

**5.22 ADALIMUMAB,
Injection 80 mg in 0.8 mL pre-filled pen
Injection 80 mg in 0.8 mL pre-filled syringe,
Yuflyma[®],
Celltrion Healthcare Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 4 submission sought to list a biosimilar brand of adalimumab (Yuflyma[®]) in the forms of 80 mg in 0.8 mL pre-filled pen (PFP) and pre-filled syringe (PFS) under the same circumstances as the PBS-listed reference biologic Humira[®] 80 mg in 0.8 mL PFP and PFS.

2 Background

Registration status

- 2.1 Yuflyma 80 mg in 0.8 mL in PFP and PFS were Therapeutic Goods Administration (TGA) registered on 30 June 2023 and determined to be biosimilar to Humira 80 mg in 0.8 mL PFP and PFS for the same indications.
- 2.2 Humira, the reference biologic, and the Amgevita[®], Hadlima[®], Hyrimoz[®] and Idacio[®] biosimilar brands of adalimumab are listed on the PBS.

Previous PBAC consideration

- 2.3 This is the first PBAC submission for Yuflyma 80 mg in 0.8 mL PFS and PFP.
- 2.4 The PBAC recommended Yuflyma 40 mg in 0.4 mL PFS and PFP at its July 2022 meeting.

3 Requested listing

- 3.1 The submission requested listing Yuflyma under the same circumstances as the PBS-listed reference biologic Humira 80 mg in 0.8 mL PFS and PFP.
- 3.2 The indications for which Yuflyma 80 mg in 0.8 mL PFS and PFP requested listing were as follows:
- Complex refractory fistulising Crohn disease
 - Severe Crohn disease
 - Moderate to severe ulcerative colitis
 - Moderate to severe hidradenitis suppurativa
 - Severe chronic plaque psoriasis

- 3.3 The comparator, Humira 80 mg in 0.8 mL, is Authority required (Written) General Schedule for all listed indications.
- 3.4 Moderate to severe hidradenitis suppurativa is the only indication that has a continuing treatment phase listing for adalimumab 80 mg in 0.8 mL. All other listings for adalimumab 80 mg in 0.8 mL are for initial treatment only.
- 3.5 The submission requested that the above restrictions apply to Yuflyma 80 mg in 0.8 mL and a separate Authority Required (Streamlined) listing of Yuflyma applies for subsequent continuing treatment for moderate to severe hidradenitis suppurativa.
- 3.6 If listed, Yuflyma will be the first PBS-listed biosimilar brand of adalimumab in the 80 mg in 0.8 mL presentation.
- 3.7 The PBAC was asked to advise whether biosimilar uptake drivers, including the differential authority requirements for subsequent continuing treatment between the reference and biosimilar brands and inclusion of an administrative note encouraging the use of biosimilar brands for treatment naïve patients, should apply to Yuflyma 80 mg in 0.8 mL if it is recommended for listing.
- 3.8 The PBAC was asked to advise, under Section 101(4AACD) of the *National Health Act 1953* whether, in the Schedule of Pharmaceutical Benefits:
 - Yuflyma 80 mg in 0.8 mL PFS and Humira 80 mg in 0.8 mL PFS should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule)
 - Yuflyma 80 mg in 0.8 mL PFP and Humira 80 mg in 0.8 mL PFP should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule)
- 3.9 The requested restrictions are complex due to the number of items and indications required for the listing. If recommended by the PBAC, the implementation of these listings may occur across separate stages. As the submission requested the same restrictions as the reference brand, the full restrictions have not been reproduced here.

3.10 The summary of the listings follows:

Severe Crohn disease

Name, restriction, manner of administration, form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12419P	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12426B	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12372E	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12409D	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd

Complex refractory Fistulising Crohn disease

Name, restriction, manner of administration, form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12360M	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12393G	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd

Moderate to severe ulcerative colitis

Name, restriction, manner of administration, form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12374G	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12339K	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd

Severe chronic plaque psoriasis

Name, restriction, manner of administration, form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12447D	1	1	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12394H	1	1	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd

Moderate to severe hidradenitis suppurativa

Name, restriction, manner of administration, form	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12448E	2	2	5	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12449F	2	2	2	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	12450G	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12395J	2	2	2	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12408C	2	2	5	Yuflyma® Celltrion Healthcare Australia Pty Ltd
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	12524E	3	3	0	Yuflyma® Celltrion Healthcare Australia Pty Ltd

4 Comparator

- 4.1 The submission nominated the reference brand of adalimumab, Humira, as the main comparator. The PBAC considered that this was appropriate.

5 Consideration of the evidence

Sponsor hearing

5.1 There was no hearing for this item.

Consumer comments

5.2 The PBAC noted and welcomed input from Crohn's and Colitis Australia (CCA) via the Consumer Comments facility on the PBS website. CCA supported the listing of adalimumab for the treatment of Crohn disease and ulcerative colitis. CCA supported the approval of biosimilar medications where they are clinically equivalent and provide an economic or access benefit to people living with inflammatory bowel disease and or the community. CCA noted that many consumers enjoy the freedoms associated with subcutaneous administration over infusion.

Clinical trials

5.3 The studies presented in the submission formed part of the TGA submission to register Yuflyma as a biosimilar to Humira. The submission stated that the TGA application for Yuflyma 80 mg PFS and PFP did not include any additional in vivo studies, beyond that included in the 40 mg injection TGA application since bioequivalence and clinical usability demonstrated with clinical data with a small dose is not expected to change for small differences between the two strengths (p 20. of submission main body).

5.4 The submission re-presented clinical evidence supporting the effectiveness and safety of Yuflyma, which was also provided in the earlier Yuflyma 40 mg submission at the July 2022 PBAC meeting.

5.5 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

5.6 The submission conducted a literature search, identifying 4 comparative studies of Yuflyma versus Humira. Only 2 studies were considered relevant (CT-P17 3.1 and CT-P17 3.2). The submission therefore re-provided results of CT-P17 3.1 and the supportive study (CTP-17 3.2) (Table 1). No additional relevant studies were located.

Table 1: Studies presented in the submission

Trial ID	Protocol/Publication title	Study Objectives (Related to Safety)	Study Drug and Dose	No. of Subjects/ Patients Assigned to Treatment
CT-P17 3.1	A Randomized, Active-Controlled, Double-Blind, Phase 3 Study to Compare Efficacy and Safety of CT-P17 with EU-approved Humira when Co-administered with Methotrexate in Patients with Moderate to Severe Active Rheumatoid Arthritis. PROTOCOL NUMBER CT-P17 3.1. 24 August 2020 (Celltrion Inc 2020)	Study to Compare Efficacy and Safety of CT-P17 With Humira in Patients With Active Rheumatoid Arthritis (Celltrion 2021)	Yuflyma (biosimilar CT-P17) 100 mg/mL, 40 mg dose every other week	324 (50%) for Yuflyma only (303 continued in treatment period I) 152 completed treatment period I on Humira and complete “maintenance” or period II of the study taking Yuflyma
CT-P17 3.2	Clinical Study Report: A Phase 3, Open-label, Single-arm, Multiple-dose Study to Evaluate Usability of Subcutaneous Auto-injector of CT-P17 in Patients with Moderate to Severe Active Rheumatoid Arthritis. PROTOCOL NUMBER CT-P17 3.2. 20 August 2020 (Celltrion Inc 2020)	Study to Evaluate Usability of Subcutaneous Auto-injector of CT-P17 in Patients With Active Rheumatoid Arthritis (Celltrion 2021)	Yuflyma (biosimilar CT-P17) 100 mg/mL, 40 mg dose every other week	62

Source: Table 1, paragraph 5.3, adalimumab, Public Summary Document (PSD) July 2022 PBAC Meeting

Clinical claim

- 5.7 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Yuflyma compared with Humira.
- 5.8 The PBAC considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety was reasonable.

Economic analysis

- 5.9 The submission presented a cost minimisation analysis of Yuflyma compared with Humira. The submission proposed the same AEMP for Yuflyma as Humira for the equivalent form and strength.
- 5.10 The equi-effective doses presented in the submission were 1 mg of adalimumab in Yuflyma 80 mg = 1 mg of adalimumab in Humira 80 mg.

Estimated PBS usage and financial implications

5.11 That submission stated that it is expected that Yuflyma 80 mg in 0.8 mL will substitute for Humira 80 mg in 0.8 mL over the next 6 years. The submission presented proportions of adalimumab substituted by Yuflyma 80 mg in 0.8 mL in the below table.

Table 2: Estimated proportion of other brands of adalimumab displaced by Yuflyma 80 mg in 0.8 mL

	2023	2024	2025	2026	2027	2028	2029
Estimated script volume for adalimumab 80 mg in 0.8 mL	■ ¹	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
Estimated annual rate of growth	10%	10%	10%	10%	10%	10%	10%
Proportion applicable to indication	100%	100%	100%	100%	100%	100%	100%
Proportion displaced by Yuflyma 80 mg in 0.8 mL (%)	■	■	■	■	■	■	■
Number displaced by Yuflyma 80 mg in 0.8 mL	-	■ ²	■ ³	■ ³	■ ³	■ ⁴	■ ⁴

Source: Submission main body

The redacted values correspond to the following ranges:

¹ 500 to < 5,000

² 5,000 to < 10,000

³ 10,000 to < 20,000

⁴ 20,000 to < 30,000

5.12 The submission requested the same price as the as the existing brand of adalimumab 80 mg in 0.8 mL on the PBS (Humira).

5.13 The submission stated that the listing of Yuflyma 80 mg in 0.8 mL is estimated to have no meaningful impact on the PBS/RPBS, supported by Table 3.

Table 3: Estimated net cost to the PBS/RPBS for Yuflyma 80 mg in 0.8 mL

	2024	2025	2026	2027	2028	2029
Estimated financial implications of Yuflyma 80 mg in 0.8 mL						
to PBS	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
to RPBS	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
to PBS/RPBS	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
Estimated financial implications of Adalimumab (Humira 80 mg in 0.8 mL)						
to PBS	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
to RPBS	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
to PBS/RPBS	■ ²	■ ²	■ ²	■ ²	■ ²	■ ²
Net financial implications						
to PBS (Saving)	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
to RPBS (Saving)	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹
to PBS/RPBS (Saving)	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹	■ ¹

Source: Submission main body

The redacted values correspond to the following ranges

¹ \$0 to < \$10 million

² Net cost saving

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required listing of adalimumab (Yuflyma) in the forms of 80 mg in 0.8 mL pre-filled pen (PFP) and pre-filled syringe (PFS) under the same circumstances as the PBS-listed reference biologic Humira 80 mg in 0.8 mL PFP and PFS for the following indications:
- Complex refractory fistulising Crohn disease
 - Severe Crohn disease
 - Moderate to severe ulcerative colitis
 - Moderate to severe hidradenitis suppurativa
 - Severe chronic plaque psoriasis
- 6.2 The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Yuflyma 80 mg in 0.8 mL PFP and PFS would be acceptable if it were cost-minimised to Humira.
- 6.3 The PBAC advised the equi-effective doses to be 1 mg of Yuflyma = 1 mg of Humira.
- 6.4 The PBAC accepted the claim of biosimilarity for Yuflyma 80 mg in 0.8 mL PFP and PFS compared to Humira. The PBAC noted the clinical evidence presented aligned with the evidence presented to the TGA to inform its outcome of bioequivalence.
- 6.5 The PBAC advised that biosimilar uptake drivers, including the differential authority requirements for subsequent continuing treatment between the reference and biosimilar brands and inclusion of an administrative note encouraging the use of

biosimilar brands for treatment naïve patients, should apply to Yuflyma 80 mg in 0.8 mL PFP and PFS.

- 6.6 The PBAC advised that, under Section 101(4AACD) of the National Health Act 1953 (the Act), in the Schedule of Pharmaceutical Benefits:
- Yuflyma 80 mg in 0.8 mL PFS and Humira 80 mg in 0.8 mL PFS should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule)
 - Yuflyma 80 mg in 0.8 mL PFP and Humira 80 mg in 0.8 mL PFP should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule)
- 6.7 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits, Yuflyma PFP should not be considered equivalent for the purposes of substitution with any adalimumab PFS, consistent with its previous considerations of adalimumab.
- 6.8 The PBAC considered that the listing of Yuflyma 80 mg in 0.8 mL PFP and PFS is expected to be cost-neutral to Government given that Yuflyma will likely substitute for the reference biologic Humira and therefore not increase overall market utilisation.
- 6.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Yuflyma is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Humira, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022 for Pricing Pathway A were not met.
- 6.10 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add adalimumab biosimilar brand Yuflyma, in the forms 80 mg in 0.8 mL PFS and PFP, with schedule equivalence ('a' flag) for the same indications as Humira 80 mg in 0.8 mL PFS and PFP as noted in Section 6.
- 7.2 Amend existing/recommended listing as follow:
- Authority Required listing of Yuflyma 80 mg in 0.8 mL PFS and PFP, with the Authority type for each treatment phase and indication to be consistent with current listings for Humira. A separate Authority Required (Streamlined) listing

of Yuflyma for the subsequent continuing treatment restriction for moderate to severe hidradenitis suppurativa.

- The application of the ‘Biosimilar prescribing policy’ administrative note encouraging the use of biosimilar brands for treatment naïve patients.

Prescribing of the biosimilar brand Yuflyma is encouraged for treatment naïve patients.

Encouraging biosimilar prescribing for treatment naïve patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the B Medicines webpage (www.health.gov.au/healthtopics/medicines)

Add ‘Yuflyma’ brand to existing listings below

Complex refractory Fistulising Crohn disease

PBS Number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
12360M	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	GE	3	3	0
12393G	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		3	3	0

Moderate to severe ulcerative colitis

PBS Number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
12374G	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	GE	3	3	0
12339K	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		3	3	0

Severe Crohn disease

PBS Number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
12419P	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	GE	3	3	0
12426B	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device		3	3	0

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12372E	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		3	3	0
12409D	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		3	3	0

Severe chronic plaque psoriasis

PBS Number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
12447D	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	GE	1	1	0
12394H	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		1	1	0

Moderate to severe hidradenitis suppurativa

PBS Number	MPP Preferred Term	Program	Maximum Quantity Packs	Maximum Quantity units	No. of repeats
12448E	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	GE	2	2	5
12449F	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device		2	2	2
12450G	adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device		3	3	0
12395J	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		2	2	2
12408C	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		2	2	5
12524E	adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe		3	3	0

Create new streamlined subsequent continuing listing for Moderate to severe hidradenitis suppurativa as below:

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MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ADALIMUMAB					
adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device	NEW	1	1	5	Yuflyma
adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	NEW	1	1	5	Yuflyma
Restriction Summary [NEW] / Treatment of Concept: [NEW]					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
(for internal Dept. use)	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required: Streamlined				
	Administrative Advice: Any queries concerning the arrangements to prescribe may be directed to Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).				
	Administrative Advice: Pharmaceutical benefits that have the form adalimumab 80 mg/0.8 mL injection, 0.8 mL pen device and pharmaceutical benefits that have the form adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe are equivalent for the purposes of substitution.				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Indication: Moderate to severe hidradenitis suppurativa				
	Treatment Phase: Subsequent continuing treatment				
	Clinical criteria:				
	Patient must have previously received PBS-subsidised treatment with this drug for this condition under the Continuing treatment restriction				
	AND				
	Clinical criteria:				
	Patient must have demonstrated a response to treatment with this drug for this condition				
	Treatment criteria:				
	Must be treated by a dermatologist				
	Prescribing Instructions: A response to treatment is defined as: Achieving Hidradenitis Suppurativa Clinical Response (HiSCR) of a 50% reduction in AN count compared to baseline with no increase in abscesses or draining fistulae.				
	Prescribing Instructions: A patient must not receive more than 24 weeks of treatment per subsequent continuing treatment course authorised under this restriction.				

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.