

An addendum to this minute has been included at the end of the document.

6.15 ADALIMUMAB, Injection 40 mg pre-filled syringe, Injection 40 mg auto-injector, Hadlima[®], Merck, Sharp & Dohme (Australia) Pty Ltd

1 Purpose of Application

- 1.1 The minor submission requested additional uptake drivers for biosimilar adalimumab (Hadlima[®]).

2 Background

Registration status

- 2.1 Hadlima is approved by the Therapeutics Goods Administration (TGA) for the same indications as the reference brand Humira[®], and was determined to be a biosimilar to Humira.

Previous PBAC consideration

- 2.2 The PBAC previously recommended the listing of Hadlima for all indications for which Humira is PBS listed (para 5.1, adalimumab (Hadlima) Public Summary Document (PSD), July 2018 PBAC Meeting; para 5.1, adalimumab (Hadlima) PSD, July 2020 PBAC Meeting).
- 2.3 The PBAC previously recommended the listing of two other biosimilar brands of adalimumab (Amgevita[®] in July 2018 and Hyrimoz[®] in March 2020). The PBAC advised that Hadlima cartridges should be 'a' flagged with Amgevita and Humira cartridges, and Hadlima pre-filled syringes (PFS) should be 'a' flagged to Amgevita, Hyrimoz and Humira PFS (para 5.5, adalimumab (Hadlima) PSD, July 2020 PBAC Meeting).
- 2.4 The PBAC considered that the following biosimilar uptake drivers should be applied to Hadlima, consistent with its previous recommendations regarding the application of these drivers to other biosimilar brands of adalimumab (para 5.6, adalimumab (Hadlima) PSD, July 2020 PBAC Meeting):
- Retain the Initial 1, 2 and 3 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 Authority Required (STREAMLINED) while the subsequent continuing restriction for the reference biological medicine will remain as a written authority; and

- The application of an Administrative Note encouraging the use of biosimilar brands for treatment-naïve patients.
- 2.5 The Sponsor made a minor submission to the November 2018 PBAC meeting regarding a biosimilar of etanercept, Brenzys[®], to request similar additional uptake drivers be applied:
- Changing the authority level for initial 1, initial 2 and first continuing prescribing from a written authority to a telephone authority for the Brenzys brand of etanercept;
 - For bDMARD/biologic-naïve patients, having the use of a biosimilar in the first instance not count as a treatment failure as part of a treatment cycle, as one of five agents in rheumatoid arthritis (RA) or three agents in ankylosing spondylitis (AS), psoriatic arthritis (PsA) or chronic plaque psoriasis (CPP); and
 - Re-introduction of ‘a’ flagging the Brenzys and Enbrel[®] brands for the subsequent continuing treatment phase, such that written authority prescriptions for Enbrel can be substituted for biosimilars at the pharmacy level, in addition to the streamlined authority listing of Brenzys that currently exists.

The PBAC deferred their consideration on the basis that the matters had potentially broader biosimilar policy implications and considered that further discussions between the Department and key stakeholders regarding these requests was necessary to inform decision making (para 4.1, etanercept PSD, November 2018 PBAC Meeting). The Sponsor stated that they have not gained further traction on this issue with the Department in having these discussions, which are yet to take place. The request regarding a-flagging has been addressed.

- 2.6 The sponsor stated that the current application of the biosimilar uptake drivers had led to a 30% market share for Brenzys.

For more detail on PBAC’s view, see section 5 PBAC outcome

3 Requested listing

- 3.1 The submission requested three additional uptake drivers for Hadlima:
1. Treatment Failure Exemption;
 2. Lowering the authority level for first continuing prescriptions to Authority Required (STREAMLINED); and
 3. Lowering the authority level for initial prescriptions to Authority Required (Telephone).
- 3.2 The submission did not present proposed new restrictions; however, the requested changes would require amendments to the restrictions to facilitate implementation.

Treatment Failure Exemption

3.3 Except for the limit of up to 5 treatments in a lifetime for severe active rheumatoid arthritis, a limit of up to 3 failures within a treatment cycle before an-exclusion of 5 years from treatment is applied to other indications, as shown in Table 1 below.

Table 1: Number of PBS subsidised treatments permitted per indication

Indication	Number of PBS-subsidised therapies permitted
Severe Crohn disease Complex refractory Fistulising Crohn disease Moderate to severe ulcerative colitis Severe active juvenile idiopathic arthritis Adult patients with a history of juvenile idiopathic arthritis Severe psoriatic arthritis Ankylosing spondylitis Severe chronic plaque psoriasis	3 treatments <i>then a 5 year exclusion from treatment with a bDMARD</i>
Severe active rheumatoid arthritis	5 treatments <i>in a lifetime.</i>

Source: The submission; italics = text added during evaluation

3.4 For bDMARD-naïve patients the submission proposed that the use of a biosimilar in the first instance would not count as a treatment failure. The submission claimed that the application of this uptake driver would encourage prescribers to choose biosimilars in the first instance and would increase the biosimilar market share in treatment-naïve patients. It is unclear how this would be applied in practice to allow a retrial of the same drug under Initial 2 restriction criteria, as these do not allow a retrial of the same drug that a patient had previously failed within a treatment cycle. The sponsor clarified that if a patient failed treatment on the biosimilar, they would no longer be eligible for that drug. This is in line with the current restriction which disallows retrial with the same drug.

3.5 This proposal would effectively alter the structure of treatment cycles, which is a component of the cost-effectiveness basis on which bDMARDs/biologics are listed on the PBS, and there may be economic implications associated with the potential for patients to access an additional treatment as part of a treatment cycle. The sponsor claimed that the economic implications would be limited, as few patients require more than three bDMARD treatments. The sponsor referred to evidence from two DUSC reviews to support this claim (see Table 2). Further, the sponsor claimed that any additional cost due to additional treatment within a cycle would be outweighed by price reductions due to price disclosure mechanisms.

Table 2: Proportion of Patients Requiring 3 or more bDMARDs

Indication	Patients with an Authority for 3 bDMARDs	Patients with an Authority for 4 bDMARDs	Patients with an Authority for 5 bDMARDs	Reference
Ankylosing Spondylitis	9.2%	2.0%	0.2%	2016 DUSC Review, Ankylosing Spondylitis
Psoriatic Arthritis	10-15%	"...a very small proportion..."		2015 DUSC Review, Psoriatic Arthritis

Source: pre-PBAC response

- 3.6 This proposal falls outside of the biosimilar uptake measures described in item 8.3 of the Medicines Australia Strategic Agreement, and would require consultation with Medicines Australia prior to implementation as well as consideration of any assessment of these measures by the Joint Oversight Committee established under the Strategic Agreement.
- 3.7 In its pre-PBAC response, the sponsor welcomed discussions between the Department and relevant stakeholders, including Medicines Australia, for consideration of the implementation of this uptake driver.

Lowering the Authority Level of Continuing Prescriptions

- 3.8 As noted above (para 2.4), the PBAC previously recommended the subsequent continuing treatment phase should be Authority Required (STREAMLINED) for Hadlima, while that of Humira is maintained as Authority Required (Written).
- 3.9 The submission proposed lowering the authority level for first continuing prescriptions from Authority Required (Telephone) to Authority Required (STREAMLINED) for Hadlima across all relevant indications, while Humira is maintained as Authority Required (Written). The submission noted that the PBAC previously considered that the application of Authority Required (STREAMLINED) to biosimilar listings at all phases of treatment was inappropriate, given the risk of leakage at the initial phase (para 7.11, etanercept PSD, July 2016 PBAC Meeting).
- 3.10 The submission noted that the current restriction for biosimilar infliximab for the treatment of moderate to severe ulcerative colitis (UC) allows physicians to prescribe continuing therapy with biosimilar brands of infliximab as Authority Required (STREAMLINED) after 12 weeks of initial therapy. In contrast, the submission noted that under the recommended adalimumab biosimilar restrictions, physicians are not able to prescribe under Authority Required (STREAMLINED) until after 24 weeks of initial therapy. The initial supply of infliximab for UC is only sufficient for 16 weeks treatment. To ensure there is no disruption in supply to the patient, the prescriber is encouraged to apply for the continuing treatment from week 12 for patients who are responding to treatment. There is no split between first and subsequent continuing therapy for infliximab, and the lower authority (Authority Required (STREAMLINED)) is applied for continuing treatment for the biosimilar brands.
- 3.11 This request fits within the Medicines Australia Strategic Agreement:
“a different prescribing process for biosimilars and reference biologics through allowing a lower level of authority to the biosimilar than exists for the reference biologic at the point of introduction of the biosimilar, which may at commencement of therapy or continuation of therapy (or both)”¹.

¹ Item 8.3.1, *Medicines Australia Strategic Agreement*, available at:
<https://www1.health.gov.au/internet/main/publishing.nsf/Content/landmark-compact-Medicines-Aust>

Lowering the authority level for initial prescriptions

3.12 The submission proposed lowering the authority level for initial prescriptions from Authority Required (Written) to Authority Required (Telephone) for Hadlima, while Humira is maintained as Authority Required (Written). The submission claimed that this would encourage physicians to prescribe biosimilar medicines for treatment-naïve patients. The Sponsor stated that they were willing to work with the Department on how this would be best implemented by Services Australia (SA).

3.13 This request fits within the Medicines Australia Strategic Agreement (refer para 3.11).

For more detail on PBAC's view, see section 5 PBAC outcome.

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted and welcomed the input from organisations (1) via the Consumer Comments facility on the PBS website. The comments from Crohn's and Colitis Australia described a range of benefits of listing an adalimumab biosimilar including flexibility for consumers.

Financial implications

4.3 The submission modelled the financial impact of the requested changes to three drugs: adalimumab, etanercept and infliximab.

4.4 The submission's model used PBS expenditure information derived from publicly available Medicare statistics, and applied historical growth rates to estimate ongoing PBS costs. The submission claimed that the model predicted the cost reductions that would flow on to the PBS through the operation of existing statutory price reductions and price disclosure mechanisms.

4.5 The submission estimated \$500 million to < \$600 million in savings between 2021–2030 (inclusive). The submission estimated an average of \$20 million to < \$30 million in cost reductions each year in the first 5 years. The submission claimed that adalimumab would account for 61% of the expected reductions. The Department was unable to validate the model's assumptions and estimates.

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

5 PBAC Outcome

- 5.1 The PBAC deferred its consideration of the requested biosimilar uptake drivers for adalimumab (Hadlima) on the basis that these matters had potentially broader biosimilar policy implications and required further discussions between the Department and relevant stakeholders to ensure appropriate consideration of the proposed uptake drivers.
- 5.2 The PBAC noted that recent data showed that market share of PBS listed biosimilars had increased since the implementation of biosimilar uptake drivers.
- 5.3 The PBAC noted that the request for treatment failure exemption fell outside of the biosimilar uptake measures described in the Medicines Australia Strategic Agreement and would require further consideration by the Joint Oversight Committee.
- 5.4 The PBAC considered that the requested Authority Required (Telephone) for initial prescriptions may be difficult to implement and time consuming for prescribers; Authority Required (Electronic) may be a preferred option. The PBAC considered that the implementation of the lowering of authority levels should be discussed with Services Australia prior to further consideration.
- 5.5 The PBAC considered that any changes to Hadlima should be flowed on to other biosimilar brands of adalimumab.

Outcome:

Deferred

6 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.

7 Sponsor's Comment

MSD is disappointed the PBAC has once again deferred consideration of additional biosimilar uptake drivers to support patient and clinician use of biosimilars in line with government policy. We acknowledge the PBAC has reiterated its request for additional consultation between the Department and relevant stakeholders, which should take place as soon as possible. We remain ready to assist in these discussions to progress MSD's proposal and its

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implementation. This will ensure patients and the health system benefit from the savings generated by the uptake of biosimilars in a timely manner.

Addendum to the November 2020 PBAC Minutes:

**4.03 ADALIMUMAB,
Injection 40 mg pre-filled syringe,
Injection 40 mg auto-injector,
Hadlima[®],
Merck, Sharp & Dohme (Australia) Pty Ltd**

8 Background

- 8.1 At its November 2020 meeting, the PBAC deferred making a recommendation regarding the requested biosimilar uptake drivers for adalimumab (Hadlima) on the basis that these matters had potentially broader biosimilar policy implications and required further discussions between the Department and relevant stakeholders to ensure appropriate consideration of the proposed uptake drivers.
- 8.2 The PBAC noted that, at present, prescribers can use the Online PBS Authorities (OPA) system on Health Professional Online Services (HPOS) to self-serve for authority approval of Authority Required (Telephone/electronic) items. Prescribers receive a real time 'immediate' assessment response to these requests and the patient can leave with the prescription.

9 PBAC Outcome

- 9.1 The PBAC did not recommend changing the authority levels for Hadlima from Authority Required (Written) to Authority Required (Telephone) for initial prescribing, and from Authority Required (Telephone) to Authority Required (STREAMLINED) for first continuing prescribing. For initial prescribing, the PBAC considered that a full assessment (written) is appropriate for Hadlima on the basis that the restrictions are complex and require prescribers to provide detailed clinical information to support the relevant PBS authority application. With a telephone authority, the PBAC considered it may be difficult and time consuming for Services Australia administrators to ensure that the specific entry criteria are explicitly addressed.
- 9.2 The PBAC acknowledged that the Government is committed to promoting the greater use of biosimilar medicines in Australia and will support the introduction of measures that improve the uptake of biosimilar medicines as recommended by the Committee on a case-by-case basis. The PBAC noted that the Department is working with Services Australia to assess the requirements of PBS items which require paper based evidence (such as Hadlima) and will seek the PBAC's advice for change where appropriate.
- 9.3 For bDMARD/biologic-naïve patients, the PBAC noted the sponsor's request for having the use of a biosimilar in the first instance not count as a treatment failure as part of

a treatment cycle, as one of five agents in RA or three agents in AS, PsA or CPP. The PBAC reiterated that this request fell outside of the biosimilar uptake measures as agreed under the Strategic Agreements with Medicines Australia (the Strategic Agreements) and acknowledged by GBMA, and would require further consideration by these stakeholders, as well as the Joint Oversight Committee (composed of Department of Health and Medicines Australia representatives) established under the Medicines Australia Strategic Agreement. The PBAC also noted that the pre-PBAC response (p2) stated that, if a patient failed treatment on the biosimilar, they would no longer be eligible for that drug (as per the current restriction which disallows retrieval with the same drug). The PBAC did not support this request on the basis that a biosimilar medicine is a highly similar version of a reference biological medicine and contemporary clinical evidence does not support that the biosimilar be exempt from the treatment failure rule.

Outcome:

Rejected

10 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.

11 Sponsor's Comment

MSD is disappointed the PBAC has rejected additional biosimilar uptake drivers proposed to support patient and clinician use of biosimilars. We remain ready to engage productively in discussions with the government, PBAC and relevant stakeholders to deliver benefits to patients and the health system.