

PRIOR AUTHORIZATION POLICY

POLICY: Neurology – Skyclarys Prior Authorization Policy

- Skyclarys® (omaveloxolone capsules – Reata/Biogen)

REVIEW DATE: 05/08/2024

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 electrocardiogram (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.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Skyclarys. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Skyclarys as well as the monitoring required for adverse events and long-term efficacy, approval requires Skyclarys to be prescribed by or in consultation with a physician who specializes in the condition being treated. All reviews will be forwarded to the Medical Director for evaluation.

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Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information. Subsequent coverage reviews for a patient who has previously met the documentation requirements and related criteria in the *Neurology – Skyclarys Prior Authorization Policy* through the Coverage Review Department, and who is requesting reauthorization, the criteria utilized do NOT require re-submission of documentation for reauthorization, except for the criterion requiring documentation of the trinucleotide repeat expansion assay genetic test confirming the diagnosis of Friedreich’s ataxia.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Skyclarys is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Friedreich’s Ataxia.** Approve for 1 year if the patient meets ONE of the following (A or B):
 - A) **Initial Therapy.** Approve if the patient meets ALL of the following (i, ii, iii, iv, v, vi, and vii):
 - i. Patient is ≥ 16 years of age; AND
 - ii. Patient has had genetic testing confirming biallelic pathogenic variants in the frataxin (FXN) gene consistent with a diagnosis of Friedreich’s ataxia **[documentation required]**; AND
 - iii. Patient has had ALL of the following in the last year (a, b, and c):
 - a) Patient has a B-type natriuretic peptide (BNP) ≤ 200 pg/mL **[documentation required]**; AND
 - b) Patient has a left ventricular ejection fraction $\geq 40\%$ **[documentation required]**; AND
 - c) Patient has a hemoglobin A_{1c} (HbA_{1c}) $\leq 11\%$ **[documentation required]**; AND
 - iv. Patient has been assessed using the modified Friedreich’s Ataxia Rating Scale and has a score ≥ 20 , but ≤ 80 **[documentation required]**; AND
 - v. Patient is ambulatory; AND
 - vi. Patient does not have pes cavus; AND
 - vii. The medication is prescribed by or in consultation with a neurologist or a physician who specializes in ataxias and/or neuromuscular disorders.
 - B) **Patient is Currently Receiving Skyclarys.** Approve if the patient meets ALL of the following (i, ii, iii, iv and v):
 - i. Patient is ≥ 16 years of age; AND
 - ii. Patient has had genetic testing confirming biallelic pathogenic variants in the frataxin (FXN) gene consistent with a diagnosis of Friedreich’s ataxia **[documentation required]**; AND
 - iii. Patient is ambulatory; AND
 - iv. According to the prescriber, the patient continues to benefit from therapy, as demonstrated by a slowed progression on the modified Friedreich’s Ataxia Rating Scale; AND
 - v. The medication is prescribed by or in consultation with a neurologist, or a physician who specializes in ataxias and/or neuromuscular disorders.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Skyclarys is not recommended in the following situations:

- 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 of Skyclarys for mitochondrial myopathy.
- 3.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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