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

FOR FRIEDREICH ATAXIA PROGRESSION,

READY SET SLOW*

More than 2000 patients have been prescribed SKYCLARYS worldwide†[2]

***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*=0.0138).[1]**

†Based on commercial patients, early access patients, and clinical trial participants through July 2024.

Patients featured are paid spokespersons for Biogen.

SKYCLARYS® (omaveloxolone) 50 mg capsules

Jacob, age 30
Youth mentor
Taking SKYCLARYS since 2023

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.

TABLE OF CONTENTS

SKYCLARYS® (omaveloxolone) 50 mg capsules

FRIEDREICH ATAXIA IS A PROGRESSIVE NEURODEGENERATIVE GENETIC DISEASE

Friedreich ataxia (FA) is the most common form of inherited ataxia[3]

In the United States, approximately 5000 people or more live with FA.[4]

FA often presents with nonspecific symptoms[3,5,6]

The first signs of FA typically include a combination of symptoms, such as:

Falls with gait ataxia

Loss of reflexes (areflexia)

Lack of balance (poor proprioception)

Loss of sensation (neuropathy)

Chronic fatigue

FA leads to incapacitation and, eventually, death. The average life expectancy for a patient with FA is 37.5 years.[3]

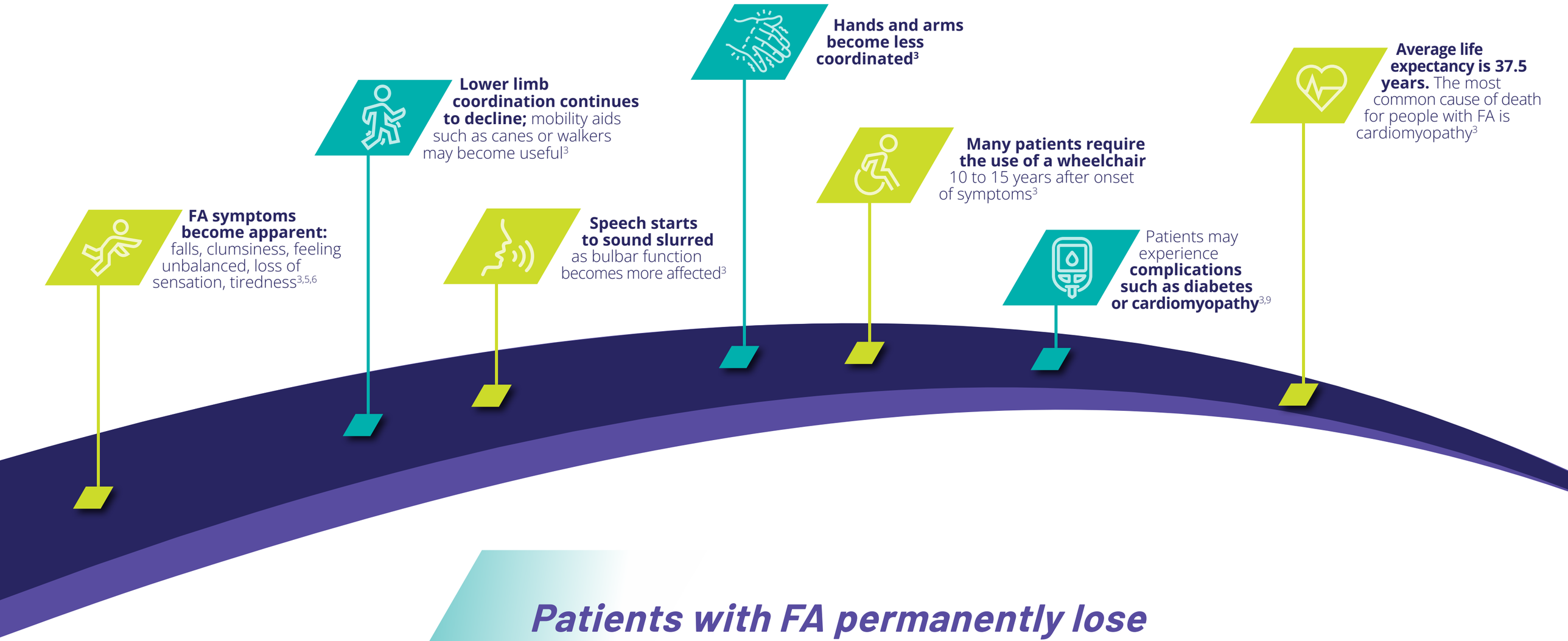
The path to an FA diagnosis is often long and frustrating for patients

Diagnostic challenges are present because of the nonspecific symptoms FA presents with:

- It is common for patients to see 4 or more doctors before a diagnosis is made[7]
- The average time to diagnosis for FA is 3 years after onset of symptoms[8]
- Older patients may go more than 8 years before a diagnosis is confirmed[7]
- FA is a commonly misdiagnosed condition. As many as 1 in 4 patients with FA have been misdiagnosed[7]

TIME IS FUNCTION FOR PATIENTS WITH FRIEDREICH ATAXIA

While each person's experience is unique, every patient with FA progresses down a neurodegenerative path toward loss of ambulation. In fact, many patients will have already lost some of their functional abilities by the time of diagnosis, typically those related to standing and mobility.[8]



Patients with FA permanently lose their physical abilities over time.[3,5,9]

AS FA PROGRESSES, A PATIENT'S mFARS SCORE WILL WORSEN (INCREASE)

The modified Friedreich Ataxia Rating Scale (mFARS) is a clinically validated neurological assessment[10]

The mFARS provides a detailed evaluation of a patient's status and is generally accepted as a clinical trial endpoint due to its correlation with disease progression.[10] In clinical practice, HCPs should use the assessment tool they feel is best for their patients.

The mFARS is made up of 4 components that focus on functional abilities

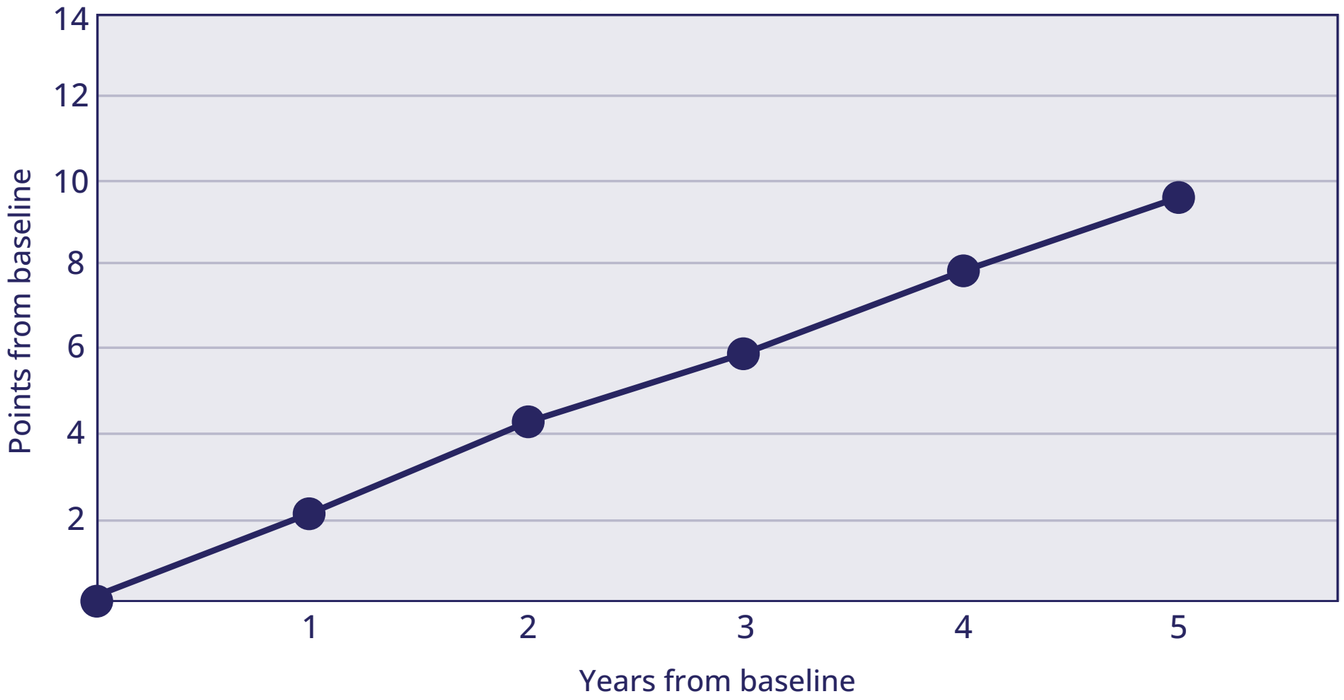
The mFARS is scored on a scale of 0 to 93, with higher scores indicating more severe physical impairment.[10]

mFARS measures[10]

Component	Assessed function	Example assessments and scoring		Clinical extrapolations of possible effects on patient abilities
Lower limb coordination	Coordination of legs and feet	▸ Heel-along-shin slide ▸ Heel-to-shin tap	16 points total	Closely related to upright stability; also an important contributor to decline in ambulatory patients.[11] Affects activities like putting on socks and shoes.
Upright stability	Sitting, standing, and walking	▸ Sitting posture ▸ Stance ▸ Gait	36 points total	Assessment of individual ambulatory ability. Affects activities like walking, sitting in a car, standing in a line, and showering.
Upper limb coordination	Fine motor coordination	▸ Finger to finger ▸ Nose to finger ▸ Dysmetria	36 points total	Ability to complete activities of daily living, such as getting dressed, eating, brushing teeth, typing, pointing, reaching, and turning a doorknob.
Bulbar function	Speech clarity; strength and volume of coughing	▸ Forceful cough ▸ Speech	5 points total	Affects the ability to communicate clearly. Patients may also be at increased risk for respiratory infection.[12]

AN INCREASE IN mFARS SCORES COULD INDICATE FURTHER LOSS OF FUNCTION THAT MAY AFFECT EVERYDAY TASKS

Mean change from baseline in mFARS[13]



A natural history study of untreated patients found that FA progresses on average ~2 points per year.[13]

SKYCLARYS WAS SHOWN TO SLOW DISEASE PROGRESSION

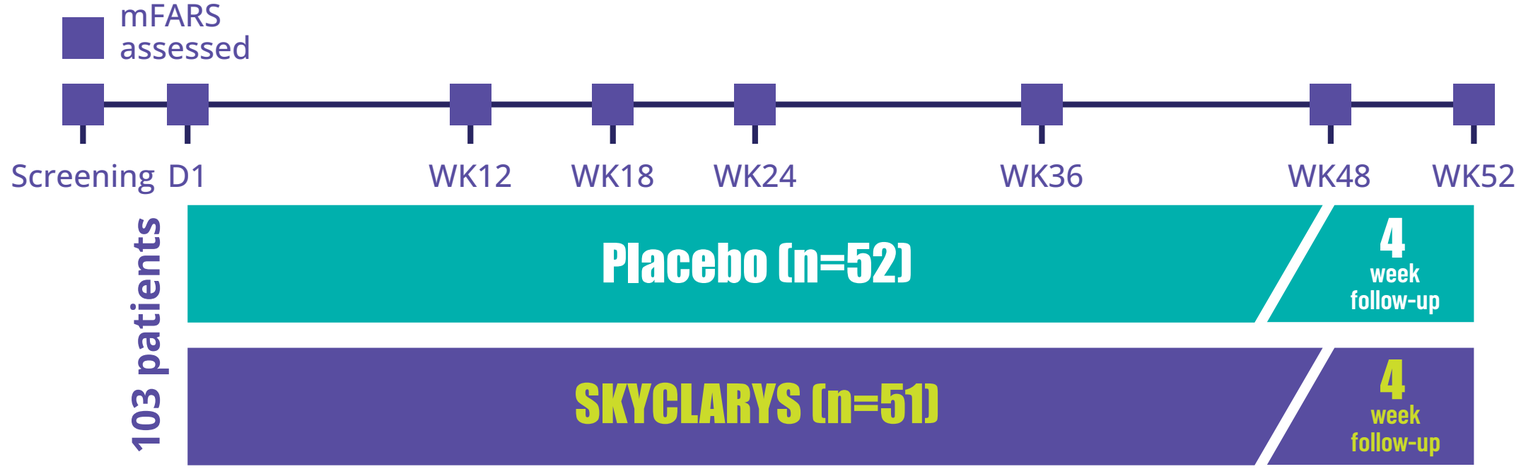
SKYCLARYS® (omaveloxolone) 50 mg capsules

The MOXIe trial was the largest clinical trial of its kind in FA[1,4]

The MOXIe trial was an international, double-blind, randomized, placebo-controlled, multicenter, registrational phase 2 trial. A total of 103 patients with genetically confirmed diagnoses were randomized in a ratio of 1:1 (the All Randomized Population) to receive SKYCLARYS 150 mg once daily (n=51) or placebo (n=52).

- 103 patients
- 11 institutions
- 3 continents
- 16 to 40 years of age
- 20 to 80 baseline mFARS score
- 53% male

The prespecified primary analysis was the change from baseline in the mFARS score compared with placebo at Week 48.[4]



IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Elevation of Aminotransferases (cont'd)

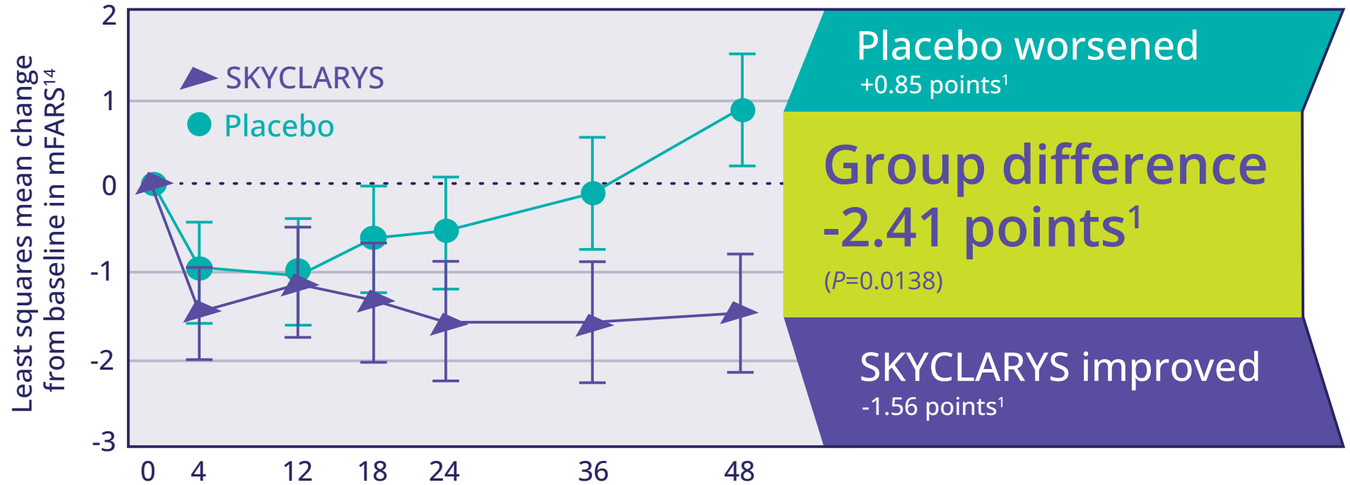
- Monitor ALT, AST, and total bilirubin prior to initiation of SKYCLARYS, every month for the first 3 months of treatment, and periodically thereafter. If transaminases increase to levels greater than 5 times the ULN, or greater than 3 times the ULN with evidence of liver dysfunction (e.g., elevated 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.

SKYCLARYS SLOWED DISEASE PROGRESSION IN THE MOXIe TRIAL[1]

SKYCLARYS® (omaveloxolone) 50 mg capsules

At 48 weeks, the study showed a difference of -2.41 points in the mFARS scores of patients in the SKYCLARYS group compared to patients in the placebo group.



SKYCLARYS (n)	40	40	40	38	36	35	34
Placebo (n)	42	42	42	41	41	41	41

In the Full Analysis Population of patients without pes cavus (n=82).

Treatment with SKYCLARYS resulted in less physical impairment relative to placebo at Week 48.[1]

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 SLOWED DISEASE PROGRESSION IN THE MOXIe TRIAL[1] (CONT'D)

SKYCLARYS® (omaveloxolone) 50 mg capsules

Results from patient subgroups numerically favored SKYCLARYS over placebo regardless of[4]:

Age

Sex

GAA repeat length

Ambulatory status

Presence of pes cavus

All 4 components of the mFARS assessment numerically favored SKYCLARYS over placebo.[4]

The greatest effects were on upper limb coordination, which has been linked to the ability to perform many activities of daily living, followed by upright stability, which defines important clinical milestones such as loss of ambulation.[8,15]

The MOXIe trial was not powered to detect a statistically significant difference among subgroups.[4]

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.

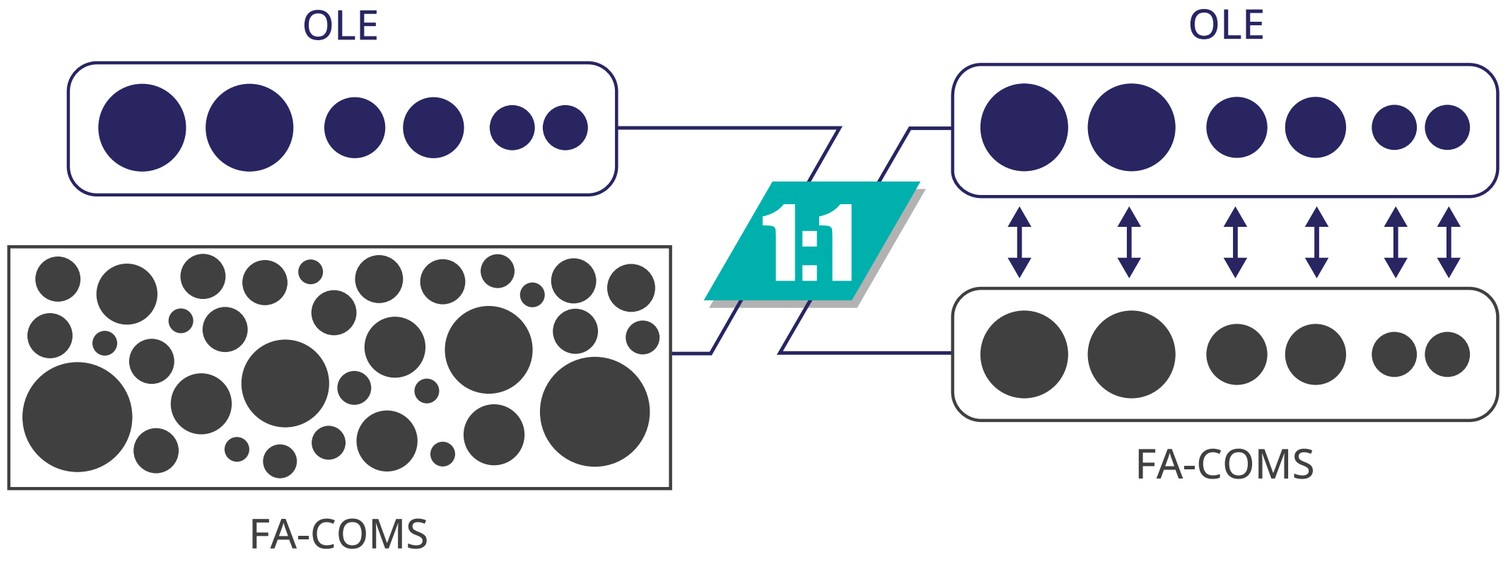
PROPENSITY MATCHING WAS USED IN A 3-YEAR POST HOC ANALYSIS OF SKYCLARYS

SKYCLARYS® (omaveloxolone) 50 mg capsules

What is propensity matching?

Propensity matching is a method of comparing patients from a clinical trial with an external control by identifying comparable prognostic characteristics. It is informative in cases where a very long follow-up period is required to assess outcomes or when it is difficult to perform randomized controlled trials, such as in certain special patient populations.[16]

An ongoing MOXIe open-label extension (OLE) assesses long-term safety and tolerability of SKYCLARYS in patients with FA who completed MOXIe Part 1 or Part 2 (n=136). A post hoc propensity-matched analysis compared patients in the MOXIe OLE with patients who were not treated with SKYCLARYS who participated in a natural history study, the Friedreich Ataxia Clinical Outcome Measures Study (FA-COMS).[17]



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

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

PATIENTS IN THE MOXIe OLE WERE CLOSELY MATCHED TO PATIENTS IN THE FA-COMS

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Patient characteristics in the propensity-matched analysis[17]

Characteristic, statistic	FA-COMS (n=136)	OLE (n=136)
Age (years), mean (SD)	26.2 (13.7)	26.6 (7.3)
Age at FA onset, mean (SD)	15.2 (10.5)	15.5 (5.3)
Sex, female, n (%)	70 (51.5%)	70 (51.5%)
mFARS, mean (SD)	41.0 (16.1)	42.2 (12.6)
Gait, mean (SD)	2.7 (1.7)	2.8 (1.4)

SD=standard deviation.

FA-COMS is a large, robust FA natural history study that has enrolled more than 1250 patients who have been followed for up to 15 years.[17]

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)
Lipid Abnormalities (cont'd)

- 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.

3-YEAR PROPENSITY-MATCHED ANALYSIS RESULTS

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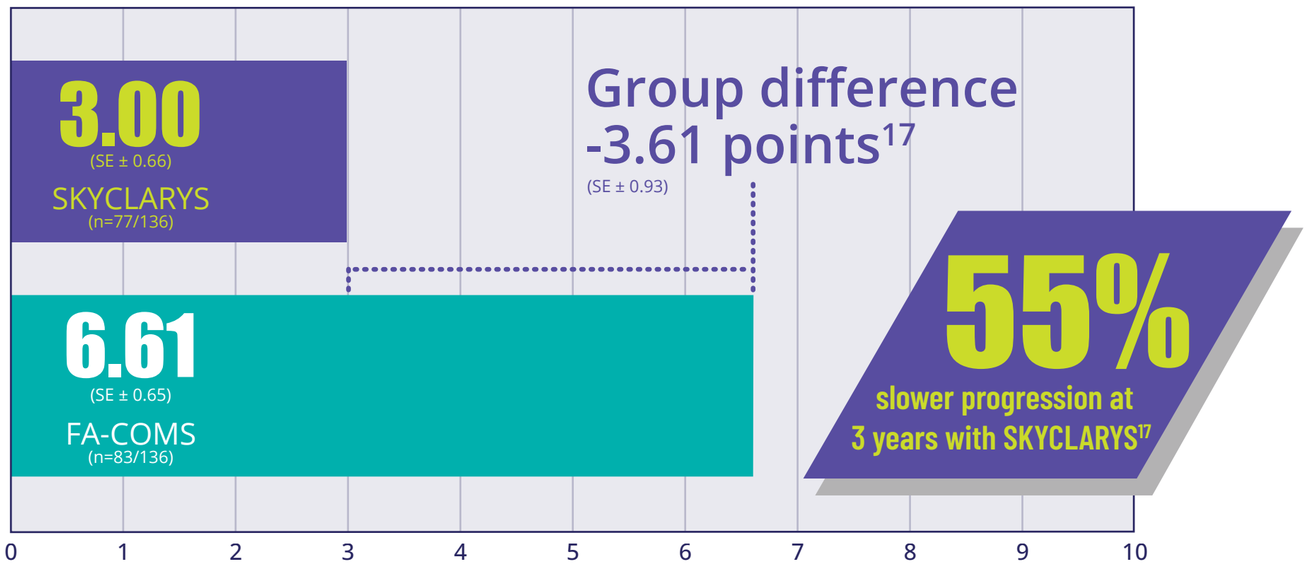
These exploratory analyses should be interpreted cautiously given the limitations of data collected outside of a controlled study, which may be subject to confounding.[1]



Lower mFARS scores were observed in patients treated with SKYCLARYS after 3 years relative to a matched set of untreated patients from a natural history study.[1]

SE=standard error.

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

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

SKYCLARYS® (omaveloxolone) 50 mg capsules

Elevation of aminotransferases[1]

Treatment with SKYCLARYS can cause an elevation in hepatic transaminases (ALT and AST).

Monitor ALT, AST, and total bilirubin prior to initiation of SKYCLARYS, every month for the first 3 months of treatment, and periodically thereafter.

Patients experiencing elevated ALT/AST[1]

>3x ULN	>5x ULN
31%	16%

If transaminases increase to levels greater than 5 times the ULN, or greater than 3 times the ULN with evidence of liver dysfunction (eg, 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.

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.

Elevation of B-type natriuretic peptide (BNP)[1]

Treatment with SKYCLARYS can cause an increase in BNP, a marker of cardiac function.[1] 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. Management of fluid overload and heart failure may require discontinuation of SKYCLARYS.

Lipid abnormalities[1]

Treatment with SKYCLARYS can cause changes in cholesterol.

Mean increases were observed within 2 weeks of initiation of SKYCLARYS and returned to baseline within 4 weeks of discontinuing treatment. Assess lipid parameters prior to initiation of SKYCLARYS and monitor periodically during treatment.

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

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

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

Lipid abnormalities

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

- Manage lipid abnormalities according to clinical guidelines

SKYCLARYS® (omaveloxolone) 50 mg capsules

Adverse events in the clinical trial were generally considered mild to moderate[4]

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

Three patients reported serious adverse events (SAEs) while taking SKYCLARYS, and 2 patients reported SAEs 2 weeks after discontinuation.[4]

Four patients in the SKYCLARYS group and 2 patients in the placebo group discontinued treatment due to adverse reactions. Reasons for discontinuation in the SKYCLARYS group included[4]:

- Ventricular tachycardia
- Elevated ALT/AST
- Muscle spasms
- Rosacea

Adverse reactions reported in ≥10% of patients and greater than placebo[1]

Adverse reactions	SKYCLARYS (n=51)	Placebo (n=52)
Elevated liver enzymes (AST/ALT)	37%	2%
Headache	37%	25%
Nausea	33%	13%
Abdominal pain	29%	6%
Fatigue	24%	14%
Diarrhea	20%	10%
Musculoskeletal pain	20%	15%
Oropharyngeal pain	18%	6%
Influenza	16%	6%
Vomiting	16%	12%
Muscle spasms	14%	6%
Back pain	13%	8%
Decreased appetite	12%	4%
Rash	10%	4%

DURATION OF ADVERSE REACTIONS

SKYCLARYS® (omaveloxolone) 50 mg capsules

Data for the duration of adverse reactions is represented by median and quartile values:

- **The median value** divides the data set in half, meaning 50% of patients saw their adverse reaction resolve before that point and 50% after
- **The first quartile** is the point before which 25% of patients experienced resolution
- **The third quartile** is the point before which 75% of patients experienced resolution

Dividing data into quartiles helps illustrate the distribution of data points and variability of the duration of adverse reactions.

Data here is limited to the duration of the MOXIe trial. Remember that adverse reactions can occur at any time, even after 1 year.

Length in days of adverse reactions reported in ≥20% of patients[18] (SKYCLARYS, n=51; placebo, n=52)

Elevated liver enzymes (ALT/AST)	SKYCLARYS (n=19)	Placebo (n=1)
Quartile 1	21	6
Median	33	6
Quartile 3	113	6
Headache	**SKYCLARYS (n=19)**	**Placebo (n=13)**
Quartile 1	1	3
Median	3	4
Quartile 3	19	182
Nausea	**SKYCLARYS (n=17)**	**Placebo (n=7)**
Quartile 1	3	1
Median	16	2
Quartile 3	67	38
Abdominal pain	**SKYCLARYS (n=15)**	**Placebo (n=3)**
Quartile 1	2	2
Median	6	8
Quartile 3	49	15

Fatigue	SKYCLARYS (n=12)	Placebo (n=7)
Quartile 1	30	34
Median	80	225
Quartile 3	339	363
Diarrhea	**SKYCLARYS (n=10)**	**Placebo (n=5)**
Quartile 1	4	1
Median	7.5	3
Quartile 3	49	4
Musculoskeletal pain	**SKYCLARYS (n=10)**	**Placebo (n=8)**
Quartile 1	8	10
Median	15.5	24
Quartile 3	136	36

Most common adverse reactions were transient and resolved within 35 days of the event start date.[19]

SKYCLARYS IS A ONCE-DAILY ORAL PRESCRIPTION MEDICINE

SKYCLARYS® (omaveloxolone) 50 mg capsules

The recommended dose is 150 mg

Each SKYCLARYS capsule is 50 mg = **3 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 and 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)

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

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)

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.

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

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
- 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.

DOSING AND ADMINISTRATION CONSIDERATIONS (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)

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 MECHANISM OF ACTION

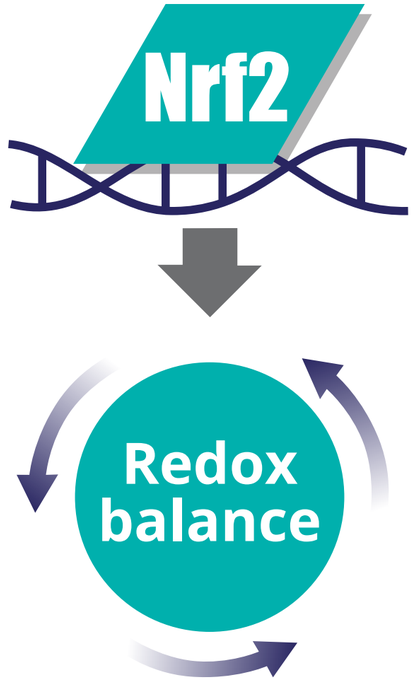
SKYCLARYS® (omaveloxolone) 50 mg capsules

How FA works

The frataxin gene mutation that causes FA results in deficiency of the frataxin protein. Frataxin protein deficiency is associated with Nrf2 dysregulation, which is linked to impaired cellular energy production, mitochondrial dysfunction, oxidative stress, and inflammation—all of which together lead to neurodegeneration.[4]

How SKYCLARYS is thought to work

The precise mechanism by which omaveloxolone exerts its therapeutic effect in patients with FA is unknown. Omaveloxolone has been shown to activate the Nrf2 pathway in vitro and in vivo in animals and humans. The Nrf2 pathway is involved in the cellular response to oxidative stress.[1]



Nrf2=nuclear factor erythroid 2-related factor 2.

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.

THE RIGHT GENETIC TEST CAN CONFIRM AN FA DIAGNOSIS

SKYCLARYS® (omaveloxolone) 50 mg capsules

Genetic testing is the only way to diagnose FA and accurately determine a patient's prognosis[20]

When diagnosing FA with a genetic test, there are multiple tests you can choose from. Make sure to request the test that will provide the most relevant information.

Diagnostic companies typically provide guidance on the correct test needed for an FA diagnosis

Most major diagnostics companies offer testing that can detect FA, whether it is caused by a GAA triplet-repeat expansion or a point mutation.

Choose a GAA triplet-repeat expansion analysis

Only a genetic test that includes a GAA triplet-repeat expansion analysis can detect pathogenic repeat expansion variants. Standard multigene panels that include only a sequence analysis cannot detect the triplet-repeat expansion variants.[20]

Genetic tests: More than just a diagnosis—a prognosis

One way to determine the anticipated severity of FA is by identifying the number of GAA triplet repeats.[3] Currently, only an FA repeat expansion analysis that includes sizing of the repeat expansion can give you this information.

If you suspect FA, confirm the diagnosis with a genetic test that detects GAA triplet repeats.

BIOGEN REACH IS HERE TO SUPPORT PATIENTS THROUGHOUT THEIR TREATMENT JOURNEY

SKYCLARYS® (omaveloxolone) 50 mg capsules

The REACH Provider Center is an informational resource for healthcare professionals and their patients who have been prescribed SKYCLARYS

Within the REACH Provider Center, you can find information about treatment support for your patient:

Lead Case Managers can help patients stay on track with SKYCLARYS by assisting with navigating insurance coverage, affordability options, prescription delivery, and connecting with the specialty pharmacy or nurses.

The REACH exclusive specialty pharmacy, Biologics, will deliver your patient's SKYCLARYS prescription and can help you and your staff with understanding insurance requirements for obtaining approval.

Options may be available to help your patients save on their SKYCLARYS prescription whether they are insured, underinsured, or uninsured.*

*Subject to eligibility and program terms and conditions. REACH affordability options are not healthcare insurance.

†Your patient is not required to enroll in REACH before you prescribe SKYCLARYS. However, their signed consent is required to access all program support services.

You must complete and submit a Start Form for your patient before they can speak with a Lead Case Manager and access REACH support offerings.†

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

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

ASSISTANCE PROGRAMS HELP KEEP SKYCLARYS AFFORDABLE FOR ELIGIBLE PATIENTS

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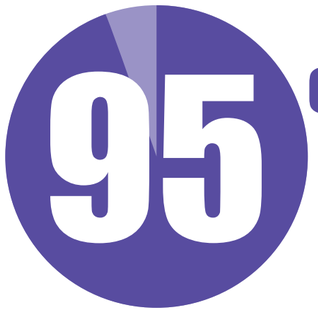
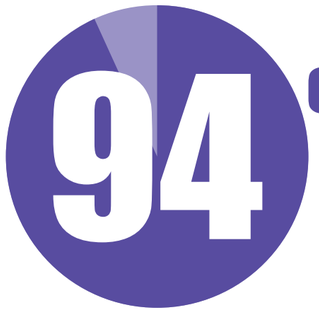
- Eligible commercially insured patients may have out-of-pocket costs as low as $0 with the Biogen Copay Program*



95%
of commercially insured patients have $0 out-of-pocket costs per month†[21]



94%
of Medicare patients have $15 or less in out-of-pocket costs per month†[21]

Low-income Medicare patients who qualify for Extra Help may pay as little as $0 to $11.20.‡[22]

- Extra Help is a low-income subsidy program available to those with limited resources and income who may be eligible for subsidized Medicare prescription drug plan premiums, deductibles, and prescription copays
- Approximately 27% of Medicare Part D enrollees already benefit from Extra Help.[23] It is estimated that 3 million patients are not currently enrolled but may be eligible for Extra Help benefits§
- Patients can apply for Extra Help online at www.ssa.gov/medicare/part-d-extra-help or by calling 1-800-772-1213

*There is an annual cap on the amount of assistance that patients can receive over a one-year period. Federal and state laws and other factors may prevent or otherwise restrict eligibility. People covered by Medicare, Medicaid, the VA/DoD, or any other federal plans are not eligible to enroll. Patients are eligible to enroll in the copay program for as long as it is offered and they are treated with SKYCLARYS.

†Data as of July 2024.

‡Data as of January 2024.

§US Department of Health and Human Services. FACT SHEET: Biden-Harris administration announces new tools to lower prescription drug costs for low-income seniors and people with disabilities. Published online June 12, 2023.

SKYCLARYS® (omaveloxolone) 50 mg capsules

A CHANCE TO SLOW FA PROGRESSION

STARTS WITH SKYCLARYS*

***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*=0.0138).[1]**

More than 2000 patients have been prescribed SKYCLARYS worldwide.†[2]

†Based on commercial patients, early access patients, and clinical trial participants through July 2024.

Patients featured are paid spokespersons for Biogen.

Libby, age 27

Interior designer

Taking SKYCLARYS since 2023

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

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Lipid Abnormalities (cont'd)

- 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.

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Intended for a US HCP audience.

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