WAYLIVRA® ▼ (volanesorsen sodium) 285 mg solution for injection in pre-filled syringe - Prescribing Information for United Kingdom

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Composition: Each ml contains 200 mg volanesorsen sodium, equivalent to 190 mg volanesorsen. Each single-dose pre-filled syringe contains 285 mg of volanesorsen in 1.5 ml solution.

Indication: As an adjunct to diet in adults with genetically confirmed familial chylomicronaemia syndrome (FCS) and at high risk for pancreatitis, in whom response to diet and triglyceride lowering therapy has been inadequate.

Dosage and administration: WAYLIVRA treatment should be initiated and remain under the supervision of a physician experienced in FCS. Secondary causes of hypertriglyceridemia should be excluded or appropriately addressed prior to initiation of treatment. Recommended starting dose is 285 mg in 1.5 ml administered subcutaneously once weekly for 3 months, after which dose frequency should be reduced to 285 mg once every 2 weeks. Treatment should be discontinued in patients with a reduction in serum triglycerides of <25% or who fail to achieve serum triglycerides below 22.6 mmol/L after 3 months on 285 mg weekly. After 6 months, an increase in dose frequency to 285 mg weekly should be considered if serum triglyceride reduction is inadequate and platelet counts are in the normal range. Patients should be re-downtitrated to 285 mg every 2 weeks if the higher 285 mg once weekly dose does not provide significant additional triglyceride reduction after 9 months. Injections should be administered on the same day of the week according to the medically determined frequency of administration. Missed doses: Missed doses noticed within 48 hours should be given as soon as possible. If not noticed within 48 hours, the missed dose should be skipped, and the next planned injection given. Platelet monitoring and dose adjustments: Refer to the SmPC for WAYLIVRA monitoring and treatment recommendations. Before initiation of treatment, platelet count should be measured. If the platelet count is below 140×10^9/L, another measurement should be taken approximately a week later to reassess. If the platelet count remains below 140×10^9/L upon a second measurement, WAYLIVRA should not be initiated. Patients on WAYLIVRA should have their platelet counts monitored at least every 2 weeks, depending on the platelet levels. If a platelet count of 100 to 139 $\times 10^9$/L is recorded, the frequency of platelet monitoring should be increased to every week. Treatment should be paused for at least 4 weeks if a platelet count lower than 100×10^9/L is recorded and treatment should not be restarted until the platelet level has reached $\geq 100 \times 10^9$/L. Platelet monitoring should be undertaken every week for patients with platelet counts in the range of 75 to 99 $\times 10^9$/L or every 2–3 days for patients with platelet counts in the range 50 to 74 $\times 10^9$/L. Treatment should be discontinued in patients with a platelet count $<50 \times 10^9$/L and glucocorticoids recommended with daily platelet monitoring. For any patient whose dose has been paused or treatment discontinued due to severe thrombocytopenia, the benefits and risks of returning to treatment once a platelet count $\geq 100 \times 10^9$/L should be carefully considered. For discontinued patients, a haematologist should be consulted prior to resuming treatment. Elderly: No starting dose adjustment is needed. Limited data exist for patients aged 65 years and over. Renal impairment: No starting dose adjustment is needed in mild to moderate renal impairment. Limited data exist for patients with severe renal impairment and should be closely observed on treatment. Hepatic impairment: No dose adjustment is expected to be required. Paediatric use: No data are available in children and adolescents below 18 years of age. Method of administration: Subcutaneous use only. Patients and/or caregivers should be trained in subcutaneous administration of WAYLIVRA. The first injection administered by a patient/caregiver should be performed under the guidance of an appropriately qualified healthcare professional. Injection sites include the abdomen, upper thigh, outer area of upper arm. If injected in the upper arm, the injection should be administered by another person. Rotate injection sites. Avoid tattoos, moles, birthmarks, bruises, rash or areas where the skin is tender, red, hard, bruised, damaged, burned or inflamed and the waistline or other sites where pressure or rubbing may occur from

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Suite 2, Riverside 3
Granta Park
Great Abington
Cambridgeshire
CB21 6AD

clothing. Remove from refrigeration at least 30 minutes before use and allow syringe to reach room temperature prior to injection. Do not use other warming methods. It is normal to see a large air bubble; there should be no attempt to remove this.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, chronic or unexplained thrombocytopenia. Treatment should not be initiated if platelet count <140 $\times 10^9$/L.

Special warnings and precautions for use: Thrombocytopenia: WAYLIVRA is very commonly associated with reductions in platelet count, which may result in thrombocytopenia. Lower body weight (less than 70 kg) may increase risk. Follow the SmPC recommendations for adjustments to frequency of platelet monitoring and dosing as necessary. Consider discontinuation of antiplatelet medicinal products/NSAIDs/anticoagulants for platelet levels < 75 $\times 10^9$/L; discontinue treatment with these products at platelet levels < 50 $\times 10^9$/L. Advise patients to report any signs of bleeding to their physician immediately, including petechiae, spontaneous bruising, subconjunctival bleeding, or other unusual bleeding (including nosebleeds, bleeding from gums, stools, or unusually heavy menstrual bleeding), neck stiffness, atypical severe headache, or any prolonged bleeding. LDL-C levels: With WAYLIVRA treatment, LDL-C levels may rise but will usually remain within the normal range. Renal toxicity: Renal toxicity has been observed after administration of WAYLIVRA. Monitor patients for evidence of nephrotoxicity by routine urine dipstick quarterly. In the case of a positive assessment, broader assessment of renal function is required as per SmPC. Discontinue treatment if proteinuria is ≥ 500 mg/24 hours, or a ≥ 0.3 mg/dL (26.5 µmol/L) increase in serum creatinine that is over the upper limit of normal (ULN) is recorded, or if creatinine clearance is ≤ 30 mL/min/1.73 m^2. Discontinue treatment if there are any clinical symptoms or signs of renal impairment pending confirmatory assessments. Hepatotoxicity: Monitor hepatotoxicity through serum liver enzymes and bilirubin quarterly. Discontinue treatment if there is a single increase in alanine transaminase (ALT) or aspartate aminotransferase (AST) > 8 × ULN, or an increase > 5 × ULN that persists for ≥ 2 weeks, or lesser increases in ALT or AST that are associated with total bilirubin > 2 × ULN or international normalised ratio (INR) > 1.5. Discontinue treatment if there are any clinical symptoms or signs of hepatic impairment or hepatitis. Immunogenicity and inflammation: No evidence of altered safety profile or clinical response was associated with presence of anti-drug antibodies. If formation of anti-drug antibodies with a clinically significant effect is suspected, contact the Marketing Authorisation Holder to discuss antibody testing. Monitoring of inflammation should be assessed through quarterly assessment of erythrocyte sedimentation rate (ESR). Sodium content: This medicine contains less than 1 mmol sodium (23 mg) per dose, it is essentially 'sodium-free'. Refer to SmPC section 4.4 for full warnings and precautions.

Interactions: No clinical drug interaction studies have been conducted. Clinically relevant interactions are not expected between WAYLIVRA and substrates, inducers, or inhibitors of cytochrome P450 (CYP) enzymes and drug transporters. No adverse events related to drug–drug interactions were reported during the clinical programme. Discontinue hepatotoxic medicinal products if signs and symptoms of hepatotoxicity develop. Risk of increased bleeding with concomitant use of WAYLIVRA and antithrombotic agents or products that lower platelet count is not known. Discontinuation of such products should be considered if platelet levels reduce to <75 $\times 10^9$/L and stopped if platelets reach < 50 $\times 10^9$/L.

Fertility, pregnancy and lactation: There are no data on the use of WAYLIVRA in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use WAYLIVRA during pregnancy. It is unknown whether WAYLIVRA or metabolites are excreted in human milk. A risk to the newborn infant cannot be excluded. A decision must be made whether to discontinue breastfeeding or discontinue/abstain from WAYLIVRA taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

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Undesirable effects: Please consult SmPC section 4.8 for the full list of possible adverse effects. The adverse reactions at least possibly related to treatment are listed below as very common (≥1/10) and common (≥1/100 to <1/10). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Very common adverse reactions: Thrombocytopenia, headache, myalgia, injection site reactions (erythema/pain/swelling/discolouration/induration/pruritus/ bruising/oedema), chills, injection site oedema, platelet count decreased. Common adverse reactions: Leukopenia, lymphopenia, eosinophilia, immune thrombocytopenic purpura, spontaneous haematoma, immunisation reaction, hypersensitivity serum sickness-like reaction, diabetes mellitus, insomnia, syncope, hypoaesthesia, presyncope, retinal migraine, dizziness, tremor, conjunctival haemorrhage, vision blurred, hypertension, haemorrhage, haematoma, hot flush, dyspnoea, pharyngeal oedema, wheezing, epistaxis, cough, nasal congestion, nausea, diarrhoea, vomiting, abdominal distension and pain, dry mouth, gingival bleeding, mouth haemorrhage, parotid gland enlargement, dyspepsia, gingival swelling, erythema, pruritus, rash, urticaria, hyperhidrosis, petechiae, ecchymosis, night sweats, papule, skin hypertrophy, swelling face, arthralgia, pain in extremity, arthritis, musculoskeletal pain, back pain, neck pain, pain in jaw, muscle spasms, joint stiffness, myositis, peripheral arthritis, haematuria, proteinuria, injection site haematoma, asthenia, fatigue, injection site reaction, pyrexia, injection site (hypoaesthesia/haemorrhage/warmth/ dryness/pallor/urticaria/vesicles), malaise, feeling hot, influenza-like illness, injection site (discomfort/inflammation/mass), oedema, pain, injection site (paraesthesia/scab/papule/rash), non-cardiac chest pain, vessel puncture site haemorrhage, haemoglobin decreased, white blood cell decreased, blood creatinine increased, blood urea increased, creatinine renal clearance decreased, hepatic enzyme increased, INR increased, transaminases increased, contusion. For uncommon adverse reactions consult the SmPC section 4.8.
Legal Category: Prescription Only Medicine (POM). **Marketing Authorisation No.:** PLGB 51704/003. **Pack size:** one pre-filled syringe. **Price:** NHS List Price £11,394.00. **Marketing Authorisation Holder:** Akcea Therapeutics Ireland Ltd. **Local Representative:** Swedish Orphan Biovitrum (UK) Ltd, Suite 2, Riverside 3, Granta Park, Great Abington, Cambridgeshire, CB21 6AD. **Date of Preparation:** January 2025 **Company Reference:** PP-25252.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Swedish Orphan Biovitrum Ltd at medical.info.uk@sobi.com or Telephone +44 (0) 800 111 4754.

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