the biosimilar and the reference biological medicine is kept within strict limits
- The same strict standards of quality, safety and efficacy apply to the biosimilar as do to the reference biological medicine.

3) Why isn't a biological medicine a generic medicine?

As biological medicines are produced by living organisms, there is an inherent degree of natural variability which is not present with chemical entities. Due to this variability, it may not be possible to produce an exact copy of a reference biological medicine. As a result, generic versions of biological medicines are not feasible.[1]

Due to the natural variability of the biological source and to the manufacturing process unique to each manufacturer, minor differences can occur between the biosimilar and the reference biological medicine. Strict controls are in place during the manufacturing process to ensure that the minor

differences do not affect the way the biosimilar works or its safety. These differences, therefore, are not clinically meaningful in terms of efficacy or safety.[2]

Biosimilars are similar but not identical versions of their reference biological medicine. They have an overall degree of comparability to the reference biological medicine.[1]

4) Where can I find further information on biological and biosimilar medicines?

The Health Products Regulatory Authority (HPRA), and the European Commission and the EMA have published guidance documents on biosimilars:

http://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-v3.pdf

https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf

5) The European Medicines Agency issued a joint statement with the Heads of Medicines Agencies on interchangeability of biosimilar medicines in September 2022. What did this say?

This statement confirmed that biosimilar medicines approved in the EU are interchangeable with their reference medicine or with an equivalent biosimilar medicine.[3]

Interchangeability in this context means that a prescriber can replace the reference medicine with a biosimilar medicine without a patient experiencing any changes in the clinical effect.[3]

The EMA highlighted that the experience obtained from clinical practice has shown that in terms of efficacy, safety and immunogenicity, biosimilar medicines are comparable to their reference medicine and therefore can be prescribed interchangeably.[3]

6) What are best-value biological (BVB) medicines?

The availability of biosimilars presents an opportunity to ensure the cost-effective prescribing and utilisation of biological medicines. Where a biosimilar becomes available for a biological medicine that is reimbursed through the community drug schemes, the Medicines Management Programme (MMP) may evaluate the biological medicines in question and issue a recommendation as to the best-value biological (BVB) medicine. The criteria that may be considered by the MMP in identifying a BVB medicine, and the evaluation process are outlined in the MMP roadmap for the prescribing of best-value biological (BVB) medicines in the Irish healthcare setting.

7) Why is it important that a BVB medicine is identified and used?

Biological medicines account for a significant amount of the total annual expenditure on medicines by the state. For example, biological medicines reimbursed on the High Tech Arrangement containing a TNF-α inhibitor accounted for expenditure* of approximately €190 million in 2021. This represented 21.2% of expenditure on medicines on the High Tech Arrangement in 2021.[4]

Prescribing of the BVB medicine in a therapeutic area will ensure that available efficiencies are realised and savings for the health service are achieved.

* Expenditure reflects ingredient cost, and is exclusive of pharmacy fees and VAT where applicable, based on claims submitted by pharmacists

Tumour Necrosis Factor-α Inhibitors

8) Which biological medicines containing TNF-α inhibitors are reimbursed on the High Tech Arrangement?

There are five biological medicines within this category that are reimbursed on the High Tech Arrangement:

- Adalimumab
- Certolizumab pegol
- Etanercept
- Golimumab
- Infliximab

The products containing a TNF-α inhibitor that are available on the High Tech Arrangement are included in the table below.

TNF-α Inhibitor	Reference Biological Medicine	Biosimilar(s)
Adalimumab	Humira®	Amgevita® Hukyndra® Hulio® Idacio® Imraldi® Yuflyma®
Certolizumab pegol	Cimzia®	Not currently available
Etanercept	Enbrel®	Benepali® Erelzi®
Golimumab	Simponi®	Not currently available
Infliximab	Not available on High Tech Arrangement	Remsima®

9) Are there biosimilars of biological medicines containing TNF-α inhibitors reimbursable on the High Tech Arrangement?

Within the TNF-α inhibitor category, biosimilars for adalimumab, etanercept and infliximab are available and reimbursable on the High Tech Arrangement. There are no biosimilars of certolizumab pegol and golimumab available at present. It is anticipated that they will become available in the future.

10) What are the BVB Medicines for adalimumab and etanercept?

The MMP recommends the following BVB medicines for adalimumab and etanercept:

- Adalimumab 40 mg:[1]
  - Citrate-containing: **Idacio®**
  - Citrate-free: **Amgevita®, Hukyndra®, Humira®, Hulio®, Imraldi®, Yuflyma®**
- Etanercept: **Benepali®, Erelzi®**

The MMP recommends **Amgevita®** 80 mg, **Humira®** 80 mg and **Yuflyma®** 80 mg as the BVB medicines for presentations of adalimumab 80 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

The MMP recommends **Amgevita®** 20 mg as the BVB medicine for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement. This presentation of adalimumab is predominately used in paediatric patients.

Prescribing the BVB medicines will lead to significant savings for the health service, in the order of millions of euros.

11) How are BVB medicines for adalimumab and etanercept identified?

BVB medicines are identified in line with the evaluation process outlined in the MMP roadmap for the prescribing of best-value biological (BVB) medicines in the Irish healthcare setting. The criteria that are considered by the MMP in identifying the BVB medicines are outlined in the MMP roadmap.

Evaluation reports are available at www.hse.ie/mmp in the section entitled *Best-value medicines*.

12) What is the difference in cost between the reference biological medicines (Enbrel® and Humira®) and the BVB medicines (Amgevita®, Benepali®, Erelzi®, Idacio®, Imraldi®, Hukyndra®, Hulio® and Yuflyma®)?

The reimbursement prices of the biological medicines containing adalimumab or etanercept, including biosimilars, are available on the website of the PCRS; www.pcrs.ie. The reimbursement price listed may not represent the final acquisition cost of the biological medicine to the HSE, as it not does not include any rebates and commercial-in-confidence arrangements that are in place.

As of 1 July 2023, all medicinal products containing adalimumab 40 mg and 80 mg in self-administered injections devices (i.e. pre-filled pen/syringe) that are available for prescribing on the High Tech Arrangement are recommended as BVB medicines for adalimumab. This means that the

[1] The MMP recommended Hyrimoz® 40 mg as a BVB medicine for adalimumab 40 mg in May 2022. In June 2024, the MMP received notification of the discontinuation of Hyrimoz®. It is, therefore, no longer recommended as a BVB medicine.

final acquisition cost of these medicines to the HSE is similar across all of the BVB medicines for adalimumab.

Branded etanercept is substantially more expensive than the identified BVB medicines for etanercept. Prescribing of the BVB medicines for etanercept will result in significant savings in comparison to the reference biological medicine, Enbrel®. This is due to commercial-in-confidence arrangements that are in place with the HSE arising from the evaluation process for the BVB medicines.

13) When should the BVB medicines for adalimumab (Amgevita®, Idacio®, Imraldi®, Hukyndra®, Hulio®, Humira®and Yuflyma®) and etanercept (Benepali®, Erelzi®) be prescribed?

If a patient is being **initiated** on a biological medicine containing a TNF-α inhibitor, one of the identified BVB medicines should be selected:

- Adalimumab 40 mg:
  - Citrate-containing: **Idacio®**
  - Citrate-free: **Amgevita®, Hukyndra®, Hulio®, Humira®, Imraldi®, Yuflyma®**
- Adalimumab 20 mg: **Amgevita®**
- Adalimumab 80 mg: **Amgevita®, Humira®, Yuflyma®**
- Etanercept: **Benepali®, Erelzi®**

When **issuing a repeat prescription** for a biological medicine containing adalimumab or etanercept, patients should be considered for switching to a BVB medicine:

- Adalimumab 40 mg:
  - Citrate-containing: **Idacio®**
  - Citrate-free: **Amgevita®, Hukyndra®, Hulio®, Humira®, Imraldi®, Yuflyma®**
- Adalimumab 20 mg: **Amgevita®**
- Adalimumab 80 mg: **Amgevita®, Humira®, Yuflyma®**
- Etanercept: **Benepali®, Erelzi®**

Since June 2019, over 25,000 patients have been prescribed a biosimilar medicine of adalimumab or etanercept that has been recommended as a BVB medicine for adalimumab or etanercept, through the High Tech Hub.

14) What supports are available for consultants and clinical teams?

MMP pharmacists are available to engage with consultants and clinical teams to provide support for initiation of, and switching to the BVB medicines. Please contact the MMP (mmp@hse.ie) if you wish to avail of this support.

Resources to support prescribing of the BVB medicines are available on the MMP website (www.hse.ie/mmp) in the section entitled *Best-value biological medicines*. These include:

- Questions and Answers for Healthcare Professionals
- MMP Product Information Sheets for Amgevita®, Benepali®, Erelzi®, Idacio®, Imraldi®, Hukyndra®, Hulio®, Humira®and Yuflyma®
- Templates for switching letters for Benepali® and Erelzi®.

Support is also available for clinics and patients from the marketing authorisation holders of Amgevita® (Amgen Ireland), Benepali® and Imraldi® (Biogen Ireland), Erelzi® (Sandoz trading as Rowex Limited), Idacio® (Fresenius Kabi Ireland), Hukyndra® (Clonmel Healthcare Limited), Hulio® (Mylan Ireland), Humira® (AbbVie Ireland Limited) and Yuflyma® (Celltrion Healthcare Ireland). This includes information on the biological medicines, training in the usage of the administration devices for each of the products, and the provision of home support to patients by a nurse. The relevant contact details are provided below.

AbbVie Ireland (Humira®)

To refer a patient who has been prescribed **Humira®** to the patient support programme or to obtain training pens, please contact 1800 200 573 or www.abbviecare.ie.

Amgen Ireland (Amgevita®)

In order to avail of the patient support services for patients who have been prescribed **Amgevita®**, please contact one of the following:

- TCP Homecare at 1800 211 211 or by email at homecare.pcb@tcp.ie. Alternatively, patients can be referred through the Amgen Care online referral portal: https://www.amgencarehcp.ie/
- Hibernian Healthcare at Home at 01 460 4820. Alternatively, patients can be referred through the Hibernian online referral portal: https://schedule.hahirl.com/

In order to obtain demonstration devices and patient support materials for use in clinics, please contact TCP Homecare at 1800 211 211 or Hibernian Healthcare at Home at 01 460 4820.

Biogen Ireland (Benepali® and Imraldi®)

In order to avail of the patient support services for patients who have been prescribed **Benepali®** or **Imraldi®**, please use the Hibernian Healthcare at Home online portal www.schedule.hahirl.com. If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 460 4820 or by email at info@hibernianhealth.com, and access and support will be provided.

In order to obtain training pens, patient support materials for use in clinics, or information relating to faecal calprotectin testing, please contact:

- Email: medinfo.europe@biogen.com
- Phone: 01 513 3333

Celltrion Healthcare Ireland (Yuflyma®)

In order to avail of the patient support services for patients who have been prescribed **Yuflyma®**, please use the Hibernian Healthcare at Home online portal www.schedule.hahirl.com. If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 460 4820 or by email at info@hibernianhealth.com, and access and support will be provided.

In order to obtain training pens and patient support materials for use in clinics please contact:
Celltrion Healthcare Ireland, Unit 26, Arrow Building, Old Belgard Road, Tallaght Dublin 24 ND70.

- Email: Enquiry_IE@celltrionhc.com
- Phone: 087 3386213

Fresenius Kabi Ireland (Idacio®)

In order to avail of the patient support services for patients who have been prescribed **Idacio®**, please contact TCP Homecare at Home at 1800 810 020 (Freephone) or 01 429 1828 or by email at homecarepcb@tcp.ie.

In order to obtain training pens and patient support materials for use in clinics, please contact Fresenius Kabi Ltd:

- Phone: 01 841 3030
- Email: FK-enquiries.Ireland@fresenius-kabi.com

Mylan Ireland (Hulio®)

In order to avail of the patient support services for patients who have been prescribed **Hulio®**, please use the Hibernian Healthcare at Home online portal www.schedule.hahirl.com. If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 460 4820 or by email at info@hibernianhealth.com, and access and support will be provided.

In order to obtain training pens and patient support materials for use in clinics, please contact Mylan Ireland Limited at 01 832 2250. For medical information queries, please contact info@mylan.co.uk.

Sandoz trading as Rowex Limited (Erelzi®)

In order to avail of the patient support services for patients who have been prescribed **Erelzi®**, please use the Hibernian Healthcare at Home online portal www.schedule.hahirl.com. If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 460 4820 or by email at info@hibernianhealth.com, and access and support will be provided.

In order to obtain training pens and patient support materials for use in clinics, please contact Sandoz trading as Rowex Limited:

- Email: dgoggin@rowa-pharma.ie or pomeara@rowa-pharma.ie
- Phone: 027 50077

Further information on the supports that are available can be found in the following document in the *Best-value biological medicines: Adalimumab & Etanercept* section of the MMP website www.hse.ie/mmp:

- BVB Medicine Patient and Clinic Support Services TNF-α Inhibitors

MMP pharmacists are available to engage with consultants and clinical teams to provide support for initiation of, and switching to the BVB medicines. This includes provision of an information session on the BVB medicines and the High Tech Hub (in conjunction with the HSE-Primary Care Reimbursement Service High Tech Co-ordination Unit). Please contact the MMP (mmp@hse.ie) if you wish to avail of this support.

References:

1. Health Products Regulatory Authority. Guide to Biosimilars for Healthcare Professionals. August 2020. Accessed at www.hpra.ie on 31/12/2024.
2. European Medicines Agency and the European Commission. Biosimilars in the EU. Information guide for healthcare professionals. October 2019. Last updated 13 November 2023. Accessed at https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf on 31/12/2024.
3. European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA). Statement on the scientific rationale supporting interchangeability of biosimilar medicines in the EU. 19 September 2022. Last updated 26 April 2023. Accessed at https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf on 31/12/2024.
4. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Pharmacy Reports. Top 100 Products by Ingredient Cost. HTS 2021. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 31/12/2024.