

6.17 EVOLOCUMAB

**Injection 420 mg in 3.5 mL single use pre-filled cartridge,
Injection 140 mg in 1 mL single use pre-filled pen,
Repatha[®],
Amgen Australia Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested an amendment to the Authority Required listings of evolocumab for all indications to allow general practitioners (GPs) to initiate treatment, but only after having consulted a specialist.

2 Background

- 2.1 Historically, the treatment criterion for evolocumab for the homozygous familial hypercholesterolaemia (ho-FH) listing (for initiation) was, “Must be treated by or in consultation with a specialist physician”.
- 2.2 In March 2018, when evolocumab was recommended for listing in heterozygous FH (he-FH), the treatment criterion was changed to “Must be treated by a specialist physician” as a means of tightening the restriction for the larger he-FH population. The existing ho-FH listing was changed accordingly to align the restrictions. The current minor submission explained that, as the overall FH population is relatively small, evolocumab treatment for both homozygous and heterozygous eligible patients could reasonably be managed by specialists, particularly those practising in lipid clinics, due to the hereditary nature of the disease.
- 2.3 The July 2019 submission for non-FH, followed by the November 2019 minor resubmission (effective 1 May 2020), requested that, for all evolocumab initiation listings across all indications, the treatment criterion should be “Must be treated by or in consultation with a specialist physician”. The current minor submission stated that the eligible non-FH patient population is substantially larger and is predominantly managed in the community by GPs. Furthermore, the sponsor claimed that the patient numbers that informed the financial estimates of the current evolocumab risk sharing arrangement (RSA) were calculated based on the assumption that GPs would be able to initiate treatment in consultation with a specialist physician. However, in its consideration of the November 2019 minor resubmission, the PBAC considered that the treatment criterion “Must be treated by a specialist physician” for initiation of treatment should remain for all indications, consistent with its previous advice (paragraph 2.7, evolocumab Public Summary Document (PSD), November 2019).

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

3 Requested listing

- 3.1 The minor submission requested amendments to the treatment criteria for all evolocumab initial treatment restrictions from “Must be treated by a specialist physician” to “Must be treated by or in consultation with a specialist physician”.
- 3.2 It was requested that the amendments would apply to all existing evolocumab initial treatment restrictions, including any remaining grandfathering restrictions:
- Evolocumab homozygous familial hypercholesterolaemia restrictions (Item codes 10958R, 11193D); and
 - Evolocumab heterozygous familial hypercholesterolaemia and non-familial hypercholesterolaemia restriction (Item codes 11484K, 11485L).
- 3.3 Under the proposed changes, the existing Authority Required restriction types would remain unchanged as:
- Authority Required (online/telephone) for initial treatment; and
 - Authority Required (STREAMLINED) for continuing treatment (which is silent on prescriber type).
- 3.4 The minor submission stated that patient eligibility criteria to initiate evolocumab treatment would continue to be assessed by Services Australia. GPs would need to provide and document evidence of patient eligibility, as specialists currently do. The sponsor stated that the expansion of the prescriber type to include GPs to initiate evolocumab treatment in consultation with a specialist should therefore not result in utilisation outside of the eligible population.
- 3.5 The PBAC noted that the nature of “in consultation with a specialist” has never been defined in PBS restrictions because the consultation could, in practice, occur through a variety of reasonable means (e.g. formalised management plan in writing or a telephone conversation).
- 3.6 The PBAC noted the options for the requested listing presented below.

Option 1 – proposed by sponsor:

Treatment criteria:
Must be treated by <i>or in consultation with</i> a specialist physician

Option 2 – proposed by sponsor, re-phrased by the Secretariat:

Treatment criteria:
Must be treated by a specialist physician; or
Must be treated by a physician who has consulted a specialist physician.

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 health care professionals (12) via the Consumer Comments facility on the PBS website. The comments described the benefits of treatment with evolocumab in terms of lipid-lowering effects and prevention of cardiovascular events. The majority of comments were in support of the proposed listing as a means of allowing timely access to the drug, particularly for rural and remote patients. One comment, from a consultant physician, stated that patients, in most cases, should see a specialist before evolocumab is prescribed, and that treatment by a GP in collaboration with a consultant physician would only be appropriate for continuing therapy.

Supporting evidence

4.3 The minor submission provided several arguments to support the requested expanded listing. These are outlined in the table below.

Table 1: Arguments to support the expanded evolocumab listing

Argument	Supporting evidence
Specialist physician numbers are insufficient to initiate evolocumab treatment for the number of high-risk atherosclerotic cardiovascular disease (ASCVD) patients deemed eligible by the PBAC.	<ul style="list-style-type: none"> • The financial estimates provided by the sponsor in December 2019 calculated that up to ██████ 1 patients would receive PBS-funded treatment. • In 2020, the Australian Health Practitioner Regulation Agency reported that there are 1,535 cardiologists, 1,940 general medicine physicians and 805 endocrinologists registered in Australia¹. • Of these specialists, approximately 1000 appear to be involved in prescribing lipid lowering therapies². Each specialist is therefore tasked with initiating over 500 eligible patients in addition to their current case load.
Restricting treatment initiation to specialist physicians only creates inequity of access.	<ul style="list-style-type: none"> • Geography: <ul style="list-style-type: none"> ○ One in four Australians living in non-urban regions suffer from CVD. People living in remote and very remote areas have 30% higher hospitalisation rates for CVD compared to those living in metropolitan areas, and CVD death rates are 1.4 times higher in remote and very remote areas than metropolitan areas^{3,4}. ○ Only 11.5% of cardiologists are located in regional, rural and remote areas and the availability of local specialist services diminishes with population remoteness^{5,6}. • Socio-economic status: <ul style="list-style-type: none"> ○ In 2016, Australians living in the lowest socioeconomic areas reported 1.76 times the heart attack rates compared to those in the highest socioeconomic areas and were 1.5 times more likely to die from their disease⁷. ○ Cardiologists are also less likely to practice in the public hospital sector, with 60% working in the private sector⁸. ○ The South Australian Health Specialist Outpatient Clinics Waiting Time Report (December 2019) reported a median waiting time of over a year to see a cardiologist at the State's largest hospital (Royal Adelaide Hospital)⁹. • Aboriginal and Torres Strait Islanders; those with mental illness; and the elderly: <ul style="list-style-type: none"> ○ Sixteen percent of Indigenous peoples aged 35-74 years have a high primary absolute CVD risk, and Indigenous people die from circulatory diseases at 1.7 times the rate of non-Indigenous Australians^{10,11}. ○ Serious mental illness patients face a 78% chance of developing CVD over the longer term¹². ○ In Australia, the AIHW reported that 30% of patients aged over 65 years report high LDL-C levels and more than 4 out of 5 CVD hospitalisations (83%) occur in high-risk patients aged 55 years or older¹³.
Evolocumab eligible patients are at even higher risk during Covid-19.	<ul style="list-style-type: none"> • The Cardiovascular Disease and Covid-19: Australian/New Zealand Consensus Statement states that “the presence of underlying cardiovascular disease (CVD) confers the highest mortality with COVID-19 disease, and thus patients with CVD must be considered a particularly high-risk population”¹⁴.

Argument	Supporting evidence
There is clinician support for the proposed amendment.	<ul style="list-style-type: none"> Of the 43,513 GPs currently registered across Australia, it is anticipated that up to 2,500 GPs who sub-specialise in ASCVD will be confident to initiate evolocumab treatment with support from their cardiologist, or endocrinologist partner. The PBAC noted that, according to the reference provided by the sponsor, the number of GPs currently registered in Australia is 27,145. There are 43,513 medical practitioners with General Registration¹. Members of the sponsor's advisory board have advised that there are several established pathways through which specialists and GPs can collaborate on appropriate patient care within the community. <ul style="list-style-type: none"> These include multidisciplinary case conferences, the hospital discharge letter, and the specialist's response to the GP patient referral letter following in-person or telehealth consultation and e-mail correspondence.
There will be no additional financial impact beyond the existing financial estimates and RSA.	<ul style="list-style-type: none"> The minor submission claimed that the patient numbers that informed the financial estimates of the current RSA were calculated based on the assumption that GPs would be able to initiate treatment in consultation with a specialist physician. In proposing the amendment, the sponsor does not anticipate any change to the special pricing arrangement (SPA) and RSA, which inform the existing Evolocumab Deed of Agreement.

Source: Minor submission, pages 4-11

The redacted values correspond to the following range:

150,000 to 60,000

Estimated PBS usage & financial implications

- 4.4 The minor submission claimed that the proposed amendment would not increase the cost of evolocumab above the financial estimates that form the basis of the RSA.
- 4.5 The minor submission also claimed that these estimates already assumed GPs would initiate treatment in consultation with specialists under an Authority Required restriction.
- 4.6 The PBAC noted that these two claims appear to be reasonable. Data extracted by the PBAC Drug Utilisation Subcommittee (DUSC) Secretariat showed that, from 2017-2019, GPs were identified as prescribers for current claims, although they tended to be more involved in prescribing continuing scripts. Further, based on the Deed for evolocumab, current use is within the RSA.
- 4.7 A summary of the evolocumab RSA subsidisation caps are included in Table 2. A tiered arrangement was agreed, with a [REDACTED] % rebate for expenditure between Tier 1 and Tier 2 and a [REDACTED] ([REDACTED] % rebate) beyond Tier 2. The maximum cost impact of the evolocumab listing is also shown in Table 2.

Table 2: Evolocumab RSA caps – commonwealth payment

	Year 1	Year 2	Year 3	Year 4	Year 5
Subsidisation Cap 1 (Tier 1)	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Subsidisation Cap 2 (Tier 2)	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
Maximum cost of PBS evolocumab	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]

Source: Table 1, page 11 of minor submission; Evolocumab Deed of Agreement signed [REDACTED]

- 4.8 The minor submission stated that the sponsor is committed to supporting the quality use of evolocumab for treatment of the eligible population. The sponsor anticipated that GPs with a cardiovascular (CV) speciality who currently work within an established care partnership with a specialist would prescribe evolocumab. The sponsor was asked to clarify whether “CV speciality” referred to any specific cardiology qualifications. The pre-PBAC response stated that those who initiate evolocumab treatment will be a subset of GPs, without any specific qualifications, but with high awareness of cardiovascular disease management, knowledge of the treatment guidelines, and recognition of the importance of treating to lipid targets.
- 4.9 The minor submission also provided an overview of planned educational activities to upskill GPs on CV health and optimal treatment, appropriate use of CV medicines, evolocumab patient eligibility and PBS restrictions.

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

5 PBAC Outcome

- 5.1 The PBAC did not recommend an amendment to the Authority Required listings of evolocumab for all indications to allow GPs to initiate treatment after having consulted a specialist. The PBAC advised that “Must be treated by a specialist physician” for initiation of treatment should remain for all indications, consistent with its previous advice.
- 5.2 The PBAC noted that the majority of consumer comments were from health professionals in support of the requested listing for evolocumab, describing the need for timely access to treatment, particularly for rural and remote patients.
- 5.3 Noting the arguments to support the requested listing, as outlined in paragraph 4.3, the PBAC recalled that it had recently considered the issue (in November 2019), and had determined that only specialists should initiate treatment. Furthermore, the PBAC considered that “consultation with a specialist physician” could, in practice, occur through a variety of means.
- 5.4 The PBAC had several concerns with expanding the prescriber types after evolocumab’s listing had just updated 5 months prior, these being:
- Evolocumab is a relatively new drug with uncertain uptake and financial estimates;
 - Evolocumab is a (novel) third-line therapy, with only 20% of GPs regularly prescribing second-line therapies;
 - Whilst there is an RSA in place, there is still the risk of use outside the intended high-risk population (particularly for non-familial hypercholesterolaemia (non-FH); and

- There is also the risk of patients undergoing inadequate trials of statin therapy before commencing treatment with evolocumab.
- 5.5 The PBAC considered there had been no material change in circumstances in terms of evolocumab's known clinical risks/benefits and the management of hypercholesterolaemia since its November 2019 recommendation. The PBAC noted that evolocumab was listed on the PBS for non-FH in May 2020 and considered it was too early to assess the combined financial impact of all indications.
- 5.6 The PBAC advised that it would be appropriate for DUSC to review the utilisation data after at least 18 months from the date evolocumab's listing was extended to include non-familial hypercholesterolaemia (1 May 2020) and the issue of GP initiation could be reassessed at that time.
- 5.7 The PBAC noted that this submission would not meet the criteria for an Independent Review because the treatment is not targeting a different population or stage of disease.

Outcome:

Rejected

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

Amgen will continue to work with the PBAC on this matter so Australians have equitable access to evolocumab.

¹ Ahpra Medical Board Registration Data Table-March 2020 <https://www.medicalboard.gov.au/News/Statistics.aspx> accessed 28th May 2020

² Nostradata (assumption based on specialist statin prescribing using 10% PBS data)

³ Cardiovascular disease in Rural Australia Fact Sheet Jan 2015 National Rural Health Alliance Inc. https://www.ruralhealth.org.au/sites/default/files/publications/cardiovascular-disease-fact-sheet_0.pdf accessed 29th May 2020

⁴ AIHW Cardiovascular Disease July 2020 update <https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium/contents/what-is-cardiovascular-disease> accessed 15th July 2020

⁵ Cardiology Fact Sheet 2016 <https://hwd.health.gov.au/webapi/customer/documents/factsheets/2016/Cardiology.pdf>

- ⁶ O'Sullivan et al 2017 Specialist Outreach Services in Regional and Remote Australia: Key Drivers and Policy Implications https://pubmed.ncbi.nlm.nih.gov/28764622/?from_term=OSullivan+BG%5BAuthor%5D&from_pos=2
- ⁷ AIHW Indicators of socioeconomic inequalities of cardiovascular disease, diabetes and chronic kidney disease <https://www.aihw.gov.au/getmedia/01c5bb07-592e-432e-9fba-d242e0f7e27e/aihw-cdk-12.pdf.aspx?inline=true>
- ⁸ Cardiology Fact Sheet 2016 <https://hwd.health.gov.au/webapi/customer/documents/factsheets/2016/Cardiology.pdf>
- ⁹ SA Health Specialist Outpatient Clinics Waiting Time Report Census date as at 31 December 2019 <https://www.sahealth.sa.gov.au/wps/wcm/connect/5865e046-a2ff-43ec-bc2f-406ee767f53f/Attachment+1+-++Specialist+Outpatient+Clinics+Waiting+Time+Report+-+Cens.....pdf?MOD=AJPERES&CACHEID=ROOTWORKSPACE-5865e046-a2ff-43ec-bc2f-406ee767f53f-n5j0Z4C>
- ¹⁰ Calabria B et al Absolute cardiovascular disease risk and lipid-lowering therapy among Aboriginal and Torres Strait Islander Australians MJA 2018 209 (1) 35: 41 <https://www.mja.com.au/journal/2018/209/1/absolute-cardiovascular-disease-risk-and-lipid-lowering-therapy-among-aboriginal>
- ¹¹ Australian Health Minister's Advisory Council. Aboriginal and Torres Strait islander health performance framework 2012 report. Canberra: AHMAC; 2012.
- ¹² Correll et al World Psychiatry 2017;16:163–180
- ¹³ AIHW Cardiovascular Disease July 2020 update <https://www.aihw.gov.au/reports/heart-stroke-vascular-diseases/cardiovascular-health-compendium/contents/what-is-cardiovascular-disease> accessed 15th July 2020
- ¹⁴ Cardiovascular disease and Covid-19: Australian/ NZ Consensus Statement MJA April 2020. <https://www.mja.com.au/journal/2020/cardiovascular-disease-and-covid-19-australiannew-zealand-consensus-statement>. Accessed 9th April 2020.