Highmark Commercial Medical Policy-PA/WV/DE/NY

Medical Policy:	I-250-00~~6~~7
Topic (or Title):	Inclisiran (Leqvio)
Section:	Injections
Effective Date:	~~October 1, 2025~~ February 2, 2026
Issued Date:	~~October 1, 2025~~ February 2, 2026
Last Revision Date:	~~September 2025~~ December 2025
Annual Review:	~~November 2024~~ December 2025
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Inclisiran (Leqvio®) is a small interfering RNA (siRNA) that directs catalytic breakdown of mRNA for PCSK9 (proprotein convertase subtilisin kexin type 9) in hepatocytes. This breakdown increases LDL-C receptor recycling and expression on the surface of hepatocyte cells which lowers LDL-C levels in circulation.

Policy Position

Preferred Products

Proprotein convertase substilisin kexin 9 (PCSK9) inhibitors (alirocumab (Praluent) or evolocumab (Repatha)) are the **preferred products** required for members initiating new therapy for indications in this policy. The **non-preferred product** Inclisiran (Leqvio) will be considered when the member has a documented therapy failure after an adequate therapeutic trial of a preferred product, the preferred product has not been tolerated or is contraindicated or the individual does not meet minimum age requirements based on FDA approval for the preferred products.

Adequate therapeutic trial is defined as three (3) months following the injection series at Food and Drug Administration (FDA) or compendia based therapeutic doses of preferred product.

New therapy is defined as no previous utilization within the last 365 calendar days.

Heterozygous Familial Hypercholesterolemia (HeFH)

Inclisiran (Leqvio) may be considered medically necessary for Heterozygous Familial Hypercholesterolemia (HeFH) when the following criteria are met:

- The individual is 18 years of age or older**; and**
- Must be prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist; **and**
- There is clinical documentation of heterozygous familial hypercholesterolemia (FH) as defined by **ONE** of the following:
    - Genetic confirmation of pathogenic variant at the LDLR, APOB, PCSK9, or LDLRAP1 gene locus; **or**
    - ~~The individual has experienced **ONE** of the following physical signs of FH:~~
        - ~~Tendon xanthomas; **or**~~
        - ~~Corneal arcus prior to age 45 years; **or**~~
        - ~~Tuberous xanthomas; **or**~~
        - ~~Xanthelasma; **or**~~
    - Clinical diagnosis based on **ONE** of the following:
        - The WHO criteria/Dutch Lipid Clinical Network criteria with a score greater than 8 points (See Table Attachment A); **or**
        - The Simon Broome Register Diagnostic Criteria with a criterion for definite familial hypercholesterolemia (See Table Attachment B); **or**

        - Familial hypercholesterolemia possibility of “definite” on the Make Early Diagnosis to Prevent Early Deaths (MEDPED) tool **or**
    - The individual meets **ONE** of the following criteria:
        - Documentation of an untreated LDL-C greater than or equal to 190 mg/dL; **or**
        - Documentation of an untreated LDL-C greater than or equal to160 mg/dL if less than 20 years of age; **and**
        - The individual has experienced **ONE** of the following physical signs of FH:
            - Tendon xanthomas; **or**
            - Corneal arcus prior to age 45 years; **or**
            - Tuberous xanthomas; **or**
            - Xanthelasma; **and**
- The individual meets **ONE** of the following criteria:
    - ~~The individual has an LDL-C greater than 100mg/dL, despite use with a maximally tolerated statin; **or**~~
    - ~~The individual has an LDL-C greater than 100mg/dL and is statin intolerant defined as one of the following:~~
    - The individual has experienced therapeutic failure to a maximally tolerated statin; **or**
    - The individual is statin intolerant defined as one (1) of the following:
        - While receiving at least two (2) separate trials of different statins, the individual experienced **ONE** of the following:
            - Statin related rhabdomyolysis, which resolved upon discontinuation of the statins; **or**
            - Skeletal-related muscle symptoms, which resolved upon discontinuation of the statins; **or**
        - Individual experienced **ONE** of the following during any course of statin therapy :
            - Creatinine kinase (CK) increase to 10 times ULN**; or**
            - Liver function tests (LFTs) increase to 3 times ULN**; or**
            - Hospitalization due to severe statin-related adverse event (e.g., rhabdomyolysis); **and**
- The individual meets **ONE** of the following criteria:
    - The individual has a current LDL-C ≥ 70 mg/dL; **or**
    - The individual has a current non-HDL-C ≥ 100 mg/dL; **or**
    - The individual meets the criteria for very high-risk (see table D: history of multiple major ASCVD events or one (1) major ASCVD event and multiple high-risk conditions) and meets one (1) of the following:
        - LDL-C ≥ 55 mg/dL; **or**
        - Non-HDL-C ≥ 85 mg/dL; **or**
    - The individual had a < 50% reduction in baseline LDL-C despite use with maximally tolerated statin therapy; **and**
- Individual has failure of proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor (e.g., alirocumab or evolocumab based upon FDA approval for age) for at least three (3) months**; and**
- Individual will use as adjunct to maximally tolerated statin therapy, unless the member is statin intolerant**; and**
- Initial authorization will be for a period of up to six (6) months.

Reauthorization Criteria

- Documentation of LDL-C reduction from baseline; **and**
- Reauthorization will be for a period of up to 12 months.

The use of inclisiran (Leqvio) not meeting the criteria as indicated in this policy is considered not medically necessary.

Procedure Codes

J1306

Hypercholesterolemia with Clinical Atherosclerotic Cardiovascular Disease (ASCVD)

Inclisiran (Leqvio) may be considered medically necessary for ASCVD when the following criteria are met:

- The individual is 18 years of age or older; **and**
- Must be prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist; **and**
- Individual has documented history of ASCVD as defined by **ONE** of the following**:**
    - Acute coronary syndrome**; or**
    - Coronary or other arterial revascularization**; or**
    - History of myocardial infarction**; or**
    - History of stroke**; or**
    - History of transient ischemic attack**; or**
    - Peripheral arterial disease presumed to be of atherosclerotic origin**; or**
    - Stable or unstable angina**; and**
- ~~Serum LDL-C greater than 70 mg/dL**; and**~~
- The individual meets **ONE** of the following criteria:
    - The individual has experienced therapeutic failure to a maximally tolerated statin; **or**
    - The individual is statin intolerant defined as one (1) of the following:
        - While receiving at least two (2) separate trials of different statins, the individual experienced **ONE** of the following:
            - Statin related rhabdomyolysis, which resolved upon discontinuation of the statins**; or**
            - Skeletal-related muscle symptoms, which resolved upon discontinuation of the statins; **or**
        - The individual experienced **ONE** of the following during any course of statin therapy:
            - Creatinine kinase (CK) increase to 10 times ULN**; or**
            - Liver function tests (LFTs) increase to 3 times ULN; **or**
            - Hospitalization due to severe statin-related adverse event (e.g., rhabdomyolysis)**; and**
- The individual meets **ONE** of the following criteria:
    - The individual has a current LDL-C ≥ 70 mg/dL; **or**
    - The individual has a current non-HDL-C ≥ 100 mg/dL; **or**
    - The individual meets the criteria for very high-risk (see table D: history of multiple major ASCVD events or one (1) major ASCVD event and multiple high-risk conditions) and meets one (1) of the following:
        - LDL-C ≥ 55 mg/dL; **or**
        - Non-HDL-C ≥ 85 mg/dL; **or**
    - The individual had a < 50% reduction in baseline LDL-C despite use with maximally tolerated statin therapy; **and**
- Individual has failure of proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor (e.g., alirocumab or evolocumab based upon FDA approval for age) for at least three (3) months; **and**
- The individual will use as adjunct to maximally tolerated statin therapy, unless the member is statin intolerant**; and**
- Initial authorization will be for a period of up to six (6) months.

Reauthorization Criteria

- Documentation of an LDL-C reduction from baseline; **and**
- Reauthorization will be for a period of up to 12 months.

The use of inclisiran (Leqvio) not meeting the criteria as indicated in this policy is considered not medically necessary.

Procedure Codes

J1306

Primary Hyperlipidemia , Not Associated with ASCVD, HeFH, or HoFH

Inclisiran (Leqvio) may be considered medically necessary for primary hyperlipidemia when the following criteria are met:

- The individual is 18 years of age or older; **and**
- Must be prescribed by or in consultation with a cardiologist, endocrinologist, or lipid specialist; **and**
- ~~The individual has serum LDL-C greater than or equal to 70 mg/dL; **and**~~
- ~~Individual has fasting triglyceride less than 400 mg/dL; **and**~~
- ~~The individual will use as adjunct to maximally tolerated statin therapy, unless the member is statin intolerant; **or**~~
- The individual has a baseline untreated LDL ≥ 190 mg/dL; **and**
- The individual meets **ONE** of the following criteria:
    - The individual has experienced therapeutic failure to a maximally tolerated statin; **or**
    - The individual is statin intolerant defined as one (1) of the following:
        - While receiving at least two (2) separate trials of different statins, the individual experienced **ONE** of the following:
            - Statin related rhabdomyolysis, which resolved upon discontinuation of the statins; **or**
            - Skeletal-related muscle symptoms, which resolved upon discontinuation of the statins; **or**
        - The individual experienced **ONE** of the following during any course of statin therapy:
            - Creatinine kinase (CK) increase to 10 times ULN; **or**
            - Liver function tests (LFTs) increase to 3 times ULN; **or**
            - Hospitalization due to severe statin-related adverse event (e.g., rhabdomyolysis); a**nd**
- The individual meets **ONE** of the following criteria:
    - The individual has a current LDL-C ≥ 70 mg/dL; **or**
    - The individual has a current non-HDL-C ≥ 100 mg/dL; **or**
    - The individual had a < 50% reduction in baseline LDL-C despite use with maximally tolerated statin therapy; **and**
- Individual has failure of proprotein convertase subtilisin kexin 9 (PCSK9) inhibitor (e.g., alirocumab or evolocumab based upon FDA approval for age) for at least three (3) months**; and**
- The individual will use as adjunct to maximally tolerated statin therapy, unless the member is statin intolerant**; and**
- Initial authorization will be for a period of up to six (6) months

Reauthorization Criteria

Continuation of therapy with inclisiran (Leqvio) may be considered medically necessary for when the following criteria are met:

- Provider attestation of positive clinical response (e.g. LDL-C reduction from baseline); **and**
- Reauthorization will be for a period of up to 12 months.

The use of inclisiran (Leqvio) not meeting the criteria as indicated in this policy is considered not medically necessary.

Procedure Codes

J1306

Quantity Level Limit

Diagnosis	Initiation Dose	Maintenance Dose
HeFH or ASCVD	Two (2) pre-filled syringes in the first three (3) months	One (1) pre-filled syringe every six (6) months

Procedure Codes

J1306

In addition to the above criteria, product specific dosage and/or frequency limits may apply in accordance with the U.S. Food and Drug Administration (FDA)-approved product prescribing information, national compendia, Centers for Medicare and Medicaid Services (CMS) and other peer reviewed resources or evidence-based guidelines. Highmark may deny, in full or in part, reimbursement for utilization that does not fall within the applicable dosage and/or frequency limits.

Diagnosis Codes

E78.011	E78.019	E78.5	E78.89	E78.9	I25.10	I25.110
I25.112	I25.118	I25.119	I25.810	I25.811	I25.812	

Removed E78.010

Place of Service: Outpatient

Inclisiran (Leqvio) is typically an outpatient procedure which is only eligible for coverage as an inpatient procedure in special circumstances, including, but not limited to, the presence of a co-morbid condition that would require monitoring in a more controlled environment such as the inpatient setting.

~~Experimental/Investigational service are not covered regardless of place of service~~

The policy position applies to all commercial lines of business

Operational Guidelines

Professional Claims

This policy is applied on a **post-payment** basis for Professional claims. **The services will pay on initial processing and are subject to retrospective review.**

Note the following **pre-payment** applications within the body of the bulletin:
The diagnosis codes are applied on a pre-payment basis.

Note: Inclisiran (Leqvio) is considered not medically necessary and, therefore, non-covered and applies to Professional claims.

Facility Claims

This policy is applied on a **post-payment** basis for Facility claims. **The services will pay on initial processing and are subject to retrospective review.**

Note the following **pre-payment** applications within the body of the bulletin:
The diagnosis codes are applied on a pre-payment basis.

Note: Inclisiran (Leqvio) is considered not medically necessary and, therefore, non-covered and applies to Facility claims.

Internal Sources

Clinical Policy Management Committee ~~November 12, 2024~~ December 9, 2025

Medical Director

Links

- Link to Provider Resource Center for the Medical Policy Update 03/2022 Criteria Established for Inclisiran (Leqvio)
- Link to References
- Link to Table Attachment(s)

This policy is designed to address medical guidelines that are appropriate for the majority of individuals with a particular disease, illness, or condition. Each person's unique clinical or other circumstances may warrant individual consideration, based on review of applicable medical records, as well as other regulatory, contractual and/or legal requirements.

Medical policies do not constitute medical advice, nor are they intended to govern the practice of medicine. They are intended to reflect Highmark's reimbursement and coverage guidelines. Coverage for services may vary for individual members, based on the terms of the benefit contract, and subject to the applicable laws of your state.

Discrimination is Against the Law
The Claims Administrator/Insurer complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. The Claims Administrator/Insurer does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex. The Claims Administrator/ Insurer:

- *Provides free aids and services to people with disabilities to communicate effectively with us, such as:*

    - *Qualified sign language interpreters*
    - *Written information in other formats (large print, audio, accessible electronic formats, other formats)*

- *Provides free language services to people whose primary language is not English, such as:*
    - *Qualified interpreters*
    - *Information written in other languages*

If you need these services, contact the Civil Rights Coordinator.

If you believe that the Claims Administrator/Insurer has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with: Civil Rights Coordinator, P.O. Box 22492, Pittsburgh, PA 15222, Phone: 1-866-286-8295, TTY: 711, Fax: 412-544-2475, email: CivilRightsCoordinator@highmarkhealth.org. You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

Insurance or benefit/claims administration may be provided by Highmark, Highmark Choice Company, Highmark Coverage Advantage, Highmark Health Insurance Company, First Priority Life Insurance Company, First Priority Health, Highmark Benefits Group, Highmark Select Resources, Highmark Senior Solutions Company or Highmark Senior Health Company, all of which are independent licensees of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield plans.

ATTENTION: If you speak English, language assistance services, free of charge, are available to you. Call the number on the back of your ID card (TTY: 711).

ATENCIÓN: Si usted habla español, servicios de asistencia lingüística, de forma gratuita, están disponibles para usted. Llame al número en la parte posterior de su tarjeta de identificación (TTY: 711).

请注意：如果您说中文，可向您提供免费语言协助服务。

请拨打您的身份证背面的号码（TTY：711）。

CHÚ Ý: Nếu quý vị nói tiếng Việt, chúng tôi cung cấp dịch vụ hỗ trợ ngôn ngữ miễn phí cho quý vị. Xin gọi số điện thoại ở mặt sau thẻ ID của quý vị (TTY: 711).

알림: 한국어를 사용하시는 분들을 위해 무료 통역이 제공됩니다. ID 카드 뒷면에 있는 번호로 전화하십시오 (TTY: 711).

ATENSYON: Kung nagsasalita ka ng Tagalog, may makukuha kang mga libreng serbisyong tulong sa wika. Tawagan ang numero sa likod ng iyong ID card (TTY: 711).

ВНИМАНИЕ: Если вы говорите по-русски, вы можете воспользоваться бесплатными услугами языковой поддержки. Позвоните по номеру, указанному на обороте вашей идентификационной карты (номер для текст-телефонных устройств (TTY): 711).

تنبيه: إذا كنت تتحدث اللغة العربية، فهناك خدمات المعاونة في اللغة المجانية متاحة لك. اتصل بالرقم الموجود خلف بطاقة هويتك (جهاز الاتصال لذوي صعوبات السمع والنطق: 711).

ATTENTION: Si c'est créole que vous connaissez, il y a un certain service de langues qui est gratis et disponible pour vous-même. Composez le numéro qui est au dos de votre carte d'identité. (TTY: 711).

ATTENTION: Si vous parlez français, les services d'assistance linguistique, gratuitement, sont à votre disposition. Appelez le numéro au dos de votre carte d'identité (TTY: 711).

UWAGA: Dla osób mówiących po polsku dostępna jest bezpłatna pomoc językowa. Zadzwoń pod numer podany na odwrocie karty ubezpieczenia zdrowotnego (TTY: 711).

ATENÇÃO: Se a sua língua é o português, temos atendimento gratuito para você no seu idioma. Ligue para o número no verso da sua identidade (TTY: 711).

ATTENZIONE: se parla italiano, per lei sono disponibili servizi di assistenza linguistica a titolo gratuito. Contatti il numero riportato sul retro della sua carta d'identità (TTY: 711).

ACHTUNG: Wenn Sie Deutsch sprechen, steht Ihnen unsere fremdsprachliche Unterstützung kostenlos zur Verfügung. Rufen Sie dazu die auf der Rückseite Ihres Versicherungsausweises (TTY: 711) aufgeführte Nummer an.

注：日本語が母国語の方は言語アシスタンス・サービスを無料でご利用いただけます。ID カードの裏に明記されている番号に電話をおかけください (TTY: 711)。

توجه : اگر شما به زبان **فارسی** صحبت می کنید، خدمات کمک زبان، به صورت رایگان، در دسترس شماست. با شماره واقع در پشت کارت شناسایی خود (TTY: 711) تماس بگیرید.