

# Best-Value Biological Medicines: Tumour Necrosis Factor- $\alpha$ 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.<sup>1</sup> 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).<sup>1</sup> 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.<sup>1</sup> The tumour necrosis factor-alpha (TNF- $\alpha$ ) 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.<sup>1</sup> The European Medicines Agency list the following specific features of biosimilar medicines:<sup>2</sup>

- 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.<sup>1</sup>

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.<sup>2</sup>

Biosimilars are similar but not identical versions of their reference biological medicine. They have an overall degree of comparability to the reference biological medicine.<sup>1</sup>

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

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

<http://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-and-patients-v2.pdf>

[https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals\\_en.pdf](https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf)

#### 5) 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) will 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](#).

#### 6) 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- $\alpha$  inhibitor accounted for total expenditure\* of approximately €224 million in 2017. This represents 10.9% of the total expenditure on medicines by the Primary Care Eligibility & Reimbursement Service (PCERS).<sup>3</sup>

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

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\* Total expenditure includes ingredient cost and VAT where applicable, based on claims submitted by pharmacists

## Tumour Necrosis Factor- $\alpha$ Inhibitors

### 7) Which biological medicines containing TNF- $\alpha$ inhibitors are reimbursed on the High Tech Arrangement?

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

- Adalimumab
- Certolizumab pegol
- Etanercept
- Golimumab

The products containing a TNF- $\alpha$  inhibitor that are available on the High Tech Arrangement as of 1 March 2020 are included in the table below.

TNF- $\alpha$ Inhibitor	Reference Biological Medicine	Biosimilar(s)
<b>Adalimumab</b>	Humira <sup>®</sup>	Amgevita <sup>®</sup> Hulio <sup>®</sup> Idacio <sup>®</sup> Imraldi <sup>®</sup>
<b>Certolizumab pegol</b>	Cimzia <sup>®</sup>	Not currently available
<b>Etanercept</b>	Enbrel <sup>®</sup>	Benepali <sup>®</sup>
<b>Golimumab</b>	Simponi <sup>®</sup>	Not currently available

### 8) Are there biosimilars of biological medicines containing TNF- $\alpha$ inhibitors reimbursable on the High Tech Arrangement?

Within the TNF- $\alpha$  inhibitor category, biosimilars for adalimumab and etanercept 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.

### 9) What are the BVB Medicines for adalimumab and etanercept?

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

- Adalimumab:
  - Citrate-containing: **Idacio<sup>®</sup>**, **Imraldi<sup>®</sup>**
  - Citrate-free: **Amgevita<sup>®</sup>**, **Hulio<sup>®</sup>**
- Etanercept: **Benepali<sup>®</sup>**

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

### 10) 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/yourmedicines](http://www.hse.ie/yourmedicines) in the section entitled *Best-value biological medicines*.

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

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

Prescribing of the BVB medicines will result in significant savings in comparison to other biological medicines. This is due to commercial in confidence arrangements that are in place with the HSE arising from the evaluation process for the BVB medicines.

### 12) When should the BVB medicines for adalimumab (Amgevita®, Idacio®, Imraldi® and Hulio®) and etanercept (Benepali®) be prescribed?

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

- Adalimumab:
  - Citrate-containing: **Idacio®**, **Imraldi®**
  - Citrate-free: **Amgevita®**, **Hulio®**
- Etanercept: **Benepali®**

When **issuing a repeat prescription** for a biological medicine containing adalimumab or etanercept, patients on the reference medicinal product (Humira® or Enbrel®) should be **considered for switching** to a BVB medicine:

- Adalimumab:
  - Citrate-containing: **Idacio®**, **Imraldi®**
  - Citrate-free: **Amgevita®**, **Hulio®**
- Etanercept: **Benepali®**

### 13) 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](mailto: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/yourmedicines](http://www.hse.ie/yourmedicines)) in the section entitled *Best-value biological medicines*. These include:

- Questions and Answers for Healthcare Professionals
- MMP Product Information Sheets for Amgevita<sup>®</sup>, Benepali<sup>®</sup>, Idacio<sup>®</sup>, Imraldi<sup>®</sup> and Hulio<sup>®</sup>
- Templates for switching letters for Amgevita<sup>®</sup>, Benepali<sup>®</sup>, Idacio<sup>®</sup>, Imraldi<sup>®</sup> and Hulio<sup>®</sup>.

Support is also available for clinics and patients from the marketing authorisation holders of Amgevita<sup>®</sup> (Amgen Ireland), Benepali<sup>®</sup> and Imraldi<sup>®</sup> (Biogen Ireland), Idacio<sup>®</sup> (Fresenius Kabi Ireland) and Hulio<sup>®</sup> (Mylan 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.

#### **Amgen Ireland (Amgevita<sup>®</sup>)**

In order to avail of the patient support services for patients who have been prescribed **Amgevita<sup>®</sup>**, please contact the TCP Homecare patient care bureau at 1800 211 211 or by email at [homecare.pcb@tcp.ie](mailto:homecare.pcb@tcp.ie). Patients can also be referred through the Amgen patient referral portal; [www.amgencarehcp.ie](http://www.amgencarehcp.ie).

In order to obtain training pens and patient support materials for use in clinics, the TCP dedicated account manager should be contacted at 1800 211 211.

#### **Biogen Ireland (Benepali<sup>®</sup> and Imraldi<sup>®</sup>)**

In order to avail of the patient support services for patients who have been prescribed Benepali<sup>®</sup> or Imraldi<sup>®</sup>, please use the Hibernian Healthcare at Home online portal [www.schedule.hahirl.com](http://www.schedule.hahirl.com). If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 4604820 or by email at [info@hibernianhealth.com](mailto: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\\_biogen@quintiles.com](mailto:Medinfo_biogen@quintiles.com)
- Phone: 01-5133333

### **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 4291828 or by email at [homecarepcb@tcp.ie](mailto: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](mailto: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](http://www.schedule.hahirl.com). If you have not registered on the Hibernian portal previously, please contact Hibernian Healthcare at Home at 01 4604820 or by email at [info@hibernianhealth.com](mailto: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 +353-1-8322250. For medical information queries, please contact [info@mylan.co.uk](mailto:info@mylan.co.uk).

Further information on the supports that are available can be found in the following two documents in the *Best-value biological medicines* section of the MMP website [www.hse.ie/yourmedicines](http://www.hse.ie/yourmedicines):

- BVB Medicine MMP initiation and switching support
- BVB Medicine Patient and Clinic Support Services TNF- $\alpha$  Inhibitors

## References:

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2. European Medicines Agency and the European Commission. Biosimilars in the EU. Information guide for healthcare professionals. April 2017. Accessed at [https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals\\_en.pdf](https://www.ema.europa.eu/documents/leaflet/biosimilars-eu-information-guide-healthcare-professionals_en.pdf) on 04/02/2019.
3. Primary Care Reimbursement Service. Statistical Analysis of Claims and Payments 2017. Accessed at <https://www.hse.ie/eng/staff/pccs/pccs-publications/annual-report-2017.pdf> on 04/02/2019.
4. HSE Medicines Management Programme. MMP roadmap for the prescribing of best-value biological (BVB) medicines in the Irish healthcare setting. December 2018. Accessed at <https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-biological-medicines/mmp-roadmap-for-the-prescribing-of-best-value-biological-bvb-medicines-in-the-irish-healthcare-setting.pdf> on 04/02/2019.