Effective Date: 08/30/2023
Current Effective Date: 08/30/2023
Last P&T Approval/Version: 07/26/2023
Next Review Due By: 07/2024
Policy Number: C25422-A

Skyclarys (omaveloxolone)

PRODUCTS AFFECTED

Skyclarys (omaveloxolone)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review.

A. FRIEDREICH'S ATAXIA:
   1. Documentation of diagnosis of Friedreich's ataxia
      AND
   2. Documentation of genetic testing for the triplet repeat expansions in the first intron of the frataxin (FXN) gene that cause Friedreich ataxia [DOCUMENTATION REQUIRED]
      AND

3. Prescriber attests to obtaining ALT, AST, bilirubin, BNP, and lipid parameters prior to initiating Skyclarys (omaveloxolone) and will continue to do so during treatment as clinically appropriate.
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Skyclarys (omaveloxolone) include Severe (Child-Pugh Class C) liver impairment, and concomitant use with Strong or Moderate CYP3A4 inducer]
   AND
5. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate of therapy at renewal [DOCUMENTATION REQUIRED]

CONTINUATION OF THERAPY:

A. ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms [DOCUMENTATION REQUIRED]

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a neurologist experienced in the management of Friedreich's ataxia [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
16 years of age and older

QUANTITY: 150 mg taken orally once daily; maximum of 90 capsules/30 days

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:

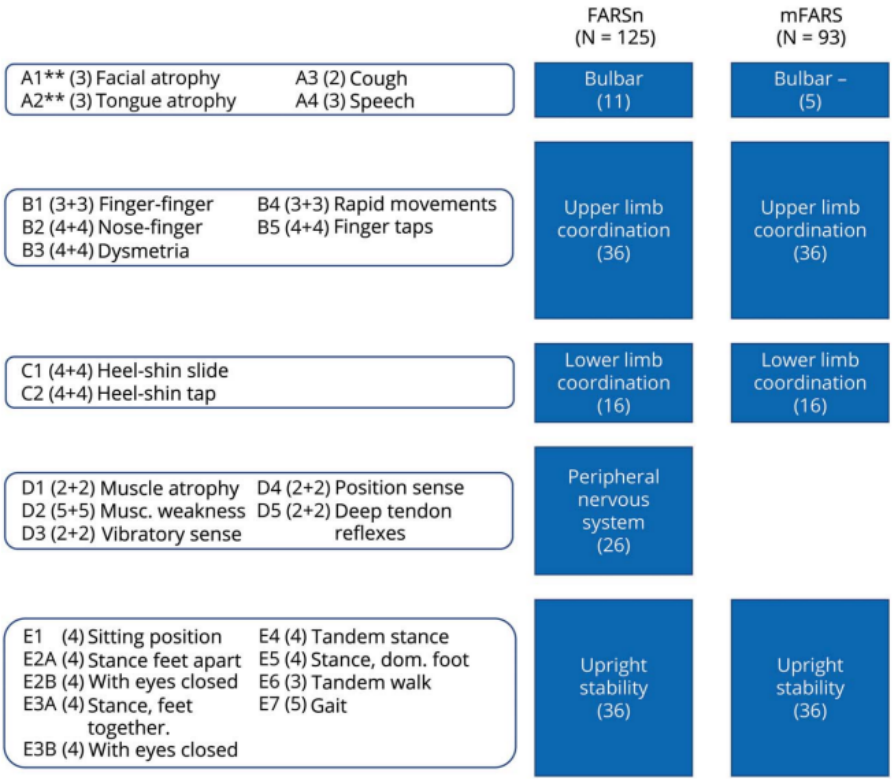
FDA-APPROVED USES: Skyclarys (omaveloxolone) indicated for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older

COMPENDIAL APPROVED OFF-LABELED USES:
N/A

APPENDIX

APPENDIX:

Rummey C, Corben LA, Delatycki MB, Subramony SH, Bushara K et al. Psychometric properties of the Friedreich Ataxia Rating Scale. Neurology Genetics 2019; 5:e371



Maximum score/subscale/item scores are shown in brackets. Items in subscales B, C, and D are conducted separately on lateral sides; ** items A1 and A2 are excluded in the mFARS examination. FARS = Friedreich Ataxia Rating Scale; mFARS = modified FARS.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Friedreich's ataxia (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 frataxin (FXN) gene, which encodes the mitochondrial protein frataxin. Frataxin is highly expressed in cardiomyocytes and in dorsal spinal column neurons. Mutations in FXN lead to impaired transcription and reduced frataxin expression (i.e. frataxin deficiency), resulting in adverse effects on mitochondrial iron metabolism that lead to iron accumulation and oxidative damage, causing cellular dysfunction.

The diagnosis of Friedreich ataxia is based upon clinical findings but should be confirmed by genetic testing. Neuroimaging of the brain and spinal cord with MRI is recommended for all patients presenting with ataxia to exclude other causes (eg, tumor or other structural lesions, inflammation, infarction, hemorrhage) and to evaluate for cerebellar atrophy, which may suggest an alternative diagnosis. Genetic testing for the triplet repeat expansions in the first intron of the frataxin (FXN) gene that cause Friedreich

ataxia should be performed in all patients with progressive cerebellar ataxia and autosomal recessive inheritance. In the case of sporadic ataxia, genetic workup should be performed if the clinical picture is consistent with a chronic and progressive ataxia and workup for other acquired ataxias is negative. Among patients with typical symptoms of Friedreich ataxia and normal vitamin E levels, the proportion who do not have a GAA expansion in either allele of the FXN gene is <1 percent

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 (Study 1; NCT02255435).
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%. In Study 1, 53% of enrolled patients were male, 97% were White, and the mean age was 24 years at study entry. Patients with or without pes cavus were included in Study 1. Pes cavus was defined as having a loss of lateral support and was determined if light from a flashlight could be seen under the patient's arch when barefoot and weight bearing.
The prespecified 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 on the mFARS signifying lesser physical impairment.

Findings showed that treatment with omaveloxolone met the prespecified primary analysis achieving statistically significantly lower mFARS scores (modified Friedreich's Ataxia Rating Scale), or less impairment, among patients without severe pes cavus at week 48 compared with placebo (placebo-adjusted difference, -2.41 [95% CI, -4.32, -0.51]; P =.0138).

Note that Skyclarys did not demonstrate significant improvements over placebo in secondary outcome measures analyzed in MOXIe Part 2, such as other neurologic measures, patient and clinician improvement assessments, and activities of daily living. These are areas, along with Skyclarys' impact on quality of life in patients with FA, that need further research and insight.
The most common adverse reactions (incidence greater than or equal to 20% and greater than placebo) are elevated liver enzymes (AST/ALT), headache, nausea, abdominal pain, fatigue, diarrhea, and musculoskeletal pain

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
None

OTHER SPECIAL CONSIDERATIONS:
Skyclarys capsules should be administered on an empty stomach, as least 1 hour before eating. The capsules should be swallowed whole. Capsules should not be opened, crushed or chewed.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
50 mg Capsules

REFERENCES

1. Skyclarys (omaveloxolone) [prescribing information]. Plano, TX: Reata Pharmaceuticals Inc; February 2023.
2. Lynch DR, et al. Safety, pharmacodynamics, and potential benefit of omaveloxolone in Friedreich ataxia. Ann Clin Transl Neurol. 2018;6(1):15–26. doi:10.1002/acn3.660
3. Lynch DR, et al. Safety and efficacy of omaveloxolone in Friedreich ataxia (MOXIe Study). Ann Neurol. 2021;89(2):212–225. doi:10.1002/ana.25934 Muscular Dystrophy Association. Friedreich's ataxia (FA). Accessed March 1, 2023. https://www.mda.org/disease/friedreichs-ataxia
4. Patel M, Isaacs CJ, Seyer L, et al. Progression of Friedreich ataxia: quantitative characterization over 5 years. Ann Clin Transl Neurol. 2016;3(9):684–694. doi:10.1002/acn3.332
5. Polek B, et al. Burden of Friedreich's ataxia to the patients and healthcare systems in the United States and Canada. Front Pharmacol. 2013;4:66. https://www.frontiersin.org/articles/10.3389/fphar.2013.00066/full
6. Rummey C, et al. Psychometric properties of the Friedreich Ataxia Rating Scale. Neurol Genet. 2019;5(6):371. doi:10.1212/NXG.0000000000000371
7. Bidichandani SI, Delatycki MB. Friedreich ataxia. GeneReviews. www.ncbi.nlm.nih.gov/books/NBK1281

SUMMARY OF REVIEW/REVISIONS	DATE
New Criteria	Q3 2023