Medicines Management Programme

Best-value biological medicine:

Tocilizumab on the High Tech Arrangement

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

AIDMP	Access & Integration Drug Management Programme
BVB	Best-value biological
BVM	Best-value medicine
CAR	Chimeric antigen receptor
COVID-19	Coronavirus disease 2019
CRS	Cytokine release syndrome
DMARDs	Disease modifying anti-rheumatic drugs
EMA	European Medicines Agency
EPAR	European public assessment report
EU	European Union
ex	Excluding
GCA	Giant cell arteritis
G-CSF	Granulocyte-colony stimulating factor
HMA	Heads of Medicines Agencies
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
IgG1	Immunoglobulin G subclass 1
IL-6	Interleukin-6
inc	Including
INN	International non-proprietary name
mg	Milligrams
mIL-6R	Membrane-bound IL-6 receptors
mL	Millilitres
mm	Millimetres
MMP	Medicines Management Programme
MTX	Methotrexate
NSAIDs	Non-steroidal anti-inflammatory drugs
PCRS	Primary Care Reimbursement Service
PD	Pharmacodynamic
PIL	Patient information leaflet
PFP	Pre-filled pen
PFS	Pre-filled syringe
pJIA	Polyarticular juvenile idiopathic arthritis
PK	Pharmacokinetic
RA	Rheumatoid arthritis
SFI	Solution for injection
sIL-6R	Soluble-bound IL-6 receptors
sJIA	Systemic juvenile idiopathic arthritis
SmPC	Summary of Product Characteristics
TNF	Tumour necrosis factor
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 tocilizumab on the High Tech Arrangement accounted for approximately €19.6 million in 2023 and €13.9 million in 2024.[1] There are now biosimilar medicines containing tocilizumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement. This provides the opportunity to identify a BVB medicine for tocilizumab 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 tocilizumab are fully realised to achieve best value. It identifies a BVB medicine for tocilizumab. It also aims to support the prescribing of the BVB medicine.

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

The MMP recommends Tyenne® (Fresenius Kabi Ireland) as the BVB medicine for tocilizumab on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Tyenne® when issuing a prescription for tocilizumab on the High Tech Arrangement.

Prescribing the recommended BVB medicine reduces the financial burdens 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 tocilizumab, the clinician should prescribe Tyenne®.

Switching

Patients currently on tocilizumab should be considered for switching to Tyenne® at the earliest possible opportunity.

2. Background

2.1 Tocilizumab

Tocilizumab is a recombinant humanised immunoglobulin G subclass 1 (IgG1) monoclonal antibody directed against the human interleukin-6 (IL-6) receptor. It is produced in Chinese hamster ovary cells by recombinant DNA technology. It binds specifically to both soluble and membrane-bound IL-6 receptors (sIL-6R and mIL-6R). Tocilizumab has been shown to inhibit sIL-6R and mIL-6R-mediated signalling. IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, monocytes and fibroblasts. IL-6 is involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, induction of hepatic acute phase protein synthesis and stimulation of haemopoiesis. IL-6 has been implicated in the pathogenesis of diseases including inflammatory diseases, osteoporosis and neoplasia.[2,3]

Expenditure[ii] on medicinal products containing tocilizumab on the High Tech Arrangement accounted for approximately €19.6 million in 2023 and €13.9 million in 2024.[1] Additional expenditure was incurred in the hospital setting arising from administration of medicinal products containing tocilizumab.

There are currently two medicinal products containing tocilizumab available on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement; the reference medicine, RoActemra® and a biosimilar medicine, Tyenne®.[4]

Tocilizumab was ranked 11th in terms of the total number of prescription claims paid (19,276) on the High Tech Arrangement in 2023.[5] There are approximately 1,900 patients in receipt of tocilizumab on the High Tech Arrangement on a monthly basis; the vast majority of these patients are currently on RoActemra®, with approximately 14% of patients in receipt of a biosimilar medicine of tocilizumab.[6]

The reference medicine, RoActemra®, first received a marketing authorisation in 2009. In September 2023, Tyenne® was the first biosimilar medicine containing tocilizumab to receive a marketing authorisation from the European Commission, following consideration of a marketing authorisation application via the European Medicines Agency (EMA) centralised procedure.

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

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.[7,8]

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 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.[6] 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.[9] 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®.[10] In July 2025, 39.5% of patients in receipt of pegfilgrastim on the High Tech Arrangement were prescribed a biosimilar medicine.[6]

The MMP has also recommended BVMs for teriparatide, two of which are biosimilar medicines (Movymia®, Sondelbay® and Terrosa®).[11] 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.[6]

There are currently three biosimilar medicines containing tocilizumab licensed by the European Commission following consideration of a marketing authorisation application via the EMA centralised procedure: Avtozma®, Tofidence® and Tyenne®.[12]

Avtozma®, RoActemra®, Tofidence® and Tyenne® are available in a concentrate for solution for infusion presentation. Avtozma®, RoActemra® and Tyenne® are also available as a solution for injection in a self-administered injection device presentation, i.e. PFP and PFS.[2,3,13,14]

3. Scope

This evaluation considers the medicinal products containing tocilizumab that have a marketing authorisation that allows for supply in Ireland. It aims to achieve efficiencies by the identification of BVB medicines for tocilizumab on the High Tech Arrangement.

Only medicinal products containing tocilizumab:

- that have a marketing authorisation that allows for supply in Ireland, and
- that are on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement, and
- for which a submission was received from the marketing authorisation holder

are included in this BVB medicine evaluation.

The following fall outside the scope of this BVB medicine evaluation process:

- Avtozma®, RoActemra®, Tofidence® and Tyenne® are available in a 20 milligrams (mg)/ millilitres (mL) concentrate for solution for infusion presentation, which are supplied and administered in the hospital setting and are not on the HSE Reimbursement List.
- Avtozma® is also available as a solution for injection in a self-administered injection device presentation, i.e. PFP and PFS; these presentations are currently not on the HSE Reimbursement List.

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 tocilizumab.

All prices and costs are correct as of 13 November 2025.

5. Best-value biological medicines – Tocilizumab

The MMP has identified a BVB medicine for tocilizumab on the High Tech Arrangement. The identification of the BVB medicine 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.[15,16] This involved a review period that included internal evaluation by the MMP and consideration of submissions received from the marketing authorisation holders/suppliers of RoActemra® and Tyenne®.

In line with the *MMP Roadmap for the prescribing of best-value biological (BVB) medicines,* the MMP considered the following criteria when identifying BVB medicines for tocilizumab:[17]

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 Tyenne® (Fresenius Kabi Ireland) as the BVB medicine for tocilizumab on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Tyenne® when issuing a prescription for tocilizumab on the High Tech Arrangement.

Prescribing the recommended BVB medicines reduces the financial burdens 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 marketing authorisation holders/suppliers of medicinal products containing tocilizumab. The consultation phase commenced on Friday 12 April 2024. The closing date for receipt of submissions was 1pm on Monday 27 May 2024.

Submissions were received from the following:

- Fresenius Kabi Ireland
- Roche Products Ireland Limited.

The MMP reviewed the information submitted by the marketing authorisation holders/suppliers and in cases where clarifications or further information was required, this was requested as part of the evaluation process. In addition, both marketing authorisation holders/suppliers were contacted by the MMP on 5 August 2025, to provide them with the opportunity to submit any additional information that had not previously been submitted to the MMP during the BVB medicine evaluation process.

6. Evaluation

As of 13 November 2025, there are two medicinal products containing tocilizumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement:[4]

- RoActemra® solution for injection (SFI) PFP/PFS (Roche Products Ireland Limited)

- Tyenne® SFI PFP/PFS (Fresenius Kabi Ireland).

RoActemra® is the reference medicinal product. Tyenne® is licensed as a biosimilar medicine of the reference medicinal product, RoActemra®.

6.1 Acquisition cost

The reimbursement price, total cost per pack and annual cost of the medicinal products containing tocilizumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement, as of 13 November 2025, are outlined in Table 1.

Table 1 Reimbursement price, total cost per pack and annual cost of medicinal products containing tocilizumab available on the HSE Reimbursement List [3]

Medicinal Product	Reimbursement Price per pack*	Total Cost per pack* (ex VAT)	Total Cost per pack* (inc VAT)	Annual Cost** (ex VAT)	Annual Cost** (inc VAT)
RoActemra® 162 mg SFI PFP/PFS	€656.23	€580.28†	€731.21†	€7,569.55†	€9,538.37†
Tyenne® 162 mg SFI PFP/PFS	€574.18	€574.18	€706.24	€7,489.97	€9,212.65

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 13 November 2025

*Each pack contains four PFP/PFS

**Annual cost reflects use of tocilizumab at the licensed dosage of 162 mg administered subcutaneously once weekly. It does not include the patient care fee paid to community pharmacies.

†The total cost per pack and annual cost of the reference medicine, RoActemra®, takes account of the price reduction to 62.86% of the 1 October 2021 ex-factory price for biological medicines that become a patent-expired non-exclusive biological medicine after 1 January 2022 (clause 8.2.2 of the 2021 Framework Agreement on the Supply and Pricing of Medicines), and the rebate of 12.5% that is applied to patent-expired non-exclusive biological medicines (clause 8.2.3 of the 2021 Framework Agreement on the Supply and Pricing of Medicines).

Submissions received during the BVB medicine evaluation process included revised commercial terms for some of the medicinal products listed in Table 1.[18,19]

Recommendation

Tyenne® has the lowest acquisition cost to the HSE, based on the proposed revised commercial terms that were contained within submissions received as part of the BVB medicine evaluation process. The acquisition cost of Tyenne® (Fresenius Kabi Ireland) falls within the range for designation as a BVB medicine for tocilizumab on the High Tech Arrangement, 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 2 summarises the licensed therapeutic indications for RoActemra® 162 mg SFI PFP/PFS and Tyenne® 162 mg SFI PFP/PFS.

Table 2 Summary of licensed therapeutic indications for RoActemra® 162 mg SFI PFP/PFS and Tyenne® 162 mg SFI PFP/PFS

Medicinal Product	Rheumatoid Arthritis (RA) in adults		Systemic Juvenile Idiopathic Arthritis		Polyarticular Juvenile Idiopathic Arthritis		Giant Cell Arteritis in adults
	Severe, active and progressive RA	Moderate-to-severe active RA	Patients aged 1 year and older	Patients aged 12 years and older	Patients aged 2 years and older	Patients aged 12 years and older	
RoActemra® 162 mg SFI PFP[2]	✓	✓		✓*		✓*	✓
RoActemra® 162 mg SFI PFS[2]	✓	✓	✓		✓		✓
Tyenne® 162 mg SFI PFP[12]	✓	✓		✓*		✓*	✓
Tyenne® 162 mg SFI PFS[12]	✓	✓	✓		✓		✓

mg: milligrams; PFP: pre-filled pen; PFS: pre-filled syringe; RA: rheumatoid arthritis; SFI: solution for injection

*RoActemra® 162 mg SFI PFP and Tyenne® 162 mg SFI PFP should not be used to treat paediatric patients < 12 years of age as there is a potential risk of intramuscular injection due to thinner subcutaneous layer.

Please refer to the relevant Summary of Product Characteristics for full prescribing information.

RoActemra® 162 mg SFI PFP/PFS and Tyenne® 162 mg SFI PFP/PFS, in combination with methotrexate (MTX), are indicated for:[2,3]

- the treatment of severe, active and progressive rheumatoid arthritis (RA) in adults not previously treated with MTX.
- the treatment of moderate-to-severe active RA in adult patients who have either responded inadequately to, or who were intolerant to, previous therapy with one or more disease modifying anti-rheumatic drugs (DMARDs) or tumour necrosis factor (TNF) antagonists.

In these patients, tocilizumab can be given as monotherapy in the case of intolerance to MTX or where continued treatment with MTX is inappropriate.[2,3]

RoActemra® 162 mg SFI and Tyenne® 162 mg SFI are indicated for the treatment of active systemic juvenile idiopathic arthritis (sJIA) in patients one year of age and older (PFS presentation)/12 years of age and older (PFP presentations), who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. Tocilizumab can be given as monotherapy (in case of intolerance to MTX or where treatment with MTX is inappropriate) or in combination with MTX.[2,3]

RoActemra® 162 mg SFI and Tyenne® 162 mg SFI, in combination with MTX, are indicated for the treatment of polyarticular juvenile idiopathic arthritis (pJIA; rheumatoid factor positive or negative and extended oligoarthritis) in patients two years of age and older (PFS presentation)/12 years of age and older (PFP presentations), who have responded inadequately to previous therapy with MTX. Tocilizumab can be given as monotherapy in case of intolerance to MTX or where continued treatment with MTX is inappropriate.[2,3]

RoActemra® 162 mg SFI PFP/PFS and Tyenne® 162 mg SFI PFP/PFS are indicated for the treatment of Giant Cell Arteritis (GCA) in adult patients.[2,3]

RoActemra® and Tyenne® are also available in a 20 mg/mL concentrate for solution for infusion presentation, which are licensed for the same range of therapeutic indications as the PFP/PFS presentations outlined above, with the exception of the treatment of GCA in adult patients. In the case of the treatment of active sJIA, RoActemra® and Tyenne® 20 mg/ml concentrate for solution for infusion are licensed in patients two years of age and older. For all other licensed therapeutic indications, RoActemra® and Tyenne® 20 mg/mL concentrate for solution for infusion are licensed in the same patient population as RoActemra® 162 mg SFI PFS and Tyenne® 162 mg SFI PFS.[2,3]

In addition, RoActemra® and Tyenne® 20 mg/mL concentrate for solution for infusion are also licensed for the:[2,3]

- treatment of coronavirus disease 2019 (COVID-19) in adults who are receiving systemic corticosteroids and require supplemental oxygen or mechanical ventilation
- treatment of chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome (CRS) in adults and paediatric patients two years of age and older.

RoActemra® and Tyenne® 20 mg/mL concentrate for solution for infusion are supplied and administered in the hospital setting and are not on the HSE Reimbursement List. As outlined in section three, these presentations of RoActemra® and Tyenne® therefore fall outside the scope of this BVB medicine evaluation.

Tyenne® 162 mg SFI PFP/PFS are licensed for the same therapeutic indications as the PFP/PFS presentations of the reference biological medicine, RoActemra®.[2,3]

The summary of product characteristics (SmPCs) of the PFP/PFS presentations of the reference biological medicine, RoActemra® and the biosimilar medicine, Tyenne®, contain the same statements in relation to the therapeutic dosage for each of the licensed therapeutic indications for tocilizumab.[2,3]

Recommendation

In relation to the criterion of therapeutic indications, the MMP is of the opinion that the medicinal products containing tocilizumab that are under evaluation for a BVB medicine for tocilizumab are equivalent.

6.3 Formulation considerations

RoActemra® 162 mg SFI PFP/PFS is formulated as a colourless to slightly yellowish solution for injection. It contains the following excipients:[2]

- L-histidine
- L-histidine monohydrochloride monohydrate
- L-arginine/L-arginine hydrochloride
- L-methionine
- polysorbate 80

- water for injections.

Each RoActemra® 162 mg SFI PFP/PFS contains 162 mg of tocilizumab in 0.9 mL; the concentration of tocilizumab is 180 mg/mL.[2]

Tyenne® 162 mg SFI PFP/PFS is formulated as a clear and colourless to pale yellow solution for injection. It contains the following excipients:[3]

- L-arginine
- L-histidine
- L-lactic acid
- sodium chloride
- polysorbate 80
- hydrochloric acid (E507) and/or sodium hydroxide (E524)
- water for injections.

Each Tyenne® 162 mg SFI PFP/PFS contains 162 mg of tocilizumab in 0.9 mL; the concentration of tocilizumab is 180 mg/mL.[3]

In terms of excipients with known effects, RoActemra® 162 mg SFI PFP/PFS does not contain sodium. Tyenne® 162 mg SFI PFP/PFS contains less than 1 millimole of sodium (23 mg) per 0.9 mL dose, i.e. it is essentially 'sodium-free'.[2,3,19] Both RoActemra® 162 mg SFI PFP/PFS and Tyenne® 162 mg SFI PFP/PFS contain polysorbate 80.[2,3]

The formulation of Tyenne® 162 mg SFI PFP/PFS is not identical to the reference medicine, RoActemra® 162 mg SFI PFP/PFS. In the quality aspects section of the European public assessment report (EPAR), this difference in formulation is noted. The EMA state that they accept the justifications provided to support that all minor differences are not clinically meaningful. The EMA conclude that, based on a review of the data provided, the marketing authorisation application for Tyenne® is considered approvable from a quality point of view.[20]

Injection site reactions are reported as a very common (≥ 1/10) adverse reaction under general disorders and administration site conditions in the section on undesirable effects in the SmPC of RoActemra® 162 mg SFI PFP/PFS. Further detail is also provided in the SmPC of the injection site reactions that were reported in the relevant clinical trials for each of the indications for which

RoActemra® 162 mg SFI PFP/PFS is licensed. The injection site reactions reported in the clinical trials included erythema, haematoma, pruritus, pain and swelling, and were mild-to-moderate in severity. None of the reported injection site reactions necessitated drug discontinuation.[2]

The SmPC for the biosimilar medicine Tyenne® 162 mg SFI PFP/PFS includes the same information as RoActemra® in relation to administration site conditions and injection site reactions.[3]

6.3.1 European Public Assessment Report – Tyenne®

In the clinical safety section of the EPAR for Tyenne®, an overview of the adverse drug reactions in the comparative pivotal pharmacokinetic (PK)/pharmacodynamic (PD) study (MS200740-001) and the comparative pivotal safety and efficacy study (FKS456-001) is provided. In both studies, injection site reactions occurred with a higher frequency in the Tyenne® PFS arm than in the EU-licensed RoActemra® PFS arm.[20]

In the PK/PD study MS200740-0001, injection site reactions were slightly more frequent in the Tyenne® arm (18/231 patients, 7.8%) than in the EU-licensed RoActemra® arm (12/225 patients, 5.3%). The same tendency was observed in the pivotal study FKS456-001, where injection site reactions were more frequent in the Tyenne® arm (34/302, 11.3%) than in the EU-licensed RoActemra® arm (14/302 patients, 4.6%) during the core 24-week period of the study. However, in the overall period (up to week 63), the difference was smaller; the proportion of patients with at least one injection site reaction in the Tyenne® and EU-licensed RoActemra® arms were 12.3% and 8.0%, respectively.[20]

The EPAR states that, given the well-characterised similarity between Tyenne® and RoActemra® from a quality and PK perspective, the observed difference in injection site reactions might be a random finding that does not indicate a true difference between Tyenne® and RoActemra®. In addition, the EPAR states that, taking the totality of data and the similarity observed in the quality and PK characterisation of the products into account, Tyenne® is considered to be a biosimilar medicine of RoActemra®.[20]

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 tocilizumab provide a similar offering.

6.4 Product range including pack sizes and strengths available

Table 3 outlines the various presentations that are available for the medicinal products that are under evaluation for a BVB medicine for tocilizumab.

Table 3 Product range of medicinal products under evaluation for a BVB medicine for tocilizumab[2,3,4]

Medicinal Product	162 mg PFP (4 PFP per pack)	162 mg PFS (4 PFS per pack)
RoActemra®	✓	✓
Tyenne®	✓	✓

mg: milligrams; PFP: Pre-filled pen; PFS: Pre-filled syringe

RoActemra® and Tyenne® are available on the HSE Reimbursement List in both single-use PFP and PFS presentations containing 162 mg of tocilizumab. Both are supplied in a pack containing four PFP/PFS.[2-4]

The majority (≈87%) of patients in receipt of a medicinal product containing tocilizumab on the High Tech Arrangement are supplied with a PFP presentation.[6]

RoActemra® and Tyenne® are also available in 4 mL, 10 mL and 20 mL vials containing a 20 mg/mL concentrate for solution for infusion.[2,3,18,19] These presentations of RoActemra® and Tyenne® are supplied and administered in the hospital setting and are not on the HSE Reimbursement List. As outlined in section three, these presentations of RoActemra® and Tyenne® therefore fall outside the scope of this BVB medicine evaluation.

Recommendation

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 tocilizumab provide a similar offering.

6.5 Product stability including storage requirements

Both RoActemra® 162 mg SFI PFS/PFP and Tyenne 162 mg SFI PFP/PFS have a shelf life of three years.[2,3] Both must be stored in a refrigerator between 2°C and 8°C, and should not be frozen.[2,3]

Once removed from the refrigerator, RoActemra® 162 mg SFI PFP/PFS can be stored for up to two weeks at or below a temperature of 30°C.

Prior to administration, RoActemra® SFI 162 mg PFS/PFS should be allowed to reach room temperature (18°C - 28°C) after removing from the refrigerator, by waiting for 25 to 30 minutes (PFS) or 45 minutes (PFP) before injecting. After removing the cap, the injection must be started within three (PFP) or five (PFS) minutes, to prevent the medicine from drying out and blocking the needle. If the injection is not used within three (PFP) or five (PFS) minutes of removing the cap, it should be disposed of in an appropriate manner and a new PFP/PFS should be used.[2]

RoActemra® SFI 162 mg PFP/PFS should be kept in the outer carton of the packaging in order to protect from light and moisture. The PFP/PFS should not be shaken.[2]

Tyenne® 162 mg SFI PFP/PFS can be stored at room temperature (up to 30°C) for a single period of up to 14 days. The PFP/PFS must be protected from light during this 14-day period, and discarded if not used within the 14-day period or by the original expiry date, whichever is earlier.

Prior to administration, Tyenne® SFI 162 mg PFP/PFS should be allowed to reach room temperature after removing from the refrigerator, by waiting for at least 30 minutes (PFS) or 45 minutes (PFP) before injecting. After removing the cap, the injection must be started right away, to prevent the medicine from drying out and blocking the needle. If the injection is not used right away after removing the cap, it should be disposed of in an appropriate manner and a new PFP/PFS should be used.[3]

Tyenne® SFI 162 mg PFP/PFS should be kept in the outer carton of the packaging in order to protect from light. The PFP/PFS should not be shaken.[3]

Recommendation

In relation to the criterion of product stability, the MMP is of the opinion that RoActemra® and Tyenne® provide a similar offering.

6.6 Administration devices

The two medicinal products that are under evaluation for a BVB medicine for tocilizumab are available in both a single-use PFP and PFS. Table 4 provides a summary of various properties for the administration devices of the medicinal products that are under evaluation for a BVB medicine for tocilizumab.

Table 4 Characteristics of administration devices for medicinal products containing tocilizumab under evaluation for a BVB medicine for tocilizumab

	RoActemra®	Tyenne®
Needle gauge†	PFP: 26	PFP: 27
	PFS: 26	PFS: 27
Needle length (mm)	PFP: 12.7	PFP: 12.7
	PFS: 12.7	PFS: 12.7
Safety feature	PFP: Yes	PFP: Yes
	PFS: Yes	PFS: Yes

mm: millimetres; 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 Pre-filled pen

From examination of the patient information leaflets (PILs), SmPCs and submissions for the PFP presentations of RoActemra® and Tyenne®, there appears to be little difference between the administration devices.

The PFP presentation of RoActemra® consists of a 0.9 mL solution for injection in a PFS (type 1 glass), with a staked-in needle, containing 162 mg of tocilizumab assembled into a PFP. The syringe is closed by a rigid needle shield (elastomer seal with a polypropylene shell) and a plunger stopper (butyl rubber with a fluororesin coating). The PFP presentation has a 26-gauge needle, with a needle length of 12.7 millimetres (mm).[2,19]

The PFP presentation of Tyenne® consists of a 0.9 mL solution for injection in a PFS (type 1 glass) with a staked stainless steel needle with a latex-free needle cap, a plunger stopper (bromobutyl rubber), containing 162 mg of tocilizumab assembled into a PFP. The PFP presentation has a 27-gauge needle, with a needle length of 12.7 mm.[3,18]

RoActemra® PFP requires the user to press an activation button to commence the delivery of the dose of tocilizumab, while Tyenne® PFP has button-free delivery, with delivery of the dose of tocilizumab commencing when the user pushes the pen firmly down against their skin. Both of the PFPs have various mechanisms to indicate to the user that the delivery of the injection has commenced, and to signify when it is completed. These include the sounding of a click when the injection has started and finished, and a coloured indicator window to show the progress and completion of the delivery of the dose of tocilizumab. Both PFP presentations have a safety feature

to guard the needle upon delivery of the dose of tocilizumab; once the PFP is lifted away from the skin, a needle shield covers the needle.[2,3]

The PILs contain instructions for the administration of a subcutaneous dose of tocilizumab from the PFP presentations of RoActemra® and Tyenne®. In both cases, the instructions are presented in the form of text with accompanying pictograms.[2,3]

6.6.2 Pre-filled syringe

From examination of the PILs, SmPCs and submissions for the PFS presentations of RoActemra® and Tyenne®, there appears to be little difference between the administration devices.

The PFS presentation of RoActemra® consists of a 0.9 mL solution for injection containing 162 mg of tocilizumab in a PFS (type 1 glass), with a staked-in needle. The syringe is closed by a rigid needle shield (elastomer seal with a polypropylene shell) and a plunger stopper (butyl rubber with a fluororesin coating). The PFS presentation of RoActemra has a 26-gauge needle, with a needle length of 12.7 mm.[2,19]

The PFS presentation of Tyenne® consists of a 0.9 mL solution for injection containing 162 mg of tocilizumab in a PFS (type 1 glass) with a staked stainless steel needle with a latex-free needle cap, a plunger stopper (bromobutyl rubber) and extended finger flanges. The PFS presentation has a 27-gauge needle, with a needle length of 12.7 mm.[3,18]

Both PFS presentations have a safety feature to guard the needle upon delivery of the dose of tocilizumab, with a passive needle guard system in place, i.e. upon release of the plunger having administered the dose, the entire needle is drawn back automatically and covered by the needle safety guard.[2,3,18,19]

The PILs contain instructions for the administration of a subcutaneous dose of tocilizumab from the PFS presentations of RoActemra® and Tyenne®. In both cases, the instructions are presented in the form of text with accompanying pictograms.[2,3]

Recommendation

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 tocilizumab provide a similar offering.

6.7 Patient factors

In their submissions, Fresenius Kabi Ireland and Roche Products Ireland Limited outlined the patient support programmes available when patients are prescribed their medicinal product containing tocilizumab.[18,19]

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

The patient support programmes that are available to patients who are prescribed RoActemra® 162 mg PFP/PFS and Tyenne® 162 mg PFP/PFS are similar in nature, based on the information provided to the MMP as part of the consultation process.

Recommendation

In relation to the criterion of patient factors, the MMP is of the opinion that the patient support programmes offered by Fresenius Kabi and Roche Products Ireland Limited provide a similar offering.

6.8 Expenditure in the therapeutic area and potential for cost savings

Figure 1 outlines total annual expenditure[iii] on medicinal products containing tocilizumab on the High Tech Arrangement from 2015 to 2024. Total annual expenditure on tocilizumab increased from €2.26 million in 2015 to €19.6 million in 2023.[1,6] There was a notable reduction in expenditure in 2024 (to €13.9 million) due to the implementation of relevant clauses of the Framework Agreement on the Supply and Pricing of Medicines and the Framework Agreement on the Supply and Pricing of Generic, Biosimilar and Hybrid Medicines.

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

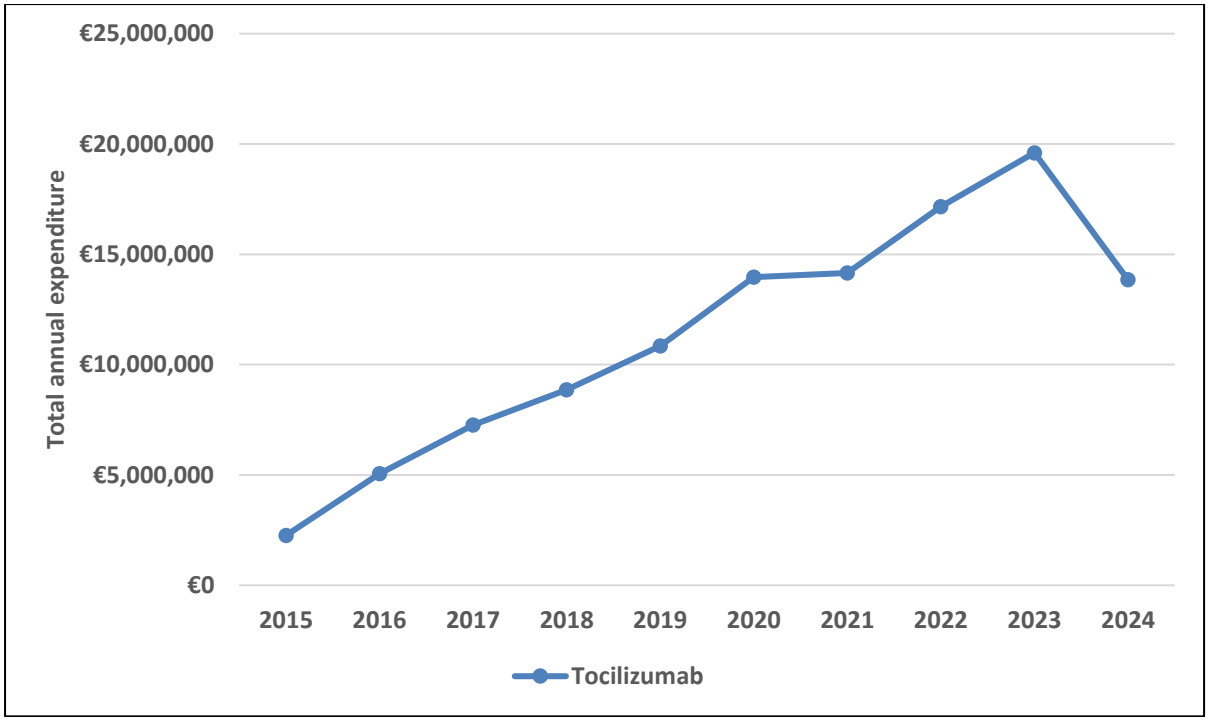

Figure 1 Total annual expenditure on tocilizumab on the High Tech Arrangement 2015 - 2024

Figure 2 outlines the total number of prescription claims per annum for medicinal products containing tocilizumab on the High Tech Arrangement from 2015 to 2023. There has been a significant increase in the number of prescription claims during this time period, from 2,331 in 2015 to 19,276 in 2023.[5]

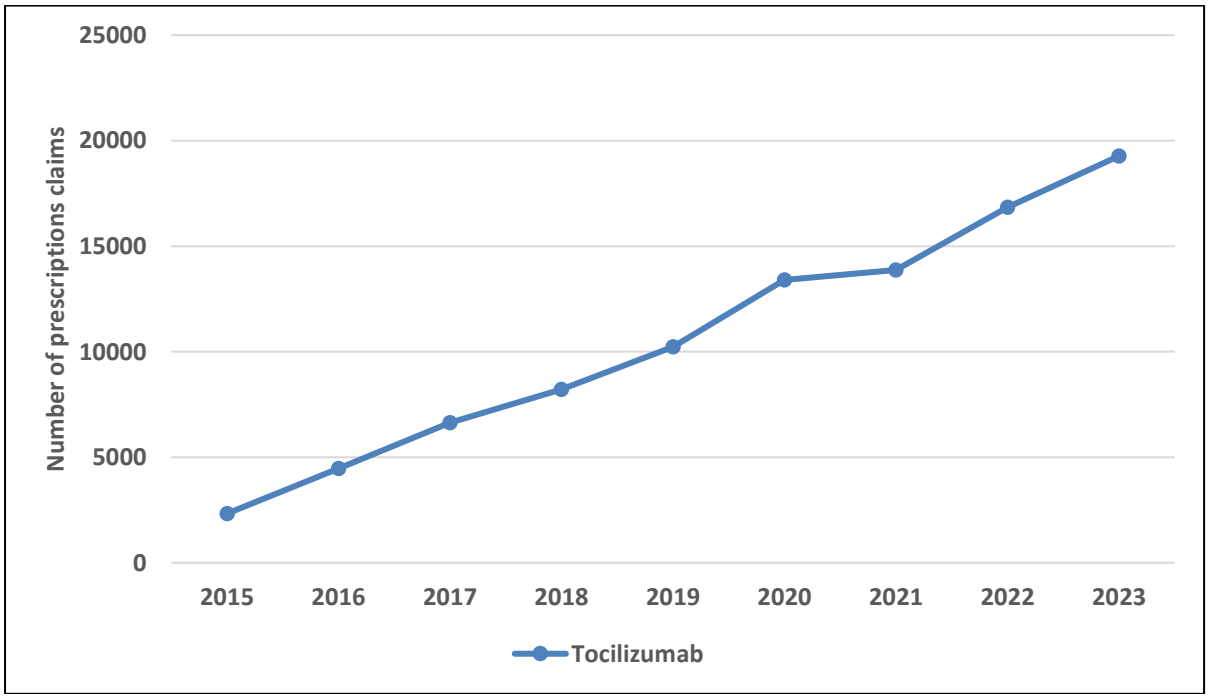

Figure 2 Total number of prescription claims per annum for medicinal products containing tocilizumab on the High Tech Arrangement from 2015 - 2023

Tocilizumab was ranked 11th in terms of the total number of prescription claims paid (19,276) on the High Tech Arrangement in 2023.[5] There are approximately 1,900 patients in receipt of tocilizumab on the High Tech Arrangement on a monthly basis; the vast majority of these patients are currently on RoActemra®, with approximately 14% of patients in receipt of a biosimilar medicine of tocilizumab.[6]

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 tocilizumab. 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.[15] This is reflected in the total cost per pack and annual cost of RoActemra® that are included in Table 1.

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 is relevant to biosimilar medicines containing tocilizumab. 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.[16] This clause applied in the case of the application for the pricing and reimbursement of Tyenne® 162 mg SFI PFP/PFS that was submitted by Fresenius Kabi Ireland.

The current total costs per pack of medicinal products containing tocilizumab on the HSE Reimbursement List, for prescribing and supply on the High Tech Arrangement, as of 13 November 2025 are outlined in Table 1. There is currently little difference (PFP/PFS: €6.10 ex VAT, €24.97 inc VAT) between the total cost per pack (four PFP/PFS) of the reference medicine (RoActemra®) and the biosimilar medicine (Tyenne®). The potential efficiencies resulting from the availability of biosimilar medicines of tocilizumab 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 a BVB medicine for tocilizumab by the

MMP, and the introduction of mechanisms to facilitate prescribing and utilisation of the BVB medicine.

Recommendation

In relation to the criterion of expenditure in the therapeutic area and potential for cost savings, the MMP recommends Tyenne® (Fresenius Kabi Ireland) as the BVB medicine for tocilizumab due to the potential for significant cost savings based on the revised commercial terms proposed in the submissions received as part of the BVB medicine evaluation process.

In addition, the MMP recommends that consideration be given to reviewing the BVB medicine recommendations for tocilizumab if other biosimilar medicines containing tocilizumab are added to the HSE Reimbursement List, due to the potential for further efficiencies arising from increased competition amongst suppliers.

6.9 Clinical guidelines

There are currently no relevant national clinical guidelines available in Ireland for the therapeutic areas or conditions for which the PFP/PFS presentations of medicinal products containing tocilizumab are indicated, i.e. 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. It also recommends that:[21]

- 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.[21]

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 tocilizumab.

6.10 Security of supply to the Irish Market

Fresenius Kabi Ireland and Roche Products Ireland Limited outlined the processes that they have in place for supply of their medicinal product containing tocilizumab to the Irish market. Both outlined the arrangements that they have in place for the supply chain management of their medicinal product containing tocilizumab, including the distribution models that they employ.[18,19]

Recommendation

In relation to the criterion of security of supply to the Irish market, the MMP is of the opinion that Fresenius Kabi Ireland and Roche Products Ireland Limited have both provided evidence of their capacity to meet the ongoing needs of Irish patients with respect to the supply of medicinal products containing tocilizumab.

6.11 Utilisation and clinical experience with the biological medicine

There is significant clinical experience with the use of tocilizumab in the Irish setting, with approximately 1,800 patients in receipt of a medicinal product containing tocilizumab on the High Tech Arrangement on a monthly basis.[6]

The concentrate for solution for infusion presentation of the reference medicine, RoActemra®, first received a marketing authorisation in 2009. RoActemra® 162 mg SFI PFS was added to the HSE Reimbursement List on 1 February 2015, for prescribing and supply on the High Tech Arrangement. The PFP presentation was added to the HSE Reimbursement List on 1 September 2018, for prescribing and supply on the High Tech Arrangement.[22]

In September 2023, Tyenne® was the first biosimilar medicine containing tocilizumab to receive a marketing authorisation from the European Commission, following consideration of a marketing authorisation application via the EMA centralised procedure. The PFP and PFS presentations of Tyenne® 162 mg SFI were added to the HSE Reimbursement List on 1 December 2023, for prescribing and supply on the High Tech Arrangement.[22]

The majority of patients accessing tocilizumab via the High Tech Arrangement are currently on RoActemra®, with approximately 14% of patients in receipt of a biosimilar medicine of tocilizumab in

July 2025.[6] Other European healthcare systems have observed higher rates of uptake of biosimilar medicines containing tocilziumab.[18]

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.[7,23]

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.[8] The clinical experience, therefore, obtained with RoActemra® is transferable to the biosimilar medicines of tocilizumab.

The MMP acknowledge the significant clinical experience that has been obtained in Ireland with the reference medicine, RoActemra®. Biosimilars of tocilizumab have only recently become available; available data indicates that these are being incorporated into clinical practice in Ireland.[6] Other European healthcare systems have observed higher rates of uptake of biosimilar medicines containing tocilizumab than those achieved in Ireland to date.[18] This demonstrates that clinical experience is being obtained for biosimilar medicines of tocilizumab within a short timeframe.

Tocilizumab is predominately prescribed in the speciality of rheumatology. The MMP has previously recommended BVB medicines for adalimumab and etanercept; both of these biological medicines are used in the treatment of conditions in the speciality of rheumatology. Since May 2019, over 17,500 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 speciality of rheumatology.[9] This demonstrates that significant experience has being obtained with biosimilar medicines in the speciality of rheumatology.

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 tocilizumab that are under evaluation for a BVB medicine for tocilizumab 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:

- innovation and research
- resources and capabilities to support healthcare professionals.

The MMP is of the opinion that no new relevant material was submitted under this criterion that had not been considered under 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 tocilizumab, were identified from the Irish clinical societies for the specialities who would be involved in prescribing medicinal products containing tocilizumab on the HSE Reimbursement List (i.e. 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.[24]

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.[25]

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 clinical 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.[23]

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.[8]

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 for tocilizumab:

1. Both medicinal products are licensed for the same range of therapeutic indications.
2. Both medicinal products are available in a PFP and PFS presentation containing 162 mg/0.9 mL of tocilizumab.
3. Both medicinal products were 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.
4. The commercially confidential pricing proposals that were included in the submissions received as part of the BVB medicine evaluation process for tocilizumab. The acquisition cost of Tyenne® (Fresenius Kabi Ireland) falls within the range for designation as a BVB medicine for tocilizumab, based on the revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.
5. The potential for significant savings that would arise from the prescribing and utilisation of Tyenne®, based on the proposed revised commercial terms included in the submissions received as part of the BVB medicine evaluation process.

The MMP recommends Tyenne® (Fresenius Kabi Ireland) as the BVB medicine for tocilizumab on the High Tech Arrangement.

7. MMP Recommendations

The MMP recommends Tyenne® (Fresenius Kabi Ireland) as the BVB medicine for tocilizumab on the High Tech Arrangement.

Clinicians should give due consideration to prescribing Tyenne® when issuing a prescription for tocilizumab on the High Tech Arrangement.

Prescribing the recommended BVB medicines reduces the financial burdens 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 tocilizumab, the clinician should prescribe Tyenne®.

Switching

Patients currently on tocilizumab should be considered for switching to Tyenne® at the earliest possible opportunity.

The MMP recommends that all new patients being initiated on tocilizumab on the High Tech Arrangement should be prescribed the MMP BVB medicine, Tyenne®. Patients currently receiving tocilizumab on the High Tech Arrangement should be considered for switching to the BVB medicine (Tyenne®) at the earliest possible opportunity.

In addition, the MMP recommends that consideration be given to reviewing the BVB medicine recommendations for tocilizumab if other biosimilar medicines containing tocilizumab are added to the HSE Reimbursement List, due to the potential for further efficiencies arising from increased competition amongst suppliers.

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