

6.13 INCLISIRAN

Injection 284 mg in 1.5 mL single use pre-filled syringe, Leqvio[®], Novartis Pharmaceuticals Australia Pty Limited

1 Purpose of Submission

- 1.1 The Category 3 submission requested an amendment to the restriction level of inclisiran (Injection 284 mg in 1.5 mL single use pre-filled syringe) for the initial and grandfathered listings for the treatment of familial heterozygous hypercholesterolaemia (FHeH) and non-familial hypercholesterolaemia (non-FH) from Authority Required (Telephone/Online) to Authority Required (STREAMLINED).

2 Background

- 2.1 Inclisiran is currently listed on the PBS as an Authority Required (Telephone/Online) listing for the initial treatment of, and Authority Required (STREAMLINED) listing for the continuing treatment of FHeH and non-FH.
- 2.2 Inclisiran also currently has an Authority Required (grandfather) listing for the treatment of FHeH and non-FH.

Registration status

- 2.3 Inclisiran was TGA registered on 14 September 2021 as an adjunct to diet and exercise to reduce low-density lipoprotein cholesterol (LDL-C) in adults with FHeH, atherosclerotic cardiovascular disease (ASCVD), or at high risk of a cardiovascular event:
- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach LDL-C goals with the maximum tolerated dose of a statin or,
 - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant.

Previous PBAC consideration

- 2.4 The PBAC has not previously considered amending the restriction level of inclisiran.
- 2.5 At its May 2023 Intracycle meeting, the PBAC recommended inclisiran for the treatment of FHeH and non-FH with ASCVD on the basis of, among other matters, a cost-minimisation to evolocumab (Paragraph 13.1, Inclisiran Public Summary Document, March 2023 PBAC Meeting with May 2023 Addendum). Inclisiran was PBS-listed on 1 April 2024.

3 Requested listing

- 3.1 The submission requested a change to the restriction level of the initial and grandfather listings of inclisiran from Authority Required (Telephone/Online) to Authority Required (STREAMLINED). The submission also requested changes to the existing administrative advice and prescribing instructions to support an Authority Required (STEAMLINED) listing by requiring prescribers to document proof of patients meeting eligibility criteria in their medical records, rather than to state this to a Services Australia representative, given no application to Services Australia would be required under an Authority Required (STREAMLINED) listing.
- 3.2 An abridged version of the requested listing is presented below. Suggested additions are in italics and deletions in strikethrough.
- 3.3 The submission requested no changes to the restriction level of the continuing treatment listing (PBS item code: 14087K).
- 3.4 The submission used the incorrect PBS item code for the non-FH Grandfather arrangement listing (Submission main body). This has been corrected in this overview.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
INCLISIRAN					
inclisiran 284 mg/1.5 mL injection, 1.5 mL syringe	14101E	1	1	1	Leqvio
Restriction Summary / Treatment of Concept:					
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system) <input checked="" type="checkbox"/> Authority Required (STREAMLINED)					
Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.					
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.					
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.					
Indication: Familial heterozygous hypercholesterolaemia					
Treatment Phase: Initial treatment					
Clinical criteria:					
The treatment must be in conjunction with dietary therapy and exercise					
AND					
Clinical criteria:					

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	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
	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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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.

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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 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: 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 Instructions: 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 / Treatment of Concept:	
	<p>Category / Program: <input checked="" type="checkbox"/>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 (telephone/online PBS Authorities system) <input checked="" type="checkbox"/>Authority Required (STREAMLINED)</p>
	<p>Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.</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>Administrative Advice: No increase in the maximum quantity or number of units may be authorised.</p>

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	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Administrative Advice: Special Pricing Arrangements apply.
	Indication: Non-familial hypercholesterolaemia
	Treatment Phase: Initial treatment
	Clinical criteria:
	The treatment must be in conjunction with dietary therapy and exercise
	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
	AND
	Clinical criteria:
	Patient must not be receiving concomitant PBS-subsidised treatment with a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) for this PBS indication
	Treatment criteria:
	Must be treated by a specialist physician; or

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	Must be treated by a physician who has consulted a specialist physician
	<p>Prescribing Instructions: Symptomatic atherosclerotic cardiovascular disease is defined as:</p> <ul style="list-style-type: none"> (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>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:</p> <ul style="list-style-type: none"> (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: 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: One of the following must be stated at the time of application and documented in the patient's medical records regarding prior statin treatment:</p> <ul style="list-style-type: none"> (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.

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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 or 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 Instructions: 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	№.of Rpts	Available brands
INCLISIRAN					
inclisiran 284 mg/1.5 mL injection, 1.5 mL syringe	14152W	1	1	0	Leqvio

Restriction Summary / Treatment of Concept:

	<p>Category / Program: <input checked="" type="checkbox"/>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 (telephone/online PBS Authorities system) <input checked="" type="checkbox"/>Authority Required (STREAMLINED)</p>
	<p>Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.</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>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: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.</p>
	<p>Indication: Familial heterozygous hypercholesterolaemia</p>
	<p>Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements</p>
	<p>Clinical criteria:</p>
	<p>Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to 1 April 2024</p>
	<p>AND</p>

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	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 prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 6 prior to starting non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have had an LDL cholesterol level in excess of 1.8 millimoles per litre in the presence of symptomatic atherosclerotic cardiovascular disease at the time non-PBS-subsidised treatment with this drug for this condition was initiated; or
	Patient must have had an LDL cholesterol level in excess of 5 millimoles per litre at the time non-PBS-subsidised treatment with this drug for this condition was initiated
	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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have developed a clinically important product-related adverse event necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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

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	(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 must have been measured 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 have been no more than 8 weeks old at the time non-PBS-subsidised treatment with this drug for this condition was initiated.
	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 retreatment should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retreatment should not occur until CK has returned to normal.
	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.
	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.
	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.
	Prescribing Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only.
	Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.
	Prescribing Instructions: 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.

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Restriction Summary / Treatment of Concept:	
	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online PBS Authorities system) <input checked="" type="checkbox"/> Authority Required (STREAMLINED)
	Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.
	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.
	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: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Indication: Non-familial hypercholesterolaemia
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
	Clinical criteria:
	Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to 1 April 2024
	AND
	Clinical criteria:
	The treatment must be in conjunction with dietary therapy and exercise
	AND
	Clinical criteria:
	Patient must have had symptomatic atherosclerotic cardiovascular disease prior to starting non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have had an LDL cholesterol level in excess of 1.8 millimoles per litre prior to starting non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have had atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories) prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels prior to starting non-PBS-subsidised treatment with this drug for this condition; 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 prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had diabetes mellitus with microalbuminuria prior to starting non-PBS-subsidised treatment with this drug for this condition; or

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	Patient must have had diabetes mellitus and be aged 60 years of more prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must be an Aboriginal or Torres Strait Islander with diabetes mellitus that was present prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had a Thrombolysis in Myocardial Infarction (TIMI) Risk Score for Secondary Prevention of 4 or higher prior to starting non-PBS-subsidised treatment with this drug for this condition
	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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have developed a clinically important product-related adverse event necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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 must have been measured 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 have been no more than 8 weeks old at the time non-PBS-subsidised treatment with this drug for this condition was initiated.

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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 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>
	<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 or 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>
	<p>Prescribing Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only.</p>
	<p>Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
	<p>Prescribing Instructions: 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>

4 Consideration of the evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from a health care professional (1) and organisations (2) via the Consumer Comments facility on the PBS website. The comment from the health care professional described the current PBS authority process as impractical and time consuming. The input emphasised that streamlining the authority level for inclisiran would increase access to patients, improve outcomes and decrease health care costs for the community.
- 4.3 The PBAC also noted the input from Hearts4heart highlighted that changing the authority level for inclisiran would significantly reduce administrative delays and enhance patient outcomes amid healthcare staff shortages. Similarly, the comment from Heart Support Australia noted the importance of inclisiran in preventing heart attacks or strokes and that streamlining the authority level would improve access particularly for patients in rural and regional areas.
- 4.4 The PBAC noted the pre-PBAC response highlighted comments from a clinician and patient organisations in support of this submission.

Justification for request

- 4.5 The submission stated that the proposed amendment in the restriction level of inclisiran for the initial treatment of FHeH and non-FH was requested to align with the recent change in restriction level for evolocumab which was recommended by the PBAC at its March 2024 meeting.
- 4.6 The submission stated that the PBAC had previously considered that the inclisiran restrictions aligned with the evolocumab restrictions. The submission stated that the PBAC had noted a lower than forecasted utilisation of evolocumab, as reported in the February 2023 DUSC review. It claimed that although similar data for inclisiran is not available, the predicted usage of inclisiran was based on the market share for evolocumab.
- 4.7 The submission claimed that the consumer comments noted by the PBAC at its March 2024 meeting, which were in support of the change to the restriction level for evolocumab, would equally be applicable to this submission.
- 4.8 The submission did not provide any clinical evidence to support its request. The submission implied that inclisiran and evolocumab are similar enough in practice to warrant the same restriction level.
- 4.9 The submission stated that the proposed change, if recommended, in conjunction with the expanded nurse practitioners (NPs) prescribing (item 6.14), would further

streamline the initiation process and improve patient access whilst reducing the potential administrative burden for health care professionals (HCPs).

Estimated PBS usage and financial implications

- 4.10 The submission adopted a market share approach to estimate the net financial impact of changing the restriction level of inclisiran.
- 4.11 The submission made its assumptions using the PBS utilisation data of inclisiran from April 2024 to July 2024 (financial workbook was provided in September 2024 upon request by the PBAC Secretariat and 4 months of data had been released at the time). The data was extrapolated to 12 months by multiplying the existing four months data by three.
- 4.12 The submission requested no change to the approved ex-manufacturer price (AEMP).
- 4.13 The submission estimated no increase in the uptake of inclisiran and a nil net financial impact to the PBS/RPBS for this population if recommended.
- 4.14 Table 1 presents the estimated extent of use 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.
- 4.15 As a Category 3 submission, the economic analysis has not been independently evaluated.

Table 1: Estimated use and financial implications

	2024	2025	2026	2027	2028	2029
Number of PBS/RPBS scripts dispensed ^a	1	2	2	2	2	2
Estimated financial implications of inclisiran (published price)						
Cost to PBS/RPBS less co-payment	3	4	4	4	4	4
Changed listing	5	5	5	5	5	5
Net cost PBS / RPBS	6	6	6	6	6	6
Estimated financial implications of inclisiran (effective price)						
Cost to PBS/RPBS less co-payment	3	3	3	3	7	7
Changed listing	5	5	5	5	5	5
Net cost PBS / RPBS	6	6	6	6	6	6

Source: Adapted from sheet 5 (impact-net) of the financial workbook

^a Assuming 2 per patient per year as estimated by the submission. The submission assumed in sheet 3a (scripts-proposed, row 174) of the financial workbook that 6 months of initiating scripts to maintain same script equivalence will result in an overall number of 3 scripts in the first year.

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

The redacted values correspond to the following ranges:

1 5,000 to < 10,000

2 10,000 to < 20,000

3 \$10 million to < \$20 million

4 \$30 million to < \$40 million

5 net cost saving

6 \$0 to < \$10 million

7 \$20 million to < \$30 million

Quality use of medicines

- 4.16 The submission stated that regular training and resources on the current treatment guidelines for cardiovascular disease, as well as the PBS eligibility criteria for inclisiran and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors therapy are provided to HCPs including specialist physicians, general practitioners and NPs to support appropriate prescribing.

Risk-sharing arrangements

- 4.17 Inclisiran is currently subject to risk-sharing arrangement (RSA) caps which are shared with evolocumab and alirocumab (soon to be removed from the PBS at the request of the sponsor).

5 PBAC Outcome

- 5.1 The PBAC recommended a change to the restriction level of inclisiran (injection 284 mg in 1.5 mL single use pre-filled syringe) from Authority Required (Telephone/Online) to Authority Required (STREAMLINED) for the initial and grandfather listings for treatment of familial heterozygous hypercholesterolaemia (FHeH) and non-familial hypercholesterolaemia (non-FH).
- 5.2 The PBAC recalled that in March 2023, it had considered the PCSK9 inhibitor therapy evolocumab an appropriate comparator and considered inclisiran an alternative to the evolocumab eligible population in FHeH and non-FH. The PBAC considered that the change in restriction level is unlikely to increase the utilisation of inclisiran or increase the eligible population. The PBAC therefore considered that the financial estimates appropriate and that the change would not result in a financial impact to Government.
- 5.3 The PBAC noted the change would reduce the administrative burden for prescribers when prescribing this medicine.
- 5.4 The PBAC considered a request to include nurse practitioners as eligible prescribers at the same meeting and noted that there would be flow-on changes to the restriction criteria for the initial treatment of FHeH and non-FH (refer to item 6.14, November 2024 PBAC meeting).
- 5.5 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for amendment to the authority level of inclisiran for the treatment of FHeH and non-FH, the amendment is not expected to address a high and urgent unmet clinical need.
- 5.6 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Amend existing listings as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
INCLISIRAN					
inclisiran 284 mg/1.5 mL injection, 1.5 mL syringe	14101E	1	1	1	Leqvio
Restriction Summary / Treatment of Concept:					
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online -PBS Authorities system) <input checked="" type="checkbox"/> Authority Required (STREAMLINED)					
	Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.				
	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.				
	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.				
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					
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					

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	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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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 <i>in consultation with a specialist physician.</i>
	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.
	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 retreatment should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retreatment 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 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 Instructions: 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>
<p>Restriction Summary / Treatment of Concept:</p>	
	<p>Category / Program: <input checked="" type="checkbox"/>GENERAL - General Schedule (Code GE)</p>
	<p>Prescriber type: : <input checked="" type="checkbox"/>Medical Practitioners <input checked="" type="checkbox"/>Nurse Practitioners</p>
	<p>Restriction type: <input checked="" type="checkbox"/>Authority Required (telephone/online PBS Authorities system) <input checked="" type="checkbox"/>Authority Required (STREAMLINED)</p>
	<p>Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.</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>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>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 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>

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	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
	AND
	Clinical criteria:
	Patient must not be receiving concomitant PBS-subsidised treatment with a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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 <i>in consultation with a specialist physician.</i>
	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)).

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	<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 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>
	<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 or 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>
	<p>Prescribing Instructions: 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>

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MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
INCLISIRAN					
inclisiran 284 mg/1.5 mL injection, 1.5 mL syringe	14152W	1	1	0	Leqvio
Restriction Summary / Treatment of Concept:					
Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction type: <input checked="" type="checkbox"/> Authority Required (telephone/online - PBS Authorities system) <input checked="" type="checkbox"/> Authority Required (STREAMLINED)					
	Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.				
	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.				
	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: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.				
Indication: Familial heterozygous hypercholesterolaemia					
Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements					
Clinical criteria:					
Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to 1 April 2024					
AND					
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 prior to starting non-PBS-subsidised treatment with this drug for this condition; or					
The condition must have been confirmed by a Dutch Lipid Clinic Network Score of at least 6 prior to starting non-PBS-subsidised treatment with this drug for this condition					
AND					
Clinical criteria:					
Patient must have had an LDL cholesterol level in excess of 1.8 millimoles per litre in the presence of symptomatic atherosclerotic cardiovascular disease at the time non-PBS-subsidised treatment with this drug for this condition was initiated; or					
Patient must have had an LDL cholesterol level in excess of 5 millimoles per litre at the time non-PBS-subsidised treatment with this drug for this condition was initiated					
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 12 consecutive weeks in conjunction with dietary therapy and exercise prior to initiating non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have developed a clinically important product-related adverse event necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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 <i>in consultation with a specialist physician.</i>
	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 must have been measured 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 have been no more than 8 weeks old at the time non-PBS-subsidised treatment with this drug for this condition was initiated.
	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: 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 Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only.</p>
	<p>Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
	<p>Prescribing Instructions: 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>
<p>Restriction Summary / Treatment of Concept:</p>	
	<p>Category / Program: <input checked="" type="checkbox"/>GENERAL - General Schedule (Code GE)</p>
	<p>Prescriber type: <input checked="" type="checkbox"/>Medical Practitioners <input checked="" type="checkbox"/>Nurse Practitioners</p>
	<p>Restriction type: <input checked="" type="checkbox"/>Authority Required (telephone/online PBS Authorities system) <input checked="" type="checkbox"/>Authority Required (STREAMLINED)</p>
	<p>Administrative Advice: Monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) medications are evolocumab or alirocumab.</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>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>

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	Administrative Advice: This grandfather restriction will cease to operate from 12 months after the date specified in the clinical criteria.
	Indication: Non-familial hypercholesterolaemia
	Treatment Phase: Transitioning from non-PBS to PBS-subsidised supply - Grandfather arrangements
	Clinical criteria:
	Patient must have received non-PBS-subsidised treatment with this drug for this condition prior to 1 April 2024
	AND
	Clinical criteria:
	The treatment must be in conjunction with dietary therapy and exercise
	AND
	Clinical criteria:
	Patient must have had symptomatic atherosclerotic cardiovascular disease prior to starting non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have had an LDL cholesterol level in excess of 1.8 millimoles per litre prior to starting non-PBS-subsidised treatment with this drug for this condition
	AND
	Clinical criteria:
	Patient must have had atherosclerotic disease in two or more vascular territories (coronary, cerebrovascular or peripheral vascular territories) prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had severe multi-vessel coronary heart disease defined as at least 50% stenosis in at least two large vessels prior to starting non-PBS-subsidised treatment with this drug for this condition; 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 prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had diabetes mellitus with microalbuminuria prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had diabetes mellitus and be aged 60 years of more prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must be an Aboriginal or Torres Strait Islander with diabetes mellitus that was present prior to starting non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have had a Thrombolysis in Myocardial Infarction (TIMI) Risk Score for Secondary Prevention of 4 or higher prior to starting non-PBS-subsidised treatment with this drug for this condition
	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 prior to initiating non-PBS-subsidised treatment with this drug for this condition; or
	Patient must have developed a clinically important product-related adverse event necessitating withdrawal of statin treatment to trials of each of atorvastatin and rosuvastatin prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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:

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	Patient must have been treated with ezetimibe for at least 12 consecutive weeks in conjunction with a statin (if tolerated), dietary therapy and exercise prior to initiating non-PBS-subsidised treatment with this drug for this condition; 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 a monoclonal antibody inhibiting proprotein convertase subtilisin kexin type 9 (PCSK9) 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 <i>in consultation with a specialist physician.</i>
	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 must have been measured 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 have been no more than 8 weeks old at the time non-PBS-subsidised treatment with this drug for this condition was initiated.
	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 retreatment should occur after a washout period of at least 4 weeks, or if the creatine kinase (CK) level is elevated, retreatment should not occur until CK has returned to normal.
	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>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:</p> <ul style="list-style-type: none"> (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>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 or 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 Instructions: A patient may qualify for PBS-subsidised treatment under this restriction once only.</p>
	<p>Prescribing Instructions: For continuing PBS-subsidised treatment, a Grandfathered patient must qualify under the Continuing treatment criteria.</p>
	<p>Prescribing Instructions: 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>

These restrictions may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7 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.

8 Sponsor's Comment

The sponsor had no comment.