

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

1 Purpose of Submission

- 1.1 The Category 3 submission requested the following changes to the existing listings for evolocumab injection 140 mg in 1 mL single use pre-filled pen and injection 420 mg in 3.5 mL single use pre-filled cartridge (Repatha[®]) for the treatment of homozygous familial hypercholesterolaemia (HoFH), heterozygous familial hypercholesterolaemia (HeFH) and non-familial hypercholesterolaemia (non-FH):
- a change to the restriction level from Authority Required (telephone/online) to Authority Required (STREAMLINED) for initial treatment.
 - a reduction in the minimum treatment duration for both the maximum tolerated dose of statin and ezetimibe, prior to initiating evolocumab in the clinical criteria (from 12 weeks to 4 weeks for each).

2 Background

- 2.1 Evolocumab 140 mg/mL and 420 mg/3.5 mL is currently listed on the Pharmaceutical Benefits Scheme (PBS) as an Authority Required (Telephone/Online) listing for initial treatment and Authority Required (STREAMLINED) for continuing treatment for the indications listed in paragraph 1.1.
- 2.2 The submission claimed the requested changes to the PBS listings of evolocumab would reduce the administrative burden on prescribers and improve patient care and outcomes through timely access to low-density lipoprotein (LDL) cholesterol lowering therapy.

Registration status

- 2.3 Evolocumab 140 mg/mL and 420 mg/3.5 mL was Therapeutic Goods Administration (TGA) registered on 4 December 2015. Repatha is indicated for the treatment of:
- primary hypercholesterolaemia in adults (including HeFH and Non-FH) to reduce LDL cholesterol, in combination with a statin or statin with other lipid-lowering therapies, or alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant.

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- HoFH in adults and adolescents ≥ 12 years in combination with other lipid-lowering therapies.
- 2.4 In August 2018, an additional TGA-registered indication was added for evolocumab 140 mg/mL and 420 mg/3.5 mL, to include prevention of cardiovascular events (myocardial infarction, stroke and coronary revascularisation) in adults with established cardiovascular disease in combination with an optimally dosed statin and/or other lipid-lowering therapies.
- 2.5 The recommended dose for primary hypercholesterolaemia and the prevention of cardiovascular events is 140 mg every 2 weeks or 420 mg once a month. The recommended dose for HoFH is 420 mg once a month (the dose can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks).

Previous PBAC consideration

- 2.6 Evolocumab 140 mg/mL was first recommended for PBS listing by the Pharmaceutical Benefits Advisory Committee (PBAC) at its March 2016 meeting for HoFH (but not the broader HeFH population) (paragraph 7.1, evolocumab, Public Summary Document (PSD), March 2016 PBAC Meeting).
- 2.7 At its July 2017 PBAC meeting, the PBAC recommended PBS listing of evolocumab 420 mg/3.5 mL for HoFH, under the same circumstances as evolocumab 140 mg/mL that was already listed (paragraphs 6.1 and 6.3, evolocumab, PSD, July 2017 PBAC Meeting).
- 2.8 At its March 2018 meeting, the PBAC recommended listing evolocumab 140 mg/mL and 420 mg/3.5 mL for the treatment of patients with both HeFH and HoFH (paragraph 5.1, evolocumab, PSD, March 2018 PBAC Meeting).
- 2.9 At its November 2019 meeting, the PBAC recommended the Authority Required listing of evolocumab in the following circumstances:
- Non-FH in patients with atherosclerotic cardiovascular disease (ASCVD), who have an LDL > 2.6 mmol/L and additional high-risk factors; and
 - Familial hypercholesterolaemia in patients with symptomatic ASCVD or HoFH who have an LDL between 2.6 and 3.3 mmol/L (paragraph 5.1, evolocumab, PSD, November 2019 PBAC Meeting).
- 2.10 For the non-FH and HeFH listing, the clinical criteria stated that the patient must have been treated with ezetimibe for at least 3 months and noted that the intent is that the ezetimibe trial must be completed prior to the patient commencing treatment with evolocumab (paragraph 2.8, evolocumab, PSD, November 2019 PBAC Meeting). The PBAC also recommended changes to the requested restriction, including adjusting the LDL prescriber instructions to clarify that the qualifying LDL cholesterol level must be following 3 months of treatment with a statin and ezetimibe (paragraph 5.4, evolocumab, PSD, November 2019 PBAC Meeting).

- 2.11 The PBAC also considered a request to change the restriction levels for evolocumab listings for familial hypercholesterolaemia, from Authority Required (Written) to Authority Required (Telephone/Online) for initial treatment, and from Authority Required (Telephone/Online) to Authority Required (STREAMLINED) for continuing treatment, at its November 2019 meeting, aligning with its requested restrictions for non-FH listings. The PBAC considered this was appropriate (paragraph 2.5, evolocumab, PSD, November 2019 PBAC Meeting).
- 2.12 At its July 2022 meeting, the PBAC recommended extending the PBAC listings for evolocumab to include patients who have an LDL cholesterol level between 1.8 and 2.6 mmol/L despite optimised treatment with statins and ezetimibe, and to allow initial prescribing by any medical practitioner in consultation with a specialist physician (paragraph 7.1, evolocumab, PSD, July 2022 PBAC Meeting). The PBAC considered there was a risk of use outside the restriction, but retaining an Authority Required (telephone/online) listing would help to mitigate this risk from the expanded listing (paragraph 7.15, evolocumab, PSD, July 2022 PBAC Meeting).
- 2.13 At its March 2023 meeting, the PBAC noted the report for evolocumab for hypercholesterolaemia from the February 2023 Drug Utilisation Sub-Committee (DUSC) meeting. The PBAC noted:
- evolocumab utilisation for non-FH was different from what was estimated.
 - the restriction changes since PBS listing of evolocumab and that the restriction changes that occurred in December 2022 (initial prescribing extended to any medical practitioner in consultation with a specialist physician and changes to the LDL cholesterol level criteria) were not included as part of the review, and that the LDL cholesterol level had been revised several times since PBS listing. The PBAC commented that utilisation of evolocumab would likely increase more rapidly as clinicians became aware of these changes.
 - there was a greater proportion of patients consistently supplied evolocumab for the same indication compared to Authority or Streamlined code in 2021. It considered this was likely due to prescriber error and noted the complexities with navigating the presentation of restriction and corresponding item codes in prescriber software (PBAC Consideration of the Report of the Drug Utilisation Sub-Committee, March 2023 PBAC Meeting).

Utilisation

- 2.14 The submission claimed utilisation of evolocumab on the PBS had been lower than forecast and had a stable initiation rate.
- 2.15 The submission stated there was an increase in use in 2020 due to the restriction changes to include patients with non-FH and symptomatic ASCVD, but stated the initiation rate is now relatively stable.

3 Requested listing

3.1 The submission requested the following changes to the existing listings of evolocumab 140 mg/mL injection (PBS Item codes 10958R and 11484K) and evolocumab 420 mg/3.5 mL injection (PBS Item codes 11193D and 11485L):

Amend restrictions as follows:

3.2 Suggested additions are in italics and deletions are in strikethrough.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EVOLOCUMAB					
evolocumab 140 mg/mL injection, 1 mL pen device	11484K	2	2	5	Repatha
evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	11485L	1	1	5	Repatha
Restriction Summary 13663 / Treatment of Concept: 13564					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.				
	Indication: Familial heterozygous hypercholesterolaemia				
	Treatment Phase Initial treatment				
	Clinical criteria:				
	The treatment must be in conjunction with dietary therapy and exercise,				
	AND				
	Clinical criteria:				
	The condition must have been confirmed by genetic testing; or				
	The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 6,				
	AND				
	Clinical criteria:				
	Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre in the presence of symptomatic atherosclerotic cardiovascular disease; or				
	Patient must have an LDL cholesterol level in excess of 5 millimoles per litre,				
	AND				
	Clinical criteria:				

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	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 4 12 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information,
	AND
	Clinical criteria:
	Patient must have been treated with ezetimibe for at least 4 12 consecutive weeks in conjunction with a statin (if tolerated), dietary therapy and exercise,
	AND
	Clinical criteria:
	Patient must not be receiving concomitant PBS-subsidised treatment with another drug that belongs to the same pharmacological class as this drug, for this PBS indication.
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.
	Prescribing Instructions: Symptomatic atherosclerotic cardiovascular disease is defined as: (i) the presence of symptomatic coronary artery disease (prior myocardial infarction, prior revascularisation procedure, angina associated with demonstrated significant coronary artery disease (50% or greater stenosis in 1 or more coronary arteries on imaging), or positive functional testing (e.g. myocardial perfusion scanning or stress echocardiography); or (ii) the presence of symptomatic cerebrovascular disease (prior ischaemic stroke, prior revascularisation procedure, or transient ischaemic attack associated with 50% or greater stenosis in 1 or more cerebral arteries on imaging); or (iii) the presence of symptomatic peripheral arterial disease (prior acute ischaemic event due to atherosclerosis, prior revascularisation procedure, or symptoms of ischaemia with evidence of significant peripheral artery disease (50% or greater stenosis in 1 or more peripheral arteries on imaging)).
	Prescribing Instructions: The qualifying LDL cholesterol level following at least 4 12 consecutive weeks of combined treatment with a statin, ezetimibe, dietary therapy and exercise (unless treatment with a statin is contraindicated, or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application, documented in the patient's medical records and must be no more than 8 weeks old.
	Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.
	Prescribing Instructions: If treatment with atorvastatin or rosuvastatin results in development of a clinically important product-related adverse event resulting in treatment withdrawal, the patient must be treated with the alternative statin (atorvastatin or rosuvastatin) unless there is a contraindication (e.g. prior rhabdomyolysis) to the alternative statin. This retrial should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retrial should not occur until CK has returned to normal.

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	<p>Prescribing Instructions: In the event of a trial of the alternative statin, it is recommended that the patient is started with the minimum dose of statin in conjunction with ezetimibe. The dose of the alternative statin should be increased not more often than every 4 weeks until the recommended or maximum tolerated dose has been reached or target LDL-c has been achieved.</p>
	<p>Prescribing Instructions: The following must be stated at the time of application and documented in the patient's medical records: (i) the qualifying Dutch Lipid Clinic Network Score; or (ii) the result of genetic testing confirming a diagnosis of familial heterozygous hypercholesterolaemia</p>
	<p>Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 4 12 consecutive weeks; or (ii) the doses, duration of treatment and details of adverse events experienced with trials with each of atorvastatin and rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information.</p>
<p>Restriction Summary 13468 / Treatment of Concept: 13563</p>	
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
	<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
	<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
	<p>Administrative Advice: Special Pricing Arrangements apply.</p>
	<p>Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.</p>
	<p>Indication: Non-familial hypercholesterolaemia</p>
	<p>Treatment Phase Initial treatment</p>
	<p>Clinical criteria:</p>
	<p>The treatment must be in conjunction with dietary therapy and exercise,</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>Patient must not be receiving concomitant PBS-subsidised treatment with another drug that belongs to the same pharmacological class as this drug,</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>Patient must have symptomatic atherosclerotic cardiovascular disease,</p>
	<p>AND</p>
	<p>Clinical criteria:</p>
	<p>Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre,</p>
	<p>AND</p>

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	Clinical criteria:
	Patient must have atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories); or
	Patient must have severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels; or
	Patient must have had at least two major cardiovascular events (i.e. myocardial infarction, unstable angina, stroke or unplanned revascularisation) in the previous 5 years; or
	Patient must have diabetes mellitus with microalbuminuria; or
	Patient must have diabetes mellitus and be aged 60 years or more; or
	Patient must be an Aboriginal or Torres Strait Islander with diabetes mellitus; or
	Patient must have a Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention of 4 or higher
	AND
	Clinical criteria:
	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 4 12 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information,
	AND
	Clinical criteria:
	Patient must have been treated with ezetimibe for at least 4 12 consecutive weeks in conjunction with a statin (if tolerated), dietary therapy and exercise.
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.
	Prescribing Instructions: Symptomatic atherosclerotic cardiovascular disease is defined as: (i) the presence of symptomatic coronary artery disease (prior myocardial infarction, prior revascularisation procedure, angina associated with demonstrated significant coronary artery disease (50% or greater stenosis in 1 or more coronary arteries on imaging), or positive functional testing (e.g. myocardial perfusion scanning or stress echocardiography); or (ii) the presence of symptomatic cerebrovascular disease (prior ischaemic stroke, prior revascularisation procedure, or transient ischaemic attack associated with 50% or greater stenosis in 1 or more cerebral arteries on imaging); or (iii) the presence of symptomatic peripheral arterial disease (prior acute ischaemic event due to atherosclerosis, prior revascularisation procedure, or symptoms of ischaemia with evidence of significant peripheral artery disease (50% or greater stenosis in 1 or more peripheral arteries on imaging)).
	Prescribing Instructions: The qualifying LDL cholesterol level following at least 4 12 consecutive weeks of combined treatment with a statin, ezetimibe, dietary therapy and exercise (unless treatment with a statin is contraindicated, or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application, documented in the patient's medical records and must be no more than 8 weeks old.

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	<p>Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.</p>
	<p>Prescribing Instructions: If treatment with atorvastatin or rosuvastatin results in development of a clinically important product-related adverse event resulting in treatment withdrawal, the patient must be treated with the alternative statin (atorvastatin or rosuvastatin) unless there is a contraindication (e.g. prior rhabdomyolysis) to the alternative statin. This retri al should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retri al should not occur until CK has returned to normal.</p>
	<p>Prescribing Instructions: In the event of a tri al of the alternative statin, it is recommended that the patient is started with the minimum dose of statin in conjunction with ezetimibe. The dose of the alternative statin should be increased not more often than every 4 weeks until the recommended or maximum tolerated dose has been reached or target LDL-c has been achieved.</p>
	<p>Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 4 12 consecutive weeks; or (ii) the doses, duration of treatment and details of adverse events experienced with tri als with each of atorvastatin and rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information.</p>
	<p>Prescribing Instructions: One or more of the following must be stated at the time of application and documented in the patient's medical records regarding the presence of cardiovascular disease or high risk of experiencing a cardiovascular event: (i) atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories); or (ii) severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels; or (iii) history of at least two major cardiovascular events (i.e. myocardial infarction, unstable angina, stroke or unplanned revascularisation) in the previous 5 years; or (iv) diabetes mellitus with microalbuminuria; or (v) diabetes mellitus and age 60 years of more; or (vi) Aboriginal or Torres Strait Islander with diabetes mellitus; or (vii) a Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention of 4 or higher</p>

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EVOLOCUMAB					
evolocumab 140 mg/mL injection, 1 mL pen device	10958R	3	3	5	Repatha
evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	11193D	1	1	5	Repatha
Restriction Summary 13623 / Treatment of Concept: 13469					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				

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	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.
	Indication: Familial homozygous hypercholesterolaemia
	Treatment Phase Initial treatment
	Clinical criteria:
	The treatment must be in conjunction with dietary therapy and exercise,
	AND
	Clinical criteria:
	The condition must have been confirmed by genetic testing; or
	The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 7,
	AND
	Clinical criteria:
	Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre,
	AND
	Clinical criteria:
	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 4 42 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information.
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.
	Prescribing Instructions: The qualifying LDL cholesterol level following at least 4 42 consecutive weeks of treatment with a statin (unless treatment with a statin is contraindicated or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application , documented in the patient's medical records and must be no more than 8 weeks old.
	Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.

	<p>Prescribing Instructions: The following must be stated at the time of application and documented in the patient's medical records: (i) the qualifying Dutch Lipid Clinic Network Score; or (ii) the result of genetic testing confirming a diagnosis of familial homozygous hypercholesterolaemia</p>
	<p>Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 4-12 consecutive weeks; or (ii) the dose, duration of treatment and details of adverse events experienced with the trial of atorvastatin or rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information</p>

3.3 Evolocumab 140 mg/mL and 420 mg/3.5 mL also have Authority Required (Telephone/Online) Grandfather listings for non-FH and HeFH. The clinical criteria for these listings state 'Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to 1 December 2022'.

Requested change in Authority requirements

3.4 The submission claimed that evolocumab was appropriate for an Authority Required (STREAMLINED) listing as it:

- is used to treat a chronic and stable long-term condition.
- has a stable dosage regime.
- is a medication that has a low risk of misuse.

3.5 The submission stated that most other medications used to treat hypercholesterolaemia on the PBS (including ezetimibe and statins) have an Authority Required (STREAMLINED) (for ezetimibe and ezetimibe/statin combinations) or Restricted Benefit listing. Statins are Restricted Benefits for 60 day prescription listings, and Unrestricted for the 1 pack quantity.

3.6 The submission considered the risk of using evolocumab outside of the PBS restriction would be low. It stated that the indications for evolocumab are well defined, there are criteria to define the eligible PBS population, prescribers are required to retain documented evidence, and therapy must be initiated by a specialist physician or a physician who has consulted a specialist physician.

Requested change in minimum treatment duration of prior therapy

3.7 The submission claimed the requirement for at least 12 weeks of maximum tolerated ezetimibe and statin therapy prior to evolocumab use does not align with local and international guidelines, which recommend re-assessing lipid levels and adding additional treatment if required after 4-8 weeks of initiating therapy. The current PBS restrictions require a patient to have received at least 12 weeks of therapy with a maximum recommended or tolerated dose of a statin (unless contraindicated or intolerant) and at least 12 weeks of ezetimibe therapy prior to receiving evolocumab.

The submission requested a reduction in the minimum treatment duration with both a statin and ezetimibe (from 12 weeks to 4 weeks for each). The request was therefore for a change from patients requiring at least 24 weeks of prior treatment before starting evolocumab to 8 weeks.

- 3.8 Ezetimibe is currently PBS-listed for the treatment of hypercholesterolaemia, with the clinical criterion ‘Patients must have cholesterol concentrations that are inadequately controlled with an HMG CoA reductase inhibitor (statin)’. Inadequate control with a statin is defined as an LDL cholesterol concentration in excess of current target lipid levels for primary and secondary prevention after at least 3 months of treatment at a maximum tolerated dose of a statin. The PBAC previously accepted the PBS definition of uncontrolled cholesterol after a minimum of 3 months of treatment for all patients (section 12, ezetimibe, PSD, November 2010 PBAC Meeting).

4 Comparator

- 4.1 The submission did not nominate a comparator.
- 4.2 The PBAC previously considered ezetimibe and placebo as appropriate main comparators to evolocumab (paragraph 5.1, evolocumab, PSD, March 2016 PBAC Meeting; paragraph 5.1, evolocumab, PSD, November 2017 PBAC Meeting) and alirocumab as a secondary comparator (paragraph 5.2, evolocumab, PSD, March 2016 PBAC Meeting; paragraph 5.2, evolocumab, PSD, November 2017 PBAC Meeting) for familial hypercholesterolaemia. The PBAC considered optimised background treatment as the appropriate comparator to evolocumab for non-FH (paragraph 7.6, evolocumab, PSD, July 2022 PBAC Meeting).
- 4.3 The human proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor inclisiran was recommended by the PBAC for PBS listing for the treatment of HeFH and non-FH with ASCVD at its May 2023 PBAC meeting (paragraph 13.1, inclisiran, PSD, March 2023 PBAC Meeting with May 2023 Addendum). Inclisiran is not yet listed on the PBS.
- 4.4 The pre-PBAC response claimed that as the submission did not propose changes to the eligible patient population accessing evolocumab, comparators were not required.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from individuals (1), health care professionals (54) and organisations (1) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with evolocumab, including:

- its effectiveness in managing hypercholesterolaemia (and subsequently cardiovascular risk), which can be challenging to treat with other medications such as statins and ezetimibe in certain patients.
 - good safety and tolerability profile, including in patients unable to tolerate statins or ezetimibe.
 - easy administration.
 - improved quality of life in patients using evolocumab.
- 5.3 Comments expressed support for an Authority Required (STREAMLINED) listing for initial treatment with evolocumab, and stated this would facilitate prescribing and improved access to patients who require this medication.
- 5.4 A number of comments noted concern with challenges accessing evolocumab on the PBS and the time required before evolocumab could be initiated. Comments stated that the time needed before patients could access evolocumab exposed them to suboptimally controlled lipid levels for longer. The majority of comments expressed support for a shorter minimal treatment duration with a statin and ezetimibe prior to initiating evolocumab. Comments also stated that the longer timeframe until patients could initiate evolocumab increased the risk of patients being missed for follow-up management. However, several comments expressed support for maintaining the current required duration of taking a maximum tolerated dose of statin and ezetimibe prior to initiating evolocumab, with one comment noting that 4 weeks was an inadequate amount of time to measure the impact of medical and dietary interventions.
- 5.5 The PBAC noted the advice received from hearts4heart that a change to an Authority Required (STREAMLINED) listing for evolocumab would reduce the administrative burden on prescribers and allow increased time for patient care, and the recommendations in Australian and international guidelines regarding timelines when LDL cholesterol levels should be re-assessed.

Clinical guidelines

- 5.6 The submission claimed that the requirement for at least 12 weeks of treatment with both a maximum tolerated dose of statin and 12 weeks of treatment with ezetimibe (24 weeks in total) prior to initiating treatment with evolocumab did not align with local and international guidelines. It cited the following guidelines:
- The Australian Therapeutic Guidelines¹ recommend:
 - To assess the response to lipid-modifying therapy, recheck lipid concentrations around 6 weeks after starting or adjusting therapy.

¹ Therapeutic Guidelines. (2023) *Cardiovascular*, Therapeutic Guidelines Limited, Melbourne.

- Use statins as first-line lipid-modifying therapy to reduce ASCVD risk in all patients with established ASCVD or at high absolute ASCVD risk.
- Consider adding ezetimibe to statin therapy if the LDL cholesterol target concentration is not met after 6 weeks with the maximum tolerated dose of a statin alone.
- If the LDL cholesterol target is not achieved with the combination of the maximum tolerated dose of a statin plus ezetimibe, consider adding a PCSK9 inhibitor.
- The Asian Pacific Society of Cardiology Consensus Recommendations on Dyslipidaemia² recommend:
 - For patients with very high risk chronic coronary syndrome, upfront initiation of combination therapy with high-dose intensity statins and ezetimibe may be considered. A PCSK9 inhibitor may be added for those who do not achieve target within 4 weeks of initial therapy.
 - Reassessment of lipid levels after 4 weeks of therapy to assess treatment response and the need for up-titration of therapy was agreed on for patients with very-high-risk chronic coronary syndrome to avoid treatment inertia and ensure that targets are reached in the shortest time possible.
- The 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk recommend³:
 - lipid levels should be assessed 8 (\pm 4) weeks after starting lipid-lowering therapy, and 8 (\pm 4) weeks after treatment is adjusted until goal is achieved.
 - In patients with acute coronary syndrome at very high risk, if the LDL cholesterol level goal is not achieved after 4-6 weeks of the maximum tolerated dose of statin, combination with ezetimibe is recommended.
 - In patients with acute coronary syndrome, if the LDL-cholesterol target goal is not achieved after 4-6 weeks despite maximum tolerated statin dose and ezetimibe, addition of a PCSK9 inhibitor is recommended.
- The 2023 ESC Guidelines for the management of acute coronary syndromes⁴ recommend:
 - Lipid levels should be measured 4-6 weeks after each treatment or dose adjustment to determine if treatment goals have been achieved.

² Koh N, Ference BA, Nicholls SJ, et al. (2021) 'Asian Pacific Society of Cardiology Consensus Recommendations on Dyslipidaemia', *Eur Cardiol*, 16:1-6.

³ Mach F, Baigent C, Catapano AL, et al. (2020) '2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk', *European Heart J*, 41(1):111-188.

⁴ Byrne RA, Rossello X, Coughlan JJ, et al (2023) '2023 ESC Guidelines for the management of acute coronary syndromes', *Eur Heart J*, 44(38):3720-3826.

- If LDL cholesterol levels are not achieved with the maximum tolerated dose of a statin alone after 4-6 weeks following acute coronary syndrome, adding ezetimibe is recommended.
- A PCSK9 inhibitor is recommended if patients do not meet their LDL cholesterol goal after 4-6 weeks of therapy with a maximum tolerated dose of statin and ezetimibe.

5.7 The submission also cited a review article from 2019 which provided an author consensus of high-risk patients who should be considered for treatment with PCSK9 inhibitors. The LDL cholesterol levels cited are for patients treated with 6 weeks of a maximum tolerated dose of a statin followed by the addition of ezetimibe for 6 weeks.⁵

Clinical trials

5.8 The submission cited the findings of two recently completed extension studies evaluating the long-term safety, tolerability, and efficacy of evolocumab in patients with established cardiovascular disease who completed the phase 3 Study 20110118 (Study 20130295 and Study 20160250). The submission stated the results of these studies showed sustained reductions in LDL cholesterol levels with evolocumab therapy, and stated there were no new safety concerns identified in these studies, with adverse events similar to those seen in previous studies.

5.9 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Safety considerations

5.10 The submission provided the latest Periodic Safety Update Report (PSUR) (covering the period from 18 July 2022 to 17 July 2023). The report concluded that the evaluation of safety data did not result in the detection of any new risks for evolocumab, and the overall benefit-risk balance of evolocumab for its approved indications remained favourable.

Pricing considerations

5.11 The submission proposed no changes to the current prices of evolocumab.

5.12 Special pricing arrangements apply to the current listings of evolocumab 140 mg/mL and 420 mg/3.5 mL.

5.13 There is an established two-tier subsidisation cap arrangement based on forecast utilisation for the PCSK9 inhibitor class for current PBS listings (paragraph 6.58, evolocumab, PSD, July 2022 PBAC Meeting).

⁵ Scherer D, Nelson AJ, O'Brien R, et al (2019) 'Status of PCSK9 Monoclonal Antibodies in Australia', *Heart Lung Circ*, 28(10):1571-1579.

Drug cost/patient/year: \$ [redacted] for evolocumab 140 mg/mL and \$ [redacted] for evolocumab 420 mg/3.5 mL

5.14 The estimated drug cost/patient per year would be \$ [redacted] for evolocumab 140 mg/mL and \$ [redacted] for evolocumab 420 mg/3.5 mL, based on an effective dispensed price for maximum quantity (DPMQ) of \$ [redacted] and \$ [redacted], respectively, and 12 prescriptions per year for ongoing treatment.

Estimated PBS usage and financial implications

5.15 Table 1 presents the estimated extent of use, cost of evolocumab to the PBS/RPBS and the net financial implications to the PBS/RPBS. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

5.16 No additional discontinuations were expected during the requested additional treatment period.

5.17 The submission estimated that 30,000 to < 40,000 patients would begin treatment with evolocumab earlier with the requested listing over the first six years of listing (500 to < 5,000 in Year 1 to 500 to < 5,000 in Year 6).

5.18 The submission stated that the estimated net financial impact to the PBS/RPBS for the requested listing to initiate earlier treatment with evolocumab is \$20 million to < \$30 million over six years (Year 1 \$0 to < \$10 million to Year 6 \$0 to < \$10 million).

5.19 At year 6, the estimated number of patients was 500 to < 5,000 and the net cost to the PBS would be \$0 to < \$10 million .

Table 1: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[redacted] ¹	[redacted] ²	[redacted] ²	[redacted] ²	[redacted] ²	[redacted] ²
Number of scripts dispensed ^a	[redacted] ³	[redacted] ⁴	[redacted] ⁴	[redacted] ⁴	[redacted] ⁴	[redacted] ⁴
Net financial implications for evolocumab 140 mg/mL and 420 mg/3.5 mL						
Net cost to PBS/RPBS	[redacted] ⁵	[redacted] ⁵	[redacted] ⁵	[redacted] ⁵	[redacted] ⁵	[redacted] ⁵

^a Assuming 4 additional prescriptions per patient on initiation of treatment as estimated by the submission.

PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Source: Financial Estimates workbook

The redacted values correspond to the following ranges

¹ 500 to < 5,000

² 5,000 to < 10,000

³ 10,000 to < 20,000

⁴ 20,000 to < 30,000

⁵ \$0 to < \$10 million

Quality use of medicines

5.20 The submission stated the sponsor provides education activities to specialist physicians and general practitioners on treatment guidelines for cardiovascular disease, as well as the PBS eligibility criteria for evolocumab to support appropriate prescribing. Both face-to-face and online education activities are provided.

6 PBAC Outcome

Requested change to the restriction level from Authority Required (telephone/online) to Authority Required (STREAMLINED) for initial treatment

- 6.1 The PBAC recommended changing the restriction level from Authority Required (telephone/online) to Authority Required (STREAMLINED) for the initial treatment listings for evolocumab injection 140 mg in 1 mL single use pre-filled pen and evolocumab injection 420 mg in 3.5 mL single use pre-filled cartridge for the treatment of homozygous familial hypercholesterolaemia (HoFH), heterozygous familial hypercholesterolaemia (HeFH) and non-familial hypercholesterolaemia (non-FH).
- 6.2 The PBAC noted findings from the report for evolocumab from the February 2023 DUSC meeting, and the submission's claims that utilisation of evolocumab on the PBS had been lower than forecast and had a stable initiation rate.
- 6.3 The PBAC noted consumer comments received which expressed support for an Authority Required (STREAMLINED) listing for initial treatment with evolocumab, stating this would facilitate prescribing and access to patients requiring this medication.

Outcome:

Recommended

Requested reduction in the minimum treatment duration for both the maximum tolerated dose of statin and ezetimibe prior to initiating evolocumab

- 6.4 The PBAC did not recommend a reduction in the minimum treatment duration for both the maximum tolerated dose of statin and ezetimibe, prior to initiating evolocumab in the clinical criteria for the PBS-listings for evolocumab.
- 6.5 The PBAC noted the guidelines referenced in the submission regarding management of hypercholesterolaemia.
- 6.6 The PBAC noted the estimated cost to the PBS for initiating evolocumab earlier would be approximately \$30 million to < \$40 million over the first six years of listing. The PBAC noted that no evidence was provided to justify a clinical need to change the listing or demonstrate benefit to patients if evolocumab is initiated earlier than what is required in the current listing (i.e., after patients have received at least 12 weeks of therapy with a maximum tolerated dose of a statin and at least 12 weeks of ezetimibe therapy). The PBAC therefore considered that there was insufficient evidence or justification to support a change in listing and a subsequent higher cost to the PBS.

Outcome:

Not recommended

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- 6.7 The PBAC recommended removing the grandfather listings for evolocumab 140 mg/mL and 420 mg/3.5 mL for non-FH and He-FH, and advised they were no longer required.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as the requested change to the restriction level from Authority Required (telephone/online) to Authority Required (STREAMLINED) for initial treatment with evolocumab received a positive recommendation.

7 Recommended listing

7.1 Amend existing listings as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
EVOLOCUMAB					
evolocumab 140 mg/mL injection, 1 mL pen device	11484K	2	2	5	Repatha
evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	11485L	1	1	5	Repatha
Restriction Summary 13663 / Treatment of Concept: 13564					
Concept ID	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
Prescribing rule level	Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised.				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Administrative Advice: Special Pricing Arrangements apply.				
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.					
Indication: Familial heterozygous hypercholesterolaemia					
Treatment Phase Initial treatment					
Clinical criteria:					
The treatment must be in conjunction with dietary therapy and exercise,					
AND					
Clinical criteria:					
The condition must have been confirmed by genetic testing; or					
The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 6,					
AND					
Clinical criteria:					
Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre in the presence of symptomatic atherosclerotic cardiovascular disease; or					
Patient must have an LDL cholesterol level in excess of 5 millimoles per litre					

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	AND
	Clinical criteria:
	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 12 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information,
	AND
	Clinical criteria:
	Patient must have been treated with ezetimibe for at least 12 consecutive weeks in conjunction with a statin (if tolerated), dietary therapy and exercise, or
	Patient must have developed clinically important product-related adverse event/contraindication as defined in the TGA approved Product Information necessitating withdrawal of ezetimibe
	AND
	Clinical criteria:
	Patient must not be receiving concomitant PBS-subsidised treatment with another drug that belongs to the same pharmacological class as this drug, for this PBS indication.
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.
	Prescribing Instructions: Symptomatic atherosclerotic cardiovascular disease is defined as: (i) the presence of symptomatic coronary artery disease (prior myocardial infarction, prior revascularisation procedure, angina associated with demonstrated significant coronary artery disease (50% or greater stenosis in 1 or more coronary arteries on imaging), or positive functional testing (e.g. myocardial perfusion scanning or stress echocardiography)); or (ii) the presence of symptomatic cerebrovascular disease (prior ischaemic stroke, prior revascularisation procedure, or transient ischaemic attack associated with 50% or greater stenosis in 1 or more cerebral arteries on imaging); or (iii) the presence of symptomatic peripheral arterial disease (prior acute ischaemic event due to atherosclerosis, prior revascularisation procedure, or symptoms of ischaemia with evidence of significant peripheral artery disease (50% or greater stenosis in 1 or more peripheral arteries on imaging)).
	Prescribing Instructions: The qualifying LDL cholesterol level following at least 12 consecutive weeks of combined treatment with a statin, ezetimibe, dietary therapy and exercise (unless treatment with a statin is contraindicated, or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application , documented in the patient's medical records and must be no more than 8 weeks old.
	Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.

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	<p>Prescribing Instructions: If treatment with atorvastatin or rosuvastatin results in development of a clinically important product-related adverse event resulting in treatment withdrawal, the patient must be treated with the alternative statin (atorvastatin or rosuvastatin) unless there is a contraindication (e.g. prior rhabdomyolysis) to the alternative statin. This retrial should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retrial should not occur until CK has returned to normal.</p>
	<p>Prescribing Instructions: In the event of a trial of the alternative statin, it is recommended that the patient is started with the minimum dose of statin in conjunction with ezetimibe. The dose of the alternative statin should be increased not more often than every 4 weeks until the recommended or maximum tolerated dose has been reached or target LDL-c has been achieved.</p>
	<p>Prescribing Instructions: The following must be stated at the time of application and documented in the patient's medical records: (i) the qualifying Dutch Lipid Clinic Network Score; or (ii) the result of genetic testing confirming a diagnosis of familial heterozygous hypercholesterolaemia</p>
	<p>Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 12 consecutive weeks; or (ii) the doses, duration of treatment and details of adverse events experienced with trials with each of atorvastatin and rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information.</p>
	<p>Prescribing Instruction: Patients with symptomatic atherosclerotic cardiovascular disease where LDL cholesterol cannot be measured due to hypertriglyceridaemia, may qualify under this authority application if they have a non-HDL in excess of 2.4 millimoles per litre.</p>
Restriction Summary 13468 / Treatment of Concept: 13563	
Prescribing rule level	<p>Concept ID</p>
	<p>Category / Program: GENERAL – General Schedule (Code GE)</p>
	<p>Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners</p>
	<p>Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)</p>
	<p>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>
	<p>Administrative Advice: No increase in the maximum number of repeats may be authorised.</p>
	<p>Administrative Advice: Special Pricing Arrangements apply.</p>
	<p>Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.</p>
	<p>Indication: Non-familial hypercholesterolaemia</p>
	<p>Treatment Phase Initial treatment</p>
	<p>Clinical criteria:</p>
	<p>The treatment must be in conjunction with dietary therapy and exercise,</p>
	<p>AND</p>
	<p>Clinical criteria:</p>

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	Patient must not be receiving concomitant PBS-subsidised treatment with another drug that belongs to the same pharmacological class as this drug,
	AND
	Clinical criteria:
	Patient must have symptomatic atherosclerotic cardiovascular disease,
	AND
	Clinical criteria:
	Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre,
	AND
	Clinical criteria:
	Patient must have atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories); or
	Patient must have severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels; or
	Patient must have had at least two major cardiovascular events (i.e. myocardial infarction, unstable angina, stroke or unplanned revascularisation) in the previous 5 years; or
	Patient must have diabetes mellitus with microalbuminuria; or
	Patient must have diabetes mellitus and be aged 60 years or more; or
	Patient must be an Aboriginal or Torres Strait Islander with diabetes mellitus; or
	Patient must have a Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention of 4 or higher,
	AND
	Clinical criteria:
	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 12 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information,
	AND
	Clinical criteria:
	Patient must have been treated with ezetimibe for at least 12 consecutive weeks in conjunction with a statin (if tolerated), dietary therapy and exercise, or
	Patient must have developed clinically important product-related adverse event/contraindication as defined in the TGA approved Product Information necessitating withdrawal of ezetimibe
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.

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	<p>Prescribing Instructions: Symptomatic atherosclerotic cardiovascular disease is defined as: (i) the presence of symptomatic coronary artery disease (prior myocardial infarction, prior revascularisation procedure, angina associated with demonstrated significant coronary artery disease (50% or greater stenosis in 1 or more coronary arteries on imaging), or positive functional testing (e.g. myocardial perfusion scanning or stress echocardiography)); or (ii) the presence of symptomatic cerebrovascular disease (prior ischaemic stroke, prior revascularisation procedure, or transient ischaemic attack associated with 50% or greater stenosis in 1 or more cerebral arteries on imaging); or (iii) the presence of symptomatic peripheral arterial disease (prior acute ischaemic event due to atherosclerosis, prior revascularisation procedure, or symptoms of ischaemia with evidence of significant peripheral artery disease (50% or greater stenosis in 1 or more peripheral arteries on imaging)).</p>
	<p>Prescribing Instructions: The qualifying LDL cholesterol level following at least 12 consecutive weeks of combined treatment with a statin, ezetimibe, dietary therapy and exercise (unless treatment with a statin is contraindicated, or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application, documented in the patient's medical records and must be no more than 8 weeks old.</p>
	<p>Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.</p>
	<p>Prescribing Instructions: If treatment with atorvastatin or rosuvastatin results in development of a clinically important product-related adverse event resulting in treatment withdrawal, the patient must be treated with the alternative statin (atorvastatin or rosuvastatin) unless there is a contraindication (e.g. prior rhabdomyolysis) to the alternative statin. This retreat should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retreat should not occur until CK has returned to normal.</p>
	<p>Prescribing Instructions: In the event of a trial of the alternative statin, it is recommended that the patient is started with the minimum dose of statin in conjunction with ezetimibe. The dose of the alternative statin should be increased not more often than every 4 weeks until the recommended or maximum tolerated dose has been reached or target LDL-c has been achieved.</p>
	<p>Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 12 consecutive weeks; or (ii) the doses, duration of treatment and details of adverse events experienced with trials with each of atorvastatin and rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information.</p>

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	<p>Prescribing Instructions: One or more of the following must be stated at the time of application and documented in the patient's medical records regarding the presence of cardiovascular disease or high risk of experiencing a cardiovascular event:</p> <ul style="list-style-type: none"> (i) atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories); or (ii) severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels; or (iii) history of at least two major cardiovascular events (i.e. myocardial infarction, unstable angina, stroke or unplanned revascularisation) in the previous 5 years; or (iv) diabetes mellitus with microalbuminuria; or (v) diabetes mellitus and age 60 years of more; or (vi) Aboriginal or Torres Strait Islander with diabetes mellitus; or (vii) a Thrombolysis in Myocardial Infarction (TIMI) risk score for secondary prevention of 4 or higher
	<p>Prescribing Instruction: Patients with symptomatic atherosclerotic cardiovascular disease where LDL cholesterol cannot be measured due to hypertriglyceridaemia, may qualify under this authority application if they have a non-HDL in excess of 2.4 millimoles per litre.</p>

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
EVOLOCUMAB					
evolocumab 140 mg/mL injection, 1 mL pen device	10958R	3	3	5	Repatha
evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	11193D	1	1	5	Repatha
Restriction Summary 13623 / Treatment of Concept: 13469					
Prescribing rule level	Concept ID	Category / Program: GENERAL – General Schedule (Code GE)			
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners			
		Restriction type: <input checked="" type="checkbox"/> Authority Required (Streamlined) [new code] <input type="checkbox"/> Authority Required (telephone/online PBS Authorities system)			
		Administrative Advice: No increase in the maximum number of repeats may be authorised.			
		Administrative Advice: Special Pricing Arrangements apply.			
		Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 888 333.			
		Indication: Familial homozygous hypercholesterolaemia			
		Treatment Phase Initial treatment			
		Clinical criteria:			
		The treatment must be in conjunction with dietary therapy and exercise,			
		AND			
		Clinical criteria:			
		The condition must have been confirmed by genetic testing; or			
		The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 7,			
		AND			
		Clinical criteria:			

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	Patient must have an LDL cholesterol level in excess of 1.8 millimoles per litre,
	AND
	Clinical criteria:
	Patient must have been treated with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily) according to the TGA-approved Product Information or the maximum tolerated dose of atorvastatin or rosuvastatin for at least 12 consecutive weeks in conjunction with dietary therapy and exercise; or
	Patient must have developed clinically important product-related adverse events necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin; or
	Patient must be contraindicated to treatment with a HMG CoA reductase inhibitor (statin) as defined in the TGA-approved Product Information.
	Treatment criteria:
	Must be treated by a specialist physician; or
	Must be treated by a physician who has consulted a specialist physician.
	Prescribing Instructions: The qualifying LDL cholesterol level following at least 12 consecutive weeks of treatment with a statin (unless treatment with a statin is contraindicated or following completion of statin trials as described in these prescriber instructions in the event of clinically important adverse events) must be stated at the time of application , documented in the patient's medical records and must be no more than 8 weeks old.
	Prescribing Instructions: A clinically important product-related adverse event is defined as follows: (i) Severe myalgia (muscle symptoms without creatine kinase elevation) which is proven to be temporally associated with statin treatment; or (ii) Myositis (clinically important creatine kinase elevation, with or without muscle symptoms) demonstrated by results twice the upper limit of normal on a single reading or a rising pattern on consecutive measurements and which is unexplained by other causes; or (iii) Unexplained, persistent elevations of serum transaminases (greater than 3 times the upper limit of normal) during treatment with a statin.
	Prescribing Instructions: The following must be stated at the time of application and documented in the patient's medical records: (i) the qualifying Dutch Lipid Clinic Network Score; or (ii) the result of genetic testing confirming a diagnosis of familial homozygous hypercholesterolaemia
	Prescribing Instructions: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment: (i) the patient was treated with atorvastatin 80 mg or rosuvastatin 40 mg or the maximum tolerated dose of either for 12 consecutive weeks; or (ii) the dose, duration of treatment and details of adverse events experienced with the trial of atorvastatin or rosuvastatin; or (iii) the patient is contraindicated to treatment with a statin as defined in the TGA-approved Product Information
	Prescribing Instruction: Patients with symptomatic atherosclerotic cardiovascular disease where LDL cholesterol cannot be measured due to hypertriglyceridaemia, may qualify under this authority application if they have a non-HDL in excess of 2.4 millimoles per litre.

7.2 Remove Grandfather listings for:

- Restriction Summary 13622 / ToC: 13467: Authority Required = Non-familial hypercholesterolaemia 11484K

