Pharmacy Policy Bulletin: J-1284 Skyclarys (omaveloxolone) – Commercial and Healthcare Reform	
Number: J-1284	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1284-003	**Original Date:** 04/05/2023
Effective Date: 04/25/2025	**Review Date:** 04/09/2025

Drugs Product(s):	• Skyclarys (omaveloxolone)
FDA-Approved Indication(s):	• Treatment of Friedreich's ataxia (FA) in adults and adolescents aged 16 years and older

Background:	• Skyclarys (omaveloxolone) is an activator of the Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathway, which is suppressed in patients with FA and involved in cellular response to oxidative stress. The exact mechanism in which Skyclarys exerts its therapeutic effect in patients with FA is unknown. By activating the Nrf2 pathway, it may reduce inflammatory response and improve mitochondrial and neurological function. • FA is a rare, inherited, neurodegenerative disease. It damages the spinal cord, peripheral nerves, and the cerebellum portion of the brain. FA is caused by a mutation in both copies of the patient's *FXN* gene, which encodes instructions for production of the protein frataxin. Without a normal level of frataxin, certain cells in the body (e.g., nerve, spinal cord, brain, and heart muscle) produce energy less effectively and undergo oxidative stress. • FA is the most common form of hereditary ataxia in the United States (US), affecting approximately one in every 50,000 people. FA tends to develop in children and teenagers and gradually worsens over time. • Neurological symptoms of FA may include ataxia, impaired sensory functions, loss of normal reflexes, dysarthria, spasticity, scoliosis, difficulty swallowing, hearing and vision loss, or fatigue. Cardiovascular symptoms of FA include hypertrophic cardiomyopathy which may present as arrhythmias, heart failure, or intolerance of cardiovascular stress. Most patients with FA are confined to a wheelchair within 10 to 20 years after the appearance of the first symptoms and may become completely incapacitated in later disease stages. FA can shorten life expectancy, and heart disease is the most common cause of death. • Prescribing Considerations:

	○ For patients with mild hepatic impairment (Child-Pugh Class A), no dosage adjustment is recommended. For patients with moderate hepatic impairment (Child-Pugh Class B), the recommended dosage of Skyclarys is 100 mg once daily. If adverse reactions emerge, reduce the dosage to 50 mg once daily. Avoid use in patients with severe hepatic impairment (Child-Pugh Class C). ○ Monitor ALT, AST, and total bilirubin prior to initiation, every month for the first 3 months of treatment, and periodically thereafter. Monitor patients for signs and symptoms of fluid overload. Cholesterol should be monitored at Skyclarys initiation and periodically during treatment. ○ Monitor for drug interactions with moderate or strong cytochrome P450 3A4 (CYP3A4) inhibitors or inducers.

Approval Criteria

I. Initial Authorization
When a benefit, coverage of Skyclarys may be approved when all of the following criteria are met **(A., B., and C.)**:
A. The member is 16 years of age or older.
B. Skyclarys is prescribed by or in consultation with a neurologist or a provider who specializes in the treatment of FA.
C. The member has a diagnosis of Friedreich's ataxia (FA) (ICD-10: G11.11), confirmed by genetic testing (i.e., *FXN* gene mutation).

II. Reauthorization
When a benefit, reauthorization of Skyclarys may be approved when the following criterion is met **(A.)**:
A. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Skyclarys [package insert]. Plano, TX: Reata Pharmaceuticals, Inc.; December 2024.
2. Friedreich's ataxia. Friedreich's Ataxia | Johns Hopkins Medicine. Available at: https://www.hopkinsmedicine.org/health/conditions-and-diseases/friedreich-ataxia. Accessed February 17, 2025.

3. Friedreich ataxia. National Institute of Neurological Disorders and Stroke. Available at: https://www.ninds.nih.gov/health-information/disorders/friedreich-ataxia. Accessed February 17, 2025.
4. Center for Drug Evaluation and Research. Notable approval. U.S. Food and Drug Administration. Available at: https://www.fda.gov/drugs/news-events-human-drugs/fda-approves-first-treatment-friedreichs-ataxia. Accessed February 17, 2025.
5. Payne RM. The heart in Friedreich's ataxia: Basic findings and clinical implications. *Progress in Pediatric Cardiology*. 2011;31(2):103-109.
6. Corben LA, Collins V, Milne S, et al. Clinical management guidelines for Friedreich ataxia: Best practice in rare diseases - orphanet journal of rare diseases. BioMed Central. Available at: https://ojrd.biomedcentral.com/articles/10.1186/s13023-022-02568-3. Accessed February 17, 2025.