Evolocumab for homozygous familial hypercholesterolaemia: predicted versus actual analysis

Drug utilisation sub-committee (DUSC)

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Abstract

Purpose

To compare the predicted and actual utilisation of evolocumab for homozygous familial hypercholesterolaemia (HoFH) in the first 24 months of PBS listing. Evolocumab was PBS listed for this indication on 1 December 2016.

Date of listing on the Pharmaceutical Benefits Scheme (PBS)

Evolocumab was first PBS listed for the treatment of homozygous familial hypercholesterolaemia on 1 December 2016.

Data Source / methodology

The analyses used data from the PBS supplied prescriptions and authority approvals databases.

Key Findings

- The actual number of patients treated with evolocumab for HoFH in the first two years of listing was higher than expected.
- In 2018, 1,098 patients were supplied at least one prescription for HoFH and, of these, 574 patients were supplied their first PBS-subsidised evolocumab prescription.
- The total number of prescriptions supplied for evolocumab for HoFH was similar to predicted in year one of listing but was greater than predicted in year two.
- In 2018, the majority of evolocumab prescriptions supplied for HoFH were for the 140 mg/mL pen device (6,996 prescriptions; 96%).

Purpose of analysis

To compare the predicted and actual utilisation of evolocumab for homozygous familial hypercholesterolaemia in the first 24 months of PBS listing. Evolocumab was PBS listed for this indication on 1 December 2016.

Background

Clinical situation

Familial hypercholesterolaemia (FH) is a dominantly inherited disorder present from birth that markedly elevates plasma low-density lipoprotein (LDL) cholesterol and causes premature coronary heart disease. Detailed information on FH is available online from the Familial Hypercholesterolaemia Australasia Network.[1]

Pharmacology

Evolocumab is a human monoclonal antibody that binds to proprotein convertase subtilisin/kexin type 9 (PCSK9) and inhibits circulating PCSK9 from binding to the LDL receptor on the liver cell surface, thus preventing PCSK9-mediated LDL receptor degradation. Increasing liver LDL receptor levels results in associated reductions in serum LDL cholesterol.[2]

Therapeutic Goods Administration (TGA) approved indications

Evolocumab is indicated as an adjunct to diet and exercise in:

Prevention of Cardiovascular Events

Evolocumab is indicated to reduce the risk 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.

[1] Familial Hypercholesterolaemia Australasia Network 2019 [Internet]. Accessed on 14 August 2018, Available from: https://www.athero.org.au/fh/

[2] Repatha® (evolocumab). Australian Approved Product Information. NSW: Amgen Australia Pty Ltd. Approved 9 December 2015, Revised 24 May 2019. Available from: https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2015-PI-02929-1&d=201908141016933

Primary Hypercholesterolaemia

Evolocumab is indicated in adults with primary hypercholesterolaemia (including heterozygous familial hypercholesterolaemia (HeFH) and non-familial hypercholesterolaemia) to reduce low-density lipoprotein cholesterol (LDL-C):

- 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.

Homozygous Familial Hypercholesterolaemia

Evolocumab is indicated in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolaemia in combination with other lipid lowering therapies.[2]

Dosage and administration

Primary hypercholesterolaemia and prevention of cardiovascular events

The recommended dose for evolocumab is either 140 mg every 2 weeks or 420 mg once monthly. The doses are clinically equivalent.

Homozygous Familial Hypercholesterolaemia

The initial recommended dose for evolocumab is 420 mg once monthly. The dose can be increased to 420 mg every 2 weeks if a clinically meaningful response is not achieved in 12 weeks. Patients on apheresis may initiate treatment with 420 mg every 2 weeks to correspond with their apheresis schedule.[2]

PBS listing details (current as at August 2019)

Table 1: PBS listing of evolocumab for homozygous familial hypercholesterolaemia

Item	Name, form & strength, pack size	Max. quant (packs)	Max. quant (units)	Rpts	DPMQ	Brand name and manufacturer
10958R	evolocumab 140 mg/mL injection, 1 mL pen device	3	3	5	$943.54	Repatha® Amgen Australia Pty Limited
11193D	evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	1	1	5	$683.24	Repatha® Amgen Australia Pty Limited

Source: the PBS website. Special Pricing Arrangements apply

Restriction

Authority Required General Schedule listing for familial homozygous hypercholesterolaemia

Treatment Phase: Initial treatment

Clinical criteria:

- The treatment must be in conjunction with dietary therapy and exercise,

AND

- 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

- Patient must have an LDL cholesterol level in excess of 3.3 millimoles per litre,

AND

- Patient must have been treated with the maximum recommended dose of atorvastatin or rosuvastatin according to the TGA-approved Product Information for at least 3 months in conjunction with dietary therapy and exercise; OR
- Patient must have developed a clinically important product-related adverse event necessitating withdrawal of statin treatment; 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.

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.

The date of the consultation with a specialist physician must be no more than 6 months prior to the application date. The full name of the specialist physician consulted and the date of consultation are to be provided at the time of application.

The qualifying LDL cholesterol level must be provided at the time of application and must be no more than 2 months old.

The physician must attempt to treat the patient with the maximum recommended dose of atorvastatin (80 mg daily) or rosuvastatin (40 mg daily).

With the exception of the situation where the patient is contraindicated to treatment with a statin, the agent, dose and duration of statin treatment must be provided at the time of application.

Contraindication to treatment with a statin is as defined in the TGA-approved Product Information.

The authority application must be made in writing and must include:

a) A completed authority prescription form; and
b) A completed familial homozygous hypercholesterolaemia Initial PBS Authority Application - Supporting Information Form; and
c) The date of consultation and the full name of the specialist physician; and
d) A copy of the qualifying Dutch Lipid Clinic Network Score or a copy of the result of genetic testing; and
e) The result of LDL cholesterol level and one of the following where appropriate: statin treatment details including agent, dose and treatment duration; or details of adverse event or contraindication to treatment with a statin as defined in the TGA-approved Product Information.

Treatment Phase: Continuing treatment

Clinical criteria:

Patient must have previously received PBS-subsidised treatment with this drug for this condition,
AND
The treatment must be in conjunction with dietary therapy and exercise.

Note: No increase in the maximum number of repeats may be authorised.

For details of the current PBS listing refer to the PBS website.

Date of listing on PBS

Evolocumab 140 mg/mL injection, 1 mL pen device was first PBS listed for the treatment of homozygous familial hypercholesterolaemia on 1 December 2016.

Changes to listing

Evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge was PBS listed for the treatment of homozygous familial hypercholesterolaemia on 1 November 2017.

Current PBS listing details are available from the PBS website.

Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

The PBAC has considered seven submissions for evolocumab since 2015. Out of these submissions, three submissions were for HoFH. Evolocumab submissions for HoFH are outlined in this section. A more detailed summary of all the evolocumab submissions can be found in Appendix 1.

March 2015 PBAC Meeting

The submission sought to open a dialogue regarding the potential future listing of evolocumab on the PBS for the treatment of hypercholesterolaemia.

The submission was considered by DUSC. DUSC considered the main issues were:

- The market share approach, based on ezetimibe utilisation, underestimated the population eligible for evolocumab.
- Changing clinical practice, including increased assessment of cardiovascular risk or more widespread treatment to target cholesterol levels, could result in many more patients being treated with evolocumab. Given the high prevalence of dyslipidaemia and the proposed price of evolocumab, small changes in practice could have a large budget impact.
- Significant potential for use beyond the restriction by patients who are not achieving target cholesterol levels, but who would not qualify for evolocumab treatment under the proposed restriction.

The PBAC rejected the request to list evolocumab for the treatment of hypercholesterolaemia on the basis of unestablished clinical place in therapy and the uncertainty surrounding its use in clinical practice.

March 2016 PBAC Meeting

The resubmission requested a Section 85 Authority Required PBS listing for evolocumab for the treatment of familial hypercholesterolaemia. This resubmission was not considered by DUSC.

The PBAC recommended the Section 85 Authority Required listing of evolocumab for homozygous familial hypercholesterolaemia (but not the broader heterozygous familial

hypercholesterolaemia population). In making this recommendation, the PBAC considered that the homozygous FH population represent a small, definable, patient group, in whom there is a high level of clinical need.

The PBAC considered that the submission's estimates of usage in the homozygous FH population were more reliable than the estimates for the heterozygous FH population, as there are likely to be less undiagnosed homozygous patients. The PBAC recommended a risk-sharing arrangement (RSA) that should include a cap based on the number of patients treated.

July 2017 PBAC Meeting

The minor submission requested PBS listing of an additional form of evolocumab 120 mg/1 mL in 3.5 mL (420 mg/3.5 mL cartridge) for the treatment of familial homozygous hypercholesterolaemia.

The PBAC recommended the listing of the new strength of evolocumab for the treatment of familial homozygous hypercholesterolaemia as the listing would reduce the number of injections that patients would be required to administer from the three injections for the currently listed strength of 140 mg/mL to a single injection and therefore would make it easier for patients to manage their condition.

The PBAC accepted the additional form of evolocumab will provide patients with an alternative dosing schedule at no additional cost to the Government.

The PBAC noted the restriction is unchanged from the currently listed strength of evolocumab.

For further details refer to the Public Summary Documents.

Medical Services Advisory Committee (MSAC) consideration

In March 2019, the MSAC considered an application received from the Royal College of Pathologists of Australasia (RCPA) for diagnostic genetic testing for heritable mutations predisposing to familial hypercholesterolaemia in clinically affected individuals, and for predictive genetic testing (or "cascade testing") of the family members of those affected individuals who are shown to have such a mutation.

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported Medicare Benefits Schedule (MBS) listing of genetic testing for heritable mutations associated with FH in affected individuals meeting defined eligibility criteria, and targeted cascade testing in first and second-degree relatives of those affected individuals with a confirmed genetic diagnosis.

MSAC queried whether the PBS criteria would lead to leakage for an MBS listing, but noted that the Dutch Lipid Clinic Network Score for identifying affected individuals in the proposed MBS item descriptor (at least 6) is similar to the Score used in the alternative option for confirming FH in the PBS restriction for evolocumab (at least 6 for HeFH, and at least 7 for HoFH). In addition, the PBS listing for HoFH patients did not appear to have resulted in large

increases in genetic testing, although the listing for HeFH patients was too recent for any data to yet be available. MSAC noted that the pool of HeFH patients is much larger than for HoFH patients.

MSAC queried the criteria for testing in the proposed MBS item descriptor, noting that it differed in some respects from the PBS listing for evolocumab. However, MSAC accepted that these criteria do not have to match. Therefore, MSAC accepted the following criteria for testing of affected individuals who do not have a previously identified FH mutation, but have one or more of the following:

- a Dutch Lipid Clinic Network Score of at least 6
- a low-density lipoprotein (LDL) cholesterol level of at least 6.5 mmol/L in the absence of secondary causes
- an LDL cholesterol level between 5.0 and 6.5 mmol/L with signs of premature/accelerated atherogenesis.

For further details refer to the MSAC Public Summary Document.

Previous reviews by the DUSC

Evolocumab has not previously been reviewed by DUSC.

Approach taken to estimate utilisation

The March 2016 PBAC submission requested a Section 85 Authority Required PBS listing for evolocumab 140 mg/mL injection prefilled syringe (pen device) for the treatment of FH (HoFH and HeFH). As the focus of this report is the use of evolocumab for HoFH, only the approach taken to estimate the utilisation in the HoFH population will be outlined in this section.

An epidemiological approach was taken to estimate the extent of use of evolocumab in the proposed HoFH population. The size of the Australian population sourced from the Australian Bureau of Statistics (ABS) was used as the starting point of the analysis to which an annual growth rate of [redacted] was applied to project into future years.

The prevalence of HoFH was taken from a publication by Cuchel et al (2014). Cuchel et al estimated that HoFH may affect as many as 1 in 160,000-300,000 people.[3] A prevalence of 1 in [redacted] was used in the financial analysis.

It was assumed in the analysis that all HoFH patients will meet the PBS eligibility criteria and uptake of evolocumab will be [redacted]. The monthly:fortnightly evolocumab dosing split was assumed to be [redacted].

[3] Cuchel M, Bruckert E, Ginsberg HN, Raal FJ, Santos RD, Hegele RA, et al. Homozygous familial hypercholesterolaemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society. Eur Heart J 2014; 35 (32):2146-2157. doi:10.1093/eurheartj/ehu274.

The July 2017 minor submission to PBAC requested PBS listing of an additional form of evolocumab 120 mg/1 mL in 3.5 mL (420 mg/3.5 mL) cartridge. The submission used the following substitution rate.

Table 2: Use of evolocumab by presentation

Name, form & strength	2016	2017	2018	2019	2020	2021	2022
evolocumab 140 mg/mL injection, 1 mL pen device	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
evolocumab 420 mg/3.5 mL injection, 3.5 mL cartridge	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Methods

The analyses used data from the PBS supplied prescriptions database, managed by Services Australia, for dates of supply up to and including 30 June 2019; extracted 29 July 2019. The PBS supplied prescriptions database includes data submitted to Services Australia for payment of a PBS or Repatriation PBS (RPBS) subsidy by the Government by all approved pharmacies in Australia. These prescription data were used to determine the number of prescriptions supplied and for the PBS expenditure analysis.

This PBS supplied prescriptions database includes a unique patient identification number (PIN) that allows supplied prescriptions to be attributed to a particular patient. The number of patients supplied evolocumab under the PBS was determined by counting the number of de-identified PINs in the prescription data over the specified time. New (initiating) patients were defined as those with no prior prescription for evolocumab and was based on the date of first supply of PBS-subsidised evolocumab from the date of listing. This group contained patients who were naïve to evolocumab and "grandfathered" patients. Grandfathered patients obtained evolocumab through other means prior to listing on the PBS and then commenced PBS-subsidised treatment. Patients were identified as being on treatment (prevalent) if they had received at least one dispensing of evolocumab in the specified period.

Prescriber type was attributed to the de-identified approval number of the prescriber by Services Australia and was based on the major field of specialty, derived from the combination of the current registered specialty and the most PBS services provided per quarter. Prescribers can work in several different specialties but are allocated by Services Australia to one major field of specialty per quarter.

Services Australia also maintains the authority approvals database. Prescribers provide necessary information to Services Australia to support approval for a PBS Authority Required prescription. De-identified information is recorded by PIN and can be matched to the prescriptions database. Approvals for the evolocumab PBS item codes 11193D, 10958R, 11484K, 11485L were extracted from the PBS authority approvals database for the period.

Data manipulation was undertaken using SAS.

As this analysis uses date of supply prescription data, there may be small differences in total number of supplies of evolocumab in the same period compared with publicly available date of processing data.[4]

Results

Analysis of drug utilisation

Overall utilisation

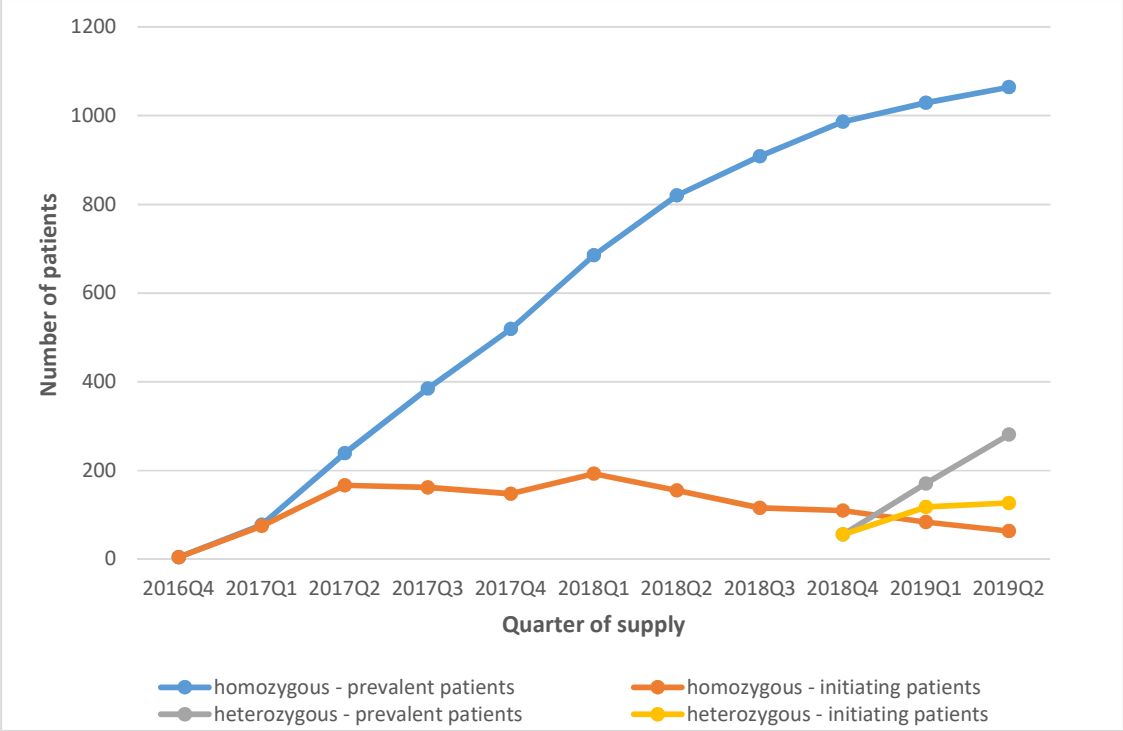

Figure 1: Prevalent and initiating patients by indication and quarter of supply

Source: PBS supplied prescriptions database; extracted July 2019.

Figure 1 depicts the number of prevalent and initiating patients to evolocumab for the treatment of HoFH and HeFH. Initially, there was a steady increase in the number of patients supplied evolocumab for HoFH, but a decreasing rate of growth was apparent, particularly in the last three quarters of available data. In 2018, there were 1,098 patients supplied a prescription for HoFH and, of these, 574 patients were supplied their first PBS-subsidised evolocumab prescription. The number of new patients starting evolocumab for the treatment of HoFH continued to decline from the first quarter of 2018.

[4] PBS statistics. Australian Government Services Australia. Canberra. Available from http://medicarestatistics.humanservices.gov.au/statistics/pbs_item.jsp

Evolocumab was listed on the PBS for the treatment of HeFH on 1 November 2018. Of the patients who had a prescription for evolocumab supplied under HeFH item codes (11484K and 11485L) since listing, 10% of patients had a previous prescription supplied under the HoFH item codes (11193D and 10958R).

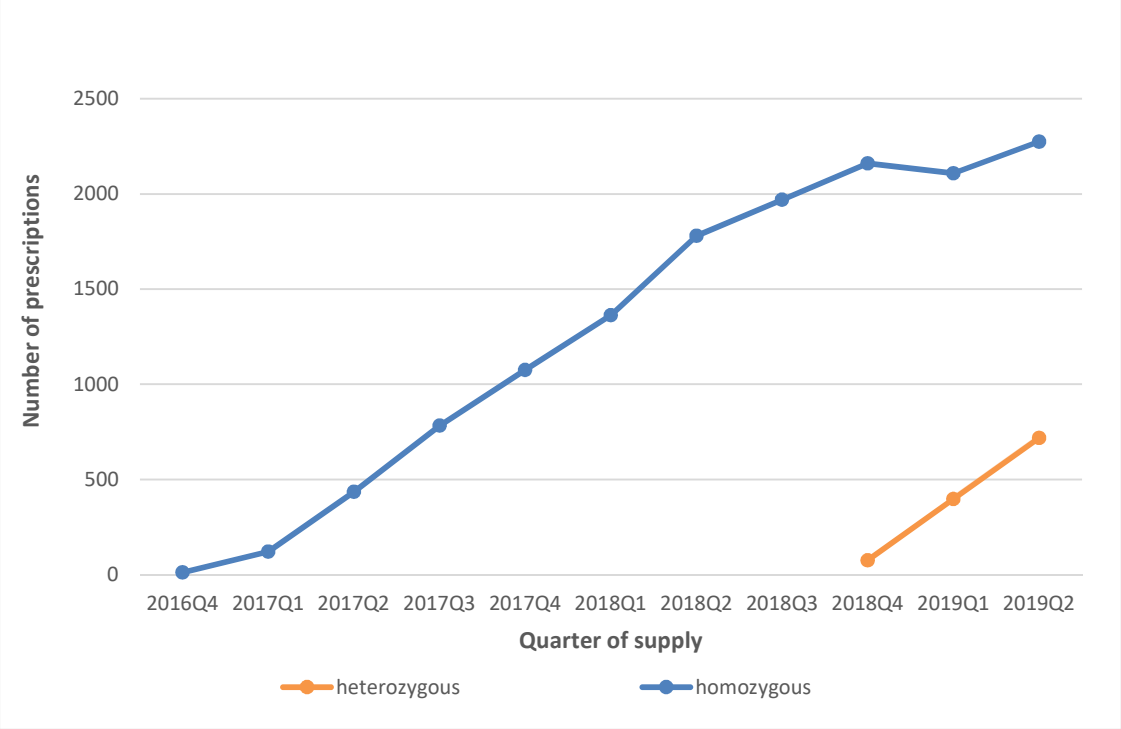

Figure 2: Number of prescriptions by indication and quarter of supply

Source: PBS supplied prescriptions database; extracted July 2019.

Figure 2 shows the number of prescriptions supplied per quarter for the treatment of HoFH has grown since listing, with a slight dip in the first quarter of 2019. The total number of PBS-subsidised evolocumab prescriptions supplied for HoFH increased from 120 prescriptions in the first quarter of 2017 to 2,108 in the first quarter of 2019. The limited data available for the HeFH indication illustrates a rapid uptake of evolocumab in this population, with 396 prescriptions of evolocumab dispensed in the first quarter of 2019 and 718 prescriptions in the second quarter.

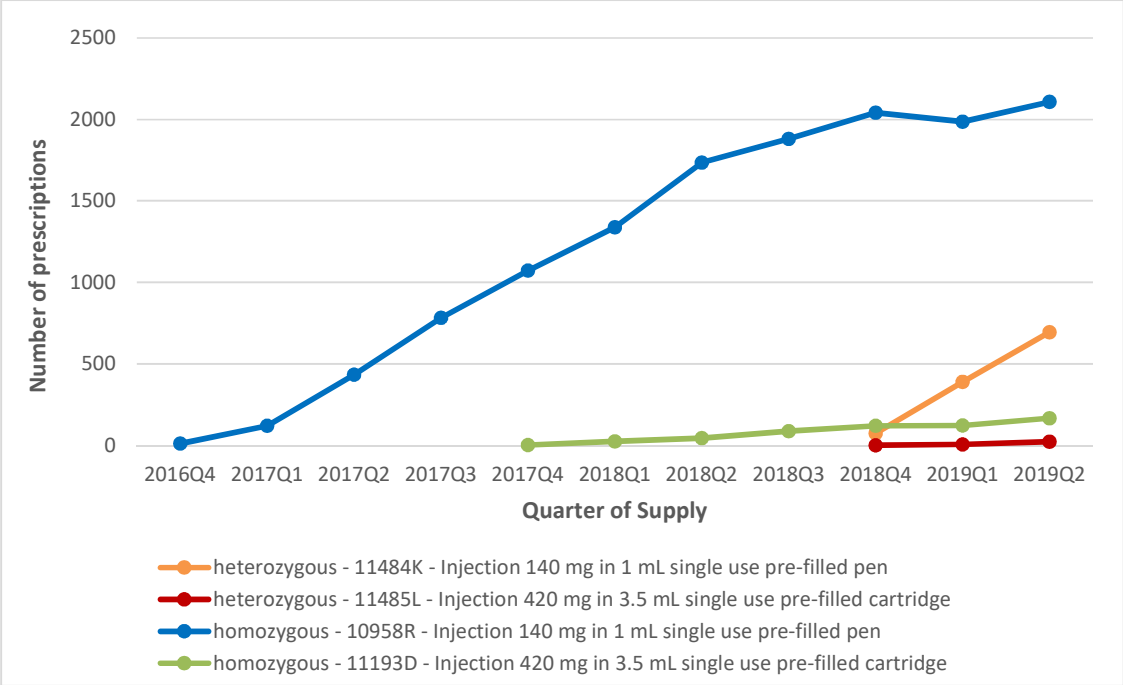

Figure 3: Number of prescriptions by item code and quarter of supply

Source: PBS supplied prescriptions database; extracted July 2019.

There are currently two different strengths of evolocumab listed on the PBS. Evolocumab 140mg/mL pen device was the most common form of evolocumab supplied for HoFH and HeFH. In 2018, 6,996 prescriptions were supplied of the 140 mg/mL pen device compared to 276 prescriptions of 420 mg/3.5 mL cartridge for the treatment of HoFH.

Utilisation by prescriber type

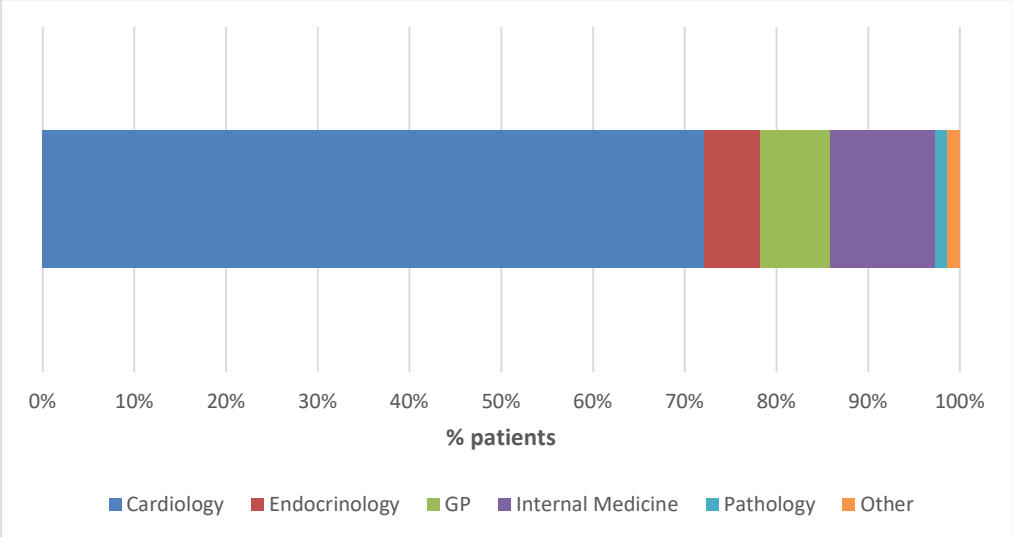

Figure 4: Proportion of patients initiating evolocumab for HoFH by prescriber type in 2018

Source: PBS supplied prescriptions database; extracted July 2019.

The PBS restriction for evolocumab requires that the patient must be treated by a specialist physician. The full name of the specialist physician consulted and the date of consultation need to be provided at the time of the authority application. The date of the consultation with a specialist physician must be no more than 6 months prior to the application date. Therefore, it is possible for non-specialist medical doctors (e.g. general practitioners) to prescribe evolocumab in consultation with the specialist managing the patient care.

Figure 4 depicts the type of prescribers who initiated PBS-subsidised evolocumab for HoFH in 2018. The largest proportion of HoFH patients initiating evolocumab had their first prescription written by a cardiologist; followed by internal medicine specialists, GPs and endocrinologists.

Analysis of actual versus predicted utilisation

A comparison of the predicted utilisation of evolocumab for HoFH versus actual use is shown in Table 3.

Table 3: Evolocumab: actual versus predicted utilisation for HoFH

		Year 1	Year 2
Patients	Predicted	[redacted]	[redacted]
	Actual	502	1,068
	%Difference	[redacted]	[redacted]
Prescriptions (total)	Predicted	[redacted]	[redacted]
	Actual	2,010	6,915
	%Difference	[redacted]	[redacted]
Prescriptions for 140 mg in 1 mL pen device (10958R)	Predicted	[redacted]	[redacted]
	Actual	2,010	6,686
	%Difference	[redacted]	[redacted]
Prescriptions for 420 mg in 3.5 mL cartridge (11193D)	Predicted	n/a	[redacted]
	Actual	n/a	229
	%Difference	n/a	[redacted]
Expenditure	Predicted	[redacted]	[redacted]
	Actual	$1,848,635	$6,319,473
	%Difference	[redacted]	[redacted]

Source: Evolocumab Final Estimates 2016 (predicted), PBS prescription database (actual), extracted July 2019. n/a = not applicable.
Note: Expenditure is reported based on published prices. Special Pricing Arrangements apply.

The sponsor's predicted number of patients, prescriptions and expenditure were very similar between listing years 1 and 2; i.e. the sponsor predicted very little growth in the market. The actual number of patients receiving evolocumab was higher than predicted in both year 1 and year 2. The number of PBS subsidised prescriptions of evolocumab was close to the

predicted number in Year 1 but was higher than predicted in year 2 of listing. The government expenditure was lower than predicted in the first year of listing but was higher than expected in the second year of listing.

In the July 2017 submission, the sponsor estimated that the 420 mg in 3.5 mL pre-filled cartridge would substitute for [redacted] of the 140 mg in 1 mL pre-filled pen prescriptions. Actual data show that the cartridge accounted for 3% of the market in its first year of listing (i.e. the second year of evolocumab listing), although use of both forms was higher than expected.

Discussion and DUSC consideration

The number of patients treated with evolocumab in the first two years of listing was higher than expected. In the Pre-Sub Committee Response (PSCR, p1), the Sponsor considered the likely reason for the greater than predicted number of patients is that the submission utilisation estimates were based on the epidemiology of true genotypic HoFH, whereas the restriction recommended by the PBAC also allows eligibility based on a phenotypic definition. DUSC noted to qualify for treatment under HoFH item codes, the condition must have been confirmed by genetic testing or by a DLCNS of at least 7. DUSC considered that DLCNS categorises patients by the likelihood of familial hypercholesterolaemia and a score of at least 7 could also encompass heterozygous patients. DUSC considered that as the DLCNS was used by the majority of prescribers to confirm the condition, the actual number of treated patients most likely included both HoFH and HeFH patients.

The analyses showed an initial steady increase in the number of patients supplied evolocumab for HoFH, but a decreasing rate of growth was apparent, particularly in the last three quarters of available data. Additionally, the number of new patients initiating evolocumab for HoFH has continued to decline since the first quarter of 2018. The listing of evolocumab for HeFH on 1 November 2018 could have contributed to the decline in the rate of growth observed for the HoFH item codes. DUSC noted that of the patients who had a prescription for evolocumab supplied under HeFH item codes since listing, 10% of patients had a previous prescription supplied under the HoFH item codes. DUSC considered the decline in the number of new HoFH patients initiating evolocumab could be due to patients now commencing on HeFH item codes or could be due to market saturation in the available population of HoFH patients.

The actual number of supplied prescriptions was very similar to the predicted number of prescriptions in the first year of listing but greater than predicted in the second year. Three possible reasons for higher than predicted number of patients but similar to predicted numbers of prescriptions are:

- a higher proportion of monthly versus fortnightly dosing than expected
- estimates may not have used “half cycle corrections” to account for people starting treatment at different points throughout the year

- more people discontinuing than expected. According to the Therapeutic Guidelines, PCSK9 inhibitors have not been associated with any notable serious adverse effects other than injection site reactions.[5]

DUSC considered another possible reason for a higher than predicted number of patients but similar to predicted numbers of prescriptions could be due to doctors prescribing 140 mg every 2 weeks instead of 420 mg every month resulting in less frequent dispensing of evolocumab. The dose recommended for HeFH is 140 mg every 2 weeks or 420 mg once monthly compared to HoFH dosing of 420 mg once monthly as the initial dose with a possible dose increase to 420 mg every 2 weeks if required.

DUSC noted that in March 2019, the MSAC supported MBS listing of genetic testing for heritable mutations associated with FH in affected individuals meeting defined eligibility criteria, and targeted cascade testing in first and second-degree relatives of those affected individuals with a confirmed genetic diagnosis. DUSC discussed that genetic testing can be expensive and may not be readily available. DUSC questioned whether this MBS listing would increase the use of this test to qualify for evolocumab. DUSC considered that, even if a genetic test is performed and a mutation is not detected, this does not automatically exclude FH. DUSC noted approximately 20% of clinically definite cases of FH will show a negative result.

DUSC noted evolocumab 140mg/mL pen device was supplied more commonly than the 420 mg/3.5 mL cartridge for the treatment of HoFH. Based on anecdotal evidence, DUSC noted a limitation for the use of the cartridge device might be pain on administration.

DUSC considered future reports of evolocumab could include analyses of the duration between supplies, and distribution by age and by the type of familial hypercholesterolaemia (HoFH or HeFH).

DUSC actions

DUSC requested that the report be provided to the PBAC for consideration.

Context for analysis

The DUSC is a Sub Committee of the Pharmaceutical Benefits Advisory Committee (PBAC). The DUSC assesses estimates on projected usage and financial cost of medicines.

The DUSC also analyses data on actual use of medicines, including the utilisation of PBS listed medicines, and provides advice to the PBAC on these matters. This may include outlining how the current utilisation of PBS medicines compares with the use as recommended by the PBAC.

[5] Lipid Modification. In: eTG complete [Internet]. Melbourne: Therapeutic Guidelines Limited; Published March 2018 (eTG June 2019 edition).

The DUSC operates in accordance with the quality use of medicines objective of the National Medicines Policy and considers that the DUSC utilisation analyses will assist consumers and health professionals to better understand the costs, benefits and risks of medicines.

The utilisation analysis report was provided to the pharmaceutical sponsors of each drug and comments on the report were provided to DUSC prior to its consideration of the analysis.

Sponsors' comments

Amgen Australia Pty Ltd: The Sponsor has no comment

Appendix 1: Relevant aspects of consideration by the Pharmaceutical Benefits Advisory Committee (PBAC)

PBAC Meeting	Indication Considered	Outcome
March 2015	Hypercholesterolaemia	The PBAC rejected the request to list evolocumab for the treatment of hypercholesterolaemia on the basis of unestablished clinical place in therapy and the uncertainty surrounding its use in clinical practice. The PBAC noted that the submission was made under the TGA-PBAC parallel process with the TGA Delegate's consideration expected in late 2015. Accordingly, the PBAC noted that there were no TGA documents available during the time of PBAC consideration to determine the indication of the drug and its clinical place in therapy.
March 2016	Familial hypercholesterolaemia	The PBAC recommended the Authority Required listing of evolocumab under Section 85, for the treatment of homozygous familial hypercholesterolaemia. In making this recommendation, the PBAC considered that the homozygous FH population (with an abnormality in both of the two copies of the specific gene) represent a small, definable, patient group, in whom there is a high level of clinical need.
July 2017	Familial homozygous hypercholesterolaemia (listing of Injection 420 mg in 3.5 mL single dose autoinjector)	The PBAC recommended the listing of the new strength of evolocumab for the treatment of familial homozygous hypercholesterolaemia. The PBAC accepted that this additional form of evolocumab would provide patients with an alternative dosing schedule to the currently listed form at no additional cost to the Government.
November 2017	Familial hypercholesterolaemia (extension of the listing to include the treatment of HeFH)/ hypercholesterolaemia with symptomatic atherosclerotic cardiovascular disease (ASCVD) who do not have underlying FH	The PBAC deferred making a recommendation to extend the PBS listing of evolocumab for patients with familial hypercholesterolaemia in order to address the residual uncertainty with the economic model following revisions provided in the pre-PBAC response. The PBAC did not recommend the listing of evolocumab for patients with non-familial hypercholesterolaemia with atherosclerotic disease on the basis of a high incremental cost effectiveness ratio (ICER) and high and uncertain patient population numbers.

PBAC Meeting	Indication Considered	Outcome
March 2018	Familial hypercholesterolaemia	The PBAC recommended extending the PBS listing for evolocumab for patients with Familial Hypercholesterolaemia to include patients with heterozygous FH, under certain conditions. The PBAC accepted that both the heterozygous and homozygous FH populations are high risk, and that the use of evolocumab could be extended to include the heterozygous population as it would be an effective and safe therapy following failed treatment with statins and ezetimibe. The PBAC considered that the revised economic model, reduced price and other arrangements proposed in the resubmission addressed the outstanding issues raised by the PBAC from the November 2017 submission.
July 2018	Non-familial hypercholesterolaemia with atherosclerotic disease.	The PBAC did not recommend the listing of evolocumab for patients with non-familial hypercholesterolaemia with atherosclerotic disease on the basis of an inadequately defined patient population, an uncertain incremental cost-effectiveness ratio (ICER) and high and uncertain patient population numbers. The PBAC considered that this population required more refined eligibility criteria in the proposed PBS listing given the very high financial estimates.
July 2019	Hypercholesterolaemia	The PBAC deferred making a recommendation on the listing of evolocumab for the treatment of non-familial hypercholesterolaemia in patients with ASCVD and additional high-risk factors. The PBAC also deferred making a recommendation on the resubmission's request to extend the existing familial hypercholesterolaemia listing in the ASCVD population to include patients with low-density lipoprotein (LDL) levels between 2.6 mmol/L and 3.3 mmol/L.

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The Department of Health (DoH) has made all reasonable efforts to ensure that information provided in this report is accurate. The information provided in this report was up-to-date when it was considered by the Drug Utilisation Sub-committee of the Pharmaceutical Benefits Advisory Committee. The context for that information may have changed since publication.

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