Medicines Management Programme

Best-value Biological Medicines:

Adalimumab 80 mg solution for injection

Approved by:	Prof. Michael Barry, Clinical Lead, HSE-Medicines Management Programme (MMP).
Date approved:	14/06/2023
Version:	1.0

Contents

Tables

List of Abbreviations

BVB	Best-value Biological
DMARDs	Disease-modifying anti-rheumatic drugs
EMA	European Medicines Agency
EPAR	European Public Assessment Report
Ex	Excluding
HMA	Heads of Medicines' Agencies
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
Inc	Including
INN	International non-proprietary name
mg	Milligrams
MMP	Medicines Management Programme
PCRS	Primary Care Reimbursement Service
PFP	Pre-filled pen
PFS	Pre-filled syringe
PIL	Patient information leaflets
PP	Plaque psoriasis
RA	Rheumatoid arthritis
SmPC	Summary of Product Characteristics
TNF-α	Tumour necrosis factor-alpha
VAT	Value-added tax

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 has previously undertaken a review of biological medicines containing adalimumab that are available on the High Tech Arrangement. Arising from this, BVB medicines have been identified for presentations of adalimumab 20 mg and 40 mg solution for injection that are available in self-administered injection devices, i.e. pre-filled pens (PFP) and pre-filled syringes (PFS).[1-7]

The MMP is now seeking to identify a BVB medicine(s) for presentations of adalimumab 80 mg solution for injection that are available in a self-administered injection device, i.e. PFP/PFS.

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

Clinicians should prescribe Humira® or Yuflyma® when issuing a prescription for adalimumab 80 mg solution for injection on the High Tech Arrangement.

Implementation of this recommendation will lead to savings for the health service.

2. Background

2.1 Best Value Biological Medicines – Adalimumab

The MMP has previously undertaken reviews of biological medicines containing adalimumab 20 mg and 40 mg that are available on the High Tech Arrangement. Arising from this, BVB medicines have been identified for presentations of adalimumab 40 mg solution for injection that are available in self-administered injection devices, i.e. PFP and PFS:[1-6]

- Citrate-containing: Hyrimoz®, Idacio®
- Citrate-free: Amgevita®, Hukyndra®, Hulio®, Imraldi®, Yuflyma®

A BVB medicine has also been identified for presentations of adalimumab 20 mg solution for injection that are available in a self-administered injection device, i.e. PFS:[7]

- Amgevita® 20 mg solution for injection

2.2 Biosimilars

A biosimilar medicine for adalimumab 80 mg solution for injection PFP, Yuflyma®, is available on the High Tech Arrangement since October 2022.[8]

3. Scope

The MMP is now seeking to identify a BVB medicine(s) for presentations of adalimumab 80 mg solution for injection that are available in self-administered injection devices. It aims to achieve efficiencies by the identification of a BVB medicine for adalimumab 80 mg solution for injection under the High Tech Arrangement.

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 HSE-Primary Care Reimbursement Service (PCRS). 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 (VAT).

Only licensed biological medicines containing adalimumab 80 mg solution for injection available on the High Tech Arrangement as of 01 October 2022 are included in this review. All prices and costs are correct as of 1 June 2023.

The term ‘adalimumab 80 mg’ is used for presentations of adalimumab 80 mg solution for injection that are available as self-administered injection devices.

5. Best-value biological medicine - adalimumab 80 mg solution for injection

The MMP has identified BVB medicines for adalimumab 80 mg solution for injection under the High Tech Arrangement. The identification of the BVB medicines was carried out in accordance with the *Processes for the Assessment and Selection of Best-Value Biological Medicines*, as outlined in schedule 2 of the Framework Agreement on the Supply and Pricing of Medicines and schedule 1 of the Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines.[9,10] This involved a review period that included internal evaluation by the MMP and consideration of submissions received from the marketing authorisation holders of Humira® and Yuflyma®.

In line with the *MMP Roadmap for the prescribing of best-value biological (BVB) medicines*, the MMP considered the following criteria when identifying a BVB medicine for adalimumab 80 mg in self-administered injection devices:[11]

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

The MMP recommends Humira® and Yuflyma® as the best-value biological medicine for presentations of adalimumab 80 mg solution for injection that are available in self-administered injection devices on the High Tech Arrangement.

Clinicians should prescribe Humira® or Yuflyma® when issuing a prescription for adalimumab 80 mg solution for injection on the High Tech Arrangement. Implementation of this recommendation will lead to significant savings for the health service.

5.1 Consultation process

As part of the evaluation process, the MMP undertook a period of consultation during which submissions were invited from all relevant stakeholders, including the marketing authorisation holders of Humira® 80 mg (AbbVie) and Yuflyma® 80 mg (Celltrion Healthcare). The consultation phase commenced on Thursday 27 October 2022. The closing date for receipt of submissions was 5pm on Thursday 8 December 2022.

Submissions were received from the following pharmaceutical companies during the consultation process:

- AbbVie Ireland Limited
- Celltrion Healthcare

6. Evaluation

As of 1 June 2023, there are two biological medicines containing adalimumab 80 mg solution for injection that are available in self-administered injection devices (i.e. PFP) available on the High Tech Arrangement:[12]

- Humira® 80 mg solution for injection PFP
- Yuflyma® 80 mg solution for injection PFP

Humira® is the reference biological medicine and Yuflyma® is a licensed as a biosimilar medicine of the reference biological medicine. Both of these biological medicines were included in the evaluation to determine the MMP BVB medicine(s) for adalimumab 80 mg.

6.1 Acquisition cost

The cost and reimbursement price of the biological medicines containing adalimumab 80 mg solution for injection that are available on the High Tech Arrangement as of 1 June 2023 are outlined in table 1.

Table 1: Cost and reimbursement price of biological medicines containing adalimumab 80 mg available on the High Tech Arrangement as of 1 June 2023[12]

Biological Medicine	Reimbursement Price per pack*	Rebate per pack*	Cost per pack* (ex VAT)	Cost per pack* (inc VAT)	Annual Cost** (ex VAT)	Annual Cost** (inc VAT)
Humira® 80 mg PFP	€883.77	€102.29	€781.49†	€984.75†	€20,388.41†	€25,691.54†
Yuflyma® 80 mg PFP	€486.08	-	€486.08	€597.87	€12,681.37	€15,598.08

ex: excluding; inc: including; mg: milligrams; PFP: Pre-filled pen; VAT: value-added tax
**Each pack contains one PFP*
***Annual cost reflects use of adalimumab at a dosage of 80 mg every two weeks*
†The cost per pack and annual cost of the reference biological medicine, Humira®, takes account of the automatic price reduction for patent-expired non-exclusive biological medicines as per the 2021 Framework Agreement on the Supply and Pricing of Medicines, and the rebate of 12.5% that is applied to patent-expired non-exclusive biological medicines.

Submissions received during the consultation process included revised commercial terms for the biological medicines listed in table 1.[13-14]

Recommendation

For the 80 mg PFP presentation of adalimumab, the proposed revised commercial terms for Humira® and Yuflyma® that were contained within submissions received as part of the consultation process, fall within the range for designation as BVB medicines.

6.2 Therapeutic indications

Table 2 summarises the licensed therapeutic indications of the biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement.

Table 2: Summary of licensed therapeutic indications for biological medicines containing adalimumab 80 mg on the High Tech Arrangement*

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	Plaque psoriasis (PP)	Hidradenitis suppurativa	Crohn's disease, Paediatric Crohn's disease	Ulcerative Colitis, Paediatric ulcerative colitis	Uveitis, Paediatric uveitis
Humira®[15] (Adalimumab)	✓	✓	✓	✓	✓	✓	✓
Yuflyma®[16] (Adalimumab)	✓	✓	✓	✓	✓	✓	✓

DMARDs: Disease-modifying anti-rheumatic drugs; INN: International non-proprietary name; PP: Plaque psoriasis; RA: Rheumatoid arthritis

*Table 3 represents a summary of the licensed indications for which an 80 mg dose of adalimumab is required. Please refer to individual SmPC for prescribing information on each of the biological medicines

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

Recommendation

In relation to the criterion of therapeutic indications, the MMP is of the opinion that the two biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement are equivalent.

6.3 Formulation considerations

Humira® 80 mg is formulated as a clear, colourless solution for injection in a PFP. One PFP of Humira® contains 80 mg of adalimumab in 0.8 ml solution, i.e. 100 mg/ml. Humira® 80 mg PFP contains the following excipients; mannitol, polysorbate 80 and water for injections.[15]

Yuflyma® 80 mg is formulated as a clear to slightly opalescent, colourless to pale brown solution for injection in a PFP. One PFP of Yuflyma® contains 80 mg of adalimumab in 0.8 ml solution, i.e. 100 mg/ml. Yuflyma® 80 mg PFP contains the following excipients; acetic acid, sodium acetate trihydrate, glycine, polysorbate 80 and water for injections.[16]

Both Humira® and Yuflyma® do not contain citrate in their formulation.[15,16]

Injection site reactions are reported in the section on undesirable effects in the Summary of Product Characteristics (SmPC) of Humira® 80 mg PFP; 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 and/or itching, haemorrhage, pain or swelling. The SmPC also states that injection site reactions did not necessitate discontinuation of the medicinal product.[15]

The SmPC for the biosimilar medicine containing adalimumab 80 mg (Yuflyma®) carries the same statement as Humira® 80 mg PFP in relation to injection site reactions.[16]

6.3.1 European Public Assessment Report – Yuflyma®

In the clinical safety section of the European Public Assessment Report (EPAR) for Yuflyma®, the incidence of injection site reactions for Yuflyma® was 4.9% in comparison to 7.1% for the reference biological medicine in the initial 26-week treatment period of the reported Phase III equivalence study. All of the injection site reactions that occurred with Yuflyma® were considered by the investigators to

be drug-related; one reaction that was reported in a patient on Humira® was not considered to be drug-related, giving a revised incidence of 6.8%. All treatment emergent adverse effects that were classified as injection site reactions for both Humira® and Yuflyma® were considered grade 1 or 2 in terms of intensity. The proportion of patients who experienced at least one treatment-emergent adverse event classified as an injection site reaction for the full duration of the Phase III study was similar across the Yuflyma® and Humira® treatment groups (5.2% versus 7.4% of patients).[17]

The EMA concluded that from a safety point of view, Yuflyma® is considered to be similar to Humira®.[17]

Recommendation
In relation to the criterion of formulation considerations, the MMP is of the opinion that there is no significant difference between the two biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement.

6.4 Product range including pack sizes and strengths available

Table 3 outlines the various presentations of the biological medicines containing adalimumab 80 mg solution for injection that are available on the High Tech Arrangement.

Table 3: Product range of reference and biosimilar medicines containing adalimumab 80 mg solution for injection available on the High Tech Arrangement[12]

Biosimilar Medicine	Product range including pack sizes and strengths available on the High Tech Arrangement
	80 mg/0.8 ml PFP x 1
Humira®	✓
Yuflyma®	✓

mg: milligrams; ml: millilitres; PFP: Pre-filled pen

Both Humira® and Yuflyma® have PFP presentations available on the High Tech Arrangement that deliver 80 mg of adalimumab.

Recommendation
In relation to the criterion of product range, the MMP is of the opinion that both biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement provide the same offering.

6.5 Product stability including storage requirements

Humira® 80 mg has a shelf life of two years.[15] Yuflyma® 80 mg has a shelf life of three years.[16] Both must be stored in a refrigerator between 2°C and 8°C, and should not be frozen.[15,16]

The SmPC of Humira® states that a single PFP containing adalimumab may be stored at a temperature of up to a maximum of 25°C for a period of up to 14 days. The SmPC also states that the PFP must be protected from light, and should be discarded if not used within the 14-day period.[15] The SmPC of Yuflyma® states that a single PFP containing adalimumab may be stored at a temperature of up to a maximum of 25°C for a period of up to 31 days. The SmPC also states that the PFP must be protected from light, and should be discarded if not used within the 31-day period.[16] The SmPCs for both biological medicines also state that the PFP must be stored in its outer carton in order to protect from light.[15,16]

Recommendation

In relation to the criterion of product stability, the MMP is of the opinion that Yuflyma® is the BVB medicine of choice due to the combination of a shelf life of three years, and the 31-day period of stability at temperatures of up to a maximum of 25°C.

6.6 Administration devices

Both biological medicines containing adalimumab 80 mg that are reimbursed under the High Tech Arrangement are available in a PFP. Table 4 provides a summary of various properties for the administration devices of the biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement.

Table 4: Characteristics of administration devices containing adalimumab 80 mg available on the High Tech Arrangement

	Humira® 80 mg PFP	Yuflyma® 80 mg PFP
Needle gauge†	29	29
Latex-containing	No	No
Safety features	Yes	Yes

PFP: Pre-filled pen

†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 leaflets (PILs) for both of the biological medicines containing adalimumab 80 mg, there appears to be little difference between the various administration devices. Both products have a 29-gauge needle and are latex-free. Both of the PFPs

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. Both of the PFPs have a safety feature; once the administration of the injection is completed, the needle retracts within the sleeve.[15,16]

The instructions within each of the PILs for the administration of a dose from the PFP presentations are clear and easy to follow. In all cases, the instructions are presented in the form of pictograms with accompanying text.[15,16]

Humira® 80 mg PFP requires the patient to press a button to commence the delivery of the dose of adalimumab, while Yuflyma® 80 mg PFP has a button-free delivery with delivery of the dose of adalimumab commencing when the patient pushes the pen down onto their skin.[15,16]

Recommendation
In relation to the criterion of administration devices, the MMP is of the opinion that both biological medicines containing adalimumab 80 mg that are available on the High Tech Arrangement provide a similar offering.

6.7 Patient factors

AbbVie Ireland Limited and Celltrion Healthcare outlined the support services that are available to patients for the biological medicine containing adalimumab 80 mg that they market.[13,14]

The MMP did not identify any published evidence that compared the patient support programmes/services that are offered by the marketing authorisation holders of medicinal products containing adalimumab 80 mg 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 AbbVie Ireland Limited and Celltrion Healthcare Ireland are similar in nature.

6.8 Expenditure in the therapeutic area and potential for cost savings

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 or one third 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]

On the addition of a biosimilar medicine to the reimbursement list, the 2016 Framework Agreement on the Supply and Pricing of Medicines provided for an automatic price reduction of 20% for the patent-expired, non-exclusive biological medicine.[19] This is reflected in the acquisition cost of Humira® 80 mg PFP that is listed in Table 1. In addition, a rebate of 12.5% is applied to Humira® 80 mg PFP.

The current acquisition cost of the biosimilar medicine containing adalimumab 80 mg, Yuflyma®, as of 1 June 2023 is also outlined in Table 1. The cost of Yuflyma® 80 mg is less than the current cost of Humira® 80 mg, therefore efficiencies can be achieved through the prescribing and utilisation of Yuflyma® on the High Tech Arrangement.

Submissions received during the consultation process included revised commercial terms for the biological medicines containing adalimumab 80 mg, resulting in significant reductions 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 Humira® and Yuflyma® are the BVB medicines of choice for adalimumab 80 mg due to the potential for significant cost savings based on the revised commercial terms proposed in the submissions received as part of the consultation process.

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

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

AbbVie Ireland Limited and Celltrion Healthcare Ireland outlined the processes that they have in place for supply of their biological medicine containing adalimumab to the Irish market.

AbbVie Ireland Limited outlined the arrangements that they have in place for the supply chain management of Humira® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[13]

Celltrion Healthcare Ireland outlined the arrangements that they have in place for the supply chain management of Yuflyma® to the Irish market, including the distribution model that they employ. They also outlined the actions that they have taken to deal with Brexit.[14]

Recommendation

In relation to the criterion of security of supply to the Irish market, the MMP is of the opinion that both AbbVie Ireland Limited and Celltrion Healthcare Ireland have provided evidence of their capacity to meet the ongoing needs of Irish patients with respect to the supply of biological medicines containing adalimumab 80 mg.

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 12,300 patients in receipt of adalimumab on the High Tech Arrangement in April 2023.[20] The loss of market exclusivity for Humira® took place on 16 October 2018, and biosimilar medicines containing adalimumab were added to the High Tech Arrangement on 1 November 2018.[8]

The MMP has identified seven BVB medicines for adalimumab 40 mg; Amgevita®, Hulio®, Hukyndra®, Hyrimoz®, Idacio®, Imraldi® and Yuflyma®.[1-6] The MMP has also identified a BVB medicine for adalimumab 20 mg; Amgevita®.[7]

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 5 June 2023, over 24,700 patients have been prescribed one of the identified BVB medicines for adalimumab or etanercept.[21] In April 2023, 81.1% of patients in receipt of adalimumab 40 mg PFP/PFS under the High Tech Arrangement were prescribed a BVB medicine.[20]

Manufacturers of biosimilar medicines 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.[22]

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 biosimilar medicines of adalimumab in a very short timeframe.

Overall, in relation to the criterion of utilisation and clinical experience with the biological medicine, the MMP is of the opinion that both biological medicines containing adalimumab 80 mg provide a similar offering.

6.12 Any other relevant factors with respect to the particular INN

AbbVie Ireland Limited submitted information in relation to biosimilarity in general.[13] Celltrion Healthcare Ireland submitted information on their biosimilar and new products pipeline under this criterion.[14]

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.

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.[23]

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.[22]

The European Medicines Agency (EMA) and the Heads of Medicines' Agencies (HMA), in a joint statement issued on 19 September 2022, have confirmed that biosimilar medicines approved in the European Union are interchangeable with their reference medicine or with an equivalent biosimilar. Interchangeability in this context means that the reference medicine can be replaced by a biosimilar without a patient experiencing any changes in the clinical effect.[24]

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 recommends Humira® and Yuflyma® as the best-value biological medicines for presentations of adalimumab 80 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

7. MMP Recommendations

The MMP recommends Humira® and Yuflyma® as the best-value biological medicine for presentations of adalimumab 80 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

Clinicians should prescribe Humira® or Yuflyma® 80 mg pre-filled pen when issuing a prescription for adalimumab 80 mg solution for injection on the High Tech Arrangement.

Implementation of this recommendation will lead to significant savings for the health service.

The MMP recommends that when issuing a prescription to a patient for adalimumab 80 mg PFP, the clinician should prescribe Humira® or Yuflyma®.

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 08/06/2023.
2. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submissions for Hulio® and Idacio®. 17 February 2020. 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 08/06/2023.
3. 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 08/06/2023.
4. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submission for Hyrimoz®. 13 May 2022. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-hyrimoz.pdf on 08/06/2023.
5. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submission for revised formulation of Imraldi®. 13 March 2023. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-imraldi.pdf on 08/06/2023.
6. HSE-Medicines Management Programme (MMP). Best-Value Biological Medicines: Review of submission for Hukyndra®. 19 May 2023. Accessed at https://www.hse.ie/eng/about/who/cspd/ncps/medicines-management/best-value-medicines/best-value-biological-medicines/mmp-report-bvb-medicine-hukyndra-may-2023.pdf on 08/06/2023.
7. 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 08/06/2023.
8. HSE Primary Care Reimbursement Service. Updates to the List of Reimbursable Items and High Tech Scheme List. Accessed at www.pcrs.ie on 08/06/2023.
9. DoH/DPER/HSE/IPHA. Framework Agreement on the Supply and Pricing of Medicines. 6 December 2021. Accessed at https://www.hse.ie/eng/about/who/cpu/ on 08/06/2023.
10. DoH/DPER/HSE/MFI. Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines. 13 December 2021. Accessed at https://www.hse.ie/eng/about/who/cpu/ on 08/06/2023.

11. 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 08/06/2023.
12. HSE-Primary Care Reimbursement Service (PCRS). Complete list of High Tech Products by Non-Proprietary Name as at 1st June 2023. Accessed at www.pcrs.ie on 08/06/2023.
13. AbbVie Ireland Limited. Submission received 8 December 2022. On file.
14. Celltrion Healthcare. Submission received 8 December 2022. On file.
15. Humira®. Summary of Product Characteristics. Last revised 11/10/2022. Accessed at https://www.ema.europa.eu/en/documents/product-information/humira-epar-product-information_en.pdf on 08/06/2023.
16. Yuflyma®. Summary of Product Characteristics. Last revised 30/01/2023. Accessed at https://www.ema.europa.eu/en/documents/product-information/yuflyma-epar-product-information_en.pdf on 08/06/2023.
17. European Medicines Agency. European Public Assessment Report. Yuflyma®. EMA/47907/2021. 26 February 2021. Accessed at https://www.ema.europa.eu/en/documents/assessment-report/yuflyma-epar-public-assessment-report_en.pdf on 08/06/2023.
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 08/06/2023.
19. DoH/DPER/HSE/IPHA. Framework Agreement on the Supply and Pricing of Medicines. July 2016. Accessed at https://www.hse.ie/eng/about/who/cpu/iphaagreement2016.pdf on 08/06/2023.
20. HSE-Primary Care Reimbursement Service (PCRS). PCRS Reimbursement report. On file
21. HSE-Primary Care Reimbursement Service (PCRS). High Tech Update for Dermatology, Gastroenterology & Rheumatology National Gainshare. 6 June 2023. On file.
22. 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 08/06/2023.
23. Government of Ireland. Health (Pricing and Supply of Medical Goods) Act 2013. S.I. No 14/2013.
24. 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. Accessed at https://www.ema.europa.eu/en/documents/public-statement/statement-scientific-rationale-supporting-interchangeability-biosimilar-medicines-eu_en.pdf on 08/06/2023.