The First and Only FDA-Approved Treatment for Friedreich Ataxia (FA) in Patients 16 Years and Older[1]

DOSING AND ADMINISTRATION

SKYCLARYS® (omaveloxolone) 50 mg capsules

Jacob, age 30
Youth mentor
Taking SKYCLARYS since 2023

Patients featured are paid spokespersons for Biogen.

INDICATION

- SKYCLARYS® (omaveloxolone) is indicated for the treatment of Friedreich ataxia in adults and adolescents aged 16 years and older

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Elevation of Aminotransferases

- Treatment with SKYCLARYS can cause an elevation in hepatic transaminases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]). The incidence of elevations of ALT or AST above 5 times and 3 times the upper limit of normal (ULN) was 16% and 31%, respectively, in patients treated with SKYCLARYS. There were no cases of concomitant elevation of transaminases and total bilirubin observed. Maximum increases in ALT and AST occurred within 12 weeks after starting SKYCLARYS. Increases in serum aminotransferases were generally asymptomatic and reversible following discontinuation of SKYCLARYS

Please see additional Important Safety Information throughout and full Prescribing Information.

ONCE-DAILY ORAL DOSING

SKYCLARYS® (omaveloxolone) 50 mg capsules

SKYCLARYS is a once-daily oral prescription medicine indicated for the treatment of Friedreich ataxia in adults and adolescents aged 16 years and older[1]:

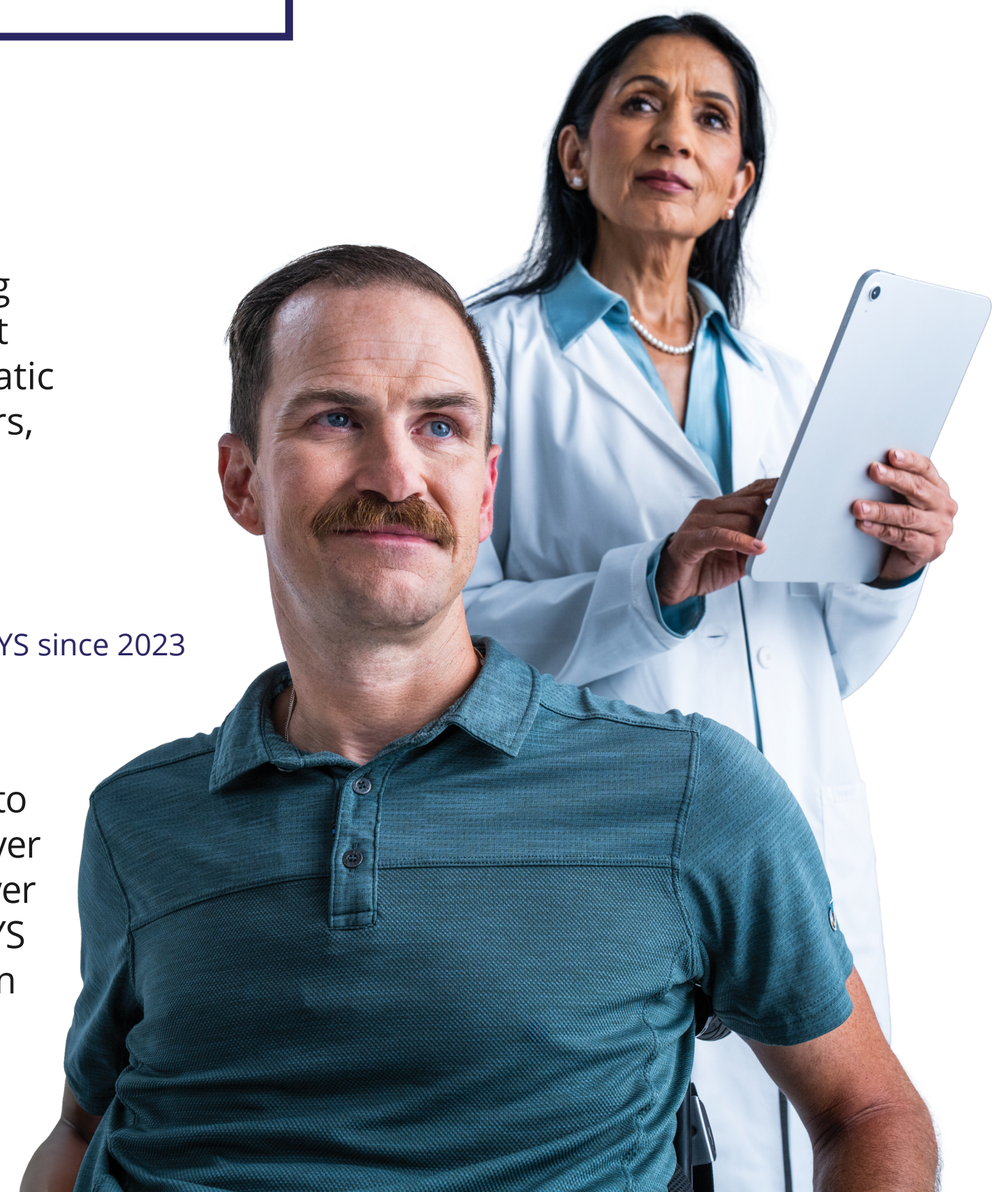
The recommended dose is 150 mg

Each SKYCLARYS capsule is 50 mg

= 3 capsules

ADHERENCE TO DOSING GUIDELINES IS CRITICAL TO SUCCESS WITH SKYCLARYS

The most effective dose of SKYCLARYS was established in a dose-ranging study that included 60 patients with FA. The 12-week study revealed that the benefits of SKYCLARYS were dose dependent. In the absence of hepatic impairment or concomitant treatment with CYP3A4 inhibitors or inducers, patients taking SKYCLARYS should be given the full 150 mg dose.[1,2]



Chris, age 42
Outdoorsman
Taking SKYCLARYS since 2023

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Elevation of Aminotransferases (cont'd)

- Monitor ALT, AST, and total bilirubin prior to initiation of SKYCLARYS, every month for the first 3 months of treatment, and periodically thereafter. If transaminases increase to levels greater than 5 times the ULN, or greater than 3 times the ULN with evidence of liver dysfunction (e.g., elevated bilirubin), immediately discontinue SKYCLARYS and repeat liver function tests as soon as possible. If transaminase levels stabilize or resolve, SKYCLARYS may be reinitiated with an appropriate increased frequency of monitoring of liver function

Please see additional Important Safety Information throughout and full Prescribing Information.

ONCE-DAILY ORAL DOSING (CONT'D)

SKYCLARYS® (omaveloxolone) 50 mg capsules

Standard administration for patients who are able to swallow whole capsules[1]:

- Administer SKYCLARYS on an empty stomach, at least 1 hour before or 2 hours after eating
- Swallow SKYCLARYS capsules whole. Do not crush or chew

Sprinkle administration for patients who are unable to swallow whole capsules[1]:

- Administer SKYCLARYS on an empty stomach, at least 1 hour before or 2 hours after eating
- SKYCLARYS capsules may be opened and the entire contents of both halves of the capsule sprinkled onto 2 tablespoons (30 mL) of applesauce
- Stir the mixture until homogenous
- Swallow all the drug/applesauce mixture immediately
- Do not store the mixture for future use
- Contents of the SKYCLARYS capsules should not be mixed with milk or orange juice
- Not for enteral feeding tube administration

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Elevation of B-Type Natriuretic Peptide

- Treatment with SKYCLARYS can cause an increase in B-type natriuretic peptide (BNP), a marker of cardiac function. A total of 14% of patients treated with SKYCLARYS had an increase from baseline in BNP value above the ULN (100 pg/mL), compared to 4% of patients who received placebo. The incidence of elevation of BNP above 200 pg/mL was 4% in patients treated with SKYCLARYS. Cardiomyopathy and cardiac failure are common in patients with Friedreich ataxia. Whether the elevations in BNP are related to SKYCLARYS or cardiac disease associated with Friedreich ataxia is unclear

Please see additional Important Safety Information throughout and full Prescribing Information.

SKYCLARYS® (omaveloxolone) 50 mg capsules

Additional dosing and administration considerations for patients taking SKYCLARYS[1]:

- If a dose of SKYCLARYS is missed, take the next dose at its scheduled time the following day. A double dose should not be taken to make up for a missed dose
- For additional information about SKYCLARYS dosing as it relates to concomitant use with strong or moderate CYP3A4 inhibitors/inducers, patients with hepatic impairment, and the use of hormonal contraceptives, please see the full Prescribing Information
- Discuss all medications your patients are taking, including other prescription medications, non-prescription medications, or herbal products (eg, St John's wort)
- Avoid grapefruit and grapefruit juice

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Elevation of B-Type Natriuretic Peptide (cont'd)

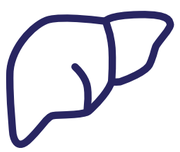
- Elevations in BNP may indicate cardiac failure and should prompt an evaluation of cardiac function. Check BNP prior to initiation of SKYCLARYS. Monitor patients for the signs and symptoms of fluid overload, such as sudden weight gain (3 pounds or more of weight gain in one day, or 5 pounds or more of weight gain in a week), peripheral edema, palpitations, and shortness of breath. If signs and symptoms of fluid overload develop, worsen, or require hospitalization, evaluate BNP and cardiac function, and manage appropriately. Management of fluid overload and heart failure may require discontinuation of SKYCLARYS

Please see additional Important Safety Information throughout and full Prescribing Information.

TESTING AND MONITORING PATIENTS ON SKYCLARYS

SKYCLARYS® (omaveloxolone) 50 mg capsules

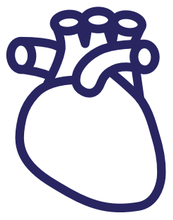
Obtain ALT, AST, bilirubin, BNP, and lipid parameters prior to initiating SKYCLARYS and during treatment[1]:



Aminotransferases

Before treatment	Every month for the first 3 months	Periodically during treatment
✔	✔	✔

- **Monitor ALT, AST, and total bilirubin** before starting SKYCLARYS. There were no cases of concomitant elevation of transaminases and total bilirubin observed in the clinical trial. **Maximum increases in ALT and AST occurred within 12 weeks after starting SKYCLARYS.** Increases in serum aminotransferases were generally asymptomatic and reversible following discontinuation of SKYCLARYS
- **If levels are >5x ULN, or >3x ULN with evidence of liver dysfunction**, immediately discontinue SKYCLARYS and repeat liver function tests as soon as possible
- **If levels stabilize or resolve**, SKYCLARYS may be reinitiated with an appropriate increased frequency of monitoring of liver function



B-type natriuretic peptide (BNP)

Before treatment	Every month for the first 3 months	Periodically during treatment
✔	—	—

- **Monitor patients for the signs and symptoms of fluid overload**, such as sudden weight gain (3 pounds or more of weight gain in one day or 5 pounds or more of weight gain in a week), peripheral edema, palpitations, and shortness of breath. Management of fluid overload and heart failure may require discontinuation of SKYCLARYS

Cholesterol

Before treatment	Every month for the first 3 months	Periodically during treatment
✔	—	✔

- Manage lipid abnormalities according to clinical guidelines

ALT=alanine aminotransferase; AST=aspartate aminotransferase; BNP=B-type natriuretic peptide; ULN=upper limit of normal.

Please see additional Important Safety Information throughout and full Prescribing Information.

RECOMMENDATIONS FOR POSSIBLE DOSAGE ADJUSTMENTS

SKYCLARYS® (omaveloxolone) 50 mg capsules

Recommended dosage of SKYCLARYS with concomitant use of CYP3A4 inhibitors and inducers[1]

Concomitant drug class	Dosage
Strong CYP3A4 inhibitor	Recommended to avoid concomitant use. If coadministration cannot be avoided: ► Reduce the dosage of SKYCLARYS to 50 mg once daily with close monitoring for adverse reactions ► If adverse reactions emerge, coadministration with strong CYP3A4 inhibitors should be discontinued
Moderate CYP3A4 inhibitor	Recommended to avoid concomitant use. If coadministration cannot be avoided: ► Reduce the dosage of SKYCLARYS to 100 mg once daily with close monitoring for adverse reactions ► If adverse reactions emerge, further reduce the dosage of SKYCLARYS to 50 mg once daily
Strong or moderate CYP3A4 inducer	Recommended to avoid concomitant use.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Lipid Abnormalities

- Treatment with SKYCLARYS can cause changes in cholesterol. In Study 1, 29% of patients treated with SKYCLARYS reported elevated cholesterol above ULN at one or more time points. Mean increases were observed within 2 weeks of initiation of SKYCLARYS and returned to baseline within 4 weeks of discontinuing treatment. A total of 16% of patients treated with SKYCLARYS had an increase in low-density lipoprotein cholesterol (LDL-C) from baseline, compared to 8% of patients who received placebo. The mean increase in LDL-C for all SKYCLARYS-treated patients was 23.5 mg/dL at 48 weeks. A total of 6% of patients treated with SKYCLARYS had decreases in high-density lipoprotein cholesterol (HDL-C) from baseline compared to 4% of patients who received placebo. The mean decrease in HDL-C for all SKYCLARYS-treated patients was 5.3 mg/dL at 48 weeks
- Assess lipid parameters prior to initiation of SKYCLARYS and monitor periodically during treatment. Manage lipid abnormalities according to clinical guidelines

Please see additional Important Safety Information throughout and full Prescribing Information.

RECOMMENDATIONS FOR POSSIBLE DOSAGE ADJUSTMENTS (CONT'D)

SKYCLARYS® (omaveloxolone) 50 mg capsules

Recommended dosage for patients with hepatic impairment[1]

Impairment classification (Child-Pugh)	Dosage
Severe (Child-Pugh Class C)	Avoid use.
Moderate (Child-Pugh Class B)	► 100 mg once daily with close monitoring for adverse reactions ► Consider lowering to 50 mg once daily if adverse reactions emerge
Mild (Child-Pugh Class A)	150 mg once daily.

Considerations for use with hormonal birth control[1]

SKYCLARYS may reduce the efficacy of hormonal contraceptives. Advise patients to avoid concomitant use with contraceptives such as the pill, patches, or rings, as well as implants and progestin-only pills.[1] See the full Prescribing Information for further details.

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS

- The most common adverse reactions in Study 1 (≥20% and greater than placebo) were elevated liver enzymes (AST/ALT), headache, nausea, abdominal pain, fatigue, diarrhea, and musculoskeletal pain

DRUG INTERACTIONS

- Avoid concomitant use of SKYCLARYS with moderate or strong CYP3A4 inhibitors. If use cannot be avoided, dosage modifications are recommended
- Avoid concomitant use of SKYCLARYS with moderate or strong CYP3A4 inducers
- Refer to the prescribing information for dosing instructions for concomitant use of CYP3A4 and CYP2C8 substrates and monitor for lack of efficacy of the concomitant treatment
- Advise patients to avoid concomitant use with combined hormonal contraceptives, implants, and progestin only pills

Please see additional Important Safety Information throughout and full Prescribing Information.

SKYCLARYS® (omaveloxolone) 50 mg capsules

A CHANCE TO SLOW FA PROGRESSION

STARTS WITH SKYCLARYS*

Libby, age 27

Interior designer

Taking SKYCLARYS since 2023

***In a clinical trial, treatment with SKYCLARYS (n=40) resulted in 2.41 lower modified Friedreich Ataxia Rating Scale scores (less impairment) relative to placebo (n=42) at Week 48 (-1.56 vs +0.85; *P*=0.01380).[1]**

Start giving your patients a chance to slow FA progression with SKYCLARYS. Visit www.SkyclarysHCP.com to learn how.

Patients featured are paid spokespersons for Biogen.

Please see additional Important Safety Information throughout and full Prescribing Information.

IMPORTANT SAFETY INFORMATION (cont'd)

SPECIFIC POPULATIONS

Pregnancy

- There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to SKYCLARYS during pregnancy. Healthcare providers are encouraged to enroll pregnant patients, or pregnant women may register themselves in the program by calling 1-866-609-1785 or by sending an email to SkyclarysPregnancySurveillance@ppd.com
- There are no adequate data on the development risks associated with the use of SKYCLARYS in pregnant women

Lactation

- There are no data on the presence of omaveloxolone or its metabolites in human milk. The effects on milk production and the breastfed infant are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for SKYCLARYS and any potential adverse effects on the breastfed infant from SKYCLARYS or from the underlying maternal condition

Hepatic Impairment

- Avoid treatment with SKYCLARYS in patients with severe hepatic impairment, including those who develop severe hepatic impairment
- Reduced dosage in patients with moderate hepatic impairment with close monitoring for adverse reactions is recommended

Please see additional Important Safety Information throughout and full Prescribing Information.

References: 1. Skyclarys. Prescribing information. Biogen; 2024. **2.** Lynch DR, Farmer J, Hauser L, et al. Safety, pharmacodynamics, and potential benefit of omaveloxolone in Friedreich ataxia. *Ann Clin Transl Neurol*. 2018;6(1):15-26.

Intended for a US HCP audience.

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