Medicines Management Programme

Best-Value Biological Medicines:

Adalimumab 20 mg solution for injection

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MEDICINES MANAGEMENT PROGRAMME

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List of Abbreviations

BVB	Best-value biological
EPAR	European Public Assessment Report
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
INN	International non-propriety name
JA	Juvenile idiopathic arthritis
MMP	Medicines Management Programme
N/A	Not applicable
PCRS	Primary Care Reimbursement Service
PIL	Patient information leaflets
PFP	Pre-filled pen
PFS	Pre-filled syringe
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 has previously undertaken a review of biological medicines containing adalimumab that are available on the High Tech Arrangement, focusing on presentations of adalimumab that are predominately used in adult patients. 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. pre-filled pens (PFP) and pre-filled syringes (PFS).[1,2]

The MMP is now seeking to identify a BVB medicine(s) for presentations of adalimumab 20 mg solution for injection that are available in self-administered injection devices i.e. PFP/PFS. These presentations of adalimumab are predominately used in paediatric patients.

The MMP recommends Amgevita® as the best-value biological medicine for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Amgevita® 20 mg pre-filled syringe when issuing a prescription for adalimumab 20 mg solution for injection on the High Tech Arrangement.

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

Initiation

When initiating a patient on a biological medicine containing adalimumab 20 mg, the clinician should prescribe Amgevita® 20 mg pre-filled syringe.

Switching

Patients currently on Humira® 20 mg pre-filled syringe should be considered for switching to Amgevita® 20 mg pre-filled syringe when their next repeat High Tech prescription is being issued.

2. Background

2.1 Best-value biological medicines – adalimumab

The MMP has previously undertaken a review of biological medicines containing adalimumab that are available on the High Tech Arrangement, focusing on presentations of adalimumab that are predominately used in adult patients. 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/PFS:[1,2]

- Citrate-containing: Idacio®, Imraldi®
- Citrate-free: Amgevita®, Hulio®

2.2 Biosimilar medicines

A biosimilar medicine for adalimumab 20 mg solution for injection PFS, Amgevita®, is available on the High Tech Arrangement since November 2018.[3]

3. Scope

This document considers the medicinal products containing adalimumab 20 mg solution for injection that are available in self-administered injection devices that are reimbursed on the High Tech Arrangement. It aims to achieve efficiencies by the identification of a BVB medicine for adalimumab 20 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 List of Prescribable High Tech Medicines 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.

Only licensed biological medicines containing adalimumab 20 mg solution for injection available on the High Tech Arrangement as of 11 December 2020 are included in this review. All prices and costs are correct as of 1 February 2021.

The term ‘adalimumab 20 mg’ is used for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices.

5. Best-value biological medicine - adalimumab 20 mg solution for injection

The MMP has identified a BVB medicine for adalimumab 20 mg solution for injection under the High Tech Arrangement. The identification of the BVB medicine was carried out in accordance with the evaluation process in the *MMP roadmap for the prescribing of best-value biological medicines:*[4] 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

The MMP considered the following criteria when identifying a BVB for adalimumab 20 mg in self-administered injection devices:

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 savings
9. Clinical guidelines
10. Robustness of supply to the Irish Market
11. Department of Health National Biosimilar Policy (awaiting publication)
12. Utilisation and clinical experience with the biological medicine
13. Any other relevant factors.

The MMP recommends Amgevita® as the best-value biological medicine for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Amgevita® 20 mg pre-filled syringe when issuing a prescription for adalimumab 20 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® (AbbVie) and Amgevita® (Amgen). Details of the consultation process were published on the website of the MMP. The MMP wrote to AbbVie Ireland and Amgen Ireland on 11 December 2020, informing them of the MMP's intention to identify a BVB medicine for presentations of adalimumab 20 mg solution for injection that are available in self-administer injection devices under the High Tech Arrangement, and inviting submissions from both parties. The closing date for receipt of submissions was 5pm on Thursday 28 January 2021.

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

- AbbVie Ireland
- Amgen Ireland

6. Evaluation

As of 11 December 2020, there are two biological medicines containing adalimumab 20 mg solution for injection that are available in self-administered injection devices reimbursed on the High Tech Arrangement:[5]

- Amgevita® 20 mg solution for injection PFS
- Humira® 20 mg solution for injection PFS

Humira® is the reference biological medicine and Amgevita® is a licensed biosimilar. Both of these biological medicines were included in the evaluation to determine the MMP BVB medicine for adalimumab 20 mg.

6.1 Acquisition cost

The acquisition cost and reimbursement price of the biological medicines containing adalimumab 20 mg solution for injection that are available on the High Tech Arrangement as of 1 February 2021 are outlined in table 1.

Table 1: Acquisition cost and reimbursement price of biological medicines containing adalimumab 20 mg available on the High Tech Arrangement as of 1 February 2021

Biological Medicine	Pack size	Reimbursement Price	Rebate	Acquisition Cost
Amgevita® 20 mg PFS	1	€155.87	-	€155.87
Humira® 20 mg PFS	2	€441.89	€51.15	€390.74*

PFS: Pre-filled syringe
Prices correct as of 1 February 2021
**The acquisition cost of the reference biological medicine, Humira®, takes account of the automatic price reduction of 20% for patent-expired non-exclusive biological medicines, and the rebate of 12.5% that is applied to patent-expired non-exclusive biological medicines.*

Both submissions received included revised commercial terms for the biological medicines listed above.

Recommendation

For the 20 mg PFS presentation of adalimumab, Amgevita® has the lowest acquisition cost to the HSE across all of the proposed revised commercial terms that were contained within submissions received as part of the consultation process.

6.2 Therapeutic indications

Table 2 summarises the licensed therapeutic indications of the biological medicines containing adalimumab 20 mg that are available on the High Tech Arrangement.

Table 2: Summary of licensed therapeutic indications for biological medicines containing adalimumab 20 mg on the High Tech Arrangement*

Brand (INN)	Juvenile idiopathic arthritis (JA) - Polyarticular JA - Enthesitis-related arthritis	Paediatric plaque psoriasis	Paediatric Crohn's disease	Paediatric uveitis
Humira®[6] (Adalimumab)	✓	✓	✓	✓
Amgevita®[7] (Adalimumab)	✓	✓	✓	✓

*Please refer to individual SmPC for prescribing information on each of the biological medicines

Recommendation

Overall, in relation to the criterion of therapeutic indications, the MMP is of the view that the two biological medicines containing adalimumab 20 mg that are available on the High Tech Arrangement are equivalent.

6.3 Formulation considerations

Amgevita® 20 mg is formulated as a clear and colourless to slightly yellow solution for injection in a PFS. One PFS contains 20 mg of adalimumab in 0.4 ml solution i.e. 50 mg/ml. Amgevita® 20 mg PFS contains the following excipients; glacial acetic acid, sucrose, polysorbate 80, sodium hydroxide and water for injections.[7]

Humira® 20 mg is formulated as a clear, colourless solution for injection in a PFS. One PFS contains 20 mg of adalimumab in 0.2 ml solution i.e. 100 mg/ml. Humira® 20 mg PFS contains the following excipients; mannitol, polysorbate 80 and water for injections.[6]

Both Amgevita® and Humira do not contain citrate in their formulation.[6,7]

Injection site reactions are reported in the section on undesirable effects in the Summary of Product Characteristics (SmPC) of Humira® 20 mg PFS; 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.[6]

The SmPC for the biosimilar containing adalimumab (Amgevita®) carries the same statement as Humira® 20 mg PFS in relation to injection site reactions.[7]

6.3.1 European Public Assessment Report – Amgevita®

In the clinical safety section of the European public assessment report (EPAR) for Amgevita®, the European Medicines Agency report that there was an imbalance in both of the Phase III studies that were undertaken for Amgevita® for injection site reactions, with fewer reactions observed for Amgevita® in comparison to the reference biological medicine in both studies (2.3% versus 5% in the rheumatoid arthritis study, and 1.7% versus 5.2% in the psoriasis study, both through week 16). After the re-randomisation at week 16, no injection site reactions occurred in the cohort of patients receiving Amgevita®.[8]

The EPAR concluded that the safety profile of Amgevita® is considered comparable to that of Humira®.[8]

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 20 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 20 mg solution for injection that are available on the High Tech Arrangement.

Table 3: Product range of reference and biosimilar medicines containing adalimumab 20 mg solution for injection available on the High Tech Arrangement[5]

Biosimilar Medicine	Product range including pack sizes and strengths available on the High Tech Arrangement	
	20 mg/0.4 ml PFS x 1	20 mg/0.2 ml PFS x 2
Amgevita®	✓	
Humira®		✓

PFS: Pre-filled syringe

Both Amgevita® and Humira® have PFS presentations available on the High Tech Arrangement that deliver 20 mg of adalimumab.

Recommendation
In relation to the criterion of product range, the MMP is of the opinion that both biological medicines containing adalimumab 20 mg that are available on the High Tech Arrangement provide the same offering.

6.5 Product stability including storage requirements

Both of the biological medicines containing adalimumab 20 mg (Amgevita® and Humira®) have a shelf life of two years. Both must be stored in a refrigerator between 2°C and 8°C, and should not be frozen.[6,7]

The SmPCs of Amgevita® and Humira® state that a single PFS 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 SmPCs also state that the PFS must be protected from light, and should be discarded if not used within 14 days. The SmPCs

for both biological medicines also state that the PFS must be stored in its outer carton in order to protect from light.[6,7]

Recommendation

In relation to the criterion of product stability, the MMP is of the opinion that Amgevita® 20 mg PFS and Humira® 20 mg PFS are equivalent.

6.6 Administration devices

Both biological medicines containing adalimumab 20 mg that are reimbursed under the High Tech Arrangement are available in a PFS. Table 4 provides a summary of various properties for the administration devices of the biological medicines containing adalimumab 20 mg that are available on the High Tech Arrangement.

Table 4: Characteristics of administration devices containing adalimumab 20 mg available on the High Tech Arrangement

	Humira® 20 mg PFS	Amgevita® 20 mg PFS
Needle gauge†	29	29
Latex-containing	No	No
Safety features	No	No

PFS: Pre-filled syringe
†A higher needle gauge is indicative of a smaller bore size for the needle i.e. a thinner needle

From examination of the patient information leaflets (PILs) for both of the biological medicines containing adalimumab 20 mg, there appears to be little difference between the various administration devices. Both products have a 29-gauge needle and are latex-free. There is no safety feature in place to guard the needle upon delivery of the dose of adalimumab with either Amgevita® 20 mg PFS and Humira® 20 mg PFS. [6,7]

The instructions within each of the PILs for the administration of a dose from the PFS presentations are clear and easy to follow. In all cases, the instructions are presented in the form of pictograms with accompanying text.[6,7]

Recommendation

In relation to the criterion of administration devices, the MMP is of the opinion that both biological medicines containing adalimumab 20 mg that are available on the High Tech Arrangement provide a similar offering.

6.7 Patient factors

AbbVie Ireland and Amgen Ireland outlined the support services that are available to patients for the biological medicine containing adalimumab 20 mg that they market.[9,10]

No robust clinical evidence was identified by the MMP that compared patient support programmes or services provided to paediatric patients who were prescribed adalimumab 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 and Amgen Ireland are similar in nature.

6.8 Expenditure in the therapeutic area and potential for cost savings

Biological medicines containing TNF-α inhibitors were the highest expenditure category on the High Tech Arrangement in 2019, accounting for approximately €295.56 million or one third of the total expenditure* on this scheme.[11,12]

Adalimumab was the most frequently prescribed of all medicines on the High Tech Arrangement (2019) with a prescribing frequency of 106,509.[13] Total expenditure* on adalimumab was approximately €133.6 million in 2019.[13] There are approximately 70 patients in receipt of adalimumab 20 mg PFS on the High Tech Arrangement on a monthly basis.[14]

On the addition of a biosimilar to the reimbursement list, the 2016 Framework Agreement on the Supply and Pricing of Medicines provides for an automatic price reduction of 20% for the patent-expired, non-exclusive biological medicine. In addition to this price reduction, a rebate of 12.5% is applied to the patent-expired, non-exclusive biological medicine.[15] This is reflected in the acquisition cost of Humira® 20 mg PFS that is listed in Table 1.

The current acquisition costs of biosimilars containing adalimumab 20 mg as of 1 February 2021 are also outlined in Table 1. The acquisition cost of Amgevita® is less than that of Humira®, therefore efficiencies can be achieved through the prescribing and utilisation of Amgevita® on the High Tech Arrangement. Data from the HSE-PCRS indicates that there is negligible usage of Amgevita® 20 mg PFS since its addition to the High Tech Arrangement in November 2018.[14] Any additional savings that could

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

have been achieved through the use of Amgevita®, which has a lower acquisition cost than Humira®, have not been realised.

Submissions received during the consultation process included revised commercial terms for the biological medicines containing adalimumab 20 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 Amgevita® is the BVB medicine of choice for adalimumab 20 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.

6.9 Clinical guidelines

There are currently no national clinical guidelines available in Ireland for the therapeutic areas or conditions for which adalimumab 20 mg 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 Robustness of supply to the Irish Market

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

According to their submission, AbbVie Ireland have provided 17 years of continuous and uninterrupted supply of Humira® to the Irish market. They outlined the arrangement they have in place with their Irish distributor, Uniphar Services, to ensure the ongoing supply of Humira®. They also outlined the steps that they have taken to ensure ongoing supply as a result of Brexit.[9]

Amgen Ireland outlined the arrangements that they have in place for the supply of Amgevita® to the Irish market, including the distribution model that they employ using United Drug. They also outlined the proactive measures that they have undertaken to mitigate risks during and after Brexit. According to their submission, Amgen Ireland has never experienced interruption in supply to the Irish market due to stock shortages.[10]

Recommendation

In relation to the criterion of robustness of supply to the Irish market, the MMP is of the opinion that both AbbVie Ireland and Amgen 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 20 mg, including the measures they are taking to mitigate the impact of Brexit.

6.11 Department of Health National Biosimilar Medicine Policy

At the time of undertaking this evaluation to identify the BVB medicine for adalimumab 20 mg, the Department of Health National Biosimilar Medicines Policy has not been published, and therefore was not a consideration in this evaluation process.

6.12 Utilisation and clinical experience with the biological medicine

There is significant clinical experience with the use of adalimumab in the Irish setting, with more than 9,000 patients in receipt of adalimumab on a monthly basis on the High Tech Arrangement.[14] The loss of market exclusivity for Humira® took place on the 16 October 2018, and biosimilars containing adalimumab were added to the High Tech Arrangement on the 1 November 2018.[3]

The MMP has identified four BVB medicines for adalimumab; Amgevita®, Hulio®, Idacio® and Imraldi®. As of December 2020, 59% of patients in receipt of adalimumab 40 mg PFP/PFS under the High Tech Arrangement were supplied with a BVB medicine.[14]

Manufacturers of biosimilars must perform an extensive head-to-head comparability exercise 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.[16]

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, the MMP is of the opinion that both biological medicines containing adalimumab 20 mg provide a similar offering.

6.13 Any other relevant factors

A variety of material was submitted under this criterion including information on:

- non-medical switching
- the Health Products Regulatory Authority (HPRA) Guide to Biosimilars for Healthcare Professionals and Patients
- resources and capabilities to support healthcare professionals.

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.

6.13.1 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 previous MMP BVB Medicine evaluation in February 2020.

6.13.2 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.[17] The updated HPRA Guide to Biosimilars for Healthcare Professionals (2020) 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 other biosimilars of that reference medicine, under the supervision of a physician.[16]

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.

Overall Recommendation

The MMP recommends Amgevita® as the best-value biological medicine for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

7. MMP Recommendations

The MMP recommends Amgevita® as the best-value biological medicine for presentations of adalimumab 20 mg solution for injection that are available as self-administered injection devices on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Amgevita® 20 mg pre-filled syringe when issuing a prescription for adalimumab 20 mg solution for injection on the High Tech Arrangement.

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

Initiation

When initiating a patient on a biological medicine containing adalimumab 20 mg, the clinician should prescribe Amgevita® 20 mg pre-filled syringe.

Switching

Patients currently on Humira® 20 mg pre-filled syringe should be considered for switching to Amgevita® 20 mg pre-filled syringe when their next repeat High Tech prescription is being issued.

The MMP recommends that when initiating a patient on adalimumab 20 mg PFS, the clinician should prescribe Amgevita®. Patients currently on Humira® 20 mg PFS should be considered for switching to Amgevita® 20 mg PFS when their next repeat High Tech prescription is being 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 01/02/2021.
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 01/02/2021.
3. HSE-Primary Care Reimbursement Service. Updates to the List of Reimbursable Items and High Tech Scheme List. Accessed at www.pcrs.ie on 01/02/2021.
4. HSE-Medicines Management Programme (MMP). 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-medicines/best-value-biological-medicines/mmp-roadmap-for-the-prescribing-of-best-value-biological-bvb-medicines-in-the-irish-healthcare-setting.pdf on 01/02/2021.
5. HSE-Primary Care Reimbursement Service. List of Prescribable High Tech Medicines December 2020. Accessed at www.pcrs.ie on 10/12/2020.
6. Humira® 20 mg solution for injection in pre-filled syringe. SmPC. Last revised 29/01/2021. Accessed at https://www.ema.europa.eu/en/documents/product-information/humira-epar-product-information_en.pdf on 01/02/2021.
7. Amgevita® 20 mg solution for injection in pre-filled syringe. SmPC. Last revised 12/03/2020. Accessed at https://www.ema.europa.eu/en/documents/product-information/amgevita-epar-product-information_en.pdf on 01/02/2021.
8. European Medicines Agency. European Public Assessment Report. Amgevita®. 26 January 2017. Accessed at https://www.ema.europa.eu/en/documents/assessment-report/amgevita-epar-public-assessment-report_en.pdf on 01/02/2021.
9. Abbvie Ireland. Submission received 28 January 2021. On file.
10. Amgen Ireland. Submission received 28 January 2021. On file.
11. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Top 20 Medicines and Appliances by Highest Expenditure. HT 2019. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 01/02/2021.
12. HSE-Primary Care Reimbursement Service (PCRS). Statistical Analysis of Claims and Payments 2019. Accessed at https://www.hse.ie/eng/staff/pcrs/pcrs-publications/annual-report-2019.pdf on 01/02/2021.
13. HSE-Primary Care Reimbursement Service (PCRS). Reporting and Open Data Area. Top 100 Products by Cost. HTS 2019. Accessed at https://www.sspcrs.ie/analytics/saw.dll?PortalPages on 01/02/2021.
14. HSE-Primary Care Reimbursement Service (PCRS). Prescribing Report 2017 - 2021. On file.
15. HSE/IPHA. Framework agreement on the supply and pricing of medicine. 2016. Accessed at https://www.hse.ie/eng/about/who/cpu/iphaagreement2016.pdf on 01/02/2021.

16. Health Products Regulatory Authority (HPRA). Guide to Biosimilars for Healthcare Professionals. 5 August 2020. Accessed at http://www.hpra.ie/docs/default-source/publications-forms/guidance-documents/guide-to-biosimilars-for-healthcare-professionals-v3.pdf?Status=Master&sfvrsn=27 on 01/02/2021.
17. Government of Ireland. Health (Pricing and Supply of Medical Goods) Act 2013. S.I. No 14/2013.