

**5.02 ADALIMUMAB,
Injection 40 mg in 0.4 mL pre-filled syringe,
Injection 40 mg in 0.4 mL pre-filled pen,
Hadlima[®],
Organon Pharma Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 4 submission sought to list a biosimilar brand of adalimumab (Hadlima[®]) in the forms of 40 mg in 0.4 mL pre-filled pen (PFP) and pre-filled syringe (PFS) under the same circumstances as the PBS-listed reference biologic Humira[®] 40 mg in 0.4 mL PFP and PFS.

2 Background

Registration status

- 2.1 Hadlima 40 mg in 0.4 mL PFP and PFS were registered on the ARTG on 15 February 2023 and determined to be biosimilars to the reference brand Humira 40 mg in 0.4 mL. Hadlima 40 mg in 0.4 mL PFP and PFS are approved for the same indication as Humira 40 mg in 0.4 mL.

Previous PBAC consideration

- 2.2 This is the first PBAC submission for Hadlima 40 mg in 0.4 mL PFS and PFP.
- 2.3 The PBAC recommended Hadlima 40 mg in 0.8 mL PFP and PFS for rheumatoid arthritis at its July 2018 meeting, and for its additional PBS-listed indications at its July 2020 meeting.

3 Requested listing

- 3.1 The submission requested listing Hadlima 40 mg in 0.4 mL under the same circumstances as the PBS-listed reference biologic Humira 40 mg in 0.4 mL PFS and PFP.
- 3.2 The submission noted there are currently two brands of adalimumab 40 mg in 0.4 mL PFP and PFS listed on the PBS: Humira and Yuflyma. These are listed for the same indications as Hadlima 40 mg in 0.8 mL, and by extension applies to all other brands of adalimumab, as noted below:
- Ankylosing spondylitis
 - Complex refractory fistulising Crohn disease
 - Severe Crohn disease

- Moderate to severe ulcerative colitis
- Moderate to severe hidradenitis suppurativa
- Severe active juvenile idiopathic arthritis
- Severe active rheumatoid arthritis
- Severe chronic plaque psoriasis
- Severe psoriatic arthritis

- 3.3 The submission requested the same biosimilar uptake drivers for listing Hadlima that were implemented for Yuflyma, including an Authority Required (Streamlined) listing of Hadlima for all subsequent continuing treatment restrictions and the application of the ‘Biosimilar prescribing policy’ administrative note encouraging the use of biosimilar brands for treatment naïve patients.
- 3.4 The submission requested that Hadlima 40 mg/0.4 mL PFP and adalimumab 40 mg/0.8 mL PFP are equivalent for the purposes of substitution, and Hadlima 40 mg/0.4 mL PFS and adalimumab 40 mg/0.8 mL PFS are equivalent for the purposes of substitution.
- 3.5 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. An example 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	Hadlima® Organon Pharma Pty Ltd
ADALIMUMAB adalimumab 40 mg/0.4 mL injection, pre-filled syringe	1	2	2	12338J	Hadlima® Organon Pharma 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)”.

4 Comparator

- 4.1 The submission nominated the reference brand of adalimumab, Humira, as the main comparator. This was appropriate because Humira has previously been accepted as a comparator to other adalimumab biosimilars, such as Amgevita (July 2018 Public Summary Document (PSD)), Hyrimoz (March 2020 PSD), Idacio (November 2020 PSD), Yuflyma (July 2022 PSD) and Adalicip (July 2023 PSD).

5 Consideration of the evidence

Sponsor hearing

5.1 There was no sponsor hearing.

Consumer comments

5.2 The PBAC noted and welcomed the input from consumer group/organisation (1) Crohn's and Colitis Australia (CCA) via the Consumer Comments facility on the PBS website. The organisation stated that it supported the listing of Hadlima for the treatment of Crohn disease and ulcerative colitis, in particular, the 0.4 mL preparation may provide reduced discomfort which is important to those who are resistant to receiving injections both paediatric and adult. Additionally, the CCA noted that having biologic/biosimilars available in this treatment space provides economic and access benefits to people living with inflammatory bowel disease and/or the community. The PBAC noted the two patient comments in the CCA input which described the patients' positive experiences with adalimumab for the treatment of Crohn disease.

Clinical trials

5.3 The submission presented the following clinical studies. The Phase I clinical study demonstrated the pharmacokinetic comparability of Hadlima 40 mg in 0.4 mL with Hadlima 40 mg in 0.8 mL. As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

Table 1: Studies and associated reports presented in the submission

Study ID	Protocol title/ Publication title	Publication citation
SB5-1003	Therapeutic equivalence (and bioequivalence) between HADLIMA® 40 mg/0.4 mL and HADLIMA® 40 mg/0.8 mL Ahn SS, Lee M, Baek Y, Lee S. A Randomized Pharmacokinetic Study in Healthy Male Subjects Comparing a High-concentration, Citrate-free SB5 Formulation (40 mg/0.4 ml) and Prior SB5 (Adalimumab Biosimilar).	August 2022 <i>Rheumatol Ther.</i> 2022 Aug;9(4):1157-1169.

Source: Submission main body

5.4 The submission noted the clinical evidence presented aligned with the evidence presented to the TGA to inform their outcome of bioequivalence. The submission noted the TGA previously approved the therapeutic equivalence (and bioequivalence) of Hadlima 40 mg in 0.8 mL to the reference product Humira 40 mg in 0.8 mL. The submission therefore concluded that Hadlima 40 mg in 0.4 mL is by extension therapeutically equivalent to Humira 40 mg in 0.4 mL. The evaluation noted the product information for Hadlima noted that Hadlima is a biosimilar medicine to Humira (p1, Hadlima Product Information).

Clinical claim

- 5.5 The submission claimed non-inferior comparative effectiveness and non-inferior comparative safety of Hadlima 40 mg/0.4 mL compared with Humira 40 mg/0.4 mL. This was appropriate.
- 5.6 The PBAC considered that the claim of non-inferior comparative effectiveness was reasonable.
- 5.7 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

- 5.8 The submission did not present an economic analysis as it was a Category 4 submission. The submission requested the same AEMP for Hadlima as the existing adalimumab 40 mg in 0.4 mL formulations listed on the PBS.
- 5.9 The submission did not propose an equi-effective dose. The PBAC previously advised 1 mg of Adalicip = 1 mg of Humira and all other biosimilar brands and formulations of adalimumab (paragraph 6.3, adalimumab Ardalicip PSD, July 2023).

Estimated PBS usage and financial implications

- 5.10 The submission stated that the listing of Hadlima 40 mg in 0.4 mL is not expected to increase the market nor is the duration of treatment with Hadlima expected to change. Additionally, the same price is being requested as the existing brands of adalimumab 40 mg in 0.4 mL on the PBS. Therefore, the listing of Hadlima 40 mg in 0.4 mL is expected to be cost-neutral to Government. It is expected that Hadlima would substitute for Humira or the other biosimilar brands of adalimumab.

6 PBAC Outcome

- 6.1 The PBAC recommended the Authority Required listing of adalimumab (Hadlima®) in the forms of 40 mg in 0.4 mL pre-filled pen (PFP) and pre-filled syringe (PFS) under the same circumstances as the PBS-listed reference biologic Humira® 40 mg in 0.4 mL PFP and PFS for the following indications:
- Ankylosing spondylitis
 - Complex refractory fistulising Crohn disease
 - Severe Crohn disease
 - Moderate to severe ulcerative colitis
 - Moderate to severe hidradenitis suppurativa
 - Severe active juvenile idiopathic arthritis
 - Severe active rheumatoid arthritis

- Severe chronic plaque psoriasis
 - Severe psoriatic arthritis
- 6.2 The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Hadlima 40 mg in 0.4 mL PFP and PFS would be acceptable if it were cost-minimised to the lowest cost PBS-listed adalimumab brand.
- 6.3 The PBAC advised the equi-effective doses to be 1 mg of Hadlima = 1 mg of Humira and all other biosimilar brands and formulations of adalimumab.
- 6.4 The PBAC accepted the claim of biosimilarity for Hadlima 40 mg in 0.4 mL PFP and PFS compared to Humira. The PBAC noted the clinical evidence presented aligned with the evidence presented to the TGA to inform their outcome of bioequivalence.
- 6.5 The PBAC considered that biosimilar uptake drivers should be applied to Hadlima, consistent with the current PBS listings for adalimumab biosimilar brands, including Amgevita, Adalicip, Hyrimoz, Idacio and Yuflyma, 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.
- 6.6 The PBAC advised that, under Section 101(4AACD) of *the National Health Act 1953* (the Act), in the Schedule of Pharmaceutical Benefits:
- Humira, Adalicip and Yuflyma PFS and Hadlima PFS should be treated as equivalent to each other; and Humira, Adalicip and Yuflyma PFP and Hadlima 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 Hadlima PFS and 40 mg in 0.4 mL Humira, Adalicip and Yuflyma and 40 mg in 0.8 mL Amgevita, Adalicip, Hadlima, Hyrimoz, Idacio and Yuflyma PFS 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 Hadlima PFP and 40 mg in 0.4 mL Humira, Adalicip and Yuflyma and 40 mg in 0.8 mL Amgevita, Adalicip, Hadlima, Hyrimoz, Idacio and Yuflyma 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, Hadlima 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 Hadlima 40 mg in 0.4 mL PFP and PFS is expected to be cost-neutral to Government given that Hadlima will likely substitute for existing adalimumab brands 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 Hadlima 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 new adalimumab form (Hadlima 40 mg in 0.4 mL PFS and PFP) with schedule equivalence ('a' flag) for the same indications as Humira 40 mg in 0.4 mL PFS and PFP as noted in Section 6.
- 7.2 Amend existing/recommended listing as follows:

- Authority Required listing of Hadlima, with the Authority type for each treatment phase and indication to be consistent with current listings for the other biosimilar brands of adalimumab.
- The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients.

Prescribing of the biosimilar brand Amgevita, Adalicip, 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.