Effective Date 10/15/2023
Next Review Date… 10/15/2024
Coverage Policy Number IP0566

Omaveloxolone

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Related Coverage Resources

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for omaveloxolone (**Skyclarys** ®).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Omaveloxolone (Skyclarys®) is considered medically necessary when the following are met:

Friedreich's Ataxia. Individual meets **ALL** of the following criteria:
A. Age 16 years or older
B. Documented genetic testing confirming biallelic pathogenic variants in the *FXN* gene consistent with a diagnosis of Friedreich's Ataxia
C. Documentation of a score of 20 to 80 on the modified Friedreich's Ataxia Rating Scale
D. Prescriber attests to **BOTH** of the following:

i. Individual is ambulatory
ii. Individual does not have pes cavus

E. Documentation of **ALL** the following in the last year:
i. B-type natriuretic peptide (BNP) less than or equal to 200 pg/mL
ii. Left ventricular ejection fraction greater than or equal to 40%
iii. Hemoglobin A_{1c} (HbA_{1c}) less than or equal to 11%

F. Medication is prescribed by, or in consultation with, a neurologist or a physician who specializes in ataxias and/or neuromuscular disorders

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Continuation of omaveloxolone is considered medically necessary for **Friedreich's Ataxia** when **ALL** of the following criteria are met:

1. Above medical necessity criteria have been met prior to the start of omaveloxolone
2. Documentation of beneficial response as demonstrated by a slowed progression on the modified Friedreich's Ataxia Rating Scale
3. Medication continues to be prescribed by, or in consultation with, a neurologist or a physician who specializes in ataxias and/or neuromuscular disorders

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

1. **Metastatic Melanoma.** Skyclarys has also been evaluated for the treatment of metastatic melanoma (in combination with Opdivo® [nivolumab intravenous infusion] or Yervoy® [ipilimumab intravenous infusion]).[9] Results have not been published. More data are needed.

2. **Mitochondrial Myopathy.** Skyclarys has also been evaluated for the treatment of mitochondrial myopathies. In one Phase II study, following 12 weeks of therapy, no differences in peak workload or 6-minute walk test were observed with Skyclarys vs. placebo.[10] More data are needed to evaluate the efficacy and safety Skyclarys for mitochondrial myopathy.

Background

OVERVIEW

Skyclarys, a nuclear factor (erythroid-derived 2)-like 2 (Nrf2) activator, is indicated for the treatment of Friedreich's ataxia in patients ≥ 16 years of age.[1]

Disease Overview
Friedreich's ataxia is an autosomal recessive, progressive, neurodegenerative disorder.[2-6] In the setting of clinical suspicion due to symptoms (e.g., ataxia, cardiomyopathy, scoliosis, and/or diabetes), genetic testing is the cornerstone of confirming a diagnosis of Friedreich's ataxia. A trinucleotide repeat expansion assay to detect biallelic mutations is used.

Clinical Efficacy
In the pivotal study of Skyclarys, patients were 16 to 40 years of age with genetically confirmed Friedreich's ataxia.[1,7] They were required to have a baseline modified Friedreich's Ataxia Rating Scale (mFARS) between 20 and 80. Patients with pes cavus were allowed to enroll in the study, but their participation was limited to 20% of patients and the primary efficacy analysis did not include patients with pes cavus. Patients with a B-type natriuretic peptide (BNP) > 200 pg/mL or a left ventricular ejection fraction < 40% were also excluded from the study. Uncontrolled diabetes mellitus, defined in a non-pivotal study as a hemoglobin A1c (HbA_{1c}) > 11%, was also part of the exclusion criteria for the pivotal trial.[7,8] The vast majority of patients enrolled in the pivotal trial were ambulatory (93%). The primary efficacy was measured using the mFARS.

Guidelines
Available consensus guidelines on Friedreich's ataxia (2022) identify Skyclarys as a potential investigative agent, but do not make any specific recommendations regarding its use.[6] According to guidelines, patients with Friedreich's ataxia should have an EKG and an echocardiogram at diagnosis and then at least annually. Patients should also be evaluated annually for diabetes mellitus. There is no cure for Friedreich's ataxia; guidelines make extensive recommendations regarding management of the symptoms and complications related to the disease, including diabetes mellitus and cardiomyopathy.

Components of the Modified Friedreich's Ataxia Rating Scale (mFARS) [16]
The mFARS is a quantifiable measurement tool that assesses four areas of neurological function: bulbar function (score 0 to 11), upper limb coordination (score 0 to 36), lower limb coordination (score 0 to 16), and upright stability (score 0 to 36). Scores range from 0 to 99 with lower scores indicative of better neurological function (i.e., lesser physical impairment).

Area of Neurologic Function (Maximum Score)	Individual Component (Maximum Score)
Bulbar function (11)	A1 Facial atrophy (3)
	A2 Tongue atrophy (3)
	A3 Cough (2)
	A4 Speech (3)
Upper limb coordination (36)	B1 Finger-finger (3+3)†
	B2 Nose-finger (4+4)†
	B3 Dysmetria (4+4)†
	B4 Rapid movements (3+3)†
	B5 Finger taps (4+4)†
Lower limb coordination (16)	C1 Heel-shin slide (4+4)
	C2 Heel-shin tap (4+4)
Upright stability (36)	E1 Sitting position (4)
	E2A Stance, feet apart (4)
	E2B With eyes closed (4)
	E3AStance, feet together (4)
	E3B With eyes closed (4)
	E4 Tandem stance (4)
	E5 Stance, dominant foot (4)
	E6 Tandem walk (3)
	E7 Gait (5)

mFARS – Modified Friedreich's Ataxia Rating Scale; † Items are evaluated separately on lateral sides.

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Supplemental References

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