Medicines Management Programme

Best-value biological medicine:

Ustekinumab

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List of Abbreviations

AIDMP	Access & Integration Drug Management Programme
AESI	Adverse event of special interest
BVB	Best-value biological
BVM	Best-value medicine
CD	Crohn's Disease
CPU	Corporate Pharmaceutical Unit
DMARD	Disease-modifying anti-rheumatic drug
EMA	European Medicines Agency
EPAR	European public assessment report
EU	European Union
Ex	Excluding
G-CSF	Granuloctye-colony stimulating factor
HMA	Heads of Medicines Agencies
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
Kg	Kilograms
IgG1κ	Immunoglobulin G subclass 1 kappa
IL	Interleukin
Inc	Including
INN	International non-proprietary name
MA	Marketing authorisation
MG	Milligrams
ML	Millilitres
MMOL	Millimole
MMP	Medicines Management Programme
MTX	Methotrexate
NK	Natural killer
PCRS	Primary Care Reimbursement Service
PIL	Patient information leaflet
PFP	Pre-filled pen
PFS	Pre-filled syringe
PP	Plaque psoriasis
PsA	Psoriatic arthritis
PTW	Price to wholesaler
PUVA	Psoralen and ultraviolet A
SC	Subcutaneous
SmPC	Summary of Product Characteristics
SFI	Solution for injection
TEAE	Treatment-emergent adverse event
TEAESI	Treatment-emergent adverse event of special interest
Th1	T helper 1
Th17	T helper 17
TNF-α	Tumour necrosis factor-alpha
UC	Ulcerative colitis
USP	United States Pharmacopeia
VAS	Visual analogue scale
VAT	Value-added tax

1. Executive Summary

The Health Service Executive (HSE)-Medicines Management Programme (MMP) aims to promote safe, effective and cost-effective prescribing of biological medicines, including biosimilar medicines. 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 or best-value medicines (BVM), including biosimilars.

Expenditure[i] on medicinal products containing ustekinumab on the High Tech Arrangement accounted for approximately €67.3 million in 2023 and €63.1 million in 2024.[1,2] Additional expenditure was incurred in the hospital setting arising from administration of medicinal products containing ustekinumab. There are now biosimilar medicines containing ustekinumab available on either the HSE Reimbursement List for prescribing and supply on the High Tech Arrangement, or with Hospital Pricing Approval. This provides the opportunity to identify BVB medicines for ustekinumab in order to achieve efficiencies in this therapeutic area.

The aim of this initiative is to ensure that the efficiencies presented by the availability of biosimilar medicines of ustekinumab are fully realised to achieve best value. It identifies BVB medicines for ustekinumab. It also aims to support the prescribing and utilisation of the BVB medicines.

[i]Expenditure reflects the ingredient cost of the medicinal product, exclusive of value-added tax and fees

The MMP recommends the following as BVB medicines for ustekinumab:

- ✓ **Imuldosa® (Accord Healthcare Ireland Limited)**
- ✓ **Otulfi® (Fresenius Kabi Ireland)**
- ✓ **Pyzchiva® (Sandoz Limited trading as Rowex)**
- ✓ **Wezenla® (Amgen Ireland Limited).**

Clinicians should give due consideration to prescribing Imuldosa®, Otulfi®, Pyzchiva® or Wezenla® when issuing a prescription for ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease.

Prescribing the recommended BVB medicines reduces the financial burden on the HSE arising out of the funding of reimbursed medicines, and can assist in facilitating access to new, innovative medicines for patients.

Initiation

When initiating a patient on ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease, the clinician should prescribe Imuldosa®, Otulfi®, Pyzchiva® or Wezenla®.

Switching

Patients currently on ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease should be considered for switching to Imuldosa®, Otulfi®, Pyzchiva® or Wezenla® at the earliest possible opportunity.

2. Background

2.1 Ustekinumab

Ustekinumab is a recombinant fully human immunoglobulin G subclass 1 kappa (IgG1κ) monoclonal antibody that binds with specificity to the shared p40 protein subunit of human cytokines interleukin (IL)-12 and IL-23. Ustekinumab inhibits the bioactivity of human IL-12 and IL-23 by preventing p40 from binding to the IL-12Rβ1 receptor protein expressed on the surface of immune cells. IL-12 and IL-23 are heterodimeric cytokines secreted by activated antigen presenting cells, such as macrophages and dendritic cells, and both cytokines participate in immune functions; IL-12 stimulates natural killer (NK) cells and drives the differentiation of CD4+ T cells toward the T helper 1 (Th1) phenotype, IL-23 induces the T helper 17 (Th17) pathway. Abnormal regulation of IL-12 and IL-23 has been associated with immune mediated diseases, such as psoriasis, psoriatic arthritis (PsA), Crohn's disease (CD) and ulcerative colitis (UC).[3]

By binding the shared p40 subunit of IL-12 and IL-23, ustekinumab may exert its clinical effects in psoriasis, PsA, CD and UC through interruption of the Th1 and Th17 cytokine pathways, which are central to the pathology of these diseases.[3]

Expenditure[ii] on medicinal products containing ustekinumab on the High Tech Arrangement accounted for approximately €67.3 million in 2023 and €63.1 million in 2024.[1,2] Additional expenditure was incurred in the hospital setting arising from administration of medicinal products containing ustekinumab.

There are currently seven medicinal products containing ustekinumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement; the reference medicine, Stelara® and six biosimilar medicines, Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla®.[4] Hospital pricing approval is also in place for each of these medicinal products for the 130 mg concentrate for solution for infusion presentation.

Ustekinumab was ranked 7th in terms of the total number of prescription claims paid (23,221) on the High Tech Arrangement in 2023.[5] There are approximately 2,400 patients in receipt of ustekinumab on the High Tech Arrangement on a monthly basis; the majority of these patients are currently on Stelara®, with approximately 5% of patients in receipt of a biosimilar medicine of ustekinumab.[2]

[ii]Expenditure reflects the ingredient cost of the medicinal product, exclusive of value-added tax and fees

The reference medicine, Stelara®, first received a marketing authorisation (MA) in 2009.[2] The Supplementary Protection Certificate for Stelara® lapsed on 19 July 2024, allowing for the availability of biosimilar medicines containing ustekinumab. It is noted, however, that the European Patent Office has granted a new patent for the use of Stelara® in a particular method of treating moderately to severely active UC.

2.2 Biosimilar medicines

There is now considerable national and international experience with the usage of biosimilar medicines. They have been used safely in clinical practice in the European Union (EU) for over 15 years and have demonstrated similar efficacy, safety and immunogenicity with their reference medicine. Analysis of more than one million patient-treatment years of safety data for biosimilar medicines did not raise any safety concerns.[6,7]

The MMP has recommended BVB medicines for adalimumab and etanercept, the majority of which are biosimilar medicines. In July 2025, all patients in receipt of adalimumab 40 milligrams (mg) pre-filled pen (PFP) or pre-filled syringe (PFS) on the High Tech Arrangement were prescribed a BVB medicine, with 69.5% of patients prescribed a biosimilar medicine of adalimumab that had been recommended as a BVB medicine. In addition, 78.6% of patients in receipt of etanercept 25/50 mg PFP or PFS on the High Tech Arrangement in July 2025 were prescribed a biosimilar medicine of etanercept that had been recommended as a BVB medicine.[5] Since May 2019, over 25,000 patients have been initiated on, or switched to a biosimilar medicine for adalimumab or etanercept that has been recommended as a BVB medicine.[8] This represents a significant increase in the prescribing and utilisation of biosimilar medicines for adalimumab and etanercept on the High Tech Arrangement since 2019. This demonstrates that significant clinical experience is being obtained for biosimilar medicines of adalimumab and etanercept in a short timeframe.

In January 2024, the MMP recommended BVB medicines for the long-acting granulocyte-colony stimulating factors (G-CSFs) (i.e. lipegfilgrastim and pegfilgrastim), two of which are biosimilar medicines of pegfilgrastim, Pelgraz® and Ziextenzo®.[9] In July 2025, 39.5% of patients in receipt of pegfilgrastim on the High Tech Arrangement were prescribed a biosimilar medicine.[2]

The MMP has also recommended BVMs for teriparatide, three of which are biosimilar medicines (Movymia®, Sondelbay® and Terrosa®).[10] In July 2025, 96.1% of patients in receipt of teriparatide on the High Tech Arrangement were prescribed a biosimilar medicine that had been recommended as a BVM.[2]

There are currently 13 biosimilar medicines containing ustekinumab licensed by the European Commission following consideration of a MA application via the European Medicines Agency (EMA) centralised procedure: Absimky®, Fymskina®, Imuldosa®, Otulfi®, Pyzchiva®, Qoyvolma®, Steqeyma®, Usgena®, Usymro®, Usrenty®, Uzpruvo®, Wezenla® and Yestinek®.[11]

3. Scope

This BVB medicine evaluation process considers the medicinal products containing ustekinumab that have a MA that allows for supply in Ireland.

This BVB medicine evaluation includes medicinal products containing ustekinumab:

- that have a MA that allows for supply in Ireland, and
- that are on the HSE Reimbursement List for prescribing and supply on the High Tech Arrangement or have hospital pricing approval in place or that are the subject of a formal pricing and reimbursement application submitted to the HSE-Corporate Pharmaceutical Unit (CPU), and
- for which a submission was received from the MA holder/supplier.

The aim of this initiative is to ensure that the efficiencies presented by the availability of biosimilar medicines of ustekinumab are fully realised to achieve best value. This BVB medicine evaluation process therefore focuses on the therapeutic indications of ustekinumab for which biosimilar medicines of ustekinumab are licensed. Licensed indications of the reference medicine, for which biosimilar medicines are not licensed, fall outside the scope of this BVB medicine process.

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 medicinal product, which may also include any rebates and commercial-in-confidence arrangements that are in place. The reimbursement price is exclusive of value-added tax (VAT), which is applicable to medicinal products containing ustekinumab.

All prices and costs are correct as of 27 November 2025.

5. Best-value biological medicines – Ustekinumab

The MMP has identified BVB medicines for ustekinumab. 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.[12,13] This involved a review period that included internal evaluation by the MMP and consideration of submissions received from the MA holders/suppliers of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla®.

In line with the *MMP Roadmap for the prescribing of best-value biological medicines (BVB) medicines,* the MMP considered the following criteria when identifying BVB medicines for ustekinumab:[14]

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 international non-proprietary name (INN).

The MMP recommends the following as BVB medicines for ustekinumab:

- ✓ **Imuldosa® (Accord Healthcare Ireland Limited)**
- ✓ **Otulfi® (Fresenius Kabi Ireland)**
- ✓ **Pyzchiva® (Sandoz Limited trading as Rowex)**
- ✓ **Wezenla® (Amgen Ireland Limited).**

Clinicians should give due consideration to prescribing Imuldosa®, Otulfi®, Pyzchiva® or Wezenla® when issuing a prescription for ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease.

Prescribing the recommended BVB medicines reduces the financial burden on the HSE arising out of the funding of reimbursed medicines, and can assist in facilitating access to new, innovative medicines for patients.

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 MA holders/suppliers of medicinal products containing ustekinumab. The consultation phase commenced on Monday 9 December 2024. The closing date for receipt of submissions was 1pm on Wednesday 22 January 2025.

Submissions were received from the following:

- Accord Healthcare Ireland Limited
- Amgen Ireland Limited
- Celltrion Healthcare Ireland Limited
- Clonmel Healthcare Limited
- Fresenius Kabi Ireland
- Johnson & Johnson Innovative Medicine
- Sandoz Limited trading as Rowex.

The MMP reviewed the information submitted by the MA holders/suppliers and in cases where clarifications or further information was required, this was requested as part of the evaluation process. In addition, all MA holders/suppliers were contacted by the MMP on 15 August 2025, to provide them with the opportunity to submit any additional information, which had not previously been submitted to the MMP during the BVB medicine evaluation process for ustekinumab.

6. Evaluation

As of 27 November 2025, there are seven medicinal products containing ustekinumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement:[4]

- Imuldosa® (Accord Healthcare Ireland Limited)
- Otulfi® (Fresenius Kabi Ireland)
- Pyzchiva® (Sandoz Limited trading as Rowex)
- Stelara® (Johnson & Johnson Innovative Medicine)
- Steqeyma® (Celltrion Healthcare Ireland Limited)
- Uzpruvo® (Clonmel Healthcare Limited)
- Wezenla® (Amgen Ireland Limited).

In addition, hospital pricing approval is also in place for the 130 mg concentrate for solution for infusion presentation for each of the medicinal products listed above.

Stelara® is the reference medicinal product. Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla® are licensed as biosimilar medicines of the reference medicinal product, Stelara®.[3,11]

The following presentations of medicinal products containing ustekinumab are the subject of a MA issued by the European Commission but are not on the HSE Reimbursement List, do not have hospital pricing approval in place or are not the subject of a formal pricing and reimbursement application submitted to the CPU; therefore, as outlined in Section 3, they fall outside the scope of this BVB medicine evaluation:

- Otulfi® vial presentation containing 45 mg/0.5 millilitre (mL) solution for injection of ustekinumab for subcutaneous (SC) administration
- Pyzchiva® vial presentation containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration
- Steqeyma® vial presentation containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration

- Uzpruvo® vial presentation containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration.

Information in relation to these presentations of medicinal products containing ustekinumab is not included in the evaluation report, and they were not considered as part of the BVB medicine evaluation process.

6.1 Acquisition cost

The reimbursement price, total cost per pack and annual cost of the medicinal products containing ustekinumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement, as of 27 November 2025 are outlined in Tables 1 and 2. The price to wholesaler (PTW) of medicinal products containing ustekinumab 130 mg in a concentrate for solution for infusion vial presentation as detailed in the approval letter for hospital pricing, is outlined in Table 3.

Table 1 Reimbursement price, total cost per PFP/PFS/vial and annual cost of medicinal products containing ustekinumab 45 mg available on the HSE Reimbursement List[4]

Medicinal Product	Reimbursement price per PFP/PFS/vial	Total cost per PFP/PFS/vial (ex VAT)	Total cost per PFP/PFS/vial (inc VAT)	Annual cost* (ex VAT)	Annual cost* (inc VAT)
Imuldosa® 45 mg SFI PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Otulfi® 45 mg SFI PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Pyzchiva® 45 mg SFI PFP/PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Stelara® 45 mg SFI PFP/PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Stelara® 45 mg SFI Vial	€1,678.26	€1,678.26	€2,064.26	€7,297.43	€8,975.84
Steqeyma® 45 mg SFI PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Uzpruvo® 45 mg SFI PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Wezenla® 45 mg SFI PFP/PFS	€1,634.66	€1,634.66	€2,010.63	€7,107.85	€8,742.65
Wezenla® 45 mg SFI Vial	€1,678.26	€1,678.26	€2,064.26	€7,297.43	€8,975.84

ex: excluding; inc: including; mg: milligrams; PFP: pre-filled pen; PFS: pre-filled syringe; SFI; solution for injection; VAT: value-added tax
Prices correct as of 27 November 2025
*Annual cost reflects use of ustekinumab at the licensed maintenance dosage of 45 mg administered subcutaneously once every 12 weeks. It does not include the patient care fee paid to community pharmacies.

Table 2 Reimbursement price, total cost per PFP/PFS and annual cost of medicinal products containing ustekinumab 90 mg available on the HSE Reimbursement List[4]

Medicinal Product	Reimbursement price per PFP/PFS	Total cost per PFP/PFS (ex VAT)	Total cost per PFP/PFS (inc VAT)	Annual cost* (ex VAT)	Annual cost* (inc VAT)
Imuldosa® 90 mg SFI PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Otulfi® 90 mg SFI PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Pyzchiva® 90 mg SFI PFP/PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Stelara® 90 mg SFI PFP/PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Steqeyma® 90 mg SFI PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Uzpruvo® 90 mg SFI PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40
Wezenla® 90 mg SFI PFP/PFS	€1,680.71	€1,680.71	€2,067.27	€10,962.13	€13,483.40

ex: excluding; inc: including; mg: milligrams; PFP: pre-filled pen; PFS: pre-filled syringe; SFI; solution for injection; VAT: value-added tax
Prices correct as of 27 November 2025
*Annual cost reflects use of ustekinumab at the licensed maintenance dosage of 90 mg administered subcutaneously once every eight weeks. It does not include the patient care fee paid to community pharmacies.

Table 3 Price to wholesaler under hospital pricing approval per one vial of medicinal products containing ustekinumab 130 mg in a concentrate for solution for infusion vial presentation[15-21]

Medicinal Product	Price to wholesaler per vial*†
Imuldosa® 130 mg concentrate for solution for infusion vial	€1,494.79
Otulfi® 130 mg concentrate for solution for infusion vial	€1,483.11
Pyzchiva® 130 mg concentrate for solution for infusion vial	n/a†
Stelara® 130 mg concentrate for solution for infusion vial	€1,647.85
Steqeyma® 130 mg concentrate for solution for infusion vial	n/a†
Uzpruvo® 130 mg concentrate for solution for infusion vial	€1,647.85
Wezenla® 130 mg concentrate for solution for infusion vial	€1,647.85

n/a: not available; mg: milligrams
*In line with the 2021 Framework Agreement on the Supply and Pricing of Medicines and the 2021 Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines, hospitals can negotiate revised arrangements with individual manufacturers.
†The PTW for the concentrate for solution for infusion vial presentation containing 130 mg of ustekinumab is included where the supplier confirmed that this information could be published in the final evaluation report. Where this confirmation was not provided, the price to wholesale was not included; this is indicated by the inclusion of n/a (not available) in Table 3.

Submissions received during the BVB medicine evaluation process included revised commercial terms for some of the medicinal products listed in Tables 1 - 3.[15-21]

Recommendation

Imuldosa®, Otulfi®, Pyzchiva® and Wezenla® have the lowest acquisition cost to the HSE, based on the proposed revised commercial terms that were contained within submissions received as part of the consultation process. The acquisition costs of Imuldosa® (Accord Healthcare Ireland Limited), Otulfi® (Fresenius Kabi Ireland), Pyzchiva® (Sandoz Limited trading as Rowex) and Wezenla® (Amgen Ireland Limited) all fall within the range for designation as BVB medicines for ustekinumab, based on the proposed revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.

6.2 Therapeutic indications

Table 4 summarises the licensed therapeutic indications of the medicinal products containing ustekinumab that fall under the scope of the BVB medicine evaluation process for ustekinumab.

Table 4 Summary of licensed therapeutic indications for medicinal products containing ustekinumab*

Brand (INN)	Plaque psoriasis	Paediatric plaque psoriasis	Psoriatic arthritis	Crohn's Disease	Paediatric Crohn's Disease	Ulcerative Colitis
Imuldosa®[22] (Ustekinumab)	✓	✓	✓	✓		
Otulfi®[23] (Ustekinumab)	✓	✓	✓	✓	✓	
Pyzchiva®[24] (Ustekinumab)	✓	✓	✓	✓	✓	
Stelara®[3] (Ustekinumab)	✓	✓	✓	✓	✓	✓
Steqeyma®[25] (Ustekinumab)	✓	✓	✓	✓	✓	
Uzpruvo®[26] (Ustekinumab)	✓	✓	✓	✓		
Wezenla®[27] (Ustekinumab)	✓	✓	✓	✓	✓	

INN: International non-proprietary name

*Please refer to individual Summary of Product Characteristics for full prescribing information.

6.2.1 Plaque Psoriasis

The reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo®, Wezenla®) are licensed for the treatment of moderate-to-severe plaque psoriasis (PP) in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or PUVA (psoralen and ultraviolet A).[3,22-27]

The licensed dosage of ustekinumab for the treatment of moderate-to-severe PP is an initial dose of 45 mg administered subcutaneously, followed by a dose of 45 mg four weeks later, and then every 12 weeks thereafter. For patients with a body weight greater than 100 kilograms (kg), the initial dose is 90 mg administered subcutaneously, followed by a dose of 90 mg four weeks later, and then every 12 weeks thereafter. In these patients, 45 mg was also shown to be efficacious. However, 90 mg resulted in greater efficacy.[3,22-27]

The PFP presentations of Pyzchiva®, Stelara® and Wezenla® and PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara® Steqeyma®, Uzpruvo® and Wezenla® containing 45 mg or 90 mg of ustekinumab, can be used to administer the licensed dosage.[3,22-27]

6.2.2 Paediatric Plaque Psoriasis

The reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo®, Wezenla®) are licensed for the treatment of moderate-to-severe PP in children and adolescent patients from the age of six years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.[2,22-27]

The licensed dosage of ustekinumab for the treatment of moderate-to-severe PP in children and adolescent patients from the age of six years and older is based on body weight at the time of dosing:[3,22-27]

- < 60 kg: 0.75 mg/kg
- ≥ 60 kg - ≤ 100 kg: 45 mg
- > 100 kg: 90 mg.

Ustekinumab should be administered subcutaneously at weeks 0 and 4, and then every 12 weeks thereafter. Further guidance is provided in relevant summary of product characteristics (SmPC) in calculating the volume of injection for patients who weigh less than 60 kg.[3,22-27]

The PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® containing 45 mg or 90 mg of ustekinumab can be used to administer the licensed dosage of 45 mg or 90 mg.[3,22-27] The PFP presentations of Pyzchiva®, Stelara® and Wezenla® have not been studied in the paediatric population and are not recommended for use in paediatric patients.[3,24,27]

Stelara® and Wezenla® are available in a solution for injection vial presentation containing 45 mg of ustekinumab; this presentation facilitates SC administration in paediatric patients weighing less than 60 kg, who need to receive less than the 45 mg dose.[3,27] The solution for injection vial presentations of Otulfi®, Pyzchiva®, Steqeyma® and Uzpruvo® containing 45 mg of ustekinumab are the subject of a MA issued by the European Commission; these presentations, however, fall outside the scope of this BVB medicine evaluation as outlined in Section 3.

There is currently no licensed presentation available of Imuldosa® that allows for weight-based dosing for paediatric patients weighing less than 60 kg.

6.2.3 Psoriatic Arthritis

The reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo®, Wezenla®), alone or in combination with MTX, are licensed for the treatment of active PsA in adult patients when the response to previous non-biological disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.[3,22-27]

The licensed dosage of ustekinumab for the treatment of active PsA in adult patients is an initial dose of 45 mg administered subcutaneously, followed by a 45 mg dose four weeks later, and then every 12 weeks thereafter. Alternatively, 90 mg may be used in patients with a body weight greater than 100 kg.[3,22-27]

The PFP presentations of Pyzchiva®, Stelara® and Wezenla® and PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara® Steqeyma®, Uzpruvo® and Wezenla® containing 45 mg or 90 mg of ustekinumab, can be used to administer the licensed dosage.[3,22-27]

6.2.4 Crohn's Disease

The SmPCs of the reference medicine (Stelara®) and the biosimilar medicines, Otulfi®, Pyzchiva®, Steqeyma® and Wezenla® state that they are licensed for the treatment of adult patients with moderately-to-severely active CD who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a tumour necrosis factor-alpha (TNF-α)

antagonist.[3,23-25,27] The SmPCs of the biosimilar medicines, Imuldosa® and Uzpruvo® state that they are licensed for the treatment of adult patients with moderately-to-severely active CD who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNF-α antagonist or have medical contraindications to such therapies.[22,26]

The licensed dosage of ustekinumab for the treatment of adult patients with moderately-to-severely active CD involves administration of an initial single intravenous dose based on body weight followed by SC maintenance dosing; details of the initial intravenous dosing are provided in Table 5.[3,22-27]

Table 5 Initial intravenous dosing of ustekinumab for treatment of adult patients with moderately-to-severely active Crohn's Disease[3,22-27]

Body weight of patient at time of initial dosing	Recommended dose*	Number of 130 mg vials
≤ 55 kg	260 mg	2
> 55 kg to ≤ 85 kg	390 mg	3
> 85 kg	520 mg	4

kg: kilograms; mg: milligrams
*Approximately 6 mg/kg

The first SC administration of ustekinumab 90 mg should take place at week eight after the intravenous dose. After this, dosing every 12 weeks is recommended. Patients who have not shown adequate response at eight weeks after the first SC dose may receive a second SC dose at this time. Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every eight weeks; the patient may subsequently be dosed every eight weeks or every 12 weeks thereafter according to clinical judgement.[3,22-27]

The concentrate for solution for infusion vial presentation of Imuldosa®, Otulfi®, Pyzchiva®, Stelara® Steqeyma®, Uzpruvo® and Wezenla® containing 130 mg of ustekinumab can be used to administer the initial intravenous dosage of ustekinumab.[3,22-27]

The PFP presentations of Pyzchiva®, Stelara® and Wezenla® and PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara® Steqeyma®, Uzpruvo® and Wezenla® containing 90 mg of ustekinumab, can be used to administer the licensed SC maintenance dosage.[3,22-27]

6.2.5 Paediatric Crohn's Disease

The reference medicine (Stelara®) and the biosimilar medicines, Otulfi®, Pyzchiva®, Steqeyma® and Wezenla® are indicated for the treatment of moderately-to-severely active CD in paediatric patients weighing at least 40 kg, who have had an inadequate response to, or were intolerant to either conventional or biologic therapy.[3,23-25,27]

At this point in time, the biosimilar medicines Imuldosa® and Uzpruvo® are not licensed for this indication.

Of note, the MA of the reference medicine (Stelara®) was amended on 31 March 2025 to reflect the extension of the licensed indications to include the treatment of paediatric CD. This licence extension took place subsequent to the availability of biosimilar medicines of ustekinumab.

The licensed dosage of ustekinumab for the treatment of moderately-to-severely active CD in paediatric patients weighing at least 40 kg involves administration of an initial single intravenous dose based on body weight followed by SC maintenance dosing; details of the initial intravenous dosing are provided in Table 6.[3,23-25,27]

Table 6 Initial intravenous dosing of ustekinumab for treatment of paediatric patients weighing at least 40 kg with moderately-to-severely active Crohn's Disease[3,23-25,27]

Body weight of patient at time of initial dosing	Recommended dose*	Number of 130 mg vials
≥ 40 kg to ≤ 55 kg	260 mg	2
> 55 kg to ≤ 85 kg	390 mg	3
> 85 kg	520 mg	4

kg: kilograms; mg: milligrams
*Approximately 6 mg/kg

The first SC administration of ustekinumab 90 mg should take place at week eight after the intravenous dose. After this, dosing every 12 weeks is recommended. Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every eight weeks; the patient may subsequently be dosed every eight weeks or every 12 weeks thereafter according to clinical judgement.[3,23-25,27]

The concentrate for solution for infusion vial presentation of Otulfi®, Pyzchiva®, Stelara®, Steqeyma® or Wezenla®, containing 130 mg of ustekinumab, can be used to administer the initial intravenous

dosage of ustekinumab. The PFS presentations of Otulfi®, Pyzchiva®, Stelara®, Steqeyma® or Wezenla®, containing 90 mg of ustekinumab, can be used to administer the licensed SC maintenance dosage. The PFP presentations of Pyzchiva®, Stelara® and Wezenla® have not been studied in the paediatric population and are not recommended for use in paediatric patients.[3,23-25,27]

6.2.6 Ulcerative Colitis

The reference medicine (Stelara®) is indicated for the treatment of adult patients with moderately-to-severely active UC who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic.[3]

At this point in time, the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo®, Wezenla®) are not licensed for this indication.

The licensed dosage of ustekinumab for the treatment of adult patients with moderately-to-severely active UC involves administration of an initial single intravenous dose based on body weight followed by SC maintenance dosing; details of the initial intravenous dosing are provided in Table 7.[3]

Table 7 Initial intravenous dosing of ustekinumab for treatment of adult patients with moderately-to-severely active ulcerative colitis[3]

Body weight of patient at time of initial dosing	Recommended dose*	Number of 130 mg vials
≤ 55 kg	260 mg	2
> 55 kg to ≤ 85 kg	390 mg	3
> 85 kg	520 mg	4

kg: kilograms; mg: milligrams
*Approximately 6 mg/kg

The first SC administration of ustekinumab 90 mg should take place at week eight after the intravenous dose. After this, dosing every 12 weeks is recommended. Patients who have not shown adequate response at eight weeks after the first SC dose may receive a second SC dose at this time. Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every eight weeks; the patient may subsequently be dosed every eight weeks or every 12 weeks thereafter according to clinical judgement.[3]

The concentrate for solution for infusion vial presentation of Stelara® containing 130 mg of ustekinumab can be used to administer the initial intravenous dosage of ustekinumab. The PFP and

PFS presentations of Stelara® containing 90 mg of ustekinumab, can be used to administer the licensed SC maintenance dosage.[3]

Recommendation

The reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo®, Wezenla®) are licensed for the treatment of:

- plaque psoriasis in adults
- paediatric plaque psoriasis
- psoriatic arthritis in adults
- Crohn's disease in adults.

In addition, the reference medicine (Stelara®) and the biosimilar medicines, Otulfi®, Pyzchiva®, Steqeyma® and Wezenla®, are licensed for the treatment of paediatric CD.

The MA of the biosimilar medicines for the indications outlined above are reflective of the MA of the reference medicine (Stelara®).

The reference medicine (Stelara®) is also licensed for the treatment of UC in adults. As outlined in Section 3, licensed indications of the reference medicine, for which biosimilar medicines are not licensed, fall outside the scope of this BVB medicine process.

Overall, in relation to the criterion of therapeutic indications, the MMP is of the opinion that the medicinal products containing ustekinumab that are under evaluation for a BVB medicine for ustekinumab are equivalent in relation to the licensed indications of PP, PsA and CD.

6.3 Formulation considerations

6.3.1 Imuldosa®

The PFS presentation of Imuldosa® is formulated as a colourless to slightly yellow and clear to slightly opalescent solution for injection. It contains the following excipients:[22]

- L-histidine
- L-histidine hydrochloride monohydrate
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Imuldosa® 45 mg/0.5 mL PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Imuldosa® 90 mg/1 mL PFS contains 90 mg of ustekinumab in 1 mL solution for injection. In both cases, the concentration of ustekinumab is 90 mg/mL.[22]

The concentrate for solution for infusion 130 mg vial presentation of Imuldosa® is formulated as a colourless to slightly yellow and clear to slightly opalescent concentrate for solution for infusion. It contains the following excipients:[22]

- EDTA disodium salt dehydrate (E385)
- L-histidine
- L-histidine hydrochloride monohydrate
- L-methionine
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each vial of Imuldosa® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[22]

6.3.2 Otulfi®

The PFS presentation of Otulfi® is formulated as a clear to slightly opalescent, colourless to light brown-yellow solution for injection. The solution may contain a few small translucent or white particles of protein.[23]

The formulation of Otulfi® PFS contains the following excipients:[23]

- L-histidine
- polysorbate 80 (E433)
- sucrose
- water for injections
- hydrochloric acid.

Each Otulfi® 45 mg/0.5 mL PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Otulfi® 90 mg/1 mL PFS contains 90 mg of ustekinumab in 1 mL solution for injection.[23]

The concentrate for solution for infusion 130 mg vial presentation of Otulfi® is formulated as a clear and colourless to slightly brown-yellow concentrate for solution for infusion. It contains the following excipients:[23]

- EDTA disodium salt dehydrate (E385)
- L-histidine
- L-histidine monohydrochloride monohydrate
- L-methionine
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each vial of Otulfi® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[23]

The solution for injection vial presentation of Otulfi® containing 45 mg of ustekinumab falls outside the scope of this BVB medicine evaluation.

6.3.3 Pyzchiva®

The PFP and PFS presentations of Pyzchiva® are formulated as a clear, colourless to light yellow solution for injection. The solution may contain a few small translucent or white particles of protein.[24]

The formulation of Pyzchiva® PFP and PFS contain the following excipients:[24]

- histidine
- histidine hydrochloride monohydrate
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Pyzchiva® 45 mg/0.5 mL PFP/PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Pyzchiva® 90 mg/1 mL PFP/PFS contains 90 mg of ustekinumab in 1 mL solution for injection. In both cases, the concentration of ustekinumab is 90 mg/mL.[24]

The concentrate for solution for infusion 130 mg vial presentation of Pyzchiva® is formulated as a clear, colourless to light yellow concentrate for solution for infusion. It contains the following excipients:[24]

- histidine
- histidine monohydrochloride monohydrate
- methionine
- disodium edetate
- sucrose
- polysorbate 80 (E433)
- water for injections.

Each vial of Pyzchiva® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[24]

The solution for injection vial presentation of Pyzchiva® containing 45 mg of ustekinumab falls outside the scope of this BVB medicine evaluation.

6.3.4 Stelara®

The PFP, PFS and 45 mg solution for injection vial presentations of Stelara® are formulated as a clear to slightly opalescent, colourless to light yellow solution for injection. The solution may contain a few small translucent or white particles of protein.[3]

The formulation of Stelara® PFP, PFS and 45 mg vial contain the following excipients:[3]

- L-histidine
- L-histidine monohydrochloride monohydrate
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Stelara® 45 mg/0.5 mL PFP/PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Stelara® 90 mg/1 mL PFP/PFS contains 90 mg of ustekinumab in 1 mL solution for injection. Each Stelara® 45 mg vial contains 45 mg of ustekinumab in 0.5 mL solution for injection. In each case, the concentration of ustekinumab is 90 mg/mL.[3]

The concentrate for solution for infusion 130 mg vial presentation of Stelara® is formulated as a clear, colourless to light yellow concentrate for solution for infusion. It contains the following excipients:[3]

- EDTA disodium salt dehydrate (E385)
- L-histidine
- L-histidine hydrochloride monohydrate
- L-methionine
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each vial of Stelara® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[3]

6.3.5 Steqeyma®

The PFS presentation of Steqeyma® is formulated as a clear to slightly opalescent, colourless to pale yellow solution for injection. The solution may contain a few small translucent or white particles of protein.[25]

The formulation of Steqeyma® PFS contains the following excipients:[25]

- L-histidine
- L-histidine monohydrochloride monohydrate
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Steqeyma® 45 mg/0.5 mL PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Steqeyma® 90 mg/1 mL PFS contains 90 mg of ustekinumab in 1 mL solution for injection.[25]

The concentrate for solution for infusion 130 mg vial presentation of Steqeyma® is formulated as a clear to slightly opalescent, colourless to pale yellow concentrate for solution for infusion. It contains the following excipients:[25]

- EDTA disodium salt dihydrate (E385)
- L-histidine

- L-histidine monohydrochloride monohydrate
- L-methionine
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each vial of Steqeyma® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[25]

The solution for injection vial presentation of Steqeyma® containing 45 mg of ustekinumab falls outside the scope of this BVB medicine evaluation.

6.3.6 Uzpruvo®

The PFS presentation of Uzpruvo® is formulated as a clear and colourless to slightly yellow solution for injection. The solution is practically free from visible particles.[26]

The formulation of Uzpruvo® PFS contains the following excipients:[26]

- histidine
- histidine monohydrochloride
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Uzpruvo® 45 mg/0.5 mL PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Uzpruvo® 90 mg/1 mL PFS contains 90 mg of ustekinumab in 1 mL solution for injection.[26]

The concentrate for solution for infusion 130 mg vial presentation of Uzpruvo® is formulated as a clear and colourless to slightly yellow concentrate for solution for infusion. The solution is practically free from visible particles. It contains the following excipients:[26]

- EDTA disodium salt dihydrate
- histidine
- histidine monohydrochloride
- methionine
- polysorbate 80 (E433)

- sucrose
- water for injections.

Each vial of Uzpruvo® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[26]

The solution for injection vial presentation of Uzpruvo® containing 45 mg of ustekinumab falls outside the scope of this BVB medicine evaluation.

6.3.7 Wezenla®

The PFP, PFS and 45 mg solution for injection vial presentations of Wezenla® are formulated as a clear to opalescent, colourless to light yellow solution for injection.[27]

The formulation of Wezenla® PFP, PFS and 45 mg vial contain the following excipients:[27]

- L-histidine
- L-histidine monohydrochloride monohydrate
- polysorbate 80 (E433)
- sucrose
- water for injections.

Each Wezenla® 45 mg/0.5 mL PFP/PFS contains 45 mg of ustekinumab in 0.5 mL solution for injection. Each Wezenla® 90 mg/1 mL PFP/PFS contains 90 mg of ustekinumab in 1 mL solution for injection. Each Wezenla® 45 mg vial contains 45 mg of ustekinumab in 0.5 mL solution for injection. In each case, the concentration of ustekinumab is 90 mg/mL.[27]

The concentrate for solution for infusion 130 mg vial presentation of Wezenla® is formulated as a clear to opalescent, colourless to light yellow concentrate for solution for infusion. It contains the following excipients:[27]

- EDTA disodium salt dihydrate
- L-histidine
- L-histidine hydrochloride monohydrate
- L-methionine
- polysorbate 80 (E433)
- sucrose

- sodium hydroxide
- water for injections.

Each vial of Wezenla® 130 mg concentrate for solution for infusion contains 130 mg of ustekinumab in 26 mL; the concentration of ustekinumab is 5 mg/mL.[27]

6.3.8 Excipients of interest

6.3.8.1 Sodium content

The majority of the sodium burden comes from the diluent used to prepare the concentrate for solution for infusion 130 mg vial presentations of the reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Uzpruvo®, Steqeyma® and Wezenla®); each of these medicinal products contain less than 1 millimole (mmol) of sodium (23 mg) per dose, i.e. they are essentially sodium-free. Each of the medicinal products, however, should be diluted with sodium chloride 9 mg/mL (0.9%) solution for infusion prior to administration. In the case of Pyzchiva®, a 250 mL infusion bag containing 0.45% sodium chloride injection, United States Pharmacopeia (USP) may also be used. This should be taken into consideration for patients on a controlled sodium diet.[3,22-27]

Sodium is not listed as an excipient in the SmPCs for any of the medical products containing ustekinumab that are intended for SC administration, i.e. PFP, PFS, 45 mg solution for injection vial. These medicinal products can therefore be considered to be sodium-free.[3,22-27]

6.3.8.2 Polysorbate 80

All presentations of the reference medicine (Stelara®) and biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Uzpruvo®, Steqeyma® and Wezenla®) contain polysorbate 80 (E433). Polysorbates may cause allergic reactions.[3,22-27]

6.3.8.3 Preservatives

There are no preservatives listed in the SmPCs for any of the medical products containing ustekinumab that are intended for SC administration, i.e. PFP, PFS, 45 mg solution for injection vial. Any unused medicinal product remaining in the PFP, PFS or 45 mg solution for injection vial presentations should therefore not be used.[3,22-27]

6.3.9 Compatibility with other medicinal products

In the absence of compatibility studies, all presentations of the reference medicine (Stelara®) and biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Uzpruvo®, Steqeyma® and Wezenla®) must not

be mixed with other medicinal products. The concentrate for solution for infusion presentations of the reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Uzpruvo®, Steqeyma® and Wezenla®) should only be diluted with sodium chloride 9 mg/mL (0.9%) solution for infusion prior to administration; in the case of Pyzchiva®, a 250 mL infusion bag containing 0.45% sodium chloride injection, USP may also be used. The concentrate for solution for infusion presentation of the reference and biosimilar medicines should not be administered concomitantly in the same intravenous line with other medicinal products.[3,22-27]

6.3.10 Injection site reactions

Injection site erythema and injection site pain are reported as a common (≥ 1/100 to < 1/10) adverse reaction and injection site reactions (including haemorrhage, haematoma, induration, swelling and pruritus) are reported as an uncommon (≥ 1/1,000 to < 1/100) adverse reaction under general disorders and administration site conditions in the section on undesirable effects in the SmPC of Stelara®.[3]

The SmPCs for the biosimilar medicines containing ustekinumab (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla®) include the same information as Stelara® in relation to injection site erythema, pain and reactions under general disorders and administration site conditions in the section on undesirable effects in their SmPCs.[22-27]

6.3.10.1 European Public Assessment Report – Imuldosa®

In the clinical safety section of the European public assessment report (EPAR) for Imuldosa®, an overview of the safety data in the safety population of the phase I (DMB-3115-1) and phase III (DMB-3115-2) clinical studies for Imuldosa® is provided. This includes 529 subjects who received at least one dose of Imuldosa® in the two clinical studies.[28]

In study DMB-3115-1, 99 healthy adult subjects received a single 45 mg SC dose of Imuldosa® on day one, 99 subjects received EU-Stelara® and 98 subjects US-Stelara®. In total, 88 injection site reactions, all of mild intensity, were reported in 27 subjects. The most common injection site reaction related to Imuldosa® was erythema, with 10 events reported in 10 subjects. All these events of erythema occurred at one hour after the treatment injection and were fully resolved at 12 hours after the treatment injection.[28]

During period one of study DMB-3115-2, 299 subjects were exposed to at least one dose of Imuldosa® and 299 subjects were exposed to at least one dose of EU-Stelara®; all 598 subjects were

included in the safety set for period one. In period two, all 531 patients who completed period one were re-randomised to either continue treatment with Imuldosa® (n=268), continue treatment with EU-Stelara® (n=132) or switch from EU-Stelara® to Imuldosa® (n=131). The safety set included 530 patients who received at least one dose of the study treatment in period two.[28]

A total of 16 treatment-emergent adverse events of special interest (TEAESI) were reported in period one for 13 (2.2%) subjects, and the incidence was comparable across treatment arms (Imuldosa®: seven [2.3%] subjects and nine TEAESIs; EU-Stelara®: six [2.0%] subjects and seven TEAESIs). Injection site reactions were reported in eight (1.3%) subjects, with a total of 10 TEAESIs (Imuldosa®: three [1.0%] subjects and four TEAESIs; EU-Stelara®: five [1.7%] subjects and six TEAESIs). The frequency of injection site reactions in Imuldosa® was numerically lower than EU-Stelara®. Injection site reactions was the only TEAESI reported for more than one subject in both treatment arms.[28]

The EMA concluded that the clinical development programme and design of the studies were adequate to evaluate the comparability of Imuldosa® and the reference medicine (EU-Stelara®) in terms of safety. It also stated that no significant differences in safety were detected based on the available data and the two products can be concluded to be biosimilar.[28]

6.3.10.2 European Public Assessment Report – Otulfi®

In the clinical safety section of the EPAR for Otulfi®, an overview of the safety data in the safety population of two phase I (FYB202-01-01 and FYB202-01-02) and the phase III (FYB202-03-01) clinical studies for Otulfi® is provided.[29]

In the phase III study, adverse events of special interest (AESIs) were reported more frequently in Otulfi® compared to EU-Stelara® (15.2% versus 11.3%); the main events reported were injection site reactions. All were rated as mild in intensity. In the initial period of the study (before re-randomisation), the incidence of injection site reactions was higher in patients treated with Otulfi® (29, 14.7%) compared to those treated with EU-Stelara® (21, 10.8%). After re-randomisation, there were three patients with injection site events, all of whom were treated with Otulfi®; two in the group who continued on treatment with Otulfi® from the initial period and one in the group who were switched from EU-Stelara® to Otulfi®.[29]

In the initial period of the phase III study, adverse events with injection site pain occurred more frequently in the Otulfi® group (32 events in 22 [11.2%] of patients) than in the EU-Stelara® group (18 events in 15 [7.7%] of patients). All events were considered a mild reaction and more frequently

occurred after the first injection. The EPAR notes that there was an overestimation of the incidence of injection site pain as the pain at the injection site was documented with high sensitivity, meaning that low scores on the visual analogue scale (VAS) were documented as treatment-emergent adverse events (TEAEs).[29]

AESIs were not defined for the phase I studies but local tolerability was assessed. In a pooled analysis of these studies, injection site pain was reported in 10 of 269 (3.7%) healthy subjects who received Otulfi®, in two of 268 (0.7%) who received EU-Stelara® and in six of 269 (2.2%) who received US-Stelara®. All reported events of injection site pain were mild in severity. The incidence of injection site pain after a 45 mg SC dosage of Otulfi® was common, which is aligned with the frequency reported in the SmPC of the reference medicine.[29]

The EMA concluded that the clinical development programme and design of the studies were adequate to evaluate the comparability of Otulfi® and the reference medicine (EU-Stelara®) in terms of safety. It also stated that no major or significant differences in safety were detected based on the available data, and the two products can be concluded to be biosimilar in terms of clinical safety.[29]

6.3.10.3 European Public Assessment Report – Pyzchiva®

In the clinical safety section of the EPAR for Pyzchiva®, an overview of the safety data in the safety population of the phase I (SB17-1001) and the phase III (SB17-3001) clinical studies for Pyzchiva® is provided.[30]

Three events of injection site reactions were reported in three subjects in the phase I study, the severity of which were classified as mild or moderate:[30]

- one event of injection site erythema in one (1.5%) subject in the Pyzchiva® group
- one event of injection site pain in one (1.5%) subject in the EU-Stelara® group
- one event of injection site reaction in one (1.5%) subject in the US-Stelara® group.

In the phase III study, injection site reactions were included as one of the categories under which information on AESIs were collected. In the main period of the study, two (0.8%) patients in the Stelara® treatment group had two events (one event of injection site erythema and injection site pain each) and none was reported in the Pyzchiva® treatment group. There were no injection site reactions reported in the transition period of the study. There were no safety concerns with regards to AESIs.[30]

The EMA concluded that the clinical development programme and design of the studies were adequate to evaluate the comparability of Pyzchiva® and the reference medicine (EU-Stelara®) in terms of safety. It also stated that no relevant differences in safety were detected based on the available data, and that the safety profile of Pyzchiva® is considered similar to and in accordance with Stelara®.[30]

6.3.10.4 European Public Assessment Report – Steqeyma®

In the clinical safety section of the EPAR for Steqeyma®, an overview of the safety data in the safety set of the two phase I (CT-P43 1.1 and CT-P43 1.2) and the phase III (CT-P43 3.1) clinical studies for Steqeyma® is provided.[31]

In the phase I study CT-P43 1.1 study, injection site reactions were reported for three (10%) subjects (two [14.3%] subjects in the Steqeyma® treatment group and one [6.3%] subject in the EU-Stelara® treatment group). In the phase I study CT-P43 1.2, 46 (14.2%) subjects experienced at least one TEAE classified as injection site reaction (22 [19.8%] subjects in the Steqeyma® treatment arm, 14 [13.0%] subjects in the EU-Stelara® treatment arm, and 10 [9.4%] subjects in the US-licensed Stelara® treatment arm). A slightly higher proportion of events were reported in the Steqeyma® treatment arm however, this was not considered clinically meaningful since all cases of injection site reactions were grade 1 in intensity, and all subjects quickly recovered from the event without any treatments given. The events were transient with most occurring on the day of administration and most recovering within 1-2 days.[31]

Five (1.0%) patients were reported to have experienced at least one TEAE classified as injection site reaction in the initial treatment period of the phase III study CT-P43 3.1; the proportion of patients was similar between the two groups (three [1.2%] and two [0.8%] patients in the Steqeyma® and EU-Stelara® groups, respectively). In the second treatment period of CT-P43 3.1, three (0.6%) patients were reported to have experienced at least one TEAE classified as injection site reactions (one [0.4%] in the Steqeyma® group, none in the EU-Stelara® group and two [1.6%] in the group that were switched from EU-Stelara® to Steqeyma®). All TEAEs classified as injection site reactions were grade 1 or 2 in intensity. All patients recovered from the event and no action was taken with the study drug.[31]

The EMA concluded that the clinical development programme and design of the studies were adequate to evaluate the comparability of Steqeyma® and the reference medicine (EU-Stelara®) in terms of safety. It also stated that no major differences in safety profile were detected based on the

available data, and that Steqeyma® and Stelara® were considered to be biosimilar in terms of clinical safety.[31]

6.3.10.5 European Public Assessment Report – Uzpruvo®

In the clinical safety section of the EPAR for Uzpruvo®, an overview of the safety data in the safety population of the phase I (AVT04-GL-101) and the phase III (AVT04-GL-301) clinical studies for Uzpruvo® is provided.[32]

In the phase I study, TEAESI in the category of general disorders and administration site conditions were reported for ten (10.2%) subjects who received Uzpruvo®, eight (8.1%) who received EU-Stelara® and eleven (11.3%) who received US-Stelara®. These included injection bruising, erythema, pain, pruritus, reaction, swelling and urticaria. All were classified as mild in severity and occurred at comparable frequencies in the three treatment groups.[32]

In the initial treatment period of the phase III study, injection site reactions was the only TEAESI reported in at least 1% of patients in any cohort (one [0.5%] patient in the Uzpruvo® cohort and seven [1.8%] patients in the EU-Stelara® cohort). From week 16 to 28 of the study, the TEAESI reported included injection site hematoma (one [0.5%] patient in the treatment group that switched from EU-Stelara® to Uzpruvo®) and injection site reaction (one [0.5%] patient in the treatment group that remained on EU-Stelara®). From week 28 to the end of the study, the TEAESI reported included injection site pain (one [0.5%] patient in the treatment group that switched from EU-Stelara® to Uzpruvo®) and injection site reaction (one [0.5%] patient in the treatment group that switched from EU-Stelara® to Uzpruvo®). All injection site reactions reported in the study were of mild severity, with a tendency of more frequent injection site reactions in the EU-Stelara® treatment group.[32]

The EMA concluded that the clinical development programme and design of the studies were adequate to evaluate the comparability of Uzpruvo® and the reference medicine (EU-Stelara®) in terms of safety. It also stated that Uzpruvo® and Stelara® were considered to be biosimilar in terms of safety.[32]

6.3.10.6 European Public Assessment Report – Wezenla®

In the clinical safety section of the EPAR for Wezenla®, an overview of the safety data in the safety population of the phase I (study 20190230) and the phase III (study 20190232) clinical studies for Wezenla® is provided.[33]

No events of injection site reaction were reported in the phase I study. In the phase III study, the number of injection site reactions that was reported is low, with one event of injection site erythema in the Wezenla® treatment group and one event of injection site inflammation in the EU-Stelara® treatment group.[33]

The EMA concluded that the size of the safety database was sufficient to enable a reasonable analysis of the comparability between Wezenla® and the reference medicine (EU-Stelara®). It also stated that the biosimilarity of Wezenla® and Stelara® from a safety perspective had been shown.[33]

Recommendation

In relation to the criterion of formulation considerations, the MMP is of the opinion that the medicinal products that are under evaluation for a BVB medicine for ustekinumab provide a similar offering.

6.4 Product range including pack sizes and strengths available

Table 8 outlines the various presentations of medicinal products containing ustekinumab that fall under the scope of the BVB medicine evaluation process.

Table 8 Product range of medicinal products containing ustekinumab[3,15-27,34]

Medicinal Product	Product range					
	130 mg/26 mL conc for soln for infusion vial	45 mg/0.5 mL SFI vial (1 vial per pack)	45 mg/0.5 mL SFI PFP (1 PFP per pack)	45 mg/0.5 mL SFI PFS (1 PFS per pack)	90 mg/1 mL SFI PFP (1 PFP per pack)	90 mg/1 mL SFI PFS (1 PFS per pack)
Imuldosa®	✓			✓		✓
Otulfi®	✓	o/s*		✓		✓
Pyzchiva®	✓	o/s*	✓	✓	✓	✓
Stelara®	✓	✓	✓	✓	✓	✓
Steqeyma®	✓	o/s*		✓		✓
Uzpruvo®	✓	o/s*		✓		✓
Wezenla®	✓	✓	✓	✓	✓	✓

Conc: concentrate; mg: milligrams; mL: millilitre; o/s: outside scope; PFP: Pre-filled pen; PFS: Pre-filled syringe; SFI: solution for injection; soln: solution
*These presentations of medicinal products containing ustekinumab fall outside the scope of this BVB medicine evaluation process, as outlined in Section 3.

Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® are available on the HSE Reimbursement List as single PFS presentations, containing 45 mg/0.5 mL or 90 mg/1.0 mL solution of injection of ustekinumab for SC administration. Pyzchiva®, Stelara® and Wezenla® are available on the HSE Reimbursement List as single PFP presentations, containing 45 mg/0.5 mL or 90 mg/1.0 mL solution for injection of ustekinumab for SC administration.[4] Stelara® and Wezenla® are available on the HSE Reimbursement List as single vial presentations, containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration.[4] Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® are available under hospital pricing approval in a vial presentation, containing 130 mg/26 mL concentrate for solution for infusion of ustekinumab.[15-21]

In terms of the reference medicine, the vial presentation of Stelara® containing 45 mg/0.5mL solution for injection of ustekinumab for SC administration was added to the HSE Reimbursement List on 1 March 2010. The PFS presentation of Stelara® containing 45 mg/0.5 mL or 90 mg/1.0 mL solution for injection of ustekinumab for SC administration was added to the HSE Reimbursement List on 1 September 2010. The PFP presentation of Stelara® containing 45 mg/0.5 mL or 90 mg/1.0 mL solution for injection of ustekinumab for SC administration was added to the HSE Reimbursement List on 1 October 2023.[4]

Figure 1 outlines the number of individuals in receipt of medicinal products containing ustekinumab on the High Tech Arrangement from January 2020 to June 2025, subdivided by the three different presentations that are available on the HSE Reimbursement List (i.e. PFP, PFS, solution for injection in a vial).

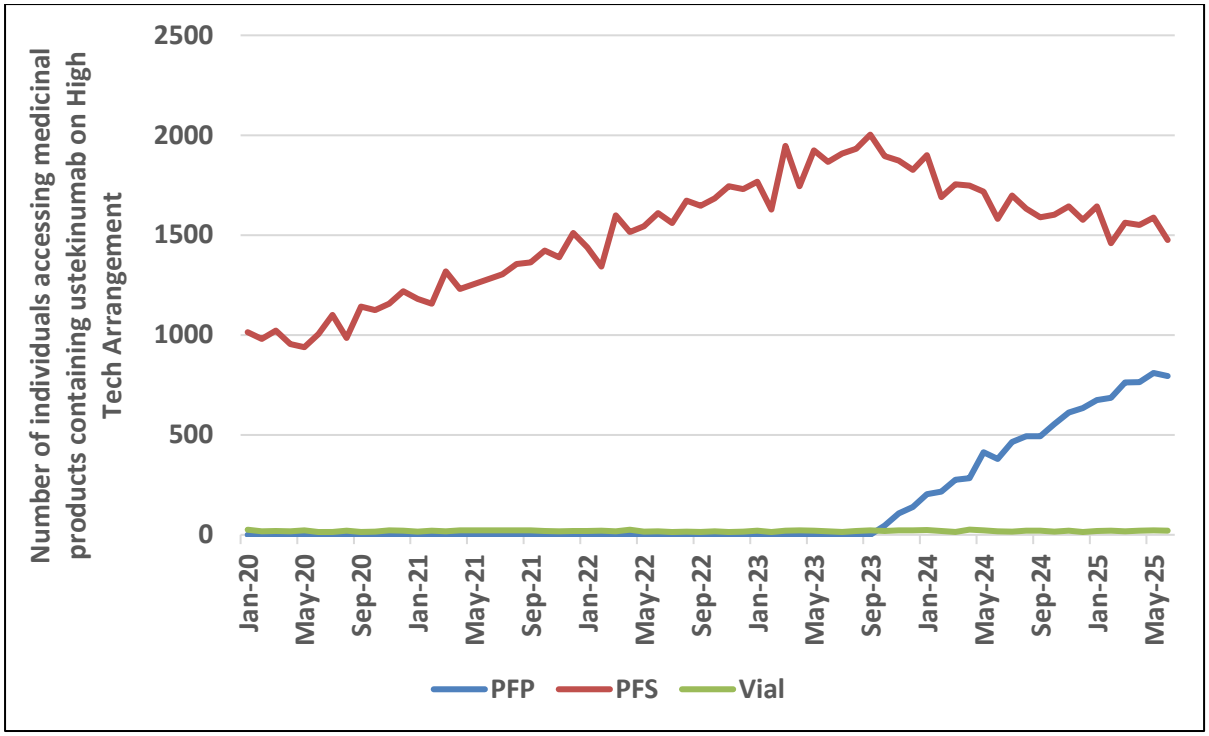


Figure 1 Number of individuals in receipt of medicinal products containing ustekinumab on the High Tech Arrangement from January 2020 - June 2025, subdivided by presentation[2]

The majority of individuals in receipt of a medicinal product containing ustekinumab on the High Tech Arrangement are supplied with a PFS presentation. All seven medicinal products that are under evaluation for a BVB medicine for ustekinumab have PFS presentations containing 45 mg/0.5 mL and 90 mg/1 mL available on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement.

The PFP presentation of the reference medicine (Stelara®) was added to the HSE Reimbursement List on 1 October 2023.[4] Since then, there has been a steady increase in the number of individuals accessing the PFP presentation of ustekinumab on the High Tech Arrangement. Prior to October 2023, all individuals in receipt of a medicinal product containing ustekinumab in a self-administered injection device on the High Tech Arrangement, were supplied with a PFS presentation.

There is limited utilisation of the vial presentation containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration, accounting for less than 1% of individuals accessing ustekinumab on the High Tech Arrangement on a monthly basis.

Recommendation

The vast majority of individuals in receipt of a medicinal product containing ustekinumab on the High Tech Arrangement are supplied with a self-administered injection device presentation. All

seven medicinal products that are under evaluation for a BVB medicine for ustekinumab have PFS presentations containing 45 mg/0.5 mL and 90 mg/1 mL available on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement. PFP presentations of Pyzchiva®, Stelara® and Wezenla® containing 45 mg/0.5 mL or 90 mg/1 mL of ustekinumab are available on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement.

Prior to October 2023, all individuals in receipt of a medicinal product containing ustekinumab in a self-administered injection device on the High Tech Arrangement, were supplied with the PFS presentation of Stelara®; there was no PFP presentation available on the HSE Reimbursement List. The availability of PFP presentations provides an alternative self-administered injection device for patients.

All seven medicinal products that are under evaluation for a BVB medicine for ustekinumab have hospital pricing approval in place for the vial presentation, containing 130 mg/26 mL concentrate for solution for infusion of ustekinumab.

Overall, in relation to the criterion of product range, the MMP is of the opinion that the medicinal products that are under evaluation for a BVB medicine for ustekinumab provide a similar offering.

6.5 Product stability including storage requirements

The shelf lives of the various presentations of medicinal products containing ustekinumab that fall under the scope of the BVB medicine evaluation process are outlined in Table 9.

Table 9 Shelf lives of presentations of medicinal products containing ustekinumab[3,22-27]

Medicinal Product	Shelf life			
	Conc for soln for infusion vial	SFI Vial	PFP	PFS
Imuldosa®	2 years	n/a	n/a	3 years
Otulfi®	3 years	o/s*	n/a	3 years
Pyzchiva®	3 years	o/s*	42 months	42 months
Stelara®	3 years	2 years	3 years	3 years
Steqeyma®	3 years	o/s*	n/a	3 years
Uzpruvo®	2 years	o/s*	n/a	3 years
Wezenla®	3 years	3 years	3 years	3 years

Conc: concentrate; o/s: outside scope; n/a: not available; PFP: Pre-filled pen; PFS: Pre-filled syringe; SFI: solution for injection; soln: solution
*These presentations of medicinal products containing ustekinumab fall outside the scope of this BVB medicine evaluation process, as outlined in Section 3.

Medicinal products containing ustekinumab on the HSE Reimbursement List were added to the High Tech Hub on 1 June 2019. In the case of supply on the High Tech Arrangement, these medicinal products are only available for ordering via the High Tech Hub.[35] This assists in minimising wastage, with ordering only occurring by the community pharmacy for individuals with a valid prescription.[36]

6.5.1 Concentrate for solution for infusion vial presentation

The concentrate for solution for infusion vial presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® must be stored in a refrigerator between 2°C and 8°C. The SmPCs state that the concentrate for solution for infusion vials should not be frozen, and the vials should be kept in the outer carton in order to protect from light.[3,22-27]

The SmPC of Pyzchiva® 130 mg concentrate for solution for infusion vial states that individual unopened vials may be stored at room temperature up to 30°C for a maximum single period of up to 35 days in the original carton in order to protect from light. At any time before the end of this 35-day period, the unopened vial can be put back in the refrigerator once and kept there until the expiry date. The vial should be discarded if it is not used after the maximum period of 35 days at room temperature storage or by the original expiry date, whichever is earlier.[24] The SmPC of Steqeyma® 130 mg concentrate for solution for infusion vial states that individual unopened vials may be stored at room temperature up to 30°C for a maximum single period of up to 31 days in the original carton

in order to protect from light. Once a vial has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The vial should be discarded if it is not used within 31 days at room temperature storage or by the original expiry date, whichever is earlier.[25] The SmPC of Uzpruvo® 130 mg concentrate for solution for infusion vial states that an unopened vial may be stored at room temperature up to 30°C for a maximum single period of up to seven days in the original carton in order to protect from light. Once a vial has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The vial should be discarded if it is not used within seven days at room temperature storage or by the original expiry date, whichever is earlier.[26] The SmPCs of the concentrate for solution for infusion vial presentations of Imuldosa®, Otulfi®, Stelara® and Wezenla® do not contain information in relation to the storage at room temperature of an unopened vial of the concentrate for solution for infusion presentation.[3,22,23,27]

The SmPC of Imuldosa® 130 mg concentrate for solution for infusion vial states that, after dilution, the chemical and physical in-use stability has been demonstrated for 24 hours at 23°C to 27°C or seven days at 2°C to 8°C. From a microbiological point of view, the product should be used immediately. If not used immediately, the SmPC states that in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C unless dilution has taken place in controlled and validated aseptic conditions. It also states that once diluted, the infusion should be completed within 24 hours of the dilution in the infusion bag.[22]

The SmPC of Otulfi® 130 mg concentrate for solution for infusion vial states that chemical and physical in-use stability has been demonstrated for 24 hours at 15°C to 25°C, and that the product should not be returned to the refrigerator after dilution. The SmPC also states that from a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. It also states that if the product is not used immediately, the in-use storage times and conditions are the responsibility of the user. Once diluted, the infusion should be completed within 24 hours of the dilution in the infusion bag.[23]

The SmPC of Pyzchiva® 130 mg concentrate for solution for infusion vial states that chemical and physical in-use stability has been demonstrated for up to 72 hours at 30°C. If necessary, the diluted infusion solution may be kept at 2°C to 8°C for up to one month and at room temperature up to 30°C for an additional 72 hours after removal from refrigeration including the infusion period. The SmPC also states that from a microbiological point of view, the infusion solution should be administered immediately. If not used immediately, in-use storage times and conditions prior to use are the

responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, unless dilution has taken place in controlled and validated aseptic conditions. Once diluted, the infusion should be completed within 72 hours (at room temperature up to 30°C) of the dilution in the infusion bag.[24]

The SmPC of Stelara® 130 mg concentrate for solution for infusion vial states that chemical and physical in-use stability has been demonstrated for eight hours at 15°C to 25°C. The SmPC also states that from a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. It also states that if the product is not used immediately, the in-use storage times and conditions are the responsibility of the user. Once diluted, the infusion should be completed within eight hours of the dilution in the infusion bag.[3]

The SmPC of Steqeyma® 130 mg concentrate for solution for infusion vial states that chemical and physical in-use stability has been demonstrated for 48 hours at refrigerated condition or room temperature up to 30°C. The SmPC also states that from a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. It also states that if the product is not used immediately, the in-use storage times and conditions are the responsibility of the user. Once diluted, the infusion should be completed within 48 hours of the dilution in the infusion bag.[25]

The SmPC of Uzpruvo® 130 mg concentrate for solution for infusion vial states that chemical and physical in-use stability has been demonstrated for eight hours at 15°C to 25°C. The SmPC also states that from a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. It also states that if the product is not used immediately, the in-use storage times and conditions are the responsibility of the user. Once diluted, the infusion should be completed within eight hours of the dilution in the infusion bag.[26]

The SmPC of Wezenla® 130 mg concentrate for solution for infusion vial states that, after dilution, chemical and physical in-use stability has been demonstrated between 0.86 mg/mL and 2.60 mg/mL for 24 hours at 15°C to 25°C, and that the product should not be returned to the refrigerator after dilution. The SmPC also states that from a microbiological point of view, unless the method of dilution precludes the risk of microbial contamination, the product should be used immediately. It

also states that if the product is not used immediately, the in-use storage times and conditions are the responsibility of the user.[27]

6.5.2 Solution for injection vial presentation

The solution for injection vial presentations of Stelara® and Wezenla® must be stored in a refrigerator between 2°C and 8°C. The SmPCs state that the solution for injection vials should not be frozen, and the vials should be kept in the outer carton in order to protect from light.[3,27]

The SmPC of Wezenla® 45 mg solution for injection vial states that individual unopened vials may be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original carton in order to protect from light. Once a vial has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The vial should be discarded if it is not used within 30 days at room temperature storage or by the original expiry date, whichever is earlier.[27] The SmPC of the solution for injection vial presentation of Stelara® does not contain information in relation to the storage at room temperature of the unopened vial of the solution for injection vial presentation.[3]

The SmPC of Wezenla® 45 mg solution for injection vial states that after withdrawing the solution for injection in a disposable syringe, the chemical and physical in-use stability has been demonstrated for 24 hours at 15°C to 25°C; this should not be returned to the refrigerator during this time. The SmPC also indicates that from a microbiological point of view, the product should be used immediately; if it is not used immediately, the in-use storage times and conditions are the responsibility of the user.[27] The SmPC of the solution for injection vial presentations of Stelara® does not contain information in relation to chemical and physical in-use stability of the solution for injection vial presentation.[3]

The solution for injection vial presentations of Otulfi®, Pyzchiva®, Steqeyma® and Uzpruvo® containing 45 mg of ustekinumab, fall outside the scope of this BVB medicine evaluation.

6.5.3 PFP presentation

The PFP presentations of Stelara®, Pyzchiva® and Wezenla® must be stored in a refrigerator between 2°C and 8°C. The SmPCs state that the PFPs should not be frozen, and they should be kept in the outer carton in order to protect from light.[3,24,27]

The SmPCs of the PFP presentations of Stelara® and Wezenla® state that individual PFPs may be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original

carton in order to protect from light. Once a PFP has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The PFP should be discarded if it is not used within 30 days at room temperature storage or by the original expiry date, whichever is earlier.[3,27]

The SmPC of the PFP presentation of Pyzchiva® states that individual PFPs may be stored at room temperature up to 30°C for a maximum single period of up to 35 days in the original carton in order to protect from light. At any time before the end of this 35-day period, the PFP can be put back into the refrigerator once and kept there until the expiry date. The PFP should be discarded if it is not used after the maximum period of 35 days at room temperature storage or by the original expiry date, whichever is earlier.[24]

6.5.4 PFS presentation

The PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® must be stored in a refrigerator between 2°C and 8°C. The SmPCs state that the PFSs should not be frozen, and they should be kept in the outer carton in order to protect from light.[2,22-27]

The SmPCs of the PFS presentations of Imuldosa®, Otulfi®, Stelara®, Uzpruvo® and Wezenla® state that individual PFS may be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original carton in order to protect from light. Once a PFS has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The PFS should be discarded if it is not used within 30 days at room temperature storage or by the original expiry date, whichever is earlier.[3,22,23,26,27]

The SmPC of the PFS presentation of Pyzchiva® states that individual PFS may be stored at room temperature up to 30°C for a maximum single period of up to 35 days in the original carton in order to protect from light. At any time before the end of this 35-day period, the PFS can be put back into the refrigerator once and kept there until the expiry date. The PFS should be discarded if it is not used after the maximum period of 35 days at room temperature storage or by the original expiry date, whichever is earlier.[24]

The SmPC of the PFS presentation of Steqeyma® states that individual PFS may be stored at room temperature up to 30°C for a maximum single period of up to 31 days in the original carton in order to protect from light. Once a PFS has been stored at room temperature (up to 30°C), it should not be returned to the refrigerator. The PFS should be discarded if it is not used within 31 days at room temperature storage or by the original expiry date, whichever is earlier.[25]

Recommendation

In relation to the criterion of product stability, the MMP is of the opinion that the medicinal products containing ustekinumab that are under evaluation for a BVB medicine provide a similar offering.

6.6 Administration devices

6.6.1 Self-administered injection devices

The seven medicinal products that fall under the scope of the BVB medicine evaluation process for ustekinumab are available in self-administered injection devices. Imuldosa®, Otulfi®, Pyzchiva®, Stelara® Steqeyma®, Uzpruvo® and Wezenla® are available in a PFS presentation. Stelara®, Pyzchiva® and Wezenla® are also available in a PFP presentation. Table 10 provides a summary of various properties of the administration devices of medicinal products containing ustekinumab that are available in self-administered injection devices.

Table 10 Characteristics of administration devices for medicinal products containing ustekinumab[3,15-27]

	Imuldosa®	Otulfi®	Pyzchiva®	Stelara®	Steqeyma®	Uzpruvo®	Wezenla®
Needle gauge†	PFS: 29	PFS: 29	PFS: 29	PFS: 27	PFS: 27	PFS: 29	PFS: 27
	PFP: n/a	PFP: n/a	PFP: 29	PFP: 27	PFP: n/a	PFP: n/a	PFP: 27
Latex	PFS: No	PFS: No	PFS: No	PFS: Yes	PFS: No	PFS: No	PFS: No
	PFP: n/a	PFP: n/a	PFP: No	PFP: Yes	PFP: n/a	PFP: n/a	PFP: No
Safety feature	PFS: Yes	PFS: Yes	PFS: Yes	PFS: Yes	PFS: Yes	PFS: Yes	PFS: Yes
	PFP: n/a	PFP: n/a	PFP: Yes	PFP: Yes	PFP: n/a	PFP: n/a	PFP: Yes

n/a: not available; PFP: Pre-filled pen; PFS: Pre-filled syringe
†A higher needle gauge is indicative of a smaller bore size for the needle, i.e. a thinner needle

6.6.1.1 Pre-filled syringe

From examination of the patient information leaflets (PILs), SmPCs and submissions for the PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® containing 45 mg/0.5mL and 90 mg/1 mL of ustekinumab, there appears to be little difference between the various administration devices. Three of the medicinal products (Stelara®, Steqeyma® and Wezenla®) have a 27-gauge needle, while the other four medicinal products (Imuldosa®, Otulfi®, Pyzchiva® and Uzpruvo®) all have a 29-gauge needle.[3,15-27] All PFS presentations of ustekinumab, therefore, use small gauge needles, with the small differences unlikely to cause a difference in practice.

The needle cover on the syringe of the PFS presentation of Stelara® is manufactured from dry natural rubber, which is a derivative of latex; this may cause allergic reactions in individuals sensitive to latex.[3] The PFS presentations of the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla®) are all latex-free.[15-17,19-21] All of the PFS presentations have a safety feature to guard the needle upon delivery of the dose of ustekinumab; they are fitted with a passive safety guard. Upon release of the plunger having administered the dose, the entire needle is drawn back automatically and covered by the needle safety guard.[3,15-27]

All of the medicinal products are supplied as sterile, single-use PFS, and do not contain preservatives; they therefore should not be re-used. Any unused medicinal product remaining in the PFS should not be used, and should be disposed of, along with any waste material, in accordance with local requirements.[3,22-27]

The PILs contain instructions for the administration of a SC dose of ustekinumab from the PFS presentations of Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla®. In all cases, the instructions are presented in the form of text with accompanying pictograms. For all the medicinal products, the PFS presentation should be allowed to reach room temperature (approximately half an hour) prior to administration.[3,22-27]

The majority of individuals in receipt of a medicinal product containing ustekinumab on the High Tech Arrangement are supplied with a PFS presentation.[2]

6.6.1.2 Pre-filled pen

From examination of the PILs, SmPCs and submissions for the PFP presentations of Pyzchiva®, Stelara®, and Wezenla® containing 45 mg/0.5 mL and 90 mg/1 mL of ustekinumab, there appears to

be little difference between the various administration devices. Stelara® and Wezenla® have a 27-gauge needle, while Pyzchiva® has a 29-gauge needle.[17,18,21] All PFP presentations of ustekinumab, therefore, use small gauge needles, with the small differences unlikely to cause a difference in practice.

The needle cover inside the bottom cap of the PFP presentation of Stelara® is manufactured from dry natural rubber, which is a derivative of latex; this may cause allergic reactions in individuals sensitive to latex.[3] The PFP presentations of Pyzchiva® and Wezenla® are latex-free.[17,21] All of the PFP presentations have a safety feature to guard the needle upon delivery of the dose of ustekinumab; they are fitted with a passive safety guard. Upon administration of the dosage of ustekinumab, the entire needle is covered by the needle safety guard.[3,17,18,21,24,27]

Stelara®, Pyzchiva® and Wezenla® are supplied as sterile, single-use PFPs, and do not contain preservatives; they therefore should not be re-used. Any unused medicinal product remaining in the PFP should not be used, and should be disposed of, along with any waste material, in accordance with local requirements.[3,24,27]

The PILs contain instructions for the administration of a SC dose of ustekinumab from the PFP presentations of Pyzchiva®, Stelara®, and Wezenla®. In all cases, the instructions are presented in the form of text with accompanying pictograms. For all the medicinal products, the PFP presentation should be allowed to reach room temperature (approximately half an hour) prior to administration.

The PFP presentation of the reference medicine (Stelara®) was added to the HSE Reimbursement List on 1 October 2023.[34] Since then, there has been a steady increase in the number of individuals accessing the PFP presentation of ustekinumab on the High Tech Arrangement.[2] Prior to October 2023, all individuals in receipt of a medicinal product containing ustekinumab in a self-administered injection device on the High Tech Arrangement, were supplied with a PFS presentation.

6.6.2 Concentrate for solution for infusion vial presentation

Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® are available in a vial presentation, containing 130 mg/26 mL concentrate for solution for infusion of ustekinumab. The vials are for single-use only and any unused medicinal product should be disposed of in accordance with local requirements. The vial presentation must be diluted, prepared and infused by a healthcare professional using aseptic technique. The PILs and SmPCs contain detailed information relevant to healthcare professionals regarding the dilution and administration of the contents of the vial as a

solution for infusion. They also indicate that the diluted solution should be administered over a period of at least one hour. The ancillaries required for administration of the solution by intravenous infusion are not provided with any of the medicinal products.[3,22-27]

6.6.3 Solution for injection vial presentation

Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® are available as single vial presentations, containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration.[3,23-27] The solution for injection vial presentations of Otulfi®, Pyzchiva®, Steqeyma® and Uzpruvo® containing 45 mg of ustekinumab, fall outside the scope of this BVB medicine evaluation.

Stelara® and Wezenla® are supplied as sterile, single-use vials, and do not contain preservatives; they therefore should not be re-used. Any unused medicinal product remaining in the vial should not be used, and should be disposed of, along with any waste material, in accordance with local requirements.[3,27]

The ancillaries required for administration of the solution by SC injection are not provided with the solution for injection vial presentations of Stelara® and Wezenla®. The SmPCs of Stelara® and Wezenla® recommend a 1 mL syringe with a 27 gauge, ½ inch (13 millimetres) needle when administering a dosage subcutaneously from the solution for injection vial presentation.[3,27]

The PILs contain instructions for the administration of a SC dose of ustekinumab from the solution for injection vial presentations of Stelara® and Wezenla®. The instructions are presented in the form of text with accompanying pictograms. For both medicinal products, the solution for injection vial presentations should be allowed to reach room temperature (approximately half an hour) prior to administration.[3,27]

There is limited utilisation of the vial presentation containing 45 mg/0.5 mL solution for injection of ustekinumab for SC administration, accounting for less than 1% of individuals accessing ustekinumab on the High Tech Arrangement on a monthly basis.[2]

Recommendation

The vast majority of individual accessing medicinal products containing ustekinumab on the High Tech Arrangement are in receipt of a self-administered injection device. All of the medicinal products that fall under the scope of the BVB medicine evaluation process are available in a PFS

presentation containing 45 mg or 90 mg of ustekinumab. Until recently, the PFS presentation was the only self-administered injection device available; PFP presentations of Pyzchiva®, Stelara® and Wezenla® are now also available.

Overall, in relation to the criterion of administration devices, the MMP is of the opinion that the medicinal products that are under evaluation for a BVB medicine for ustekinumab provide a similar offering.

6.7 Patient factors

In their submissions, Accord Healthcare Ireland Limited, Amgen Ireland Limited, Celltrion Healthcare Ireland Limited, Clonmel Healthcare Limited, Fresenius Kabi Ireland, Johnson & Johnson Innovative Medicine and Sandoz Limited trading as Rowex outlined the patient support programmes available when patients are prescribed medicinal products containing ustekinumab.

A literature review was undertaken to investigate the impact of the provision of patient support programmes on treatment with ustekinumab. No robust evidence was identified by the MMP in relation to the impact of patient support programmes on treatment with ustekinumab.

The patient support programmes that are available to individuals who are prescribed Imuldosa®, Otulfi®, Pyzchiva®, Stelara®, Steqeyma®, Uzpruvo® and Wezenla® are similar in nature, based on the information provided to the MMP as part of the BVB medicine evaluation process.

Recommendation

In relation to the criterion of patient factors, the MMP is of the opinion that the patient support programmes offered by Accord Healthcare Ireland Limited, Amgen Ireland Limited, Celltrion Healthcare Ireland Limited, Clonmel Healthcare Limited, Fresenius Kabi Ireland, Johnson & Johnson Innovative Medicine and Sandoz Limited trading as Rowex all provide a similar offering.

6.8 Expenditure in the therapeutic area and potential for cost savings

Figure 2 outlines total annual expenditure[iii] on medicinal products containing ustekinumab on the High Tech Arrangement from 2016 to 2024. Total annual expenditure on ustekinumab has increased across this period, from €11.86 million in 2016 to €67.34 million in 2023.[1] There was a reduction in expenditure in 2024 (to €63.11 million) due to the implementation of relevant clauses of the

[iii]Expenditure reflects the ingredient cost of the medicinal product, exclusive of value-added tax and fees.

Framework Agreement on the Supply and Pricing of Medicines and the Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines.[2]

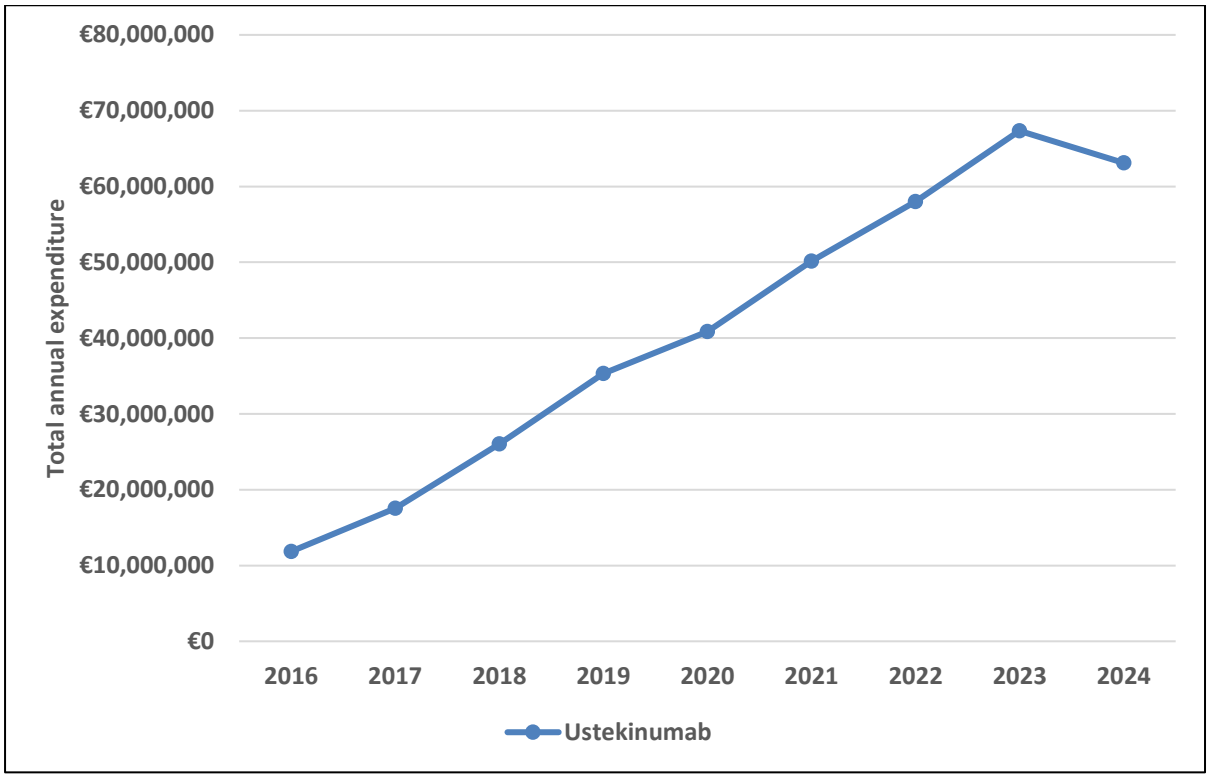


Figure 2 Total annual expenditure on ustekinumab on the High Tech Arrangement 2016 - 2024

Figure 3 outlines the total number of prescription claims per annum for medicinal products containing ustekinumab on the High Tech Arrangement from 2016 to 2023. There has been a significant increase in the number of prescription claims during this period, from 3,344 in 2016 to 23,221 in 2023.[5]

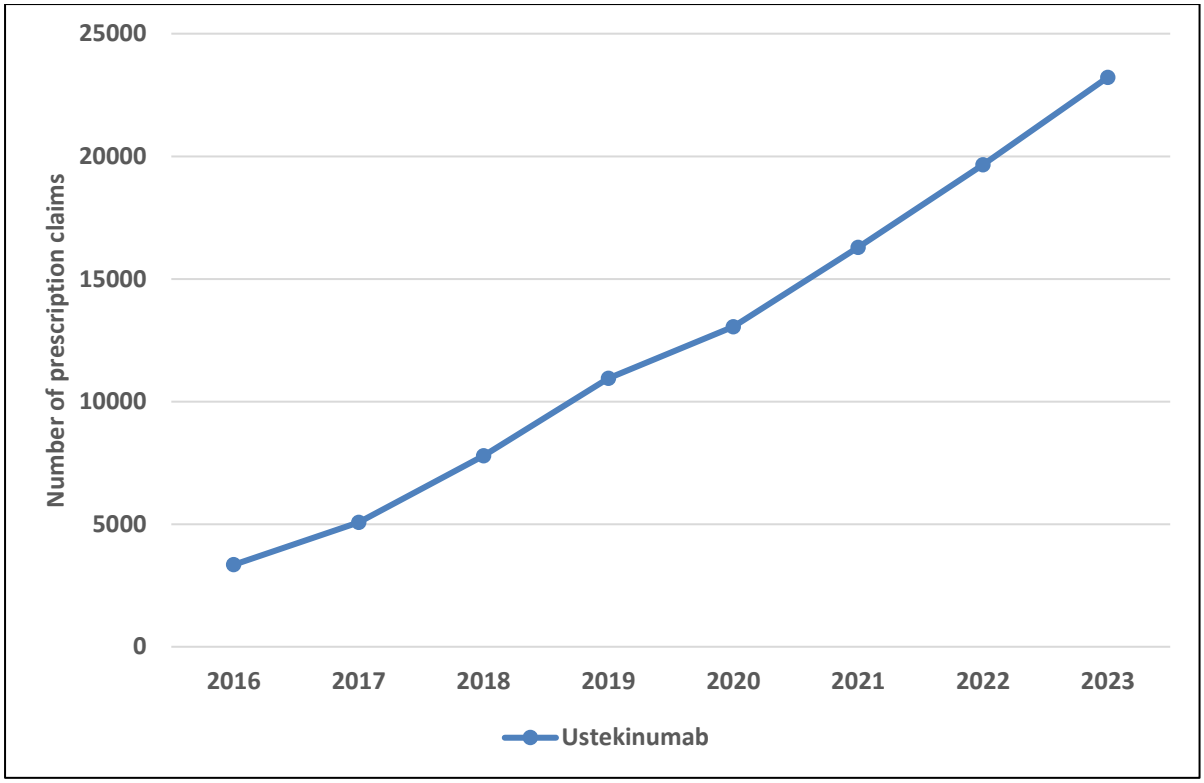


Figure 3 Total number of prescription claims per annum for medicinal products containing ustekinumab on the High Tech Arrangement from 2016 - 2023

Ustekinumab was ranked 7th in terms of the total number of prescription claims paid (23,221) on the High Tech Arrangement in 2023.[5] There are approximately 2,300 patients in receipt of ustekinumab on the High Tech Arrangement on a monthly basis; the majority of these patients are currently on Stelara®, with approximately 5% of patients in receipt of a biosimilar medicine of ustekinumab.[2]

The Framework Agreement on the Supply and Pricing of Medicines (2021) contains a number of clauses in relation to the pricing of patent-expired non-exclusive biological medicines that are relevant to medicinal products containing ustekinumab. Clause 8 applies to patent-expired biologic medicines for which a biosimilar medicine is available for supply. In relation to price reductions, clause 8.2.2 states that the price of a biological medicine that becomes a patent-expired non-exclusive biologic medicine after the 1 January 2022 shall be reduced to 62.86% of the ex-factory price of that biological medicine as of 1 October 2021. In addition to this price reduction, clause 8.2.3 states that a rebate to the HSE of a sum equal to 12.5% of the reduced price as per clause 8.2.2, is applied to the patent-expired, non-exclusive biological medicine.[12] This is reflected in the current total costs per pack of Stelara® that are included in Tables 1 - 3.

The Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines (2021) also contains a clause in relation to the pricing of biosimilar medicines that are relevant to

biosimilar medicines containing ustekinumab. Clause 8.2.2 states that the price that a supplier shall submit to the HSE of a new biosimilar medicine for which an application is made for its addition to the Reimbursement List shall be no greater than 55% of the price of the equivalent branded original medicine as of 1 October 2021.[13] This clause applied in the case of the applications for the pricing and reimbursement of Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla® that were submitted by Accord Healthcare Ireland Limited, Fresenius Kabi Ireland, Sandoz Limited trading as Rowex, Celltrion Healthcare Ireland Limited, Clonmel Healthcare Limited and Amgen Ireland Limited, respectively.

The current total costs per pack of medicinal products containing ustekinumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement, as of 27 November 2025, are outlined in Tables 1 and 2. There is currently no difference between the total cost per PFP/PFS of the reference medicine (Stelara®) and the biosimilar medicines (Imuldosa®, Otulfi®, Pyzchiva®, Steqeyma®, Uzpruvo® and Wezenla®). In addition, there is currently no difference between the total unit cost of the solution for injection vial presentation of the reference medicine (Stelara®) and the biosimilar medicine (Wezenla®). The potential efficiencies resulting from the availability of biosimilar medicines of ustekinumab are not being fully realised.

Based on the revised commercial terms outlined in the submissions received by the MMP, significant efficiencies can be achieved through the identification of BVB medicines by the MMP, and the introduction of mechanisms to facilitate prescribing and utilisation of the BVB medicines.

Recommendation

In relation to the criterion of expenditure in the therapeutic area and potential for cost savings, the MMP recommends Imuldosa® (Accord Healthcare Ireland Limited), Otulfi® (Fresenius Kabi Ireland), Pyzchiva® (Sandoz Limited trading as Rowex) and Wezenla® (Amgen Ireland Limited) as BVB medicines due to the potential for significant cost savings based on the proposed revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.

6.9 Clinical guidelines

There are currently no relevant national clinical guidelines available in Ireland for the therapeutic areas or conditions for which the medicinal products containing ustekinumab are indicated, i.e. dermatology, gastroenterology, rheumatology.

The HSE-Access & Integration Drug Management Programme (AIDMP) has published guidance for biological and biosimilar medicine use in acute hospitals (version 2, May 2024). The guidance states that for a biological medicine with a biosimilar available for the same licensed indication, the medicine offering the better value should be prescribed.[37] It also recommends that:

- all treatment-naïve patients should be initiated on the better-value medicine (whether biosimilar or reference medicine)
- all non-treatment-naïve patients currently on treatment with the reference medicine should be considered for a switch to a biosimilar if the biosimilar is better value compared to the originator or reference medicine.

The guidance highlights that the availability of biosimilar medicines brings competition to the pharmaceutical market, presenting an opportunity for significant improvement in value for patients and healthcare providers.[37]

Recommendation

In relation to the criterion of clinical guidelines, no relevant information was identified by the MMP with respect to identifying a BVB medicine for ustekinumab.

6.10 Security of supply to the Irish market

Accord Healthcare Ireland Limited, Amgen Ireland Limited, Celltrion Healthcare Ireland Limited, Clonmel Healthcare Limited, Fresenius Kabi Ireland, Johnson & Johnson Innovative Medicine and Sandoz Limited trading as Rowex outlined the processes that they have in place for supply of their medicinal product containing ustekinumab to the Irish market. Each outlined the arrangements that they have in place for the supply chain management of their medicinal product containing ustekinumab, including the distribution model that they employ.[15-21]

Recommendation

In relation to the criterion of security of supply to the Irish market, the MMP is of the opinion that Accord Healthcare Ireland Limited, Amgen Ireland Limited, Celltrion Healthcare Ireland Limited, Clonmel Healthcare Limited, Fresenius Kabi Ireland, Johnson & Johnson Innovative Medicine and Sandoz Limited trading as Rowex have all provided evidence of their capacity to meet the ongoing needs of Irish patients with respect to the supply of medicinal products containing ustekinumab.

6.11 Utilisation and clinical experience with the biological medicine

There is significant clinical experience with the use of ustekinumab in the Irish setting, with approximately 2,400 patients in receipt of ustekinumab on the High Tech Arrangement on a monthly basis.[2] The majority of patients are currently on Stelara®, with approximately 5% of patients in receipt of a biosimilar medicine of ustekinumab.[2] Approximately 5,700 unique individuals accessed treatment with ustekinumab on the High Tech Arrangement in 2024.[2]

The solution for injection vial presentation of the reference medicine, Stelara®, first received a MA in 2009.[3] Stelara® 45 mg solution for injection vial presentation was added to the HSE Reimbursement List on 1 March 2010, for prescribing and supply on the High Tech Arrangement. The PFS presentations of Stelara® containing 45 mg and 90 mg of ustekinumab were added to the HSE Reimbursement List on 1 September 2010, for prescribing and supply on the High Tech Arrangement. The PFP presentations of Stelara® containing 45 mg and 90 mg of ustekinumab were added to the HSE Reimbursement List on 1 October 2023, for prescribing and supply on the High Tech Arrangement.[34]

The Supplementary Protection Certificate for Stelara® lapsed on 19 July 2024, and biosimilar medicines containing ustekinumab were added to the HSE Reimbursement List on 1 August 2024, for prescribing and supply on the High Tech Arrangement.[34]

The majority of patients accessing ustekinumab on the High Tech Arrangement are currently on Stelara®, with approximately 5% of patients in receipt of a biosimilar medicine of ustekinumab in July 2025.[2] Other European healthcare systems have observed higher rates of uptake of biosimilar medicines containing ustekinumab.

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.[6,38]

The EMA and Heads of Medicines Agencies (HMA), in a joint statement, have confirmed that biosimilar medicines approved in the EU 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.[7] The clinical experience, therefore, obtained with Stelara® is transferable to the biosimilar medicines of ustekinumab, in line with their marketing authorisations.

The MMP acknowledge the significant clinical experience that has been obtained in Ireland with the reference medicine, Stelara®. Biosimilars of ustekinumab have only recently become available; available data indicates that these are being incorporated into clinical practice in Ireland.[2] Other European healthcare systems have observed higher rates of uptake of biosimilar medicines containing ustekinumab than those achieved in Ireland to date. This demonstrates that clinical experience is being obtained for biosimilar medicines of ustekinumab within a short timeframe.

Ustekinumab is predominately prescribed in the specialities of dermatology, gastroenterology and rheumatology. The MMP has previously recommended BVB medicines for adalimumab and etanercept; adalimumab is used in the treatment of conditions in the specialities of dermatology, gastroenterology and rheumatology, and etanercept is used in the specialities of dermatology and rheumatology. Since May 2019, over 25,000 patients have been initiated on, or switched to a biosimilar medicine for adalimumab or etanercept that has been recommended as a BVB medicine, by prescribers in the specialities of dermatology, gastroenterology and rheumatology.[8] This demonstrates that significant experience has being obtained with biosimilar medicines in these specialities.

Recommendation

Overall, in relation to the criterion of utilisation and clinical experience with the biological medicine, the MMP is of the opinion that the medicinal products containing ustekinumab that are under evaluation for a BVB medicine for ustekinumab provide a similar offering.

6.12 Any other relevant factors with respect to the particular INN

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

- biosimilar medicine pipeline
- educational support for healthcare professionals and patients on biosimilar medicines
- environmental sustainability.

The MMP is of the opinion that no new relevant material was submitted under this criterion that had not been considered under any of the other criteria.

6.12.1 Position papers

No published position papers on the usage of biosimilar medicines, either in general or specifically in relation to ustekinumab, were identified from the Irish clinical societies for the specialities who

would be involved in prescribing medicinal products containing ustekinumab (i.e. Irish Association of Dermatologists, Irish Society of Gastroenterology and Irish Society of Rheumatology).

The HSE-National Clinical Programme for Rheumatology published a model of care for rheumatology in Ireland in 2017. This proposes the development of evidence-based national guidelines for the use of biologic therapies, including biosimilars, in a cost-effective manner in conjunction with the MMP. It also highlights that significant cost savings can be achieved through consideration of the use of biosimilars.[39]

The HSE-National Clinical Programme for Dermatology published a model for care for dermatology in Ireland in 2020. This supports the work of the MMP in promoting the use of biosimilar medicines in dermatology services in the interests of significant cost savings to the health service and best-value use of limited resources.[40]

6.12.2 Legislation/Guidance from medicines regulators

The MMP reviewed the legislation and guidelines from medicines regulators that relate to the prescribing and utilisation of biosimilar medicines. Pharmacist-led substitution of biological medicines is not permitted under the Health (Pricing and Supply of Medical Goods) Act 2013.[41]

The Health Products Regulatory Authority (HPRA) published an updated version of their Guide to Biosimilars for Healthcare Professionals in September 2025. 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.[38]

The EMA and HMA, in a joint statement issued on 19 September 2022, have confirmed that biosimilar medicines approved in the EU 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.[7]

Recommendation

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

Overall Recommendation

The MMP notes the following in relation to medicinal products that fall under the scope of the BVB medicine evaluation process for ustekinumab:

1. All medicinal products are licensed for the treatment in adults of PP, PsAs and CD, and for the treatment of PP in children and adolescents aged six years and older.
2. Otulfi®, Pyzchiva®, Stelara®, Steqeyma® and Wezenla® are licensed for the treatment of CD in paediatric patients weighing at least 40 kg.
3. All medicinal products are available in a PFS presentation containing 45 mg/0.5 mL or 90 mg/1 mL of ustekinumab. Pyzchiva®, Stelara® and Wezenla® are available in a PFP presentation containing 45 mg/0.5 mL or 90 mg/1 mL of ustekinumab. The majority of individuals in receipt of a medicinal product containing ustekinumab on the High Tech Arrangement are supplied with a PFS presentation. Prior to October 2023, all individuals in receipt of a medicinal product containing ustekinumab in a self-administered injection device on the High Tech Arrangement were supplied with a PFS presentation.
4. Stelara® and Wezenla® are available in a solution for injection vial presentation containing 45 mg of ustekinumab, to facilitate weight-based dosing for the treatment of PP in paediatric patients who weigh less than 60 kg. There is limited utilisation of this presentation of ustekinumab, accounting for less than 1% of individuals accessing ustekinumab on the High Tech Arrangement on a monthly basis.
5. All medicinal products are available in a concentrate for solution for infusion vial presentation containing 130 mg of ustekinumab, to facilitate administration of the induction dosing for the treatment of CD.
6. All medicinal products are considered to provide a similar offering in relation to the criteria of formulation considerations, product range including pack sizes and strengths available, product stability including storage requirements, administration devices, patient factors, security of supply to the Irish market, and utilisation and clinical experience with the biological medicine, with no material differences identified.
7. The commercially confidential pricing proposals that were included in the submissions received as part of the BVB medicine evaluation process for ustekinumab. The acquisition costs of Imuldosa® (Accord Healthcare Ireland Limited), Otulfi® (Fresenius Kabi Ireland), Pyzchiva® (Sandoz trading as Rowex) and Wezenla® (Amgen Ireland Limited) all fall within the range for designation as BVB medicines for ustekinumab, based on the proposed revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.

8. The potential for significant savings that would arise from the prescribing and utilisation of Imuldosa®, Otulfi®, Pyzchiva® and Wezenla®, based on the proposed revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.

Overall, the MMP recommends Imuldosa® (Accord Healthcare Ireland Limited), Otulfi® (Fresenius Kabi Ireland), Pyzchiva® (Sandoz Limited trading as Rowex) and Wezenla® (Amgen Ireland Limited) as the BVB medicines for ustekinumab.

7. MMP Recommendations

The MMP recommends the following as BVB medicines for ustekinumab:

- ✓ **Imuldosa® (Accord Healthcare Ireland Limited)**
- ✓ **Otulfi® (Fresenius Kabi Ireland)**
- ✓ **Pyzchiva® (Sandoz Limited trading as Rowex)**
- ✓ **Wezenla® (Amgen Ireland Limited).**

Clinicians should give due consideration to prescribing Imuldosa®, Otulfi®, Pyzchiva® or Wezenla® when issuing a prescription for ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease.

Prescribing the recommended BVB medicines reduces the financial burden on the HSE arising out of the funding of reimbursed medicines, and can assist in facilitating access to new, innovative medicines for patients.

Initiation

When initiating a patient on ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease, the clinician should prescribe Imuldosa®, Otulfi®, Pyzchiva® or Wezenla®.

Switching

Patients currently on ustekinumab for the treatment of plaque psoriasis, psoriatic arthritis or Crohn's disease should be considered for switching to Imuldosa®, Otulfi®, Pyzchiva® or Wezenla® at the earliest possible opportunity.

The MMP recommends that all new patients being initiated on ustekinumab for the treatment of PP, PsA or CD should be prescribed a BVB medicine, i.e. Imuldosa®, Otulfi®, Pyzchiva® or Wezenla®. Patients currently on ustekinumab for the treatment of PP, PsA or CD should be considered for switching to a BVB medicine (Imuldosa®, Otulfi®, Pyzchiva® or Wezenla®) at the earliest possible opportunity.

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