omaveloxolone (Skyclarys™)

Policy # 00853
Original Effective Date: 10/09/2023
Current Effective Date: 10/09/2023

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 May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider omaveloxolone (Skyclarys™)‡ for the treatment of Friedreich's ataxia to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for omaveloxolone (Skyclarys) when the below patient selection criteria are met:

- Patient has a diagnosis of Friedreich's Ataxia; AND
- Patient is greater than or equal to 16 years of age; AND
- Diagnosis of Friedreich's Ataxia has been confirmed by genetic testing showing biallelic pathogenic variants in the frataxin gene (*FXN*); AND
- Patient is ambulatory; AND
  *(Note: This specific patient selection criterion is an additional company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient does not have severe hepatic impairment (i.e., Child-Pugh class C).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of omaveloxolone (Skyclarys) for non-ambulatory patients to be **not medically necessary.****

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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 omaveloxolone (Skyclarys) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Skyclarys is the first pharmacological agent to be approved for the treatment of Friedreich's Ataxia (FA), a rare genetic condition caused by a mutation in the frataxin (*FXN*) gene. Skyclarys is thought to work by impacting the cellular response to oxidative stress by activating the nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway. It should be dosed as 150 mg (3 capsules) taken orally once daily on an empty stomach at least 1 hour before eating.

FA is an ultra-rare, progressive, autosomal recessive genetic neurodegenerative disorder. It primarily affects the function of the cerebellum, spinal cord, and peripheral nervous system. FA is caused by mutations in the *FXN* gene which encodes the mitochondrial protein frataxin. Mutations in *FXN* lead to adverse effects on mitochondrial iron metabolism that lead to iron accumulation and oxidative damage, causing cellular dysfunction. FA affects approximately 1 in 29,000 individuals with Caucasian ancestry and 1 in every 50,000 people in the United States. Patients with FA primarily have ataxia, or impaired muscle coordination, which worsens over time. Patients also experience loss of sensation and reflexes, speech and swallowing difficulties, fatigue, scoliosis, and foot deformities (pes cavus [abnormal elevation of the arch of the foot that does not flatten with weightbearing; reported in 50-70% of patients with FA]). They are also more likely to develop insulin-dependent diabetes mellitus and hypertrophic cardiomyopathy and arrhythmias. The mean life expectancy of a patient with FA is around 40 years, but patients with less severe features may live into their 60s and beyond.

Diagnosis of FA requires clinical evaluation for balance difficulty, loss of join sensation, absence of reflexes, and signs of neurological problems. It must be confirmed by genetic testing demonstrating a mutation in the *FXN* gene. Prior to the approval of Skyclarys, treatment involved supportive

measures with mobility aids such as prostheses, canes, walkers, and wheelchairs as well as treatment of associated diabetes and heart disease.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Skyclarys was approved in February 2023 for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.

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 Skyclarys was evaluated in a 48-week, randomized, double-blind, placebo-controlled study in patients 16 to 40 years of age with Friedreich's Ataxia. A total of 103 patients were randomized 1:1 to receive Skyclarys 150 mg once daily (n=51) or placebo (n=52). Enrolled patients had to have a stable modified Friedreich's Ataxia Rating Scale (mFARS) score between 20 and 80, be able to complete maximal exercise testing, and have a left ventricular ejection fraction of at least 40%. This study included patients with or without pes cavus, defined as having a loss of lateral support and determined if light from a flashlight could be seen under the patient's arch when barefoot and weight bearing.

The primary analysis was the change from baseline in the mFARS score compared to placebo at Week 48 in the Full Analysis population of patients without pes cavus (n=82). The mFARS is a clinical assessment tool to assess patient function, which consists of 4 domains to evaluate bulbar function, upper limb coordination, lower limb coordination, and upright stability. The mFARS has a maximum score of 99 with a lower score indicating lesser physical impairment. In the population without pes cavus, treatment with Skyclarys resulted in statistically significantly lower mFARS scores relative to placebo at Week 48. The least squares mean change from baseline in the Skyclarys group was -1.56 and it was 0.85 in the placebo group (p=0.0138). The all randomized population

group that included patients with pes cavus demonstrated similar results with a nominally significant least squares mean difference between treatment groups of -1.94 (95% CI: -3.71, -0.16, p=0.0331).

References

1. Skyclarys [package insert]. Reata Pharmaceuticals, Inc. Plano, TX. Updated May 2023.
2. Skyclarys for the Treatment of Friedreich's Ataxia. IPD Analytics. Updated March 2023.

Policy History

Original Effective Date: 10/09/2023
Current Effective Date: 10/09/2023
09/07/2023 Medical Policy Committee review
09/13/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 09/2024

*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.

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**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.