

**5.17 Adalimumab,
Injection 40 mg in 0.4 mL pre-filled pen,
Injection 40 mg in 0.4 mL pre-filled syringe,
Yuflyma[®],
Celltrion Healthcare Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission sought Section 85 and Section 100 Highly Specialised Program (HSD) listings of a new biosimilar brand of adalimumab (Yuflyma[®]) 40 mg in the forms of 0.4 mL solution for injection in pre-filled pen (PFP) and pre-filled syringe (PFS) presentations under the same circumstances as the PBS-listed reference biologic Humira[®].

2 Background

Registration status

- 2.1 Yuflyma was registered with the Therapeutic Goods Administration (TGA) on 25 March 2022 and was determined to be a biosimilar to the reference brand Humira. Yuflyma 40 mg has the same indications as Humira 40 mg.

Previous PBAC consideration

- 2.2 Yuflyma has not previously been considered by the PBAC.

Current status

- 2.3 Humira the reference biologic and the Amgevita[®], Hadlima[®], Hyrimoz[®] and Idacio[®] biosimilar brands of adalimumab are listed on the PBS.
- 2.4 If listed, Yuflyma will be the first PBS-listed biosimilar brand of adalimumab in the 40 mg in 0.4 mL presentation. Amgevita, Hadlima, Hyrimoz and Idacio are PBS-listed in the 40 mg in 0.8 mL presentation.

For more detail on PBAC's view, see section 6 PBAC outcome.

3 Requested listing

- 3.1 The submission requested listing Yuflyma under the same circumstances as the PBS-listed reference biologic Humira 40 mg in 0.4 mL PFS and PFP.
- 3.2 The PBAC was asked to advise whether biosimilar uptake drivers which currently apply to Amgevita, Hadlima, Hyrimoz and Idacio, including the differential authority requirements for subsequent continuing treatment with 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 if it is recommended for listing.

3.3 The PBAC was asked to advise, under Section 101(4AACD) of the Act whether, in the Schedule of Pharmaceutical Benefits:

- Humira and Yuflyma PFS should be treated as equivalent to each other; and Humira and Yuflyma PFP should be treated as equivalent to each other for the purposes of substitution (i.e. ‘a’ flagged in the schedule)
- 40 mg in 0.4 mL Yuflyma PFS and 40 mg in 0.8 mL Amgevita, Hadlima, Hyrimoz and Idacio PFS should be treated as equivalent to each other for the purpose of substitution
- 40 mg in 0.4 mL Yuflyma PFP and 40 mg in 0.8 mL Amgevita, Hadlima, Hyrimoz and Idacio PFP should be treated as equivalent to each other for the purpose of substitution

3.4 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.

3.5 The summary of the listing follows:

Name, restriction, manner of administration, form	Max. Qty (packs)	Max. Qty (units)	No. of repeats	PBS item code	Proprietary name and manufacturer
ADALIMUMAB adalimumab 40 mg/0.4 mL injection, pre-filled pen	1	2	2	12345R	Yuflyma® Celltrion Healthcare Australia Pty Ltd
ADALIMUMAB adalimumab 40 mg/0.4 mL injection, pre-filled syringe	1	2	2	12338J	Yuflyma® Celltrion Healthcare Australia Pty Ltd

The sponsor has requested the same number of items and indications as Humira 40 mg in 0.4 mL. Maximum quantity packs and units and number of repeats will change to match the item code and indication. The example indication used is “Severe Crohn disease Treatment Phase: Initial treatment - Initial 1 (new patient)”.

For more detail on PBAC’s view, see section 6 PBAC outcome.

4 Comparator

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

For more detail on PBAC’s view, see section 6 PBAC outcome.

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 the input from Crohn's & Colitis Australia (CCA) via the Consumer Comments facility on the PBS website. CCA's comments described a range of benefits for patients with Crohn's disease and ulcerative colitis associated with treatment with adalimumab. The organisation noted that the subcutaneous administration of Yuflyma improves quality of life and access for patients, and that not needing to attend a medical facility for treatment decreases absence from work and reduces travel, particularly for those in remote or regional areas or with restricted mobility.

Clinical studies

- 5.3 The submission presented the following clinical studies. As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

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

5.4 The studies presented in the submission formed part of the TGA submission to register Yuflyma as a biosimilar to Humira.

Clinical claim

5.5 The submission claimed the comparability of Yuflyma with Humira had been demonstrated with regard to physiochemical characteristics and efficacy and safety outcomes. While the sponsor did not provide a clinical evaluation report, the TGA has confirmed that Yuflyma is biosimilar to Humira and that there were no clinically meaningful differences between Yuflyma and Humira in the submitted comparative pharmacology, pharmacokinetic and toxicity studies.

5.6 The PBAC considered that the claims of non-inferior comparative effectiveness and safety compared to Humira were reasonable.

Economic analysis

- 5.7 The submission did not present an economic analysis as it was a Category 3 submission. The submission proposed the same AEMP for Yuflyma as Humira for the equivalent form and strength.
- 5.8 The equi-effective doses presented in the submission were 1 mg of Yuflyma = 1 mg of Humira. The PBAC considered that this was appropriate.

Estimated PBS utilisation and financial implications

- 5.9 The submission stated that the listing of Yuflyma would not increase the overall market for adalimumab, and therefore would be cost-neutral to Government. The PBAC considered that this was appropriate as it is expected that Yuflyma would substitute for Humira or the other biosimilar brands of adalimumab.

For more detail on PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required listing of adalimumab (Yuflyma) in the form of 40 mg in 0.4 mL PFS and PFP as a biosimilar brand of Humira on the General Schedule (Section 85) and Section 100 (Highly Specialised Drug Program). The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Yuflyma PFP and PFS would be acceptable if it were cost-minimised to Humira for the following indications:
- Severe Crohn disease
 - Moderate to severe ulcerative colitis
 - Severe active juvenile idiopathic arthritis
 - Complex refractory fistulising Crohn disease
 - Severe active rheumatoid arthritis
 - Severe psoriatic arthritis
 - Ankylosing spondylitis
 - Severe chronic plaque psoriasis
 - Moderate to severe hidradenitis suppurativa
- 6.2 The PBAC advised the equi-effective doses to be 1 mg of Yuflyma = 1 mg of Humira and all other biosimilar brands and formulations of adalimumab.
- 6.3 The PBAC considered that the claim of biosimilarity for Yuflyma compared to Humira was reasonably supported by the data. The TGA Delegate noted that Yuflyma is biosimilar to Humira and that there were no clinically meaningful differences in the comparative pharmacology, pharmacokinetic and toxicity studies.

6.4 The PBAC considered that biosimilar uptake drivers should be applied to Yuflyma, consistent with the current PBS listings for adalimumab biosimilar brands, including:

- Authority Required listing of Yuflyma for the initial and first continuing treatment restrictions, with the Authority type for each indication to be consistent with current listings for the other biosimilar brands of adalimumab.
- A separate Authority Required (Streamlined) listing of Yuflyma for the subsequent continuing treatment restrictions.
- The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients (this note will need to be updated for the other biosimilar brands of adalimumab to include Yuflyma in the list):

Prescribing of the biosimilar brand, Amgevita, Hadlima, Hyrimoz, Idacio or 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 Medicines webpage (www.health.gov.au/health-topics/medicines)

6.5 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits:

- Humira and Yuflyma PFS should be treated as equivalent to each other; and Humira and Yuflyma PFP should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the Schedule).
- 40 mg in 0.4 mL Yuflyma PFS and 40 mg in 0.8 mL Amgevita, Hadlima, Hyrimoz and Idacio PFS should be treated as equivalent to each other for the purpose of substitution (i.e. 'a' flagged in the Schedule).
- 40 mg in 0.4 mL Yuflyma PFP and 40 mg in 0.8 mL Amgevita, Hadlima, Hyrimoz and Idacio PFP should be treated as equivalent to each other for the purpose of substitution (i.e. 'a' flagged in the Schedule).

6.6 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.

6.7 The PBAC noted that the listing of Yuflyma will not increase overall market utilisation as it is expected that Yuflyma would substitute for Humira or other biosimilar brands of adalimumab.

6.8 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.

- 6.9 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 new adalimumab brand (Yuflyma) with schedule equivalence ('a' flag) for the same indications as Humira as noted in Section 3.

- 7.2 Amend existing/recommended listing as follows:

- Authority Required listing of Yuflyma for the initial and first continuing treatment restrictions, with the Authority type for each indication to be consistent with current listings for the other biosimilar brands of adalimumab.
- A separate Authority Required (Streamlined) listing of Yuflyma for the subsequent continuing treatment restriction.
- The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients (this note will need to be updated for the other biosimilar brands of adalimumab to include Yuflyma in the list):

Prescribing of the biosimilar brand Amgevita, Hadlima, Hyrimoz, Idacio or 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/health-topics/medicines)

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.