Prescribing Information: Waylivra▼ (volanesorsen 285 mg solution for injection in pre-filled syringe)
Consult Summary of Product Characteristics (SmPC) before prescribing
Indications: 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: Treatment should be initiated and supervised by a physician experienced in FCS. 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. 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 down titrated to 285 mg every 2 weeks if there is no 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, a missed dose should be skipped, and the next planned injection given. *Platelet monitoring and dose adjustments:* Before initiation of treatment, platelet count should be measured. If the platelet count is below 140 x 10^9/L, another measurement should be taken approximately a week later to reassess. If the platelet count remains below 140 x 10^9/L upon a second measurement, Waylivra should not be initiated. Patients on Waylivra should have their platelet counts monitored every 2 weeks. If a platelet count of 100 to 139 x10^9/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 x 10^9/L is recorded and treatment should not be restarted until the platelet level has reached ≥100x10^9/L. Platelet monitoring should be undertaken every week for patients with platelet counts in the range of 75 to 99 x 10^9/L or every 2–3 days for patients with platelet counts in the range 50 to 74 x 10^9/L. Treatment should be discontinued in patients with a platelet count <50 x 10^9/L. For any patient dose paused or discontinued due to severe thrombocytopenia, the benefits and risks of returning to treatment once a platelet count ≥100 x 10^9/L should be carefully considered. For discontinued patients, a haematologist should be consulted prior to resuming treatment. *Elderly:* Limited data exist for patients aged 65 years and over. *Renal impairment:* Limited data exist for patients with severe renal impairment; patients with severe renal impairment should be closely observed on treatment. *Hepatic impairment:* Waylivra is not metabolised via the cytochrome P450 enzyme system; 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 under the guidance of an appropriately qualified healthcare professional. Injection sites include the abdomen, upper thigh, outer area of upper arm. Rotate injection sites. Avoid tattoos, scars, birthmarks, rash or injured skin. 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 active substance or excipients, chronic or unexplained thrombocytopenia. Treatment should not be initiated if platelet count <140 x 10^9/L. **Warnings and precautions:** Consult SmPC for full details. **Thrombocytopenia:** Waylivra is very commonly associated with reductions in platelet count, which may result in thrombocytopenia. Lower body weight (≤70kg) 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 x 10^9/L; discontinue treatment with these products at platelet levels <50 x 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:** Monitor patients for evidence of nephrotoxicity by routine urine dipstick quarterly. In the case of a positive result, broader assessment of renal function is required. Discontinue treatment if proteinuria is ≥500 mg/24 hours, 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:** Assess 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 x ULN, an increase >5 x ULN that persists for ≥2 weeks, or lesser increases in ALT or AST that are associated with total bilirubin >2 x ULN or international normalised ratio >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). **Interactions:** No clinical drug interaction studies have been conducted. Clinically relevant interactions are not expected between volanesorsen and substrates, inducers or inhibitors of cytochrome P450 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 antithrombotics or products that lower platelet count is not known. Discontinuation of such products should be considered if platelet levels reduce to <75 x 10^9/L and stopped if platelets reach <50 x 10^9/L. **Pregnancy and lactation:** Avoid the use of Waylivra in pregnancy. Decision to be made whether to discontinue breastfeeding or discontinue Waylivra during lactation, taking into account the relative benefits for the woman and child. **Undesirable effects:** Consult SmPC for full details. Very common (≥1/10): thrombocytopenia, injection-site reactions, platelet-count reductions. Common (≥1/100 to <1/10): leukopenia, eosinophilia, immune thrombocytopenic purpura, spontaneous haematoma, immunisation reaction, hypersensitivity, serum sickness-like reaction, diabetes mellitus, insomnia, headache, hypoaesthesia, presyncope, retinal migraine, syncope, dizziness, tremor, conjunctival haemorrhage, vision blurred, haematoma, hypertension, haemorrhage, hot flush, epistaxis, cough, dyspnoea, nasal congestion, pharyngeal oedema, wheezing, gastrointestinal disorders including nausea, diarrhoea, vomiting and abdominal pain, skin and subcutaneous disorders including erythema, pruritis, rash and urticaria, musculoskeletal and connective tissue disorders including myalgia, arthralgia and pain in extremities, renal and urinary disorders including haematuria and proteinuria, general disorders including asthenia and fatigue, and changes in lab parameters including renal, hepatic and haematological, and contusion.
Legal Category: POM
Package Quantities and Basic NHS Price: £11,394.00
Marketing Authorisation Holder: Akcea Therapeutics Ireland Ltd, Regus House,
Harcourt Centre, Harcourt Road
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Marketing Authorisation Number: EU/1/18/1296/001, EU/1/18/1296/002
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Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/
Adverse events should also be reported to Akcea Therapeutics UK Ltd
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