

## **5.18 ADALIMUMAB, Injection 80 mg in 0.8 mL pre-filled syringe, Humira<sup>®</sup>, AbbVie Pty Ltd**

### **1 Purpose of Submission**

- 1.1 The Category 4 submission requested General Schedule listings of adalimumab 80 mg/0.8 mL pre-filled syringe (PFS) (1 pack) as an induction dose for patients weighing less than 40 kg, with moderate to severe ulcerative colitis (herein referred to as UC) or severe Crohn disease (herein referred to as CD). The requested listings are in addition to the existing adalimumab 40 mg (2 pack) listings for this patient population and are not intended to replace them.

### **2 Background**

- 2.1 The Sponsor confirmed in their pre-PBAC response that the submission was for the PFS only and intentionally did not include the 80 mg/0.8 mL pre-filled pen (cartridge) form.

#### ***Previous PBAC consideration***

- 2.2 At its July 2018 meeting, the PBAC recommended listing an 80 mg form of adalimumab in a PFS and pre-filled pen (cartridge) to substitute for two 40 mg injections for those conditions that require a dose of 80 mg or higher.
- 2.3 The PBAC recommended an Authority Required listing for a new form and strength of adalimumab as follows:
- 80 mg/0.8 mL in PFS and pre-filled pen (cartridge) for the treatment of moderate to severe UC, fistulising CD, severe CD, moderate to severe hidradenitis suppurativa and chronic severe plaque psoriasis.
- 2.4 In making the recommendation, the PBAC noted that the 80 mg/0.8 mL forms of adalimumab have different pack sizes to adalimumab 40 mg/0.8 mL and advised that the new forms should be cost neutral.

#### ***Registration status***

- 2.5 Adalimumab (Humira) 80 mg/0.8 mL was registered on the Australian Register of Therapeutic Goods (ARTG) on 3 January 2018 for the following indications:
- Rheumatoid Arthritis

- Juvenile Idiopathic Arthritis
- Psoriatic Arthritis
- Ankylosing Spondylitis
- CD in Adults and Children ( $\geq 6$  years)
- UC
- Psoriasis in Adults and Children
- Hidradenitis Suppurativa in Adults and Adolescents (from 12 years of age)
- Uveitis.

### 3 Requested listing

#### 3.1 Add new medicinal product pack as follows:

For patients with moderate to severe UC weighing less than 40 kg

Name, restriction, manner of administration, form	Max. Qty (packs)	Max. Qty (units)	No. of repeats	PBS item code	Proprietary name and manufacturer
ADALIMUMAB adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	1	1	0	NEW	Humira® AbbVie Pty Ltd

For patients with severe CD weighing less than 40 kg

Name, restriction, manner of administration, form	Max. Qty (packs)	Max. Qty (units)	No. of repeats	PBS item code	Proprietary name and manufacturer
ADALIMUMAB adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	1	1	0	NEW	Humira® AbbVie Pty Ltd

- 3.2 The Sponsor requested the restriction wording of the new listings above to be consistent with the existing listings for adalimumab 40 mg formulations listed for the same indications.
- 3.3 The Secretariat suggested changes in italics for additions and strikethrough for deletions to the existing Administrative Advice [27132] under the current 80 mg listing for moderate to severe UC is presented below.

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**Note**

Two completed authority prescriptions should be submitted with every initial application for this biological medicine.

**Prescribing the 40 mg presentation:**

For patients weighing at least 40 kg, one prescription should be for the induction doses, containing a quantity of 6 doses of 40 mg and no repeats and the second prescription should be written for 2 doses of 40 mg and 2 repeats.

*For patients weighing less than 40 kg, one prescription should be written for 2 doses of 40 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.*

**Prescribing the 80 mg presentation:**

For patients weighing at least 40 kg, one prescription should be for the 80 mg presentation with a quantity of 3 units and zero repeats. This will enable doses at week 0 and week 2 to be completed. The second prescription should be written for 2 doses of 40 mg and 2 repeats.

**Patient weighing less than 40 kg:**

For patients weighing less than 40 kg, one prescription should be written for ~~2 doses of 40 mg~~ 1 dose of 80 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.

3.4 The Secretariat suggested changes to the existing Administrative Advice [27131] under the current 80 mg listing for severe CD is presented below.

[27131]	<p><b>Administrative Advice:</b> Two completed authority prescriptions should be submitted with every initial application for this biological medicine.</p> <p><b>Prescribing the 40 mg presentation:</b> For patients weighing at least 40 kg, one prescription should be for the induction doses, containing a quantity of 6 doses of 40 mg and no repeats and the second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><i>For patients weighing less than 40 kg, one prescription should be written for 2 doses of 40 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</i></p> <p><b>Prescribing the 80 mg presentation:</b> For patients weighing at least 40 kg, one prescription should be for the 80 mg presentation with a quantity of 3 units and zero repeats. This will enable doses at week 0 and week 2 to be completed. The second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><b>Patient weighing less than 40 kg:</b> For patients weighing less than 40 kg, one prescription should be written for <del>a single doses of 480 mg</del> with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</p> <p><b>Requests for quantities/repeats insufficient to complete 16 weeks:</b> If fewer than 2 repeats (for patients 40 kg or greater) or 3 repeats (for patients less than 40 kg) are requested at the time of the application, authority approvals for sufficient repeats to complete a maximum of 16 weeks of treatment with this drug may be sought through the 'Balance of Supply' PBS restriction.</p>
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For more detail on PBAC's view, see section 6 PBAC outcome.

## 4 Comparator

- 4.1 The submission nominated two adalimumab 40 mg injections administered by subcutaneous injection in a PFS as the comparator for one dose of adalimumab 80 mg via PFS.
- 4.2 The PBAC considered that the proposed comparator 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 that this item received no consumer comments.

### ***Clinical trials***

- 5.3 As a Category 4 submission, no new clinical trials were presented in the submission.

### ***Clinical claim***

- 5.4 The submission claimed that one injection of adalimumab 80 mg/0.8 mL via PFS is equivalent to two injections of adalimumab 40 mg via PFS with respect to bioequivalence, safety, and efficacy.
- 5.5 The submission claimed that availability of the adalimumab 80 mg/0.8 mL PFS form on the PBS will reduce the treatment burden for patients weighing less than 40 kg, with moderate to severe UC or severe CD who require one dose of 80 mg at induction, as patients will require only one injection instead of two. The PBAC considered that this was reasonable.

### ***Economic analysis***

- 5.6 As a Category 4 submission, there was no economic comparison presented.

### ***Estimated PBS usage & financial implications***

- 5.7 The submission estimated there to be no financial implications to the PBS as the adalimumab 80 mg/0.8 mL PFS (1 pack) formulation would only substitute for adalimumab 40 mg/0.4 mL PFS (2 pack) at the same price with no expected change to current utilisation.

- 5.8 The PBAC noted that the proposed approved ex-manufacturer price (AEMP) for the requested listings are identical to existing adalimumab 40 mg/0.4 mL PFS (2 pack) listings.
- 5.9 The PBAC noted that the requested listings of adalimumab 80 mg/0.8 mL PFS may substitute for the existing treatment initiation listings of adalimumab 40 mg/0.8 mL that have biosimilar brands available. However, the PBAC noted that the affected patient population is expected to be small and therefore any impact to the PBS would likely be negligible.
- 5.10 The PBAC also noted that there are currently no biosimilar brands for adalimumab 80 mg listed on the PBS and considered that the requested listings may encourage Sponsors to bring an adalimumab 80 mg biosimilar product to market.

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

## **6 PBAC Outcome**

- 6.1 The PBAC recommended Authority Required listings of adalimumab 80 mg/0.8 mL PFS (1 pack) as an induction dose for patients with moderate to severe UC or severe CD weighing less than 40 kg, on the basis of cost-neutrality with the existing listings of adalimumab 40 mg PFS (2 pack).
- 6.2 The PBAC considered the proposed maximum quantities and repeats for the requested new listings of adalimumab 80 mg/0.8 mL PFS appropriate for its intended use, replacing two doses of the 40 mg formulation in treatment induction.
- 6.3 The PBAC accepted that one dose of adalimumab 80 mg/0.8 mL via PFS provides an alternative for patients weighing less than 40 kg, with moderate to severe UC or severe CD to its comparator (two adalimumab 40 mg injections administered by subcutaneous injection in a PFS).
- 6.4 The PBAC considered that the requested listings of adalimumab 80 mg/0.8 mL PFS may substitute for the existing treatment initiation listings of adalimumab 40 mg/0.8 mL that have biosimilar brands. However, the PBAC noted that the affected patient population is expected to be small and therefore any impact to the PBS would likely be negligible.
- 6.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because adalimumab 80 mg/0.8 mL PFS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over adalimumab 40 mg PFS, 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.

- 6.6 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 item for Moderate to Severe Ulcerative Colitis (11640) with restriction wording consistent with 12347W and for Severe Crohn disease (11290) with restriction wording consistent with 12373F:

Name, restriction, manner of administration, form	Max. Qty (packs)	Max. Qty (units)	No. of repeats	PBS item code	Proprietary name and manufacturer
ADALIMUMAB adalimumab 80 mg/0.8 mL injection, 0.8 mL syringe	1	1	0	NEW	Humira® AbbVie Pty Ltd

- 7.2 Amend the following Administrative Advice in 12374G and flow on to the new item listed above for Moderate to Severe Ulcerative Colitis, 12347W, 12346T, 12359L, 12382Q, 12344Q, 10944B and 12333D.

Edit 27132	<p><b>Administrative Advice:</b></p> <p>Two completed authority prescriptions should be submitted with every initial application for this biological medicine.</p> <p><b>Prescribing the 40 mg presentation:</b></p> <p>For patients weighing at least 40 kg, one prescription should be for the induction doses, containing a quantity of 6 doses of 40 mg and no repeats and the second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><i>For patients weighing less than 40 kg, one prescription should be written for 2 doses of 40 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</i></p> <p><b>Prescribing the 80 mg presentation:</b></p> <p>For patients weighing at least 40 kg, one prescription should be for the 80 mg presentation with a quantity of 3 units and zero repeats. This will enable doses at week 0 and week 2 to be completed. The second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><b>Patient weighing less than 40 kg:</b></p> <p>For patients weighing less than 40 kg, one prescription should be written for <del>2 doses of 40 mg</del> 1 dose of 80 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</p>
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Amend the following Administrative Advice in 12426B and flow on to the new item listed above for Severe Crohn disease, 12373F, 12441T, 12338J, 12455M, 12392F, 12416L and 10419J.

Edit [27131]	<p><b>Administrative Advice:</b></p> <p>Two completed authority prescriptions should be submitted with every initial application for this biological medicine.</p> <p><b>Prescribing the 40 mg presentation:</b></p> <p>For patients weighing at least 40 kg, one prescription should be for the induction doses, containing a quantity of 6 doses of 40 mg and no repeats and the second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><i>For patients weighing less than 40 kg, one prescription should be written for 2 doses of 40 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</i></p> <p><b>Prescribing the 80 mg presentation:</b></p> <p>For patients weighing at least 40 kg, one prescription should be for the 80 mg presentation with a quantity of 3 units and zero repeats. This will enable doses at week 0 and week 2 to be completed. The second prescription should be written for 2 doses of 40 mg and 2 repeats.</p> <p><del>Patient weighing less than 40 kg:</del></p> <p>For patients weighing less than 40 kg, one prescription should be written for <del>2 doses of 40 mg</del> 1 dose of 80 mg with no repeats and the second prescription should be written for 2 doses of 20 mg with 3 repeats.</p> <p><b>Requests for quantities/repeats insufficient to complete 16 weeks:</b></p> <p>If fewer than 2 repeats (for patients 40 kg or greater) or 3 repeats (for patients less than 40 kg) are requested at the time of the application, authority approvals for sufficient repeats to complete a maximum of 16 weeks of treatment with this drug may be sought through the 'Balance of Supply' PBS restriction.</p>
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***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.