TEGSEDI® (inotersen) 284 mg solution for injection in pre-filled syringe - Prescribing Information for United Kingdom & Republic of Ireland

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

Composition: Each ml contains 189 mg inotersen (as inotersen sodium). Each pre-filled syringe contains 284 mg inotersen (as inotersen sodium) in 1.5 mL of solution.

Indication: Treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis (hATTR).

Dosage and administration: Treatment should be initiated by and remain under the supervision of a physician experienced in the treatment of hATTR. Recommended dose is 284 mg administered subcutaneously once per week, on the same day every week. Dose adjustment in case of reduction in platelet count: TEGSEDI is associated with reductions in platelet count, which may result in thrombocytopenia. Frequency of monitoring and dosing should be adjusted where platelet count is below 100×10^9/L. Treatment should be discontinued, and corticosteroids are recommended if platelet count is below 25×10^9/L. See SmPC for full recommendations on TEGSEDI dosing adjustments and platelet count monitoring frequency. Missed doses: If a dose is missed, administer the next dose as soon as possible unless it is scheduled within 2 days, in which case skip the missed dose and administer the next dose as scheduled. Elderly: No dose adjustment required. Renal impairment: No dose adjustment required in mild or moderate renal impairment. TEGSEDI should not be used in patients with a urine protein to creatinine ratio (UPCR) ≥ 113 mg/mmol (1 g/g) or estimated glomerular filtration rate (eGFR) < 45 ml/min/1.73m^2. Monitor UPCR and eGFR during treatment. If acute glomerulonephritis is confirmed, consider permanent treatment discontinuation. Hepatic impairment: No dose adjustment required for mild or moderate hepatic impairment. TEGSEDI must not be used in patients with severe hepatic impairment. Patients undergoing liver transplant: Discontinue dosing in patients undergoing liver transplantation. 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 TEGSEDI. The first injection administered by a patient/caregiver should be under 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 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.

Contraindications: Hypersensitivity to the active substance or to any of the excipients, platelet count < 100×10^9/L prior to treatment, UPCR ≥ 113 mg/mmol (1 g/g) prior to treatment, eGFR < 45 ml/min/1.73m^2, severe hepatic impairment.

Special warnings and precautions for use: Thrombocytopenia: TEGSEDI is associated with reductions in platelet count, which may result in thrombocytopenia at any time during treatment. Monitor platelet count every 2 weeks during the entire course of treatment and for 8 weeks following treatment discontinuation. Follow recommendations for adjustments to frequency of monitoring and dosing as necessary. Advise patients to immediately report any signs of unusual or prolonged bleeding (e.g. petechia, spontaneous bruising, subconjunctival bleeding, nosebleeds, bleeding from the gums, blood in urine or stools, bleeding in the whites of eyes), neck stiffness or atypical severe headache because these symptoms may be caused by bleeding in the brain. Use with caution in elderly patients, those taking antithrombotic or antiplatelet/platelet-lowering medicines and those with prior history of major bleeding events. Glomerulonephritis/renal function decline: Glomerulonephritis and renal function decline without signs of glomerulonephritis have been seen in some patients. Monitor UPCR and eGFR every 3 months or more frequently, as clinically indicated, based on history of chronic kidney disease and/or renal amyloidosis. Monitor UPCR and eGFR for 8 weeks following treatment

SWEDISH ORPHAN BIOVITRUM LTD
Suite 2, Riverside 3
Granta Park
Great Abington
Cambridgeshire
CB21 6AD

discontinuation. If repeated UPCR is more than or equal to twice the upper limit of normal or eGFR < 60 ml/min, which has no alternative explanation, monitor every 4 weeks. Consider pausing dosing if there is a decrease in eGFR >30% with no alternative explanation. If repeated UPCR is ≥ 2 g/g (226 mg/mmol), pause dosing and evaluate for acute glomerulonephritis. Permanently discontinue TEGSEDI if acute glomerulonephritis is confirmed. If glomerulonephritis is excluded, resume dosing if clinically indicated and renal function has improved. Consider early initiation of immunosuppressive therapy if glomerulonephritis is confirmed. Use caution with nephrotoxic medicines or those that may impair renal function. Vitamin A deficiency: TEGSEDI is expected to reduce plasma vitamin A (retinol) below normal levels. Before TEGSEDI initiation, correct levels below the lower limit of normal and ensure any ocular symptoms or signs of vitamin A deficiency have resolved. Oral supplementation of approximately 3000 IU per day of vitamin A should be taken to reduce potential risk of ocular toxicity. Refer for ophthalmological assessment if patients develop ocular symptoms consistent with vitamin A deficiency, e.g., reduced night vision or night blindness, persistent dry eyes, eye inflammation, corneal inflammation or ulceration, corneal thickening, corneal perforation. Liver monitoring and drug-induced liver injury: Elevated transaminases occur commonly in patients. Serious cases of drug induced liver injury (DILI) have also been reported, including cases with a long time to onset (up to 1 year). Liver function should be assessed before initiating treatment with TEGSEDI. Measure hepatic enzymes 4 months after initiation of treatment and at least annually or more frequently as clinically indicated thereafter. Prompt clinical evaluation and measurement of liver function tests should be performed preferably within 72 hours in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine or jaundice. Dose interruption should be considered until clinical and liver function evaluation is performed. If a patient is suspected to have developed liver injury induced by TEGSEDI, it should be permanently discontinued. Liver transplant rejection: Cases of liver transplant rejection have been reported in patients treated with TEGSEDI. Patients with a prior liver transplant should be monitored for signs and symptoms of transplant rejection during treatment with TEGSEDI. In these patients, liver function tests should be performed monthly. Discontinuation of TEGSEDI should be considered in patients who develop liver transplant rejection. Precautions prior to initiation of TEGSEDI: Prior to initiation, measure platelet count, eGFR, UPCR, hepatic enzymes, pregnancy and vitamin A levels. Transient increases of CRP and platelet levels may occur in some patients after initiation of TEGSEDI. This reaction typically resolves spontaneously after a few days of treatment. 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: Caution should be used with antithrombotic medicinal products, antiplatelet medicinal products and other medicines that may lower platelet count, for example, acetylsalicylic acid, clopidogrel, warfarin, heparin, low-molecular weight heparins, Factor Xa inhibitors such as rivaroxaban and apixaban, and thrombin inhibitors such as dabigatran. Caution should be exercised with concomitant use of nephrotoxic products and other medicines that may impair renal function, such as sulfonamides, aldosterone antagonists, anilides, natural opium alkaloids and other opioids. A systematic assessment of co-administration of TEGSEDI and potentially nephrotoxic medicinal products has not been conducted.

Fertility, pregnancy and lactation: There are no or limited data on the use of TEGSEDI in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Pregnancy should be excluded before initiation of TEGSEDI and effective contraception should be in place. TEGSEDI should not be used in pregnancy, unless required by clinical condition of the woman. TEGSEDI and vitamin A supplementation should be discontinued, and vitamin A levels should have returned to normal before conception is attempted. In the event of unplanned pregnancy, discontinue TEGSEDI. Vitamin A deficiency may develop after cessation of treatment. No recommendation can be given whether to continue/discontinue vitamin A supplementation during the first trimester. If treatment with TEGSEDI

is continued, the daily dose should not exceed 3000 IU/day. 3000 IU/day should be resumed in the second and third trimester if plasma retinol levels have not yet returned to normal due to increased risk of vitamin A deficiency in the third trimester. A decision must be made whether to discontinue breastfeeding or discontinue/abstain from TEGSEDI taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman.

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 drug reactions are presented in order of decreasing seriousness. Very common: thrombocytopenia, anaemia, platelet count decreased, headache, vomiting, nausea, pyrexia, chills, injection site reactions, peripheral oedema. Common: eosinophilia, decreased appetite, orthostatic hypotension, hypotension, haematoma, transaminases increased, pruritus, rash, glomerulonephritis, proteinuria, renal failure, acute kidney injury, renal impairment, influenza-like illness, peripheral swelling, injection site discolouration, contusion. For uncommon adverse reactions consult the SmPC section 4.8.

Legal Category: Prescription Only Medicine (POM). **Marketing Authorisation Nos.:** PLGB 51704/0002 and EU/1/18/1296/001-002. **Pack size:** 4 pre-filled syringes. **Price:** NHS List Price £23,700. Eire List Price available on request. **Marketing Authorisation Holder:** Akcea Therapeutics Ireland Ltd, Ireland. **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-25251.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard (for United Kingdom) and www.hpra.ie (for Republic of Ireland). Adverse events should also be reported to Swedish Orphan Biovitrum Ltd at medical.info.uk@sobi.com or Telephone +44 (0) 800 111 4754.

SWEDISH ORPHAN BIOVITRUM LTD
Suite 2, Riverside 3
Granta Park
Great Abington
Cambridgeshire
CB21 6AD