

5.18 ADALIMUMAB
Injection 40 mg in 0.8 mL pre-filled syringe
Injection 40 mg in 0.8 mL pre-filled pen
Injection 40 mg in 0.8 mL vial
Idacio[®], Fresenius Kabi Australia Pty Ltd

1 Purpose of Application

- 1.1 The minor submission sought an Authority Required listing for a new biosimilar brand of adalimumab (Idacio[®]) in the form of 40 mg in 0.8 mL pre-filled syringe (PFS), pre-filled pen (PFP) and vial.

2 Background

Registration status

- 2.1 Idacio was TGA approved on 17 June 2020, and was determined to be a biosimilar to the reference brand Humira[®].

Previous PBAC consideration

- 2.2 Idacio has not previously been considered by the PBAC.
- 2.3 The PBAC has recommended other biosimilar brands of adalimumab, including Amgevita[®] (PFS and PFP), Hadlima[®] (PFS and cartridges) in July 2018 and Hyrimoz[®] (PFS and PFP) in March 2020. As of November 2020, none of these brands were listed on the PBS.
- 2.4 The PBAC recommended the listing of a vial form of Humira in July 2017 with the same restrictions as the listed forms of Humira cartridge and PFS at the time. The vial form of adalimumab has not been listed on the PBS.

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

3 Requested listing

- 3.1 The submission requested Section 85 and Section 100 (Highly Specialised Drug Program) listings of Idacio PFS and PFP for all indications for which Humira is PBS-listed, except those for paediatric patients with certain conditions which require dosing of less than 40 mg (see paragraph 3.3). The requested listings are the same as those recommended for Amgevita and Hyrimoz.
- 3.2 The proposed PBS indications for Idacio are:
- 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.
- 3.3 The pre-PBAC response clarified that the submission also requested Section 85 and Section 100 (Highly Specialised Drug Program) listings of Idacio vial for the following Humira indications for paediatric patients with certain conditions which require dosing of less than 40 mg:
- Paediatric patients with severe Crohn disease: treatment for patients weighing less than 40 kg (Humira PBS codes 10389T, 10396E, 10422M)
 - Patients with moderate to severe ulcerative colitis: treatment for patients weighing less than 40 kg (Humira PBS codes 11121H, 11127P)
 - Patients with severe juvenile idiopathic arthritis: treatment for patients weighing less than 30 kg (Humira PBS codes 9661L, 9678J).
- 3.4 The pre-PBAC response noted that the vial form would provide greater flexibility and choice for patients and clinicians, particularly for paediatric patients weighing less than 40 kg who require a low dose maintenance schedule of 10 mg a fortnight of adalimumab. The approved Product Information (PI) for Idacio states that paediatric patients requiring a dose less than 40 mg should use the vial presentation of Idacio and that healthcare providers should consider the risk of medication errors and the appropriateness of using the vial presentation for any dose less than 40 mg (PI, p3). Humira is currently available on the PBS as PFS and PFP, where there is a 20 mg/0.4 mL PFS that caters for the paediatric indications. The PBAC previously considered that the evidence of a clinical need for a vial presentation of adalimumab was not convincing when it was recommended in July 2017 (paragraph 5.2, Humira Public Summary Document (PSD), July 2017 PBAC Meeting).
- 3.5 The minor submission stated that the sponsor intends to supply only the pack sizes of two PFP/PFS and one vial. The submission proposed that where Humira has pack sizes of 4 and 6 listed for certain treatment phases and conditions, the listing for Idacio should have maximum quantities to provide the same number of injections (i.e. maximum quantities of 2 and 3 for PFP/PFS in place of the 4- and 6-pack; and maximum quantities of 2, 4 and 6 for vials in place of the 2-, 4- and 6-pack). This

approach was consistent with the PBAC's recommendation for Hyrimoz (paragraph 6.4, Hyrimoz PSD, March 2020 PBAC Meeting).

3.6 The sponsor requested the following biosimilar uptake drivers to apply to the listing of Idacio:

- Retain the Initial 1 and 2 restrictions as Authority Required (written) benefits
- Split the continuation criteria into 'first continuing' and 'subsequent continuing', to allow for the subsequent continuing restriction for the biosimilar to be Streamlined Authority while the subsequent continuing restriction for the reference biological medicine will remain as a written authority and
- The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients.

The biosimilar uptake drivers requested are consistent with PBAC's recommendations for Amgevita, Hadlima and Hyrimoz (Amgevita and Hadlima PSDs, July 2018 PBAC Meeting; Hyrimoz PSD, March 2020 PBAC Meeting).

3.7 The restriction was considered to be complex because of the number of items and indications required for the listing.

3.8 The submission requested that all dose forms of Idacio be 'a' flagged for pharmacy level substitution to the reference brand, Humira.

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

4 Comparator

4.1 The minor submission nominated the reference brand of adalimumab, Humira, as the main comparator. 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 as it was a minor submission.

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. The PBAC specifically noted the advice that the use of injectable biosimilars that do not require infusion in a medical facility would provide flexibility for consumers including reducing absence from work and travel due to treatment. CCA also noted that consumers would welcome an alternative to Humira that does not have associated injection site pain, which may also increase treatment adherence for children. The PBAC noted that this advice was supportive of the evidence provided in the submission.

Clinical trials

5.3 As this was a minor submission, no evaluation of the clinical evidence was undertaken.

5.4 Details of the studies presented in the submission are provided in the table below.

Table 1. Studies presented in the submission

Trial ID (Full Study No.)	Protocol title/publication title	Publication citation
Direct randomised trial(s)		
EMR200588-001 (Phase I PK study)	A 3-arm, randomised, double-blind, parallel-group, single-dose study in 237 healthy male and female subjects. Objective: to demonstrate pharmacokinetic (PK) bioequivalence, safety, immunogenicity and tolerability of Idacio, Humira (EU) and Humira (US) in terms of C_{max} and AUC_{0-inf} and AUC_{0-last} after a single s.c. injection of 40 mg of adalimumab	Clinical Study Report
EMR200588-002 (Phase III PK study)	A 2-arm, randomised, multi-centre, double-blind, parallel-group confirmatory trial in 443 subjects with moderate to severe plaque psoriasis. Objective: to evaluate the efficacy, safety and immunogenicity of Idacio with HUMIRA (EU) in terms of Psoriasis Area and Severity Index (PASI) score, anti-drug-antibody (ADA) and neutralising antibody (Nab) after fortnightly s.c. injections of 40 mg of adalimumab over 52 weeks, starting at Week 1 with an 80 mg initial baseline dose.	Clinical Study Report

5.5 Source: Table 6 of minor submission The clinical trials presented in the submission formed part of the TGA submission to register Idacio as a biosimilar of Humira. The TGA Delegate noted the efficacy and safety of the biosimilar Idacio was compared to Humira and that no significant differences were found in the main clinical study, Study EMR200588-002 (TGA Australian Public Assessment Report, p18).

Clinical claim

5.6 The minor submission claimed that Idacio was biosimilar to Humira.

5.7 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonably supported by the data.

Estimated PBS usage & financial implications

5.8 The minor submission requested listing of Idacio on a cost-minimisation basis to Humira.

5.9 The submission proposed a 1:1 unit equivalence for Idacio to Humira and all other biosimilar brands and formulations of adalimumab.

5.10 The minor submission estimated that the PBS listing of Idacio is expected to have no change in the overall net cost to the government given that Idacio will replace existing adalimumab therapies at the equivalent cost.

5.11 In formulating the financial estimates, the sponsor made the following assumptions:

- A 6.55% annual growth rate for adalimumab services, based on calculations from PBS services over the last three calendar years (Hyrimoz applied a 6.6% annual growth rate (paragraph 5.16, Hyrimoz PSD, March 2020 PBAC Meeting))
- A statutory 25% price reduction was applied to the price of Humira in line with the 'First New Brand Price Reductions' if any of the recommended biosimilar brands of adalimumab was to be listed on the PBS, triggering a move of the drug to F2
- The vial form would displace currently listed PFP, as the PFP listings had a much higher utilisation than PFS.

5.12 As a minor submission, the financial estimates have not been independently evaluated.

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 (Idacio) in the form of a 40 mg in 0.8 mL pre-filled pen (PFP) and pre-filled syringe (PFS) 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 Idacio 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 noted the sponsor for Idacio had not pursued PBAC listing of PFP and PFS dose forms for the following paediatric indications due to the absence of a 20 mg/0.4 mL injection presentation of Idacio:

- Paediatric patients with severe Crohn disease: treatment for patients weighing less than 40 kg (Humira PBS codes 10389T, 10396E, 10422M)
- Patients with moderate to severe ulcerative colitis: treatment for patients

weighing less than 40 kg (Humira PBS codes 11121H, 11127P)

- Patients with severe juvenile idiopathic arthritis: treatment for patients weighing less than 30 kg (Humira PBS codes 9661L, 9678J).
- 6.3 The PBAC did not recommend the listing of Idacio in the 40 mg/0.8 mL vial form. The PBAC noted the request was for the vial to be listed for paediatric use only. Although a vial form was recommended in July 2017, the PBAC considered there was not a sufficient clinical need at this time to support the listing given the 20 mg/0.4 mL syringe was currently available for paediatric listings and the need for a vial in the outpatient paediatric population was minimal. Additionally, the PBAC noted that having a 40 mg/0.8 mL vial alternative to the currently listed 20 mg/0.4 mL syringe may cause confusion and would result in wastage of medicine.
- 6.4 The PBAC advised the equi-effective doses to be a 1:1 unit equivalence for Idacio to Humira and all other biosimilar brands and formulations of adalimumab.
- 6.5 The PBAC considered that the claim of non-inferior comparative effectiveness and safety for Idacio compared to Humira was reasonably supported by the data. The TGA Delegate noted that there were no significant differences found in the main clinical study, Study EMR200588-002, when Idacio was compared to Humira.
- 6.6 The PBAC noted that the sponsor intended to supply only the pack size of 2 for PFP and PFS. Where Humira has pack sizes of 4 and 6 listed for certain treatment phases and conditions, the PBAC considered it would be appropriate to list Idacio with equivalent maximum quantity units to provide the same number of injections (i.e. maximum quantities of 2 and 3 for PFP/PFS in place of the 4- and 6-pack respectively). The PBAC noted that this approach was consistent with the PBAC's recommendation for Hyrimoz. The PBAC also noted that new PBS item codes may need to be created for Idacio for the different maximum quantities.
- 6.7 The PBAC considered that the following biosimilar uptake drivers should be applied to Idacio PFP and PFS, consistent with its previous recommendations regarding the application of these drivers to other biosimilar brands of adalimumab:
- Retain the Initial 1 and 2 restrictions as Authority Required (written) benefits.
 - Split the continuation criteria into 'first continuing' and 'subsequent continuing', to allow for the subsequent continuing restriction for Idacio to be Streamlined Authority, while the subsequent continuing restriction for Humira will remain as a written authority.
 - The application of the 'Biosimilar prescribing policy' administrative note encouraging the use of biosimilar brands for treatment naïve patients:

Note

Biosimilar prescribing policy

Prescribing of the biosimilar brand IDACIO 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).

- 6.8 The PBAC reiterated its previous advice that adalimumab should not be available for nurse practitioner prescribing.
- 6.9 The PBAC has previously considered that adalimumab should not be exempt from the Early Supply Rule.
- 6.10 The PBAC advised that, under Section 101(4AACD) of the *National Health Act 1953*, in the Schedule of Pharmaceutical Benefits, Idacio, Amgevita, Hadlima, Hyrimoz and Humira pre-filled syringes should be treated as equivalent ('a' flagged) to each other; and Idacio, Amgevita, Hadlima, Hyrimoz and Humira pre-filled pens should be treated as equivalent ('a' flagged) to each other for the purpose of substitution, for respective PBS-listed indications. The PBAC noted its previous advice that the different dose forms of adalimumab (i.e. vial, PFS and auto-injector forms) should not be considered equivalent for the purpose of substitution (i.e. 'a' flagged on the Schedule) due to the differences in the administration techniques between the devices (paragraph 9.1, Humira PSD, July 2017 PBAC meeting).
- 6.11 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Idacio 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.
- 6.12 The PBAC advised 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 (Idacio) with schedule equivalence ('a' flag) for the same indications as Humira, except for:
- Paediatric patients with severe Crohn disease: treatment for patients weighing less than 40 kg (Humira PBS codes 10389T, 10396E, 10422M)
 - Patients with moderate to severe ulcerative colitis: treatment for patients weighing less than 40 kg (Humira PBS codes 11121H, 11127P)
 - Patients with severe juvenile idiopathic arthritis: treatment for patients weighing less than 30 kg (Humira PBS codes 9661L, 9678J).

7.2 Amend existing/recommended listing as follows:

- Retain the Initial 1 and 2 restrictions as Authority Required (written) benefits.
- Split the continuation criteria into ‘first continuing’ and ‘subsequent continuing’, to allow for the subsequent continuing restriction for Idacio to be Streamlined Authority, while the subsequent continuing restriction for Humira will remain as a written authority.
- Add an administrative note encouraging biosimilar prescribing for treatment naïve patients:

Note

Biosimilar prescribing policy

Prescribing of the biosimilar brand IDACIO 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.