# inclisiran (Leqvio®)

**Policy #** 00786
Original Effective Date: 06/13/2022
Current Effective Date: 06/12/2023

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

# When Services Are Eligible for Coverage

Based on review of available data, the Company may consider inclisiran (Leqvio®) ‡ for cholesterol lowering in patients with familial hypercholesterolemia or atherosclerotic cardiovascular disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for inclisiran (Leqvio) when the following criteria are met (I, II, III, IV, V, VI, and VII):

I. Patient is 18 years of age or older; AND
II. Patient is adherent to any medications required for therapy prior to receiving authorization for inclisiran (Leqvio); AND
III. inclisiran (Leqvio) will NOT be used in combination with lomitapide (Juxtapid®)‡, mipomersen (Kynamro®)‡, evolocumab (Repatha™)‡, alirocumab (Praluent®)‡, evinacumab-dgnb (Evkeeza™)‡, or bempedoic acid products (Nexletol®, Nexlizet®)‡ AND
IV. inclisiran (Leqvio) will be used along with a maximally tolerated statin [in those who are not considered statin intolerant (see below for statin intolerance)]; AND
V. inclisiran (Leqvio) is dosed as 284 mg given initially, at 3 months, and then every 6 months thereafter; AND
VI. Patient must meet one of the following (A, B, C, or D):
    A. Patient has a diagnosis of Familial Hypercholesterolemia (FH) withOUT atherosclerotic cardiovascular disease, defined as a WHO (World Health Organization)/Dutch Lipid Clinic Network score of >8; AND
        i. Patient's low density lipoprotein cholesterol (LDL-C) is not adequately controlled [e.g., not at the LDL-C treatment goal for a "high risk" (LDL-C goal <100 mg/dL) or "very high risk" (LDL-C goal <70 mg/dL) patient based on the current National Lipid Association (NLA) guidelines and the patient's specific characteristics] with a high potency maximum daily dose statin

[rosuvastatin (Crestor®)‡ 40 mg, atorvastatin (Lipitor®)‡ 80 mg] for at least 3 months; OR
*(Note that the 3 month timeframe is an additional Company requirement and will be denied as not medically necessary** if not met)*

ii. Patient's LDL-C is not adequately controlled [e.g., not at the LDL-C treatment goal for a "high risk" (LDL-C goal <100 mg/dL) or "very high risk" (LDL-C goal <70 mg/dL) patient based on the current NLA guidelines and the patient's specific characteristics] with a maximally tolerated stable daily statin (of any potency) for at least 3 months ONLY if proof is given that a high potency maximum daily dose statin was not well tolerated; OR
*(Note that the 3 month timeframe is an additional Company requirement and will be denied as not medically necessary** if not met)*

B. Patient has a diagnosis of FH withOUT atherosclerotic cardiovascular disease, defined as a WHO/Dutch Lipid Clinic Network score of >8; AND
   i. Patient's LDL-C is not adequately controlled [e.g., not at the LDL-C treatment goal for a "high risk" (LDL-C goal <100 mg/dL) or "very high risk" (LDL-C goal <70 mg/dL) patient based on the current NLA guidelines and the patient's specific characteristics] due to statin intolerance; AND
   ii. Patient meets all of the following criteria confirming statin intolerant:
      1. Patient was unable to tolerate at least 2 different statins. [The inability to tolerate one statin will be accepted if the patient experienced rhabdomyolysis or clinically-significant myonecrosis secondary to a statin. Rhabdomyolysis/myonecrosis is considered to be a muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness ALONG WITH either: a.) acute renal failure or myoglobinuria AND elevated creatine kinase levels (e.g., ≥ 10 times the upper limit of normal) OR b.) elevated creatine kinase levels (e.g., ≥ 10 times the upper limit of normal) alone]; AND
      2. Patient's intolerance was associated with confirmed, intolerable statin-related adverse effects [e.g., skeletal related muscle symptoms (myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness])]; AND
      3. Patient's symptoms or biomarker changes resolved or showed significant improvement on dose decrease or discontinuation; OR

C. Patient has the presence of atherosclerotic cardiovascular disease (either FH or non-FH); AND
   i. Patient's LDL-C is not adequately controlled [e.g., not at the LDL-C treatment goal of <70 mg/dL based on the current NLA guidelines] with a high potency maximum daily dose statin [rosuvastatin (Crestor) 40 mg, atorvastatin (Lipitor) 80 mg] for at least 3 months; OR
   *(Note that the 3 month timeframe is an additional Company requirement and will be denied as not medically necessary** if not met)*
   ii. Patient's LDL-C is not adequately controlled [e.g., not at the LDL-C treatment goal of <70 mg/dL based on the current NLA guidelines] with a maximally tolerated stable daily statin (of any potency) for at least 3 months ONLY if proof is given that a high potency maximum daily dose statin was not well tolerated; OR
   *(Note that the 3 month timeframe is an additional Company requirement and will be denied as not medically necessary** if not met)*

D. Patient has the presence of atherosclerotic cardiovascular disease (either FH or non-FH); AND
   i. Patient's LDL-C is not adequately controlled [e.g., not at the LDL-C treatment goal of <70 mg/dL based on the current NLA guidelines] due to statin intolerance; AND
   ii. Patient meets all of the following criteria confirming statin intolerance:
      1. Patient was unable to tolerate at least 2 different statins. [The inability to tolerate one statin will be accepted if the patient experienced rhabdomyolysis or clinically-significant myonecrosis secondary to a statin. Rhabdomyolysis/myonecrosis is considered to be a muscle breakdown with signs and symptoms such as muscle pain, weakness, tenderness ALONG WITH either: a.) acute renal failure or myoglobinuria AND elevated creatine kinase levels (e.g., ≥ 10 times the upper limit of normal) OR b.) elevated creatine kinase levels (e.g., ≥ 10 times the upper limit of normal) alone]; AND
      2. Patient's intolerance was associated with confirmed, intolerable statin-related adverse effects [e.g., skeletal related muscle symptoms (myopathy [muscle weakness] or myalgia [muscle aches, soreness, stiffness, or tenderness])]; AND

3. Patient's symptoms or biomarker changes resolved or showed significant improvement on dose decrease or discontinuation; AND

VII. Patient meets one of the following criteria (A or B):
   A. Patient meets both of the following criteria (i and ii):
      i. Patient has tried a proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor for ≥ 12 continuous weeks at the FDA approved maximum dose for atherosclerotic cardiovascular disease or heterozygous familial hypercholesterolemia; AND
      *(Note: Examples of PCSK9 inhibitors at their maximum dose for the same conditions as Leqvio include Repatha (evolocumab)140 mg once every 2 weeks or 420 mg once every 4 weeks and Praluent (alirocumab) 150 mg once every 2 weeks or 300 mg once every 4 weeks)*
      *(Note that the 12 week trial of a PCSK9 inhibitor is an additional Company requirement and will be denied as not medically necessary** if not met)*
      ii. Patient's LDL-C level after the max PCSK9 inhibitor dosing regimen remains ≥ 70 mg/dL or ≥100 mg/dL based on "high risk" or "very high risk" classifications of the patient; OR
   B. Patient is known to have two LDL-receptor negative alleles.

**Re-authorization**: (Patient must meet I, II, III, and IV)

I. Patient previously met the initial criteria and received an approval for inclisiran (Leqvio); AND
II. inclisiran (Leqvio) is dosed as 284 mg every 6 months; AND
III. inclisiran (Leqvio) will NOT be used in combination with lomitapide (Juxtapid), mipomersen (Kynamro), evolocumab (Repatha), alirocumab (Praluent), evinacumab-dgnb (Evkeeza), or bempedoic acid products (Nexletol, Nexlizet); AND

IV. Patient has achieved clinically significant LDL-C lowering AND is adherent to inclisiran (Leqvio).
*(Note: This specific patient criterion is an additional Company requirement and will be denied as not medically necessary** if not met)*

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# When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of inclisiran (Leqvio) when the patient has NOT tried and failed the required pre-requisite medications for a timeframe of at least 3 months to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of inclisiran (Leqvio) when the patient has NOT achieved clinically significant LDL-C lowering OR is NOT adherent to inclisiran (Leqvio) to be **not medically necessary.****

Based on review of available data, the Company considers the use of inclisiran (Leqvio) when the patient has NOT tried and failed 12 weeks of therapy with a PCSK9 inhibitor (e.g., Repatha, Praluent) to be **not medically necessary.****

# When Services Are Considered Investigational

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers the use of inclisiran (Leqvio) when patient selection criteria are not met (except those listed above as **not medically necessary****) to be **investigational.***

# Background/Overview

Leqvio is a small interfering RNA (siRNA) directed to proprotein convertase subtilisin kexin type 9 (PCSK9) mRNA indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C (low density lipoprotein cholesterol). In hepatocytes, Leqvio utilizes the RNA interference mechanism and directs catalytic breakdown of mRNA for PCSK9. This increases LDL-C receptor recycling and expression on the hepatocyte cell surface, which increases LDL-C uptake and lowers LDL-C levels in the circulation. Leqvio's dosage is 284 mg administered as a subcutaneous injection initially, again at 3 months, and then every 6 months. Leqvio should be administered by a healthcare professional.

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It should be noted that the effects of Leqvio on cardiovascular morbidity and mortality have not been determined. Leqvio and the PCSK9 inhibitors have not been studied head to head, but have similar LDL-C reductions. Currently, the PCSK9 inhibitors offer an equally efficacious and more cost-effective option for the lowering of cholesterol in patients with HeFH or atherosclerotic cardiovascular disease.

**Hypercholesterolemia/Treatment Guidelines**

Approximately 30% of the United States population has elevated LDL-C (low density lipoprotein cholesterol). There is also a subset of hypercholesterolemia, known as familial hypercholesterolemia, which can affect nearly 1 in 300 individuals. Familial hypercholesterolemia can further be broken down into homozygous and heterozygous forms of familial hypercholesterolemia. The homozygous form is by far the rarest with an estimated incidence of 1 in 1,000,000 individuals. The gold standard for the treatment of elevated LDL-C levels is a statin given along with ezetimibe (Zetia) to provide the greatest amount of LDL-C lowering. Statin products also have proven cardiovascular outcomes.

Genetic testing is available to determine whether or not an individual has familial hypercholesterolemia, however clinical signs/symptoms are often a more practical method of diagnosing this condition. Clinical studies have used the WHO/Dutch Lipid Clinic Network Familial Hypercholesterolemia diagnostic criteria to determine if an individual had familial hypercholesterolemia. A score of >8 is representative of “definite” familial hypercholesterolemia. The criteria are located in the following chart:

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**WHO (World Health Organization)/Dutch Lipid Clinic Network Familial Hypercholesterolemia Criteria**

| | Points |
|---|---|
| Criteria<br>**Family history** | |
| First-degree relative with known premature* coronary and vascular disease, OR<br>First-degree relative with known LDL-C level above the 95th percentile | 1 |
| First-degree relative with tendinous xanthomata and/or arcus cornealis, OR<br>Children aged less than 18 years with LDL-C level above the 95th percentile | 2 |
| **Clinical history** | |
| Patient with premature* coronary artery disease | 2 |
| Patient with premature* cerebral or peripheral vascular disease | 1 |
| **Physical examination** | |
| Tendinous xanthomata | 6 |
| Arcus cornealis prior to age 45 years | 4 |
| **Cholesterol levels mg/dl (mmol/liter)** | |
| LDL-C >= 330 mg/dL ( ≥8.5) | 8 |
| LDL-C 250 – 329 mg/dL (6.5–8.4) | 5 |
| LDL-C 190 – 249 mg/dL (5.0–6.4) | 3 |
| LDL-C 155 – 189 mg/dL (4.0–4.9) | 1 |
| **DNA analysis** | |
| Functional mutation in the *LDLR, apo B or PCSK9* gene | 8 |
| **Diagnosis (diagnosis is based on the total number of points obtained)** | |
| Definite Familial Hypercholesterolemia | >8 |
| Probable Familial Hypercholesterolemia | 6 – 8 |
| Possible Familial Hypercholesterolemia | 3 – 5 |
| Unlikely Familial Hypercholesterolemia | <3 |

Premature = < 55 years in men; < 60 years in women

The 95th percentile in the "WHO/Dutch Lipid Clinic Network Familial Hypercholesterolemia Criteria" chart refers to the following LDL cholesterol values:

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| Men | | | | Women | | | |
|---|---|---|---|---|---|---|---|
| **Age (yr)** | **5th Percentile (LDL-C, mg/dL)** | **75th Percentile (LDL-C, mg/dL)** | **95th percentile (LDL-C, mg/dL)** | **Age (yr)** | **5th Percentile (LDL-C, mg/dL)** | **75th Percentile (LDL-C, mg/dL)** | **95th Percentile (LDL-C, mg/dL)** |
| 0–19 | 65 | 105 | 130 | 0–19 | 65 | 110 | 140 |
| 20–24 | 65 | 120 | 145 | 20–24 | 55 | 120 | 160 |
| 25–29 | 70 | 140 | 165 | 25–34 | 70 | 125 | 160 |
| 30–34 | 80 | 145 | 185 | 35–39 | 75 | 140 | 170 |
| 35–39 | 80 | 155 | 190 | 40–44 | 75 | 145 | 175 |
| 40–44 | 85 | 155 | 185 | 45–49 | 80 | 150 | 185 |
| 45–69 | 90 | 165 | 205 | 50–54 | 90 | 160 | 200 |
| 70 + | 90 | 165 | 185 | 55 + | 95 | 170 | 215 |

The above chart comes from Lipid Research Clinic Data 1983. Available at: http://www.ncbi.nlm.nih.gov/books/NBK351/table/A968/?report=objectonly

The following link for the ATP III- A distribution of LDL Cholesterol in the US Adult Population also provides percentile values. It is located at: http://circ.ahajournals.org/content/106/25/3237/T2.expansion.html.

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The American College of Cardiology (ACC)/American Heart Association (AHA) treatment guidelines no longer set treatment goals for hyperlipidemia. The guidelines instead emphasize the appropriate intensity of statin therapy to reduce cardiovascular risk in patients who will benefit. These guidelines also emphasize the benefits of LDL-C reduction. The National Lipid Association does set LDL-C treatment goal levels for patients at various risk stratifications. Those with clinical atherosclerotic cardiovascular disease would fall into the "very high risk" category and would therefore be treated to an LDL-C of less than 70 mg/dL. Patients with familial hypercholesterolemia could fall into either the "very high risk" or "high risk" categories, based on their patient characteristics and would therefore have a treatment goal of less than 70 mg/dL or 100 mg/dL (respectively). Risk stratification (per the National Lipid Association) is as follows:

**Risk Classifications:**

**Very High Risk:**

I. ASCVD (atherosclerotic cardiovascular disease)[#]; OR
II. Diabetes Mellitus with ≥2 other Major ASCVD risk factors^ OR diabetes mellitus with end organ damage [e.g., increased albumin/creatinine ratio (≥30mg/g), chronic kidney disease, or retinopathy]

**High Risk:**

I. ≥ 3 major ASCVD risk factors^; OR
II. Diabetes Mellitus with 0-1 other Major ASCVD risk factors^; OR
III. Chronic kidney disease (GFR ≤44 mL/min); OR
IV. LDL-C ≥190 mg/dL (untreated); OR
V. Quantitative risk score reaching the high risk threshold (one of the following)
    A. ≥10% using Adult Treatment Panel III Framingham risk score for hard coronary heart disease (CHD, MI, or CHD death); OR
    B. ≥15% using the 2013 Pooled Cohort Equations for hard ASCVD (MI, stroke, or death from CHD or stroke); OR
    C. ≥45% using the Framingham long-term CVD (MI, CHD death or stroke) risk calculator

**[#]ASCVD (includes one of more of the following):**

I. Myocardial infarction or other acute coronary syndrome
II. Coronary or other revascularization procedure

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III. Transient ischemic attack
IV. Ischemic stroke
V. Atherosclerotic peripheral arterial disease (ABI of <0.90)
VI. Other documented atherosclerotic diseases such as
    A. Coronary atherosclerosis
    B. Renal atherosclerosis
    C. Aortic aneurysm secondary to atherosclerosis
    D. Carotid plaque (≥50% stenosis)

**^ASCVD Risk factors:**

I. Age
    A. Male ≥45 years
    B. Female ≥55 years
II. Family history of early CHD (MI, death, or coronary revascularization procedure)
    A. <55 years of age in a male first degree relative or
    B. <65 years of age in a female first degree relative
III. Current cigarette smoking
IV. High blood pressure (≥140/≥90 mm Hg) or on a blood pressure medication)
V. Low HDL-C
    A. Male <40 mg/dL
    B. Female <50 mg/dL

**Treatment Goals:**

| Risk | LDL-C Treatment Goal |
|---|---|
| Very High Risk | <70 mg/dL |
| High Risk | <100 mg/dL |

**Primary Hypercholesterolemia/Atherosclerotic Cardiovascular Disease**

These products do not have any cardiovascular outcomes data to date.

**Statin Intolerance**

Statins have been associated with muscle-related adverse effects such as myalgia (e.g., muscle aches, soreness, stiffness, or tenderness), myopathy (muscle weakness), and/or myositis (muscle inflammation). Although the incidence is variable, muscle adverse effects are reported in around 5%

of patients receiving statins, but may be due to other causes (e.g., excessive exercise, other medical conditions [hypothyroidism], non-statin medications). It is advisable to assess for drug interactions as well as to check vitamin D levels and thyroid function status. Rhabdomyolysis, which is uncommon with statin therapy, is a severe muscle-related adverse effect that results in muscle breakdown associated with muscle-related symptoms (e.g., muscle pain, weakness, tenderness) along with acute renal failure and elevated creatine kinase [CK] levels (myonecrosis). In patients with statin-related muscle adverse events, symptoms may not re-occur if the patient switches to a different statin therapy. Pravastatin and fluvastatin appear to have much less intrinsic muscle toxicity than other statins and could be considered for those who had statin related intolerable muscle symptoms.

In 2014, the NLA Statin Intolerance Panel published an update. It was stated that most statin intolerance is due to myalgia. The strongest evidence at present for statin intolerance in a population is that myalgia appears but then remits with withdrawal but reoccurs with re-challenge. The incidence of statin intolerance is widely variable. The Panel states that statins are among the safest medications available. The Panel does advise that due to statin benefits, it is safe to recommend a patient continue statin therapy even when some degree of statin intolerance is present, if the patient can reasonably tolerate the statin. A pivotal trial with Praluent called ODYSSEY ALTERNATIVE defined statin intolerance as the inability to take at least two different statins due to muscle-related adverse effects, of which one statin was administered at the lowest approved starting dose. Data also suggest that many patients who are re-challenged with statin therapy after an adverse event may be able to tolerate statin therapy long-term. Of note, in the ODYSSEY ALTERNATIVE trial with Praluent, 69.8% of patients who were considered statin intolerant were treated with atorvastatin 20 mg daily and completed the double-blind 24-week portion of the trial. This suggests that re-challenge with a statin in those purported to be statin intolerant is reasonable and may lead to successful use of a statin therapy.

# FDA or Other Governmental Regulatory Approval

**U.S. Food and Drug Administration (FDA)**

Leqvio is indicated as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease who require additional lowering of LDL-C (low density lipoprotein cholesterol).

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# Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Leqvio was investigated in three randomized, double-blind, placebo-controlled trials that enrolled 3,457 adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD), who were taking maximally tolerated statin therapy and who required additional LDL-C (low density lipoprotein cholesterol) lowering. Demographics and baseline disease characteristics were balanced between the treatment arms in all trials.

**LDL-C Reduction in Patients with ASCVD**

Study 1 (ORION-10) was a multicenter, double-blind, randomized, placebo-controlled 18-month trial in which 1,561 patients with ASCVD were randomized 1:1 to receive subcutaneous injections of either Leqvio 284 mg (n = 781) or placebo (n = 780) on Day 1, Day 90, Day 270, and at Day 450. Patients were taking a maximally tolerated dose of statin with or without other lipid modifying therapy, and required additional LDL-C reduction. Patients were stratified by current use of statins or other lipid-modifying therapies. Patients taking PCSK9 inhibitors were excluded from the trial. The mean baseline LDL-C was 105 mg/dL. At the time of randomization, 89% of patients were receiving statin therapy and 69% were receiving high-intensity statin therapy. The primary efficacy outcome measure in Study 1 was the percent change from baseline to Day 510 in LDL-C. The difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to Day 510 was -52% (95% CI: -56%, -49%; $p < 0.0001$)

Study 2 (ORION-11) was a multicenter, double-blind, randomized, placebo-controlled 18-month trial in which 1,414 adults with ASCVD were randomized 1:1 to receive subcutaneous injections of either Leqvio 284 mg (n = 712) or placebo (n = 702) on Day 1, Day 90, Day 270, and Day 450. Patients were taking a maximally tolerated dose of statin with or without other lipid modifying therapy, and required additional LDL-C reduction. Patients were stratified by country and by current use of statins or other lipid-modifying therapies. Patients taking PCSK9 inhibitors were excluded

from the trial. The mean baseline LDL-C was 101 mg/dL. At the time of randomization, 96% of patients were receiving statin therapy and 80% were receiving high-intensity statin therapy. The primary efficacy outcome measure in Study 2 was the percent change from baseline to Day 510 in LDL-C. The difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to Day 510 was -51% (95% CI: -54%, -47%; $p < 0.0001$).

**LDL-C Reduction in Patients with HeFH**

Study 3 (ORION-9) was a multicenter, double-blind, randomized, placebo-controlled 18-month trial in which 482 patients with HeFH were randomized 1:1 to receive subcutaneous injections of either Leqvio 284 mg (n = 242) or placebo (n = 240) on Day 1, Day 90, Day 270, and at Day 450. Patients with HeFH were taking a maximally tolerated dose of statin with or without other lipid modifying therapy, and required additional LDL-C reduction. The diagnosis of HeFH was made either by genotyping or clinical criteria using either the Simon Broome or WHO/Dutch Lipid Network criteria. Patients were stratified by country and by current use of statins or other lipid-modifying therapies. Patients taking PCSK9 inhibitors were excluded from the trial. The mean baseline LDL-C was 153 mg/dL. At the time of randomization, 90% of patients were receiving statin therapy and 74% were receiving high-intensity statin therapy. Fifty-two percent (52%) of patients were treated with ezetimibe. The most commonly administered statins were atorvastatin and rosuvastatin. The primary efficacy outcome measure in Study 3 was the percent change from baseline to Day 510 in LDL-C. The difference between the Leqvio and placebo groups in mean percentage change in LDL-C from baseline to Day 510 was -48% (95% CI: -54%, -42%; $p < 0.0001$).

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# Policy History

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05/05/2022 Medical Policy Committee review
05/11/2022 Medical Policy Implementation Committee approval. New policy.

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05/04/2023 Medical Policy Committee review
05/10/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 05/2024

# Coding

*The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.*

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

| Code Type | Code |
|---|---|
| CPT | No codes |
| HCPCS | J1306<br>Delete codes effective 06/01/2023: J3490, J3590, C9399 |
| ICD-10 Diagnosis | All related diagnoses |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.