Medicines Management Programme

Best-Value Biological Medicines:

Review of submission for Hyrimoz®

Approved by:	Prof. Michael Barry, Clinical Lead, HSE-Medicines Management Programme (MMP).
Date approved:	13/05/2022
Version:	1.0

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List of Abbreviations

BVB	Best-Value Biological
CPU	Corporate Pharmaceutical Unit
DMARDs	Disease-modifying anti-rheumatic drugs
EPAR	European Public Assessment Report
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
Inj	Injection
INN	International non-propriety name
JA	Juvenile idiopathic arthritis
MMP	Medicines Management Programme
PCRS	Primary Care Reimbursement Service
PIL	Patient information leaflets
PFP	Pre-filled Pen
PFS	Pre-filled syringe
PP	Plaque psoriasis
RA	Rheumatoid arthritis
Soln	Solution
SmPC	Summary of Product Characteristics
TNF-α	Tumour Necrosis Factor-alpha

1. Executive Summary

The Health Service Executive (HSE)-Medicines Management Programme (MMP) supports the safe, effective and cost-effective use of biological medicines including biosimilar medicines (or 'biosimilars'). The MMP recognises the potential savings arising from the availability of biosimilars. These savings, however, can only be realised by increased utilisation of best-value biological (BVB) medicines, including biosimilars.

The MMP published a report on 2 May 2019 in which it identified BVB medicines for adalimumab and etanercept:[1]

- Adalimumab: **Imraldi®**. Where the clinician wishes to prescribe a citrate-free formulation of adalimumab, the MMP recommends **Amgevita®**.
- Etanercept: **Benepali®**

On 17 February 2020, the MMP published a report in which it recommended two further BVB medicines for adalimumab, **Hulio®** and **Idacio®**.[2] On 31 March 2021, the MMP published a report in which it recommended **Amgevita®** 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.[3] On 21 September 2021, the MMP published a report in which it recommended an additional BVB medicine for adalimumab, **Yuflyma®**.[4] On 30 December 2021, the MMP published a report in which it recommended a second BVB medicine for etanercept, **Erelzi®**.[5]

The MMP has reviewed a submission received from Novartis Ireland Limited at the request of the Corporate Pharmaceutical Unit (CPU) of the HSE-Primary Care Reimbursement Service (PCRS). The MMP considers **Hyrimoz®** to be comparable to the MMP BVB medicines for adalimumab. The MMP recommends that BVB medicine status be assigned to **Hyrimoz®**.

The MMP recommends the following BVB medicines:

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

Clinicians should give due consideration to the prescription of these agents when prescribing a TNF-α inhibitor. Implementation of the BVB medicines will lead to significant savings for the health service, in the order of millions of euros.

Initiation

When initiating a patient on a biological medicine containing a TNF-α inhibitor, the clinician should prescribe a BVB medicine:

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

Switching

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: **Hyrimoz®, Idacio®, Imraldi®**
  - Citrate-free: **Amgevita®, Hulio®, Yuflyma®**
- Etanercept: **Benepali®, Erelzi®**

2. Background

2.1. Best-Value Biological Medicines -Adalimumab & Etanercept

The MMP published a report on 2 May 2019 in which it identified BVB medicines for adalimumab and etanercept:[1]

- Adalimumab: **Imraldi®**. Where the clinician wishes to prescribe a citrate-free formulation of adalimumab, the MMP recommends **Amgevita®**.
- Etanercept: **Benepali®**

On 17 February 2020, the MMP published a report in which it recommended two further BVB medicines for adalimumab**, Hulio®** and **Idacio®**.[2] On 31 March 2021, the MMP published a report in which it recommended **Amgevita®** 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.[3] On 21 September 2021, the MMP published a report in which it recommended an additional BVB medicine for adalimumab, **Yuflyma®**.[4] On 30 December 2021, the MMP published a report in which it recommended a second BVB medicine for etanercept, **Erelzi®**.[5]

2.2 Biosimilars

Biosimilars for adalimumab and etanercept are available on the High Tech Arrangement:[6]

- Benepali®, a biosimilar containing etanercept, is available on the High Tech Arrangement since September 2016; Erelzi® was added to the High Tech Arrangement in March 2022.
- Amgevita®, Hulio® and Imraldi® biosimilars containing adalimumab, are available on the High Tech Arrangement since November 2018; Idacio® was added to the High Tech Arrangement in December 2019; Yuflyma® was added to the High Tech Arrangement in November 2021.

2.3 HSE-Primary Care Reimbursement Service Request

The CPU of the PCRS requested the MMP to review a submission for BVB medicine status from Novartis Ireland Limited in relation to their biosimilar medicine containing adalimumab, Hyrimoz®.

3. Scope

In line with the original BVB medicine evaluation process (May 2019), the presentation of Hyrimoz® for which Novartis Ireland Limited have provided a submission is considered to be within scope of evaluation for BVB medicine status as it contains a 40 mg dose of adalimumab within a self-administered injection device.

4. Definitions

For the purposes of this document, the reimbursement price refers to the reimbursed price of the medicinal product as listed in the High Tech Drug File maintained by the CPU. It may not represent the final acquisition cost to the HSE of the biological medicine, which may also include any rebates and commercial-in-confidence arrangements that are in place. Both the reimbursement price and the acquisition cost are exclusive of value added tax. Costs are correct as of 4th May 2022.

5. Evaluation Process

The review of the submission received from Novartis Ireland Limited was carried out in accordance with the evaluation process in the *MMP roadmap for the prescribing of best-value biological (BVB) medicines.*[7]

In line with the *MMP roadmap for the prescribing of best-value biological (BVB) medicines*, the MMP considered the following criteria when reviewing the BVB medicine submission received from Novartis Ireland Limited:[7]

1. Acquisition cost
2. Therapeutic indications
3. Formulation considerations
4. Product range including pack sizes and strengths available
5. Product stability including storage requirements
6. Administration devices
7. Patient factors
8. Expenditure in the therapeutic area and potential for cost efficiencies
9. Clinical guidelines
10. Security of supply to the Irish Market
11. Utilisation and clinical experience with the biological medicine
12. Any other relevant factors with respect to the particular INN

6. Evaluation

6.1 Acquisition cost

The proposed reimbursement price of Hyrimoz® under the High Tech Arrangement is outlined in table 1.

Table 1: Proposed reimbursement price of Hyrimoz® under the High Tech Arrangement[8]

Biological Medicine	Pack size	Reimbursement Price
Hyrimoz® PFP 40 mg	2	€617.07

PFP: Pre-filled pen

The submission received from Novartis Ireland Limited included revised commercial terms for the biological medicine listed above, resulting in significant reductions in the acquisition costs to the HSE.

Recommendation

For the 40 mg dosage of adalimumab formulated as a pre-filled pen (PFP), the acquisition cost to the HSE for Hyrimoz® is in line with the acquisition cost of the BVB medicines for adalimumab currently recommended by the MMP.

6.2 Therapeutic indications

Table 3 summarises the licensed therapeutic indications of Hyrimoz®, and compares them to the licensed indications of the reference medicine, Humira®.

Table 2: Summary of licensed therapeutic indications for Humira® and Hyrimoz®*

Brand (INN)	Rheumatoid arthritis (RA) Moderate to severe, active RA when response to DMARDs has been inadequate	Rheumatoid arthritis (RA) Severe, active and progressive RA in adults not previously treated with methotrexate	Juvenile idiopathic arthritis (JA) -Polyarticular JA -Enthesitis-related arthritis	Psoriatic arthritis	Axial spondyloarthritis -Ankylosing spondylitis -Non-radiographic axial spondyloarthritis	Plaque psoriasis (PP), Paediatric PP	Hidradenitis suppurativa	Crohn's disease, Paediatric Crohn's disease	Ulcerative Colitis, Paediatric ulcerative colitis	Uveitis, Paediatric uveitis
Humira®[9] (Adalimumab)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Hyrimoz®[10] (Adalimumab)	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

DMARDs: Disease-modifying anti-rheumatic drugs; INN: International non-proprietary name; JA: Juvenile idiopathic arthritis; PP: Plaque psoriasis; RA: Rheumatoid arthritis
*Please refer to individual SmPC for prescribing information on each of the biological medicines

Humira® is licensed for the full range of therapeutic indications. Hyrimoz® is also licensed for the full range of therapeutic indications in line with the reference biological medicine.

Recommendation
Overall, in relation to the criterion of therapeutic indications, the MMP is of the view that Hyrimoz® is equivalent to the reference medicine, Humira®. Hyrimoz® is licensed for all of the therapeutic indications that the MMP BVB medicines for adalimumab are licensed for.

6.3 Formulation considerations

Citrate is present as an excipient in Hyrimoz®.[10] Citrate is used to maintain the pH of the injection solution within a defined range, thus ensuring the stability of the biological medicine.

Injection site reactions are reported in the section on undesirable effects in the Summary of Product Characteristics (SmPC) of the reference biological medicine Humira®; this states that in pivotal clinical trials in adults and children, 12.9% of patients treated with Humira® developed injection site reactions, compared to 7.2% of patients who received treatment with placebo or active control. The injection site reactions are described as erythema, itching, haemorrhage, pain or swelling. The SmPC also states that injection site reactions did not necessitate discontinuation of the medicinal product.[9]

The SmPC for Hyrimoz® carries the same statement as Humira® in relation to injection site reactions.[10]

6.3.1 European Public Assessment Report - Hyrimoz®

In the clinical safety section of the European Public Assessment Report (EPAR) for Hyrimoz®, the incidence of injection site reactions reported for Hyrimoz® and Humira® were similar among healthy patients. Mild injection site reactions were mainly reported in all of the treatment groups. In the confirmatory efficacy and safety study in patients with psoriasis, the proportion of patients with injection site reactions were slightly higher in the Hyrimoz® treatment group than in the Humira® treatment group (6.5% versus 3.4%, respectively) during randomisation to week 17. This difference disappears over time and no imbalance was recorded at later time points of safety assessment.[11]

The EPAR concluded that the safety and immunogenicity results of the comparative studies in healthy volunteers and patients with psoriasis broadly support biosimilarity of Hyrimoz® and Humira®, with only some minor differences identified. The observed adverse effects for Hyrimoz® mirror those outlined in the SmPC of Humira®.[11]

Recommendation

In relation to the criterion of formulation considerations, the MMP is of the opinion that there is no robust evidence available that differentiates any of the biological medicines containing adalimumab. Hyrimoz® is therefore considered comparable to the MMP BVB medicines for adalimumab 40 mg for this criterion.

6.4 Product range including pack sizes and strengths available

Table 4 outlines the various presentations that will be available on the High Tech Arrangement for Hyrimoz® and those that are available for the MMP BVB medicines for adalimumab.

Table 3: Product range of biosimilar medicines containing adalimumab

Biosimilar Medicine	Product range including pack sizes and strengths available				
	20 mg/0.4 ml PFS x 1	40 mg/0.8 ml PFP x 2	40 mg/0.8 ml PFS x 2	40 mg/0.4 ml PFP x 2	40 mg/0.8 ml Soln for Inj 0.8 ml x 2
Amgevita®	✓	✓	✓		
Hulio®		✓	✓		✓
Hyrimoz®		✓			
Idacio®		✓	✓		✓
Imraldi®		✓	✓		
Yuflyma®				✓	

PFP: Pre-filled pen; PFS: Pre-filled syringe; Soln: Solution; Inj: Injection

Amgevita®, Hulio®, Hyrimoz®, Idacio®, Imraldi® and Yuflyma® have a PFP presentation available that delivers 40 mg of adalimumab. In addition, Amgevita®, Hulio®, Idacio® and Imraldi® have pre-filled syringe (PFS) presentations that deliver 40 mg of adalimumab. Data from claims submitted under the High Tech Arrangement indicates that there is a very low level of dispensing of the PFS presentations of products containing 40 mg of adalimumab, and that the vast majority of patients are in receipt of the 40 mg PFP presentation of adalimumab.[12]

Recommendation
In relation to the criterion of product range, the MMP is of the opinion that Hyrimoz® provides a similar offering when compared to the MMP BVB medicines for adalimumab 40 mg.

6.5 Product stability including storage requirements

Three of the biosimilar medicines containing adalimumab (Amgevita®, Idacio®, Yuflyma®) have a shelf life of two years. [13,14,15] Hyrimoz® has a shelf life of 30 months.[10] Imraldi® has a shelf life of 42 months.[16] Hulio® has a shelf life of three years.[17] All biosimilar medicines containing adalimumab must be stored in a refrigerator between 2°C and 8°C, and should not be frozen.[10, 13-17]

The SmPCs of Amgevita® and Hulio® state that a single PFP or PFS may be stored at a temperature of up to a maximum of 25°C for a period of up to 14 days. The SmPCs also state that the PFP or PFS must be protected from light, and should be discarded if not used within the 14-day period.[13,17] The SmPC of Hyrimoz® state that a single PFP may be stored at a temperature of up to a maximum of 25°C for a period of up to 21 days. The SmPC also states that the PFP must be protected from light and discarded if not used within the 21-day period.[10] The SmPCs of Idacio® and Imraldi® state that a single PFP or PFS may be stored at a temperature of up to a maximum of 25°C for a period of up to 28 days. The SmPC also states that the PFP or PFS must be protected from light, and should be discarded if not used within the 28-day period.[14,16] The SmPC of Yuflyma® states that a single PFP may be stored at a temperature of up to a maximum of 25°C for a period of up to 30 days. The SmPC also states that the PFP must be protected from light, and should be discarded if not used within the 30-day period.[15]

Recommendation
In relation to the criterion of product stability, the MMP is of the opinion that Imraldi® is the BVB medicine of choice due to the additional period of shelf life when compared with the other biosimilar medicines containing adalimumab, and the 28-day period of stability at temperatures up to 25°C. Hyrimoz® is comparable to the BVB medicines for adalimumab 40 mg in terms of product stability, including storage requirements.

6.6 Administration devices

The BVB medicines containing adalimumab 40 mg that are reimbursed under the High Tech Arrangement are available in a PFP, with Amgevita®, Hulio®, Idacio® and Imraldi® also available in a PFS. Novartis Ireland Limited are seeking reimbursement under the High Tech Arrangement for Hyrimoz® in a PFP presentation that delivers 40 mg of adalimumab. Table 5 provides a summary of various properties for the administration devices of the PFP presentations of the MMP BVB medicines for adalimumab 40 mg, and for Hyrimoz® 40 mg.

Table 4: Characteristics of administration devices for PFP presentations of biosimilar medicines containing adalimumab 40 mg

	Amgevita®	Hulio®	Hyrimoz®	Idacio®	Imraldi®	Yuflyma®
Needle gauge†	27	29	27	29	29	29
Latex	Yes	No	Yes	No	No	No
Safety features	Yes	Yes	Yes	Yes	Yes	Yes

†A higher needle gauge is indicative of a smaller bore size for the needle i.e. a thinner needle.

6.6.1 Pre-filled pen

From examination of the patient information leaflet (PIL) for the PFP presentation of Hyrimoz®, there appears to be little difference between the administration device when compared to those of the MMP BVB medicines for adalimumab 40 mg. Two products (Amgevita® and Hyrimoz®) have a 27-gauge needle, while all other products have a 29-gauge needle. The needle cover of the PFP of both Amgevita® and Hyrimoz® is made from dry natural rubber, which is a derivative of latex, and therefore both of these biosimilar medicines cannot be used in patients with a latex allergy; the PFP presentations of the other products are all latex-free. All of the PFP have various mechanisms to indicate to the patient that the delivery of the injection has commenced, and to signify when it is completed. These include the sounding of a click when the injection has started and/or finished, and an indicator window to show the progress and completion of the delivery of the biological medicine. All of the PFP have a safety feature; once the administration of the injection is completed, the needle retracts within the sleeve.[10,13-17]

The instructions within the PIL for the administration of a dose from the PFP presentation of Hyrimoz® are clear and easy to follow. The instructions are presented in the form of pictograms with accompanying text.[10]

Two of the biosimilar medicines containing adalimumab formulated in a PFP require the patient to press a button to commence the delivery of the dose of adalimumab (Amgevita® and Idacio®), while the other four (Hulio®, Hyrimoz®, Imraldi® and Yuflyma®) have button-free delivery with delivery of the dose of adalimumab commencing when the patient pushes the pen down onto their skin.[10,13-17]

Recommendation
Overall, in relation to the criterion of administration devices, the MMP is of the opinion that Hyrimoz® provides a similar offering to the MMP BVB medicines for adalimumab 40 mg.

6.7 Patient factors

Novartis Ireland Limited outlined the services that are available to patients when they are prescribed the biological medicine containing adalimumab that they market:[8]

The offerings that are available to patients who are prescribed Hyrimoz® are very similar in nature to those available to patients who are prescribed the MMP BVB medicines for adalimumab 40 mg, based on the information provided to the MMP in the submission received from Novartis Ireland Limited. Novartis Ireland Limited have engaged a third-party provider for provision of support services to patients who are prescribed Hyrimoz®.[8] A similar approach has been adopted by the marketing authorisation holders of the MMP BVB medicines for adalimumab 40 mg.

No robust clinical evidence was identified by the MMP that compared patient support services with each other.

Recommendation
In relation to the criterion of patient factors, the MMP is of the opinion that the patient support services offered by Novartis Ireland Limited are similar in nature to those offered by the marketing authorisation holders of the MMP BVB medicines for adalimumab 40 mg.

6.8 Expenditure in the therapeutic area and potential for cost efficiencies

Biological medicines containing tumour necrosis factor-alpha (TNF-α) inhibitors were the highest expenditure category on the High Tech Arrangement in 2021, accounting for approximately €232.66 million of the total expenditure* on this scheme.[18]

Adalimumab was the most frequently prescribed of all medicines on the High Tech Arrangement (2021) with a prescribing frequency of 135,062. Total expenditure* on adalimumab was approximately €143.60 million in 2021.[18]

The proposed reimbursement price of Hyrimoz® is outlined in Table 1. The acquisition cost of this biosimilar is less than that of Humira® therefore efficiencies can be achieved through utilisation of this biosimilar medicine.

The submission received from Novartis Ireland Limited included revised commercial terms for the PFP presentation of Hyrimoz®, resulting in a significant reduction in the acquisition cost to the HSE.

Recommendation

In relation to the criterion of expenditure in the therapeutic area and potential for cost savings, the MMP is of the opinion that for the 40 mg PFP presentation of adalimumab, the acquisition cost to the HSE for Hyrimoz® is in line with the acquisition cost of the BVB medicines for adalimumab 40 mg identified by the MMP.

6.9 Clinical guidelines

There are currently no relevant national clinical guidelines available in Ireland for the therapeutic areas or conditions for which adalimumab is indicated i.e. dermatology, gastroenterology, ophthalmology and rheumatology.

Recommendation

In relation to the criterion of clinical guidelines, no relevant information was identified by the MMP.

6.10 Security of supply to the Irish Market

Novartis Ireland Limited outlined the processes that they have in place for supply of their biosimilar medicine containing adalimumab to the Irish market.

* Total expenditure includes ingredient cost and value added tax where applicable, based on claims submitted by pharmacists.

Novartis Ireland Limited outlined the manufacturing and distribution channels that they have in place in Ireland for Hyrimoz®. They also outlined the arrangements that they have in place to ensure sufficient supply of Hyrimoz® to the Irish market. Novartis Ireland Limited also outlined the systems that they have in place for the supply of others medicines that they market in Ireland and the steps that they have taken to ensure ongoing supply as a result of Brexit.[8]

Recommendation
In relation to the criterion of robustness of supply to the Irish market, the MMP is of the opinion that Novartis Ireland Limited have provided evidence of their capacity to meet the ongoing needs of Irish patients with respect to the supply of Hyrimoz®.

6.11 Utilisation and clinical experience with the biological medicine

There is significant clinical experience with the use of adalimumab in the Irish setting, with approximately 11,500 patients in receipt of adalimumab on the High Tech Arrangement in March 2022.[12] The loss of market exclusivity for Humira® took place on 16 October 2018, and biosimilars containing adalimumab were added to the High Tech Arrangement on 1 November 2018.

The MMP published a report on 2 May 2019 in which it identified BVB medicines for adalimumab and etanercept:[1]

- Adalimumab: **Imraldi®**. Where the clinician wishes to prescribe a citrate-free formulation of adalimumab, the MMP recommends **Amgevita®**.
- Etanercept: **Benepali®**

On 17 February 2020, the MMP published a report in which it recommended two further BVB medicines for adalimumab, **Hulio®** and **Idacio®**.[2] On 31 March 2021, the MMP published a report in which it recommended **Amgevita®** 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.[3] On 21 September 2021, the MMP published a report in which it recommended an additional BVB medicine for adalimumab, **Yuflyma®**.[4] On 30 December 2021, the MMP published a report in which it recommended a second BVB medicine for etanercept, **Erelzi®**.[5]

Medicines available on the High Tech Arrangement that are used in the specialities of dermatology, rheumatology and gastroenterology were added to the High Tech Hub in June 2019. As of 2 May 2022, over 18,900 patients have been prescribed one of the identified BVB medicines for adalimumab or

etanercept.[19] In March 2022, 73.3% of patients in receipt of adalimumab 40 mg PFP/PFS under the High Tech Arrangement were prescribed a BVB medicine.[12]

Manufacturers of biosimilars must perform an extensive head-to-head comparability with the reference medicine and demonstrate to regulators that they have similar quality, safety and efficacy to the reference medicine such that there are no clinically meaningful differences between the two.[20]

Recommendation
There has been a significant increase in the prescribing of biosimilar medicines of adalimumab under the High Tech Arrangement since June 2019. This demonstrates that significant clinical experience is being obtained for biosimilars of adalimumab in a very short timeframe.

Overall, in relation to the criterion of utilisation and clinical experience with the biological medicine, given that Hyrimoz® has been deemed to be a biosimilar version of the reference medicine Humira®, the MMP is of the opinion that it provides a similar offering to the MMP BVB medicines for adalimumab 40 mg.

6.12 Any other relevant factors with respect to the particular INN
Novartis Ireland Limited submitted information on their biosimilar products pipeline under this criterion.[8]

6.12.1 Position papers
No new published position papers on the usage of biosimilars, either in general or specifically in relation to TNF-α inhibitors, were identified from the Irish clinical societies for the specialities for which adalimumab is prescribed (i.e. Irish Association of Dermatologists, Irish College of Ophthalmologists, Irish Society of Gastroenterology and Irish Society of Rheumatology) since the initial MMP publication in May 2019.

6.12.2 Legislation/Guidance from Medicines Regulators
The MMP also felt there was merit in reviewing any legislation or guidelines from medicines regulators that relate to the prescribing and utilisation of biosimilars. Pharmacist-led substitution of biological medicines is not permitted under the Health (Pricing and Supply of Medical Goods) Act 2013.[21]

The Health Products Regulatory Authority (HPRA) published an updated version of their Guide to Biosimilars for Healthcare Professionals in August 2020. This guide defines interchangeability as “the possibility of exchanging one medicine with another that is expected to have the same effect. This could mean replacing a reference medicine with a biosimilar (or vice versa), or replacing one biosimilar

with another". The guide states that, once approved, biosimilars can be used interchangeably with the reference medicine, or with biosimilars of that reference medicine.[20]

Recommendation

In relation to the criterion of any other relevant factors, the MMP is of the opinion that no new relevant material was submitted under this criterion that had not been considered under one of the other criteria.

Overall Recommendation

The MMP considers Hyrimoz® 40 mg to be comparable to the MMP BVB medicines for adalimumab 40 mg. The MMP recommends that BVB medicine status be assigned to Hyrimoz® 40 mg.

7. MMP Recommendations - May 2022

The MMP recommends the following BVB medicines:

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

Clinicians should give due consideration to the prescription of these agents when prescribing a TNF-α inhibitor. Implementation of the BVB medicines will lead to significant savings for the health service, in the order of millions of euros.

Initiation

When initiating a patient on a biological medicine containing a TNF-α inhibitor, the clinician should prescribe a BVB medicine:

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

Switching

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: **Hyrimoz®, Imraldi®, Idacio®**
  - Citrate-free: **Amgevita®, Hulio®, Yuflyma®**
- Etanercept: **Benepali®, Erelzi®**

The MMP recommends that all new patients being initiated on a biological medicine containing a TNF-α inhibitor should be prescribed one of the BVB medicines. Patients currently on the reference medicine for adalimumab (Humira®) or etanercept (Enbrel®) should be considered for switching to a BVB medicine when their next repeat prescription is issued.

8. References

1. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Tumour Necrosis Factor-α Inhibitors on the High Tech Drug Scheme. 2 May 2019. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp%20report%20bvb%20medicines%20tnf%20alpha%20inhibitors%20may%202019.pdf on 08/04/2022.
2. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submissions for Hulio® and Idacio®. 17 February 2021. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicines-hulio-idacio-feburary-2020.pdf on 08/04/2022.
3. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Adalimumab 20 mg solution for injection. 31 March 2021 Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-adalimumab-20mg-march-2021.pdf on 08/04/2022.
4. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submission for Yuflyma®. 21 September 2021. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-yuflyma.pdf on 08/04/2022.
5. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submission for Erelzi®. 30 December 2021. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-erelzi-february-2022.pdf on 03/05/2022.
6. HSE-Corporate Pharmaceutical Unit. High Tech Drug File May 2022. On file.
7. HSE-Medicines Management Programme (MMP). MMP roadmap for the prescribing of best-value biological (BVB) medicines in the Irish healthcare setting. Version 3, March 2022. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-roadmap-for-the-prescribing-of-best-value-biological-bvb-medicines-in-the-irish-healthcare-setting.pdf on 08/04/2022.
8. Novartis Ireland Limited. Submission received 21 March 2022. On file.
9. Humira®: EPAR – Product Information. Last revised 14/09/2021. Accessed at https://www.ema.europa.eu/en/documents/product-information/humira-epar-product-information_en.pdf on 12/05/2022.
10. Hyrimoz®: EPAR – Product Information. Last revised 03/03/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/hyrimoz-epar-product-information_en.pdf on 12/05/2022.
11. European Medicines Agency. European Public Assessment Report. Hyrimoz®. 2 August 2018. Accessed at https://www.ema.europa.eu/en/documents/assessment-report/hyrimoz-epar-public-assessment-report_en.pdf on 08/04/2022.
12. HSE-Primary Care Reimbursement Service (PCRS). PCRS Reimbursement report. On file

13. Amgevita®: EPAR – Product Information. Last revised 17/12/2021. Accessed at https://www.ema.europa.eu/en/documents/product-information/amgevita-epar-product-information_en.pdf on 12/05/2022.
14. Idacio®: EPAR – Product Information. Last revised 01/03/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/idacio-epar-product-information_en.pdf on 12/05/2022.
15. Yuflyma®: EPAR – Product Information. Last revised 11/03/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/yuflyma-epar-product-information_en.pdf on 12/05/2022.
16. Imraldi®: EPAR – Product Information. Last revised 12/05/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/imraldi-epar-product-information_en.pdf on 12/05/2022.
17. Hulio®: EPAR – Product Information. Last revised 12/01/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/hulio-epar-product-information_en.pdf on 12/05/2022.
18. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Pharmacy Reports. Top 20 Medicines and Appliances. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 11/04/2022.
19. HSE-Primary Care Reimbursement Service (PCRS). High Tech Update for Dermatology, Gastroenterology & Rheumatology National Gainshare. 3 May 2022. On file.
20. Health Products Regulatory Authority (HPRA). Guide to Biosimilars for Healthcare Professionals and Patients. 5 August 2020. Accessed at https://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-v3.pdf?sfvrsn=22 on 11/04/2022.
21. Government of Ireland. Health (Pricing and Supply of Medical Goods) Act 2013. S.I. No 14/2013.