continue to swirl the upright vial for 5 to 10 seconds every 5 minutes until no gel-like particles are visible in the solution; do not use if contents are not completely dissolved after 40 minutes. Resulting solution is 150 mg/1.2 mL. Invert the vial for 15 seconds so the solution drains toward the stopper. Remove all of the solution by inserting a new 3 mL syringe with a 1-inch, 18-gauge needle into the inverted vial. Replace the 18-gauge needle with a 25-gauge needle for subcutaneous injection and expel any air or bubbles. **Vial contains overfill;** expel excess solution to obtain the resulting dose of 150 mg/1.2 mL or 75 mg/0.6 mL. **Note:** Vial contains 202.5 mg including overfill (ISMP 2019). Concentrations following reconstitution of the vial differ from concentrations of prefilled syringes.

Administration: Pediatric Note: Omalizumab prefilled syringes and reconstituted lyophilized powder are different concentrations; use extra precaution during product selection and during dose volume calculations

Parenteral: SUBQ: Doses >150 mg should be divided into more than 1 injection site (eg, 225 mg or 300 mg administered as 2 injections, 375 mg administered as 3 injections); each injection site should be separated by ≥1 inch; do not inject into moles, scars, bruises, tender areas, or broken skin. Due to viscosity, injection may take 5 to 10 seconds to administer. Administer initial doses and any doses prepared from vials by a health care professional. Observe patient for a minimum of 2 hours after the first 3 injections and 30 minutes after subsequent injections (Lieberman 2015) or in accordance with individual institution policies and procedures.

Lyophilized powder (vial): Recommended injection sites include the upper arm, stomach, or the front and middle of the thighs.

Prefilled syringe: Allow to warm to room temperature for 15 to 30 minutes; leave in carton to protect from light. Do not speed warming process in any way (eg, microwave, warm water). Recommended injection sites include the upper arm and the front and middle of the thighs.

Note: In patients 6 to 11 years of age, doses should be administered by a trained caregiver; patients ≥12 years may self-administer after training. Candidates for self-administration should be determined following a risk-benefit assessment using the following criteria: Patient has no prior history of anaphylaxis related or unrelated to omalizumab; patient has previously received ≥3 doses of omalizumab; patient/caregiver has the ability to recognize and manage signs/symptoms of a severe hypersensitivity reaction, including anaphylaxis; and patient/caregiver has the ability to perform injections with proper technique and per the prescribed dosing regimen.

Monitoring Parameters Anaphylactic/hypersensitivity reactions (observe patients for 2 hours after the first 3 injections and 30 minutes after subsequent injections [Lieberman 2015] or in accordance with individual institution policies and procedures); baseline serum total IgE; FEV_1, peak flow, and/or other pulmonary function tests; monitor for signs of infection.

Dosage Forms: US Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution Prefilled Syringe, Subcutaneous [preservative free]:
Xolair: 75 mg/0.5 mL (0.5 mL); 150 mg/mL (1 mL)

Solution Reconstituted, Subcutaneous [preservative free]:
Xolair: 150 mg (1 ea)

Dosage Forms: Canada Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution Prefilled Syringe, Subcutaneous:
Xolair: 75 mg/0.5 mL (0.5 mL); 150 mg/mL (1 mL)

Solution Reconstituted, Subcutaneous:
Xolair: 150 mg (1 ea)

Omaveloxolone

Medication Safety Issues

Sound-alike/look-alike issues:
Omaveloxolone may be confused with oxandrolone.

Brand Names: US Skyclarys

Therapeutic Category Nuclear Factor Erythroid 2-Related Factor 2 Activator

Generic Availability (US) No

Use Treatment of Friedreich ataxia (FDA approved in ages ≥16 years and adults).

Breastfeeding Considerations

It is not known if omaveloxolone is present in breast milk. According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother.

Contraindications There are no contraindications listed in the manufacturer's labeling.

Warnings/Precautions B-type natriuretic peptide increases may occur during therapy and may indicate cardiac failure. Cardiac failure and cardiomyopathy may also occur with Friedreich ataxia. Associated signs/symptoms of cardiac failure–associated fluid overload include sudden weight gain (eg, ≥1.4 kg [3 lb] in 1 day or ≥2.3 kg [5 lb] in 1 week), palpitations, peripheral edema, and shortness of breath. Elevated ALT and AST may occur with treatment. Maximum increases in ALT and AST typically occur within 12 weeks of initiation of therapy. Transaminase elevation may be asymptomatic and reversible with discontinuation of therapy. Increases in cholesterol and LDL and decreases in HDL may occur during therapy. Cholesterol increases typically occur within 2 weeks of initiation of therapy and return to baseline within 4 weeks of therapy discontinuation. At 48 weeks of therapy, a mean LDL increase of 23.5 mg/dL and a mean HDL decrease of 5.3 mg/dL have been measured. Use with caution in patients with preexisting liver impairment.

Adverse Reactions The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified. Adverse reactions reported in adolescents and adults.

>10%:
Endocrine & metabolic: Increased LDL cholesterol (16%), increased serum cholesterol (29%)
Gastrointestinal: Abdominal pain (29%), decreased appetite (12%), diarrhea (20%), nausea (33%), vomiting (16%)
Hepatic: Increased serum alanine aminotransferase (≤37%), increased serum aspartate aminotransferase (≤37%)
Infection: Influenza (16%)
Nervous system: Fatigue (24%), headache (37%)
Neuromuscular & skeletal: Back pain (13%), muscle spasm (14%), musculoskeletal pain (20%)
Respiratory: Oropharyngeal pain (18%)

1% to 10%:
Dermatologic: Skin rash (10%)
Endocrine & metabolic: Decreased HDL cholesterol (6%)

Drug Interactions

Metabolism/Transport Effects Substrate of CYP2C8 (minor), CYP2J2 (minor), CYP3A4 (major); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential; **Induces** BCRP/ABCG2, CYP2C8 (weak), CYP3A4 (weak), OATP1B1/1B3 (SLCO1B1/1B3)

Avoid Concomitant Use
Avoid concomitant use of Omaveloxolone with any of the following: CYP3A4 Inducers (Moderate); CYP3A4 Inducers (Strong); Fexinidazole; Fusidic Acid (Systemic); Hormonal Contraceptives; Zavegepant

Storage/Stability Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F).

Mechanism of Action Omaveloxolone activates Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) pathways, which are involved in the cellular response to oxidative stress; in vitro, omaveloxolone restores mitochondrial function in fibroblasts obtained from patients with Friedreich ataxia (Abeti 2018; Lynch 2021; manufacturer's labeling).

Pharmacokinetics (Adult Data Unless Noted)

Absorption: C_{max} and AUC are increased (350% and 15%, respectively) with administration with a high-fat meal (800 to 1,000 calories; ~150, 250, and 500 to 600 calories from protein, carbohydrate, and fat, respectively) compared to fasted conditions.

Distribution: V_d: 7,361 L.

Protein binding: 97%.

Metabolism: Primarily metabolized via CYP3A with minor metabolism via CYP2C8 and CYP2J2.

Half-life elimination: 57 hours (range: 32 to 90 hours).

Time to peak: Median: 7 to 14 hours; range: 1 to 24 hours.

Excretion: Feces: 92%; urine: 0.1%.

Pharmacokinetics: Additional Considerations (Adult Data Unless Noted)

Hepatic function: Moderate and severe hepatic impairment (Child-Pugh class B and C): Clearance is reduced, resulting in increased AUC and C_{max} (increased by 1.65-fold and 1.83-fold, respectively, in moderate hepatic impairment; AUC variably increased by up to 2.17-fold in severe hepatic impairment). Dosage reduction is recommended.