MEDICAL MUTUAL®

Drug Policy

Policy:	Skyclarys (omaveloxolone)	Annual Review Date: 06/20/2024 Last Revised Date: 06/20/2024

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] 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.

POLICY STATEMENT

This policy involves the use of Skyclarys. Prior authorization is recommended for pharmacy benefit coverage of Skyclarys. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

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, initial approval requires Skyclarys be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

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

1. **Friedreich's Ataxia.** Approve if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve if the patient meets ALL the following criteria (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 within 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.

B) Patient is Currently Receiving Skyclarys. Approve if the patient meets ALL the following criteria (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.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 1 year
B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Skyclarys has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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.
3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

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The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational, or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Skyclarys™ capsules [prescribing information]. Plano, TX: Reata; February 2023.
2. Cook A, Giunti P. Friedreich's ataxia: clinical features, pathogenesis and management. *Br Med Bull*. 2017;124(1):19-30.
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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.
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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.
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