BlueCross BlueShield Federal Employee Program

PRALUENT
(alirocumab)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Praluent (alirocumab) is a human monoclonal antibody that binds to proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 binds to the low-density lipoprotein cholesterol (LDL-C) receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. By blocking PCSK9's ability to work, more receptors are available to clear LDL cholesterol from the blood, thereby lowering LDL cholesterol levels (1).

Regulatory Status

FDA-approved indications: Praluent is a PCSK9 (Proprotein Convertase Subtilisin Kexin Type 9) inhibitor indicated: (1)

- To reduce the risk of myocardial infarction, stroke, and unstable angina requiring hospitalization in adults with established cardiovascular disease.
- As adjunct to diet, alone or in combination with other low-density lipoprotein cholesterol (LDL-C)-lowering therapies, in adults with primary hyperlipidemia, including heterozygous familial hypercholesterolemia (HeFH), to reduce LDL-C.
  As an adjunct to other LDL-C-lowering therapies in adult patients with homozygous familial hypercholesterolemia (HoFH) to reduce LDL-C.
- As an adjunct to diet and other LDL-C-lowering therapies in pediatric patients aged 8 years and older with HeFH to reduce LDL-C.

Physicians often measure creatine kinase (CK) in patients about to begin statins or already on statins. CK is an enzyme that leaks out of damaged muscle. Many physicians will not start or continue statins to lower LDL-C in asymptomatic patients with high CK because of concern regarding possible statin-induced myositis-rhabdomyolysis. High pretreatment CK, predominantly 3 to 5 times the upper normal limit (UNL), should not be an impediment to start or continue statins to lower LDL-C (2).

Spectrum of statin-associated muscle adverse events: (3)

1. Myalgia: unexplained muscle discomfort often described as ‘‘flu-like’’ symptoms with normal CK level. The spectrum of myalgia complaints includes:
    - Muscle aches
    - Muscle soreness

- Muscle stiffness
- Muscle tenderness
- Muscle cramps with or shortly after exercise (not nocturnal cramping)

2. Myopathy: muscle weakness (not attributed to pain and not necessarily associated with elevated CK)
3. Myositis: muscle inflammation
4. Myonecrosis: muscle enzyme elevations or hyperCKemia
    - Mild > 3-fold greater than baseline untreated CK levels or normative upper limit that are adjusted for age, race, and sex
    - Moderate ≥ 10-fold greater than untreated baseline CK levels or normative upper limit that are adjusted for age, race, and sex
    - Severe ≥ 50-fold above baseline CK levels or normative upper limit that are adjusted for age, race, and sex
5. Myonecrosis with myoglobinuria or acute renal failure (increase in serum creatinine ≥ 0.5 mg/dL (clinical rhabdomyolysis)

Statin intolerance is widely defined as not being able to tolerate a registered statin dose, due to side effects such as myalgia-myopathy, myositis, or elevation of serum liver enzyme activities. Statin intolerance has been also described as a clinical syndrome with the following characteristics: (4)

1. The inability to tolerate at least 2 different statins – one statin at the lowest starting average daily dose and the other statin at any dose
2. Intolerance associated with confirmed, intolerable statin-related adverse effect(s) or significant biomarker abnormalities
3. Symptom or biomarker changes resolution or significant improvement upon dose decrease or discontinuation
4. Symptoms or biomarker changes not attributable to established predispositions such as drug-drug interactions and recognized conditions increasing the risk of statin intolerance

The ACC Statin Intolerance Tool guides clinicians through the process of managing and treating patients who report muscle symptoms while on statin therapy. The tool is available for free online at *Tools.ACC.org/StatinIntolerance* or for download in the App stores. Search “ACC Statin Intolerance”.

The safety and efficacy of Praluent in pediatric patients with HeFH less than 8 years of age have not been established. The safety and efficacy of Praluent in pediatric patients less than 18 years of age with other types of hyperlipidemia have not been established (1).

Summary

Praluent (alirocumab) is a human monoclonal antibody that binds to proprotein convertase subtilisin kexin type 9 (PCSK9). PCSK9 binds to the low-density lipoprotein cholesterol (LDL-C) receptors (LDLR) on the surface of hepatocytes to promote LDLR degradation within the liver. By blocking PCSK9's ability to work, more receptors are available to clear LDL cholesterol from the blood, thereby lowering LDL cholesterol levels. The safety and efficacy of Praluent in pediatric patients with HeFH less than 8 years of age have not been established. The safety and efficacy of Praluent in pediatric patients less than 18 years of age with other types of hyperlipidemia have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Praluent while maintaining optimal therapeutic outcomes.

References

1. Praluent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; March 2024.
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3. Rosenson R, Baker S, et al. An assessment by the Statin Muscle Safety Task Force: 2014 update. Jrnl Clin Lipid, 2014; 8, S58–S71.
4. Banach M, Rizzo M, et al. Statin intolerance – an attempt at a unified definition. Position paper from an International Lipid Expert Panel. Arch Med Sci 2015; 11, 1: 1–23.