VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Proprotein Convertase Subtilisin Kexin Type 9 Related Products – Leqvio Utilization Management Medical Policy
- Leqvio® (inclisiran subcutaneous injection – Novartis)

REVIEW DATE: 05/28/2025

OVERVIEW

Leqvio, a small interfering ribonucleic acid (RNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) messenger RNA, is indicated as an adjunct to diet and statin therapy for the treatment of adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce low-density lipoprotein cholesterol (LDL-C).[1] The safety and effectiveness have not been established in pediatric patients.

Repatha® (evolocumab subcutaneous injection) and Praluent® (alirocumab subcutaneous injection) are PCSK9 inhibitor products.[2,3]

Dosing Information

Leqvio is given as a subcutaneous injection and should be administered by a healthcare professional.[1] The dose is 284 mg given as a single subcutaneous injection initially, again at 3 months, and then once every 6 months.

Guidelines

Many guidelines are available regarding the treatment of patients with dyslipidemia which include the management of HeFH and atherosclerotic cardiovascular disease (ASCVD).[4-9] For patients with elevated LDL-C, statins are the cornerstone of therapy and recommended first-line to be used at maximally tolerated doses due to the established benefits regarding the reduction of cardiovascular (CV) risks. Atorvastatin 40 mg to 80 mg once daily (QD) and rosuvastatin 20 mg to 40 mg QD are considered high-intensity statins as they achieve LDL-C lowering of ≥ 50%.

- The **American College of Cardiology (ACC) Expert Consensus Decision Pathway on the Role of Non-Statin Therapies** for LDL-Cholesterol Lowering in the Management of Atherosclerotic cardiovascular disease (ASCVD) Risk (2022) make several recommendations regarding PCSK9 inhibitors.[4] For adults with clinical ASCVD at very high risk (e.g., patients with major ASCVD events, HeFH, diabetes) who are on statin therapy for secondary prevention, the general goal is ≥ 50% LDL-C reduction and an LDL-C < 55 mg/dL with maximally tolerated statin therapy. If the above goals are not achieved, the initial non-statin agents recommended include ezetimibe and/or a PCSK9 monoclonal antibody (i.e., Repatha or Praluent). Leqvio may be considered. For adults without clinical ASCVD or diabetes or LDL-C ≥ 190 mg/dL who have undergone subclinical atherosclerosis imaging, if the coronary artery calcium score is ≥ 1,000 Agatston units, PCSK9 monoclonal antibodies (i.e., Repatha or Praluent) may be non-statin agents to consider following high-intensity statin therapy and ezetimibe to achieve the goal of a ≥ 50% LDL-C reduction (and LDL-C threshold < 70 mg/dL).
- The **American Heart Association (AHA)/ACC guidelines on the management of blood cholesterol** (updated 2018) defines ASCVD as an acute coronary syndrome, those with a history of myocardial infarction, stable or unstable angina or coronary or other revascularizations, stroke, transient ischemic attack, or peripheral arterial disease.[5,6] Although LDL-C thresholds are not always recognized, in general, an LDL-C < 70 mg/dL is recommended for most patients with

ASCVD to reduce CV risk. Use of a PCSK9 as an adjunct is justified if this goal is not met with maximally tolerated statins.[5,6] Additionally, reviews have recognized that patients with an elevated coronary artery calcium or calcification score (e.g., ≥ 300 Agatston units) are at an increased risk of CV events.[11-14]

- The **ACC/AHA Guideline for the management of Patients with Acute Coronary Syndrome (ACS)** [2025] states that patients who are already on maximally tolerated statin therapy with LDL-C ≥ 70 mg/dL, adding a nonstatin lipid-lowering agent is recommended to further reduce the risk of a major adverse cardiac event (MACE).[15] Some recommendations also provide for a lower goal LDL-C level (55 to 69 mg/dL).
- The **American Diabetes Association Standards of Care for Diabetes** discuss CV disease and risk management (2025).[7] For patients with diabetes who are 40 to 75 years of age at higher CV risk (including those with one or more ASCVD risk factors) it is recommended to use high-intensity statin therapy to reduce LDL-C by ≥ 50% of baseline and to target an LDL-C of < 70 mg/dL. Also, for patients with diabetes who are 40 to 75 years of age at higher CV risk, especially those with multiple ASCVD risk factors and an LDL-C ≥ 70 mg/dL, it may be reasonable to add ezetimibe or a PCSK9 inhibitor to a maximum tolerated statin.
- Guidelines for **Chronic Coronary Disease from the AHA and ACC** (along with other organizations) [2023] state in such patients who are judged to be at very high risk and on maximally tolerated statin therapy and an LDL-C ≥ 70 mg/dL, ezetimibe can be beneficial to further reduce the risk of a major adverse coronary event.[8] Patients with chronic coronary disease who are considered to be at very high risk who have and LDL-C ≥ 70 mg/dL who are receiving maximally tolerated statins and ezetimibe, a PCSK9 monoclonal antibody can be beneficial to further reduce the risk of a major adverse coronary event.
- The **American Association of Clinical Endocrinology** (AACE) clinical practice guideline on the pharmacologic management of adults with dyslipidemia (2025) make many recommendations.[16] In adults with dyslipidemia who are receiving maximally tolerated statins and have ASCVD or are an increased risk for ASCVD but who are not at goal (LDL-C < 70 mg/dL), AACE suggests therapy with Praluent or Repatha. In adults with dyslipidemia who do not have ASCVD, AACE suggests against the use of Praluent or Repatha. There is insufficient evidence to formulate a recommendation for or against use of Leqvio in adults with dyslipidemia. Overall, there were very few trials and CV events, preventing determination of the balance of potential benefits and harms of Leqvio in addition to usual care.
- A **Scientific Statement from the AHA on Familial Hypercholesterolemia** (2015),[9] as well as other information,[10] provide additional guidance on diagnosing familial hypercholesterolemia (e.g., HeFH). For HeFH, Dutch Lipid Network criteria scoring is used, as well the Simon Broome criteria.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Leqvio. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. A patient who has previously met Initial Therapy criteria for Leqvio for the requested indication under the Coverage Review Department and is currently receiving Leqvio is only required to meet continuation of therapy criteria (i.e., currently receiving therapy). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Leqvio, or is restarting Leqvio, Initial Therapy criteria must be met.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Leqvio is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. **Heterozygous Familial Hypercholesterolemia (HeFH).*** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient meets ONE of the following (a, b, or c):
       - **a)** Patient has an untreated low-density lipoprotein cholesterol (LDL-C) level ≥ 190 mg/dL (prior to treatment with antihyperlipidemic agents); OR
       - **b)** The diagnosis has been confirmed by genetic testing; OR
         Note: Examples include pathogenic variants at the low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), proprotein convertase subtilisin kexin type 9 (PCSK9), or low-density lipoprotein receptor adaptor protein 1 (LDLRAP1) gene.
       - **c)** Patient has been diagnosed with heterozygous familial hypercholesterolemia meeting ONE of the following diagnostic criteria thresholds [(1) or (2)]:
         - **(1)** Prescriber confirms that the Dutch Lipid Network criteria score was > 5; OR
         - **(2)** Prescriber confirms that Simon Broome criteria met the threshold for "definite" or "possible (or probable)" familial hypercholesterolemia; AND
     - **iii.** Patient meets ONE of the following (a or b):
       - **a)** Patient meets ALL of the following [(1), (2), and (3)]:
         - **(1)** Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single entity or as a combination product]); AND
         - **(2)** Patient has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND
         - **(3)** LDL-C level after this treatment regimen remains ≥ 70 mg/dL; OR
       - **b)** Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:
         - **(1)** Patient experienced statin-related rhabdomyolysis; OR
           Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).
         - **(2)** Patient meets ALL of the following [(a), (b), and (c)]:
           - **(a)** Patient experienced skeletal-related muscle symptoms; AND
             Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).
           - **(b)** The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
           - **(c)** When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
             Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

B) Patient Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):
A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR
B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

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2. Primary Hyperlipidemia.* Approve for 1 year if the patient meets ONE of the following (A or B):
Note: This is not associated with established cardiovascular disease or heterozygous familial hypercholesterolemia (HeFH) and may be referred to as combined hyperlipidemia, hypercholesterolemia (pure, primary), dyslipidemia, or increased/elevated low-density lipoprotein cholesterol (LDL-C) levels.

A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has a coronary artery calcium or calcification score ≥ 300 Agatston units; OR
  - **b)** Patient has diabetes; AND
- **iii.** Patient meets ONE of the following (a or b):
  - **a)** Patient meets ALL of the following [(1]), (2), and (3)]:
    - **(1)** Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single-entity or as a combination product]); AND
    - **(2)** Patient has tried the one high-intensity statin therapy above along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND
    - **(3)** LDL-C level after this treatment regimen remains ≥ 70 mg/dL; OR
  - **b)** Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:
    - **(1)** Patient experienced statin-related rhabdomyolysis; OR
      Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).
    - **(2)** Patient meets ALL of the following [(a), (b), and (c)]:
      - **(a)** Patient experienced skeletal-related muscle symptoms; AND
        Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).
      - **(b)** The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND
      - **(c)** When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR
        Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

B) Patient Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.
Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):
A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR
B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

Other Uses with Supportive Evidence

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3. Established Cardiovascular Disease.* Approve for 1 year if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
i. Patient is ≥ 18 years of age; AND
ii. Patient has had one of the following conditions or diagnoses (a, b, c, d, e, or f):
a) A previous myocardial infarction or a history of an acute coronary syndrome; OR
b) Angina (stable or unstable); OR
c) A past history of stroke or transient ischemic attack; OR
d) Coronary artery disease; OR
e) Peripheral arterial disease; OR
f) Patient has undergone a coronary or other arterial revascularization procedure in the past; AND
Note: Examples include coronary artery bypass graft surgery, percutaneous coronary intervention, angioplasty, and coronary stent procedures.
iii. Patient meets ONE of the following (a or b):
a) Patient meets all of the following [(1), (2), and (3)]:
(1) Patient has tried one high-intensity statin therapy (i.e., atorvastatin ≥ 40 mg daily; rosuvastatin ≥ 20 mg daily [as a single entity or as a combination product]); AND
(2) Patient has tried one high-intensity statin along with ezetimibe (as a single-entity or as a combination product) for ≥ 8 continuous weeks; AND
(3) Low-density lipoprotein cholesterol (LDL-C) level after this treatment regimen remains ≥ 55 mg/dL; OR
b) Patient has been determined to be statin intolerant by meeting ONE of the following [(1) or (2)]:
(1) Patient experienced statin-related rhabdomyolysis; OR
Note: Rhabdomyolysis is statin-induced muscle breakdown that is associated with markedly elevated creatine kinase levels (at least 10 times the upper limit of normal), along with evidence of end organ damage which can include signs of acute renal injury (noted by substantial increases in serum creatinine [Scr] levels [a ≥ 0.5 mg/dL increase in Scr or doubling of the Scr] and/or myoglobinuria [myoglobin present in urine]).
(2) Patient meets ALL of the following [(a), (b), and (c)]:
(a) Patient experienced skeletal-related muscle symptoms; AND
Note: Examples of skeletal-related muscle symptoms include myopathy (muscle weakness) or myalgia (muscle aches, soreness, stiffness, or tenderness).

(b) The skeletal-muscle related symptoms occurred while receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or combination products); AND

(c) When receiving separate trials of both atorvastatin and rosuvastatin (as single-entity or as combination products) the skeletal-related muscle symptoms resolved upon discontinuation of each respective statin therapy (atorvastatin and rosuvastatin); OR

Note: Examples of skeletal-related muscle symptoms include myopathy and myalgia.

B) Patient Currently Receiving Leqvio. Approve if according to the prescriber, the patient has experienced a response to therapy.

Note: Examples of a response to therapy include decreasing LDL-C, total cholesterol, non-high-density lipoprotein (non-HDL-C), or apolipoprotein B levels. Also, if the patient is currently receiving the requested therapy but has not previously received approval of Leqvio for this specific indication through the Coverage Review Department, review under criteria for Initial Therapy. If the patient is restarting therapy with Leqvio, Initial Therapy criteria must be met.

Dosing. Approve ONE of the following dosage regimens (A or B):

A) Initial dose is 284 mg given as a single subcutaneous injection, again at 3 months, and then once every 6 months; OR

B) Maintenance dose is 284 mg given as a subcutaneous injection once every 6 months.

Note:

* A patient may have a diagnosis that pertains to more than one indication, therefore, consider review under different approval conditions, if applicable (e.g., a patient with heterozygous familial hypercholesterolemia may have established cardiovascular disease, a patient with primary hyperlipidemia may have heterozygous familial hypercholesterolemia).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Leqvio is not recommended in the following situations:

1. **Concurrent use of Leqvio with Repatha (evolocumab subcutaneous injection) or Praluent (alirocumab subcutaneous injection).** Repatha and Praluent are PCSK9 inhibitors and should not be used with Leqvio due to a similar mechanism of action.[1] Patients receiving PCSK9 inhibitors were excluded from the pivotal trials with Leqvio.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	It was added to the Policy Statement that a patient who has previously met initial therapy criteria for Leqvio for the requested indication under the Coverage Review Department and is currently receiving Leqvio is only required to meet continuation of therapy criteria (i.e., currently receiving therapy). If past criteria have not been met under the Coverage Review Department and the patient is currently receiving Leqvio, or is restarting Leqvio, initial criteria must be met. In addition, the following changes were made: **Atherosclerotic Cardiovascular Disease:** Requirements were divided to distinguish between initial therapy and patient currently receiving Leqvio (previously there was only one criteria set). For a patient who is currently receiving Leqvio and has previously met initial therapy criteria for the requested indication under the Coverage Review Department, only the continuation of therapy criteria has to be met. The continuation of therapy criteria states that according to the prescribing physician, the patient has experienced a response to therapy with examples provided in a Note. **Heterozygous Familial Hypercholesterolemia:** Requirements were divided to distinguish between initial therapy and patient currently receiving Leqvio (previously there was only one criteria set). The criteria to confirm the diagnosis of heterozygous familial hypercholesterolemia were reworded regarding the use of the Dutch Lipid Network criteria and the Simon Broome criteria; also, the phrase "prescriber used" was changed to "the prescribing physician confirms". For a patient who is currently receiving Leqvio and has previously met initial therapy criteria for the requested indication under the Coverage Review Department, only the continuation of therapy criteria has to be met. The continuation of therapy criteria states that according to the prescribing physician, the patient has experienced a response to therapy with examples provided in a Note.	04/26/2023
Selected Revision	**Atherosclerotic Cardiovascular Disease:** The condition was moved from FDA-Approved Indications to Other Uses with Supportive Evidence. Also, coronary artery disease was added as a condition or diagnosis that represents this indication of use in this related requirement. A Note was added that a patient may have a diagnoses that pertains to more than one indication, therefore, consider review under different approval conditions, if applicable. **Heterozygous Familial Hypercholesterolemia:** A Note was added that a patient may have a diagnoses that pertains to more than one indication, therefore, consider review under different approval conditions, if applicable. **Primary Hyperlipidemia:** This was added as a new FDA-approved indication.	08/30/2023

HISTORY (CONTINUED)

Type of Revision	Summary of Changes	Review Date
Annual Revision	It was removed from the Policy Statement that the agent is prescribing by or in consultation with a physician who specializes in the condition being treated. In addition, the following changes were made: **Established Cardiovascular Disease:** The name of the indication was changed to as stated (previously "Atherosclerotic Cardiovascular Disease"). For Initial Therapy, the requirement that the medication is prescribed by, or in consultation with a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders was removed. The requirement that the low-density lipoprotein cholesterol level after treatment with one high-intensity statin therapy and ezetimibe be ≥ 70 mg/dL was changed to ≥ 55 mg/dL. For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber". **Heterozygous Familial Hypercholesterolemia:** For Initial Therapy, the requirement that the medication is prescribed by, or in consultation with a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders was removed. The requirement that the patient has had genetic confirmation of heterozygous familial hypercholesterolemia by mutations in the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin kexin type 9, or low-density lipoprotein receptor adaptor protein 1 gene was changed to state that the patient has had phenotypic confirmation of heterozygous familial hypercholesterolemia with the above examples moved to a Note. Regarding the diagnosis of heterozygous familial hypercholesterolemia by meeting the Dutch Lipid Network criteria score or the Simon Broome criteria, the requirement that this be confirmed by the "prescribing physician" was changed to "prescriber". For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber". **Primary Hyperlipidemia:** For Initial Therapy, the requirement that the medication is prescribed by, or in consultation with a cardiologist; an endocrinologist; or a physician who focuses in the treatment of cardiovascular risk management and/or lipid disorders was removed. A patient with diabetes now qualifies for this indication (if requirements are met); previously, high risk was only defined by a patient who had a "coronary artery calcium or calcification score ≥ 300 Agatston units". The requirement that the low-density lipoprotein cholesterol level after treatment with one high-intensity statin therapy, along with ezetimibe, be ≥ 100 mg/dL was changed to ≥ 70 mg/dL. For a Patient Currently Receiving the Medication, the requirement that the "prescribing physician" notes that the patient has experienced a response to therapy was changed to "prescriber".	05/08/2024
Annual Revision	**Heterozygous Familial Hypercholesterolemia (HeFH):** For Initial Therapy, the phrase "phenotypic confirmation of heterozygous familial hypercholesterolemia" was replaced with "The diagnosis has been confirmed by genetic testing". Also, "apo B" was changed to "APOB".	05/28/2025

APPENDIX A

Simon Broome Register Diagnostic Criteria.[9,10]

Definite Familial Hypercholesterolemia
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
--Tendon xanthomas in the patient or in a first (parent, sibling, or child) or second-degree relative (grandparent, aunt, or uncle);
OR
DNA-based evidence of LDL-receptor, familial defective APOB, or PCSK9 mutation.
Possible (or Probable) Familial Hypercholesterolemia
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
Family history of premature myocardial infarction younger than 50 years of age in second-degree relative or younger than 60 years of age in first-degree relative;
OR
Raised cholesterol
--Total cholesterol greater than 6.7 mmol/L (260 mg/dL) or LDL-C > 4.0 mmol/L (155 mg/dL) in a patient < 16 years of age; OR
--Total cholesterol > 7.5 mmol/L (290 mg/dL) or LDL-C > 4.9 mmol/L (190 mg/dL) in a patient > 16 years of age;
AND
Family history of raised cholesterol > 7.5 mmol (290 mg/dL) in adult first-degree or second-degree relative or > 6.7 mmol/L (260 mg/dL) in child or sibling aged < 16 years.

LDL-C – Low-density lipoprotein cholesterol; LDL – Low-density lipoprotein; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.

APPENDIX B.

Dutch Lipid Network Criteria.[9,10]

Criteria	Score
Family History	
First-degree relative with known premature coronary and/or vascular disease (men < 55 years, women < 60 years)	1
First degree relative with known LDL-C > 95th percentile for age and sex	1
First-degree relative with tendon xanthomata and/or arcus cornealis, OR	2
Patient is < 18 years of age with LDL-C > 95th percentile for age and sex	2
Clinical History	
Patient with premature CAD (age as above)	2
Patient with premature cerebral or peripheral vascular disease (age as above)	1
Physical Examination	
Tendon xanthomas	6
Arcus cornealis at age < 45 years	4
LDL-C	
LDL-C ≥ 8.5 mmol/L (330 mg/dL)	8
LDL-C 6.5 to 8.4 mmol/L (250 to 329 mg/dL)	5
LDL-C 5.0 to 6.4 mmol/L (190 to 249 mg/dL)	3
LDL-C 4.0 to 4.9 mg/dL (155 to 189 mg/dL)	1
DNA Analysis	
Functional mutation LDLR, APOB or PCSK9 gene	8
Stratification	**Total score**
Definite familial hypercholesterolemia	> 8
Probable familial hypercholesterolemia	6 to 8
Possible familial hypercholesterolemia	3 to 5
Unlikely familial hypercholesterolemia	< 3

LDL-C – Low-density lipoprotein cholesterol; CAD – Coronary artery disease; LDLR – Low-density lipoprotein receptor; APOB – Apolipoprotein B; PCSK9 – Proprotein convertase subtilisin kexin type 9.