PRIOR AUTHORIZATION POLICY

POLICY: Neurology – Skyclarys Prior Authorization Policy
- Skyclarys® (omaveloxolone capsules – Reata/Biogen)

REVIEW DATE: 05/14/2025

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

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.

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.

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is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 ≥ 40% **[documentation required]**; AND
         c) Patient has a hemoglobin A_{1c} (HbA_{1c}) ≤ 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;
      OR
   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 COVERED

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is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

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.

REFERENCES

1. Skyclarys® capsules [prescribing information]. Cambridge, MA: Reata/Biogen; December 2024.
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4. Lynch DR, Schadt K, Kichula E, et al. Friedreich ataxia: multidisciplinary clinical care. *J Multidiscip Healthc*. 2021;14:1645-1658.
5. Patel M, Isaacs CJ, Seyer L, et al. Progression of Friedreich ataxia: quantitative characterization of 5 years. *Ann Clin Trans Neurol*. 2016;3(9)684-694.
6. Corben LA, Collins V, Milne S, et al. Clinical management guidelines for Friedreich ataxia: best practice in rare diseases. Clinical Management Guidelines Writing Group. *Orphanet J Rare Dis*. 2022;17(1):415. Available at: www.frdaguidelines.org.
7. Lynch DR, Chin MP, Delatycki MB, et al. Safety and efficacy of omaveloxolone in Friedreich ataxia (MOXIe study). *Ann Neurol*. 2021;89(2):212-225.
8. Lynch DR, Farmer J, Hauser L, et al. Safety, pharmacodynamics, and potential benefit of omaveloxolone in Friedreich ataxia. *Ann Clin Trans Neurol*. 2018;6(1):15-26.
9. US National Institutes of Health. In: ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). 2000- [cited 2025 May 8]. Available from: https://clinicaltrials.gov/. Search term: omaveloxolone.
10. Madsen KL, Buch AE, Cohen BH, et al. Safety and efficacy of omaveloxolone in patients with mitochondrial myopathy: MOTOR trial. *Neurology*. 2020;94(7):e687-e698.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	04/19/2023
Selected Revision	**Friedreich's Ataxia (Initial Therapy and Patients Currently Receiving Skyclarys):** Criteria were updated to require the patient to have had genetic testing confirming biallelic pathogenic variants in the frataxin (FX) gene consistent with a diagnosis of Friedreich's ataxia. Previously, criteria required the patient to have had a trinucleotide repeat expansion assay genetic test confirming the diagnosis of Friedreich's ataxia.	05/24/2023
Annual Revision	No criteria changes.	05/08/2024
Annual Revision	No criteria changes.	05/14/2025