

**5.17 ADALIMUMAB,
Injection 40 mg in 0.8 mL pre-filled syringe,
Injection 40 mg in 0.8 mL pre-filled pen,
Hulio[®],
Viatrix (Alphapharm Pty Ltd)**

1 Purpose of Submission

- 1.1 The Category 3 submission sought Section 85 and Section 100 Highly Specialised Drugs Program listings of a new biosimilar brand of adalimumab (Hulio[®]) in the form of 40 mg in 0.8 mL pre-filled syringe (PFS) and pre-filled pen (PFP) under the same circumstances as the PBS-listed reference biologic Humira[®] 40 mg in 0.8 mL PFS and PFP.

2 Background

Registration status

- 2.1 Hulio was TGA registered on 14 May 2021 and was determined to be a biosimilar to the reference brand Humira. Hulio 40 mg has the same indications as Humira 40 mg.

Previous PBAC consideration

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

Current status

- 2.3 Humira and the following biosimilar brands of adalimumab, Amgevita[®], Hadlima[®], Hyrimoz[®] and Idacio[®], are listed on the PBS.

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

3 Requested listing

- 3.1 The submission requested the following PBS indications for Hulio under the same circumstances as the PBS-listed reference biologic Humira 40 mg in 0.8 mL PFS and PFP:

- Severe Crohn disease
- Moderate to severe ulcerative colitis
- Severe active juvenile idiopathic arthritis
- Complex refractory fistulising Crohn's disease

- Severe active rheumatoid arthritis
- Severe psoriatic arthritis
- Ankylosing spondylitis
- Severe chronic plaque psoriasis
- Moderate to severe hidradenitis suppurativa

The submission requested a listing for uveitis, which is not a PBS-listed indication for adalimumab. This request would not be considered in this submission because a Category 3 submission is not the appropriate pathway for this type of request. Neither the submission nor the pre-PBAC response provided any data to support the request of listing Hulo for the treatment of uveitis.

- 3.2 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 restrictions have not been reproduced.

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 the Centre for Community Driven Research (1) via the Consumer Comments facility on the PBS website. The input included structured interviews and quantitative questionnaires from 100 participants with ulcerative colitis or Crohn's Disease. The repository provided participants' personal experiences on their quality of life, side effects and effectiveness of treatment.

Clinical studies

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

Public Summary Document – November 2021 PBAC Meeting

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
FKB327-001	Phase 1, randomized, double-blind, parallel group study in healthy male volunteers and healthy female volunteers of non-child bearing potential.	To compare the safety of FKB327 and EU-approved and US-licensed Humira after single doses, by SC injection in healthy volunteers. To assess tolerability after single doses of FKB327 and EU-approved and US-licensed Humira, by SC injection	FKB327 (from vial), EU-approved Humira (from PFS) or US-licensed Humira (from PFS): single 40 mg SC injection	FKB327: 60 EU-approved Humira: 60 US-licensed Humira: 60
FKB327-002	Phase 3, multi-centre, randomized, double-blind, parallel arm, active-comparator, equivalence study patients with active RA taking concomitant MTX.	To compare the safety profiles of FKB327 with Humira	FKB327 (vial): 40 mg eow by SC by injection. Humira (PFS) 40 mg eow by SC injection.	FKB327:324 Humira:321
FKB327-003	Phase 3, Period 1: open-label, randomized, comparative, multi-centre, 2-arm extension in patients with RA taking concomitant MTX who continued from the preceding Study FKB327-002. Period 2: open-label, multi-centre, single arm extension in which all patients received prolonged FKB327 treatment	To compare the safety of long-term treatment with FKB327 and Humira in patients with RA. To evaluate safety in patients who were switched from Humira in the preceding FKB327-002 double-blind study to FKB327 in the FKB327-003 OLE study, and of patients who were switched from FKB327 to Humira, respectively. To evaluate safety in patients who were switched from FKB327-003 OLE study, and then switched back to FKB327 in the second part of the FKB327-003 OLE study (from Week 30; double switch).	FKB327 (PFS or AI): 40 mg eow SC by injection. Humira (PFS) 40 mg eow by SC injection	FKB327: 324 Humira:321
FKB321-005	Phase 1, randomized, open-label, parallel group, single SC dose study in healthy male and female subjects.	To compare the safety of FKB327 after a single SC dose delivered by vial, PFS and AI in healthy subjects	FKB327: single 40 mg SC injection via vial/syringe, PFS or AI	FK327: 367 [treated=366] Humira:363 [treated=362]

FKB327 = adalimumab (Hulio); AI = auto injector; eow = every other week; MTX = methotrexate; OLE = open label extension; PFS = pre-filled syringe; RA = rheumatoid arthritis; SC = subcutaneous

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

Clinical claim

- 5.5 The submission claimed that the comparability of Hulo with Humira had been demonstrated with regards to physiochemical characteristics, and efficacy and safety outcomes. While the sponsor had not provide a clinical evaluation report, the TGA has confirmed that Hulo is biosimilar to Humira and that there were no clinically meaningful differences between Hulo and Humira in the submitted comparative pharmacology, pharmacokinetic and toxicity studies. The clinical safety and efficacy of Hulo were found to be comparable to Humira.
- 5.6 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonably supported by the data.

Economic analysis

- 5.7 The submission did not present an economic analysis as it was a Category 3 submission. The submission proposed that Hulo is priced with the same AEMP as Humira for the same form and strength. The PBAC considered this to be appropriate.
- 5.8 The equi-effective doses were not presented in the submission.

Estimated PBS utilisation and financial implications

- 5.9 The submission estimated that the listing of Hulo will not increase the overall market utilisation.

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 (Hulo) in the form of 40 mg in 0.8 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 Hulo 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 suppuratives
- 6.2 The PBAC advised the equi-effective doses to be a 1:1 unit equivalence for Hulio to Humira and all other biosimilar brands and formulations of adalimumab.
- 6.3 The PBAC considered that the claim of biosimilarity for Hulio compared to Humira was reasonably supported by the data. The TGA Delegate noted that Hulio is biosimilar to Humira and that there were no clinically meaningful differences in the comparative pharmacology, pharmacokinetic and toxicity studies.
- 6.4 The PBAC noted that the sponsor intended to supply only the pack size of two PFP/PFS. Where Humira has pack sizes of 4 and 6 listed for certain treatment phases and conditions, the PBAC considered that it is appropriate to list Hulio with the equivalent maximum quantity units to provide the same number of injections (i.e. maximum pack quantities of 2 and 3 in place of 4-pack and 6-pack, respectively).
- 6.5 The PBAC considered that the biosimilar uptake drivers should be applied to Hulio, consistent with the current PBS listings for adalimumab biosimilar brands, including:
- Authority Required (Written) listing of Hulio for the initial and first continuing treatment restrictions.
 - A separate Authority Required (Streamlined) listing of Hulio 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 Hulio in the list):

Prescribing of the biosimilar brand, HULIO, 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 Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars)
- 6.6 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits, Abrilada, Amgevita, Hadlima, Hulio, Humira, Hyrimoz and Idacio PFS should be treated as equivalent to each other; and Abrilada, Amgevita, Hadlima, Hulio, Humira, Hyrimoz and Idacio PFP should be treated as equivalent to each other for the purpose of substitution (i.e. 'a' flagged in the Schedule).

- 6.7 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits, Hulio 40 mg/0.8 mL PFP and PFS and adalimumab 40 mg/0.4 mL PFP and PFS should be considered equivalent for the purposes of substitution, respectively.
- 6.8 The PBAC advised that, under Section 101(4AACD) of the Act, in the Schedule of Pharmaceutical Benefits, Hulio PFP should not be considered equivalent for the purposes of substitution with any adalimumab PFS, consistent with its previous considerations of adalimumab.
- 6.9 The PBAC noted that the listing of Hulio will not increase overall market utilisation as it is expected that Hulio would substitute for the Humira or other biosimilar brands of adalimumab.
- 6.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Hulio 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 2009* for Pricing Pathway A were not met.
- 6.11 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 (Hulio) 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 (Written) listing of Hulio for the initial and first continuing treatment restrictions.
 - A separate Authority Required (Streamlined) listing of Hulio 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 Hulio in the list):

Prescribing of the biosimilar brand, HULIO, 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 Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars)

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.