

**5.15 ADALIMUMAB,  
Injection 20 mg in 0.2 mL pre-filled syringe,  
Injection 40 mg in 0.4 mL pre-filled syringe,  
Injection 40 mg in 0.4 mL pre-filled pen,  
Injection 80 mg 0.8 mL pre-filled syringe,  
Injection 80 mg in 0.8 mL pre-filled pen,  
Hyrimoz<sup>®</sup>,  
SANDOZ PTY LTD**

**1 Purpose of Submission**

- 1.1 The Category 4 submission sought to list a biosimilar brand of adalimumab (Hyrimoz<sup>®</sup>) in the forms and strengths of 40 mg in 0.4 mL, 80 mg in 0.8 mL pre-filled pen (PFP) and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL pre-filled syringe (PFS) under the same circumstances as the currently PBS-listed reference biologic, Humira<sup>®</sup>.

**2 Background**

***Registration status***

- 2.1 The requested forms and strengths of Hyrimoz were registered on the Australian Register of Therapeutic Goods Administration (ARTG) on 15 May 2024, and determined to be biosimilar to the reference brand Humira.

***Previous PBAC consideration***

- 2.2 This is the first PBAC submission for the requested forms and strengths of Hyrimoz (the submission refers to these as high concentration formula Hyrimoz; hereafter referred to as 'Hyrimoz HCF').
- 2.3 The PBAC recommended 40 mg in 0.8 mL PFP and PFS at its March 2020 meeting and is currently listed on the PBS (the submission refers to these as low concentration formula Hyrimoz; hereafter referred to as 'Hyrimoz LCF').
- 2.4 Table 1 provides a summary of the forms and strengths requested in the submission against the current forms and strengths of adalimumab available in the different brands on the PBS.

**Table 1: Summary of the submission's request and the current brands of adalimumab available on the PBS**

	Brands available	Form requested of Hyrimoz in the submission
High concentration formulation (HCF)		
adalimumab 20 mg in 0.2 mL pre-filled syringe	Humira	Yes
adalimumab 20 mg in 0.4 mL pre-filled syringe	Amgevita	No
adalimumab 40 mg in 0.4 mL pre-filled pen	Humira, Adalicip, Yuflyma	Yes
adalimumab 40 mg in 0.4 mL pre-filled syringe	Humira, Adalicip, Yuflyma	Yes
adalimumab 80 mg in 0.8 mL pre-filled pen	Humira	Yes
adalimumab 80 mg in 0.8 mL pre-filled syringe	Humira	Yes
Low concentration formulation (LCF)		
adalimumab 40 mg in 0.8 mL pre-filled pen	Amgevita, Hadlima, Hyrimoz, Idacio	No

Table compiled during evaluation.

### 3 Requested listing

- 3.1 The submission requests listing Hyrimoz HCF under the same circumstances as the PBS-listed reference biologic Humira. If listed, Hyrimoz HCF will be the first PBS-listed biosimilar brand of adalimumab in the 20 mg in 0.2 mL and 80 mg in 0.8 mL presentations.
- 3.2 The PBS indications requested in the submission for Hyrimoz HCF 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 submission did not request Hyrimoz be listed for vision-threatening non-infectious uveitis. At its March 2024 meeting, the PBAC recommended the General Schedule, Authority Required listing of adalimumab (Humira) for the treatment of vision-threatening non-infectious uveitis (adalimumab (Humira), March 2024 PBAC meeting outcome). In its March 2024 consideration, the PBAC noted multiple biosimilars were available for adalimumab and considered existing 'a' flagging arrangements should be implemented for the listing for non-infectious uveitis (paragraph 7.20, adalimumab (Humira) Public Summary Document (PSD), March 2024 PBAC meeting). The PBAC was asked to advise whether it would consider Hyrimoz cost-effective under the same circumstances as Humira, including for those in which it recommended listing Humira for uveitis, noting that Hyrimoz is TGA approved for this indication (Hyrimoz TGA approval letter).
- 3.4 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 Hyrimoz HCF PFS and PFP if it is recommended for listing.

- 3.5 Table 2 is a summary of the current brands, forms and strengths of adalimumab available on the PBS which are equivalent to each other for the purposes of substitution. The PBAC was asked to advise, under Section 101(4AACD) of the *National Health Act 1953* whether, in the Schedule of Pharmaceutical Benefits:
- i) The PFS of Hyrimoz HCF should be treated as equivalent to the different brands of adalimumab of the same strength for specific indications (see Table 2) for the purposes of substitution (i.e. 'a' flagged in the schedule); with the exception that the 40 mg in 0.4 mL PFS of the different brands of adalimumab should be treated as equivalent to the 40 mg in 0.8 mL PFS of the different brands of adalimumab.
  - ii) The PFP of Hyrimoz HCF should be treated as equivalent to the different brands of adalimumab of the same strength for specific indications (see Table 2) for the purposes of substitution (i.e. 'a' flagged in the schedule), with the exception that the 40 mg in 0.4 mL PFP of the different brands of adalimumab should be treated as equivalent to the 40 mg in 0.8 mL PFP of the different brands of adalimumab.

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**Table 2: Summary of the current brands, forms and strengths of adalimumab available on the PBS which are equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule)**

Form	Brand Name	a-flagged (Y/N/if an exception applies)
'a' flagging for 20mg adalimumab syringe		
20 mg/0.2 mL injection, 2 x 0.2 mL syringes	Humira	Y
20 mg/0.4 mL injection, 0.4 mL syringe	Amgevita	Y, except for item codes 12351C <sup>a</sup> & 12436M <sup>b</sup>
'a' flagging for 40mg adalimumab pen devices		
40 mg/0.4 mL injection, 2 x 0.4 mL pen devices **	Adalicip	Y
	Humira	Y, except for item codes 13211H <sup>a</sup> , 13214L <sup>c</sup> , 13215M <sup>d</sup> , 13221W <sup>e</sup> , 13223Y <sup>f</sup> , 13224B <sup>b</sup> , 13225C <sup>b</sup> , 13226D <sup>g</sup> , 13230H <sup>h</sup> , 13691N <sup>i</sup> , 13703F <sup>i</sup> & 13764K <sup>g</sup>
	Yuflyma	Y
40 mg/0.8 mL injection, 2 x 0.8 mL pen devices**	Amgevita	Y
	Hadlima	Y
	Hyrimoz	Y
	Idacio	Y
'a' flagging for 40mg adalimumab syringes		
40 mg/0.4 mL injection, 2 x 0.4 mL syringes*	Adalicip	Y
	Humira	Y, except for item codes 13208E <sup>g</sup> , 13209F <sup>f</sup> , 13213K <sup>a</sup> , 13216N <sup>c</sup> , 13217P <sup>d</sup> , 13218Q <sup>b</sup> , 13219R <sup>b</sup> , 13220T <sup>h</sup> , 13704G <sup>i</sup> , 13732R <sup>i</sup> & 13763J <sup>g</sup>
	Yuflyma	Y
40 mg/0.8 mL injection, 2 x 0.8 mL syringes*	Amgevita	Y
	Hadlima	Y
	Hyrimoz	Y
	Idacio	Y
'a' flagging for 80mg adalimumab pen device		
80 mg/0.8 mL injection, 0.8 mL pen device	Humira	N
'a' flagging for 80mg adalimumab syringes		
80 mg/0.8 mL injection, 0.8 mL syringe	Humira	N

Table compiled during evaluation.

a Indicated for moderate to severe ulcerative colitis.

b Indicated for severe Crohn disease.

c Indicated for severe psoriatic arthritis.

d Indicated for severe chronic plaque psoriasis.

e Indicated for moderate to severe hidradenitis suppurativa.

f Indicated for severe active juvenile idiopathic arthritis.

g Indicated for ankylosing spondylitis.

h Indicated for complex refractory Fistulising Crohn disease.

i Indicated for severe active rheumatoid arthritis.

\*40 mg in 0.4 mL PFS of the different brands of adalimumab should be treated as equivalent to the 40 mg in 0.8 mL PFS of the different brands of adalimumab for the purposes of substitution (i.e. 'a' flagged in the schedule).

\*\*40 mg in 0.4 mL PFP of the different brands of adalimumab should be treated as equivalent to the 40 mg in 0.8 mL PFP of the different brands of adalimumab for the purposes of substitution (i.e. 'a' flagged in the schedule).

3.6 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	Hyrimoz® Sandoz Pty Ltd
ADALIMUMAB adalimumab 40 mg/0.4 mL injection, pre-filled syringe	1	2	2	12338J	Hyrimoz® Sandoz Pty Ltd

The sponsor has requested the same number of items and indications as Humira. 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. 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 that no consumer comments were received for this item.

### *Clinical trials*

- 5.3 The submission presented the following clinical trials to support the claim that Hyrimoz HCF is similar to Humira in terms pharmacokinetics, efficacy and safety. The evaluation noted the clinical trials reported in this submission were the same as the trials included with Hyrimoz LCF March 2020 PBAC submission, with the addition of CGPN017B12101 which compares Hyrimoz LCF and HCF. As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

**Table 3: Studies and associated reports presented in the submission**

Trial ID (Full Study No.)	Protocol title/publication title	Publication citation
CGPN017B12101	<p>A randomized, double-blind, parallel, two-arm study compared the pharmacokinetics, safety and immunogenicity of HYRIMOZ HCF (100 mg/mL) with HYRIMOZ LCF (50mg/mL) after a single dose of 40 mg subcutaneous injection in healthy male subjects</p> <p>Objective: To demonstrate PK comparability between Hyrimoz-HCF and Hyrimoz- LCF in terms of:</p> <ul style="list-style-type: none"> <li>• C<sub>max</sub> and AUC<sub>inf</sub> (as agreed with FDA)<sup>1</sup></li> <li>• C<sub>max</sub> and AUC<sub>0-360</sub> (as agreed with EMA)<sup>1</sup></li> </ul> <p>Healthy male subjects</p>	Clinical Study Report Report date: 25-Jan-2024
GP17-101 (supportive PK study)	<p>A single-centre, randomised, double-blind, single-dose, three-arm, parallel group study in 219 healthy male and female subjects.</p> <p>Objective: to demonstrate PK bioequivalence of Hyrimoz, Humira (EU) and Humira (US) in terms of C<sub>max</sub> and AUC<sub>0-inf</sub> and AUC<sub>0-last</sub> after a single s.c. injection of 40 mg of adalimumab</p>	Clinical Study Report Report date: 11-May-2017
GP17-102 (supportive PK study – device development)	<p>A single-centre, randomised, open-label, single-dose, two-arm, parallel group study in 108 healthy male subjects</p> <p>Objective: to describe PK of Hyrimoz administered by autoinjector or pre-filled syringe (PFS) as a single s.c injection of 40 mg to healthy adult male subjects with body weights between 50 and 94.9kg in terms of AUC<sub>0-360h</sub> (device comparison).</p>	Clinical Study Report Report date: 11-May-2017
GP17-103 (supportive PK study – technical transfer)	<p>A multi-centre, randomised, double-blind, parallel group, two-arm study in 178 healthy male subjects</p> <p>Objective: to demonstrate PK bioequivalence (90% CI of ratio of geometric means within the margins of [0.8; 1.25]) of Hyrimoz-Cook and Hyrimoz-Schaftenau in terms of C<sub>max</sub>, AUC<sub>0-inf</sub> and AUC<sub>0-last</sub> after a single s.c. injection of 40 mg of adalimumab.</p>	Clinical Study Report Report date: 11-May-2017
GP17-104 (pivotal PK study)	<p>A single-centre, randomized, double-blind, single-dose, three-arm, parallel group study in 318 healthy male subjects comparing Hyrimoz with Humira (EU) and Humira (EU) with Humira (US).</p> <p>Objective: To demonstrate PK bioequivalence (90% CI of ratio of geometric means within the margins of [0.8; 1.25]) of Hyrimoz and Humira (EU), and PK bioequivalence of Humira (EU) and Humira (US) in terms of C<sub>max</sub> and AUC<sub>0-inf</sub> after a single s.c. injection of 40 mg of adalimumab</p>	Clinical Study Report Report date: 11-May-2017
GP17-301 (pivotal confirmatory efficacy and safety study)	<p>A multi-center, randomized, double-blind, comparator-controlled study with treatment switches in 465 male and female patients with moderate to severe chronic plaque-type psoriasis. Patients enrolled in the EU received either Hyrimoz or Humira (EU), and patients enrolled in the US received either Hyrimoz or Humira (US).</p> <p>Objective: To demonstrate equivalent efficacy of Hyrimoz and Humira with respect to PASI75 response rate at Week 16 and similar safety and immunogenicity in patients with moderate to severe chronic plaque-type psoriasis</p>	Clinical Study Report Report date: 11-May-2017

Source: Table 1-1, p8 A5-clinical overview LCF and Table 1-1, p8 A6-clinical overview addendum HCF.

### **Clinical claim**

- 5.4 The submission claimed that Hyrimoz HCF is non-inferior in terms of comparative efficacy and safety to Humira. The PBAC noted the TGA Delegate found that the results of the clinical and pharmacokinetic trials showed that the two products were similar in terms of both efficacy and safety and were biosimilar to one other.
- 5.5 The PBAC considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety to Humira was reasonable.

### **Economic analysis**

- 5.6 The submission did not present an economic analysis as it was a Category 4 submission. The submission requested listing of Hyrimoz HCF on a cost-minimisation basis to Humira. The submission requested the same AEMP for Hyrimoz HCF as Humira for the equivalent form and strength.
- 5.7 The submission did not propose an equi-effective dose. The PBAC previously advised 1 mg of Hadlima = 1 mg of Humira and all other biosimilar brands and formulations of adalimumab (paragraph 6.3, adalimumab (Hadlima) PSD, November 2023 PBAC Meeting).

### **Estimated PBS usage and financial implications**

- 5.8 The submission considered listing Hyrimoz HCF on the PBS is not expected to increase overall use of adalimumab.
- 5.9 The requested price was based on the AEMP of the PBS listed adalimumab brands.
- 5.10 The submission estimated a save to the PBS of > \$1 billion over six years, claiming there would be savings from price disclosure reductions of the PBS listed adalimumab LCF and the HCF brands, as well as savings associated with patients switching from LCF to HCF (submission). However, in the Pre-PBAC Response, the sponsor noted the estimated saving was a transcript error and that it should have been stated as < \$100 million to < \$200 million over six years. Further, the sponsor no longer deemed the estimated savings to be realistic based on market changes that have occurred since the date of the submission. The sponsor revised the claim of cost saving to the PBS to cost neutral based on the following assumptions:
- Base case does not consider any further price reductions resulting from the PBS listing of Hyrimoz HCF
  - Base case does not consider any savings associated with switching between LCF and HCF
  - Calculations did not include injection 20 mg in 0.2 mL pre-filled syringe as it represents less than 0.5% of the spend
- 5.11 The Pre-PBAC Response presented a scenario analysis to demonstrate that the listing of Hyrimoz HCF could result in an incremental 5% reduction each year for all adalimumab brands due to the continued effect of statutory price disclosure. The

sponsor estimated potential savings of up to \$200 million to < \$300 million over a 6-year period.

- 5.12 The evaluation noted that if Hyrimoz HCF were recommended to be listed on the PBS, it is expected that Hyrimoz HCF would substitute for the other brands of PBS listed adalimumab and provide more adalimumab options for patients. However, the evaluation estimated the likely net financial impact to Government would be nil as the additional biosimilar would not result in additional savings to Government.

## **6 PBAC Outcome**

- 6.1 The PBAC recommended the Authority Required listing of adalimumab (Hyrimoz) in the forms and strengths of 40 mg in 0.4 mL, 80 mg in 0.8 mL PFP and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL PFS under the same circumstances as the currently PBS-listed reference biologic, Humira® and other brands of adalimumab 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
- Vision-threatening non-infectious uveitis

- 6.2 The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Hyrimoz 40 mg in 0.4 mL, 80 mg in 0.8 mL PFP and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL PFS would be acceptable if it were cost-minimised to Humira and all other biosimilar brands and formulations of adalimumab.

- 6.3 The PBAC noted the submission did not request Hyrimoz be listed for vision-threatening non-infectious uveitis, which was recommended for Humira at the March 2024 PBAC meeting. The PBAC noted Hyrimoz is TGA approved for this indication. Therefore, the PBAC considered that Hyrimoz would be cost-effective under the same circumstances as Humira, including for those in which it recommended listing Humira for vision-threatening non-infectious uveitis.

- 6.4 The PBAC advised the equi-effective doses to be 1 mg of Hyrimoz = 1 mg of Humira and all other biosimilar brands and formulations of adalimumab.

- 6.5 The PBAC accepted the claim of biosimilarity for Hyrimoz 40 mg in 0.4 mL, 80 mg in 0.8 mL PFP and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL PFS compared to Humira. The PBAC noted the TGA Delegate found that the results of the clinical and

pharmacokinetic trials showed that the two products were similar in terms of both efficacy and safety and were biosimilar to one other.

- 6.6 The PBAC advised that biosimilar uptake drivers, including the differential authority requirements for subsequent continuing treatment between the reference and biosimilar brands of adalimumab and inclusion of an administrative note encouraging the use of biosimilar brands for treatment naïve patients, should apply to Hyrimoz 40 mg in 0.4 mL, 80 mg in 0.8 mL PFP and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL PFS.
- 6.7 The PBAC advised that, under Section 101(4AACD) of the *National Health Act 1953* (the Act), in the Schedule of Pharmaceutical Benefits:
- PFS of Hyrimoz HCF should be treated as equivalent to the different brands of adalimumab of the same strength for specific indications (see Table 2) for the purposes of substitution (i.e. 'a' flagged in the schedule); with the exception that the 40 mg in 0.4 mL PFS of the different brands of adalimumab should also be treated as equivalent to the 40 mg in 0.8 mL PFS of the different brands of adalimumab.
  - PFP of Hyrimoz HCF should be treated as equivalent to the different brands of adalimumab of the same strength for specific indications (see Table 2) for the purposes of substitution (i.e. 'a' flagged in the schedule), with the exception that the 40 mg in 0.4 mL PFP of the different brands of adalimumab should also be treated as equivalent to the 40 mg in 0.8 mL PFP of the different brands of adalimumab.
  - The PBAC reaffirmed its advice from November 2023 that adalimumab PFP formulation should not be considered equivalent for the purposes of substitution with any adalimumab PFS formulation.
- 6.8 The PBAC considered that the listing of Hyrimoz 40 mg in 0.4 mL, 80 mg in 0.8 mL PFP and 20 mg in 0.2 mL, 40 mg in 0.4 mL, 80 mg in 0.8 mL PFS is expected to be cost-neutral to Government given that Hyrimoz will likely substitute for other brands of PBS listed adalimumab and therefore not increase overall market utilisation or result in additional savings to Government.
- 6.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Hyrimoz 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 brand (Hyrimoz) with schedule equivalence ('a' flag) for the same indications as Humira as noted in Section 3, including the treatment of vision-threatening non-infectious uveitis for which Humira and all other biosimilar brands and formulations of adalimumab was recommended to be listed on the PBS.
- 7.2 Amend existing/recommended listing as follows:
- Authority Required listing of Hyrimoz, 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 (this note will need to be updated for the other biosimilar brands of adalimumab to include Hyrimoz in the list):

*Prescribing of the biosimilar brand Amgevita, Ardalicip, 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](http://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.