OMALIZUMAB

Breastfeeding Considerations

Use
Treatment of Friedreich ataxia (FDA approved in ages ≥ 12 and adults).

Generic Availability (US)
Therapeutic Category
Brand Names: US
Dosage Forms: US

Monitoring Parameters
According to the manufacturer, the decision to breastfeed should be made with consideration of the benefits of breastfeeding and the potential risk of exposure to omaveloxolone. It is not known if omaveloxolone is present in breast milk. In animal studies, there have been no data on the effects of omaveloxolone on the breastfed infant.

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

Dosage Forms:
Solution Reconstituted, Subcutaneous: 202.5 mg including overfill (ISP 2019). Concentrations following reconstitution of the vial differ from concentrations of prefilled syringe.

Solution Prefilled Syringe, Subcutaneous [preservative free]: Injections and 30 minutes after subsequent injections (Lieberman 2015) or in accordance with individual institution policies and procedures. Loyoehilized 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 use if solution is visibly undissolved 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 202.5 mg including overfill 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 (ISP 2019). Concentrations following reconstitution of the vial differ from concentrations of prefilled syringe.

Adминистration: Pediatric Note: Omaveloxolone prefilled syringes and reconstituted lypoehilized powder are different concentrations; use separate vials/dilution 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. Lypoehilized powder (vial): Recommended injection sites include the upper arm, stomach, or 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/syptoms of a severe hypersensitivity reaction, including anaphylaxis; and patient/caregiver has the ability to perform injections without technical assistance and 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; FEV1, peak flow, and/or other pulmonary function tests; blood pressure; pulse; temperature; weight; and vital signs (including pulse oximetry and the benefits of treatment to the mother.

Contraindications
There are no contraindications listed

Warnings/Precautions
B-type natriuretic peptide
Pharmacokinetics: Additional Considerations
Time to peak: Median: 7 to 14 hours; range: 1 to 24 hours. Excretion: Feces ≥ 1.4 kg [3 lb] in 1 day or ≥ 2.3 kg [5 lb] in 4 weeks. Associated signs/syptoms of fluid overload include sudden weight gain (eg, ≥1.4 kg [3 lb] in 1 day or ≥2.3 kg [5 lb] in 4 weeks), 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 ≥ 12 years:

Endocrine & metabolic: Increased LDL cholesterol (16%), increased serum cholesterol (29%) and triglyceride (12%); decreased HDL cholesterol (29%), decreased apolipoprotein A (ApoA) (12%), diastolic blood pressure (33%), and systolic blood pressure (33%).

Hepatic: Increased serum alanine aminotransferase (>373), increased serum aspartate aminotransferase (>373), and increased serum alkaline phosphatse (>373)

Nervous system: Fatigue (24%), headache (37%), dizziness (16%), increased serum cholesterol (29%), increased serum triglyceride (29%), and increased serum lactate dehydrogenase (20%).

Respiratory: Cough (10%), wheezing (10%), shortness of breath (10%), wheezing (10%), and irritation (10%).

Dermatologic: Skin rash (10%)

Gastrointestinal: Abdominal pain (29%), diarrhea (29%), nausea (33%), vomiting (16%)

Hypersensitivity: Anaphylaxis (16%) and angioedema (16%)

Infections: Infection (16%) and respiratory infection (16%)

Metabolic & Endocrine: 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; Inducers BCRP/ABCG2, CYP2C8 (weak), and CYP3A4 (weak), OATP1B1/1B3 (SLC01B1/1B3)

Avoid Concomitant Use
Use of concomitant use of Xolair: 150 mg (1 ea) with the following:

- Inducers (Strong): Fexinidazole; Fusidic Acid (Systemic); Haloperidol; Hydrocortisone; Lithium; Mitotane; Orphan; Oxytocin; Roaccutane; Tolbutamide

- Inducers (Moderate): Loratadine; Midazolam; Nifedipine; Omeprazole; Paxil; Pramipexole; Quetiapine; Rosuvastatin; Sildenafil; Simvastatin; Tryptophan; Zolpidem (Hypnotic Use of)

- Inducers (弱): Alprazolam; Amiodarone; Amoxicillin; Atorvastatin; Clonazepam; Codeine; Concerta; Diltiazem; Dobutamine; Domperidone; Etoricoxib; Fosphenytoin; Gabapentin; Hydralazine; Lamotrigine; Lamotrigrine; Levothyroxine; Lisinopril; Lisdexamfetamine; Lioton; Lurasidone; Metolazone; Metoprolol; Mesalamine; Mexiletine; Modafinil; Nisoldipine; Olanzapine; Opiates; Phenytoin; Prazosin; Prochlorperazine; Quetiapine; Ritalin; Rosuvastatin; Saxagliptin; Sertindole; Sinemet; Somatropin; Spironolactone; St. John’s Wort; Telmisartan; Topiramate; Valproic Acid; Vortioxetine

- Inhibitors (Strong): Cimetidine; Darapladib; Enalapril; Etoradiral; Fosphenytoin; Lasix; Lurasidone; Metoprolol; Midazolam; Omeprazole; Opiates; Phenytoin; Pramipexole; Prazosin; Quetiapine; Ritalin; Rosuvastatin; Sertindole; Sinemet; Spironolactone; St. John’s Wort; Telmisartan; Topiramate; Vortioxetine; Zopiclone

- Inhibitors (Weak): Amlodipine; Diltiazem; Enalapril; Losartan; Nitrofurantoin; Omeprazole; Opiates; Phenytoin; Propranolol; Quetiapine; Ritalin; Rosuvastatin; Sertindole; Sinemet; Spironolactone; St. John’s Wort; Telmisartan; Topiramate; Vortioxetine; Zopiclone

- P-Glycoprotein: Pimavanserin

- Transporter: OATP1B1/1B3

- Transporter: OCT2

- Transporter: OAT3

- Transporter: OCT1

- Transporter: OCT3

- Transporter: ABCC1

- Transporter: ABCG2

Note: Variability may occur 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.

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