Prescribing Information: Tegsedi ▼
(inotersen 284 mg solution for injection in pre-filled syringe)

Consult Summary of Product Characteristics (SmPC) before prescribing

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

Dosage and administration: Treatment should be initiated and supervised by a physician experienced in 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 $100x10^9$/L. Treatment should be discontinued and corticosteroids are recommended if platelet count is below $25x10^9$/L. See SmPC for full recommendations. *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. *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:* Tegsedi must not be used in patients with severe hepatic impairment. 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 health care professional. Injection sites include abdomen, upper thigh, outer area of upper arm. Rotate injection sites. Avoid tattoos, scars, areas of skin disease or injury. 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 active substance or excipients, platelet count < 100 x 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.

Warnings and precautions: Consult SmPC for full details. Tegsedi is associated with reductions in platelet count, which may result in thrombocytopenia. Monitor platelet count every 2 weeks during 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), neck stiffness or atypical severe headache. Use caution in elderly patients, those taking antithrombotic or antiplatelet/platelet-lowering medicines and those with history of major bleeding events. 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 discontinuation. If repeated UPCR is ≥ 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. 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. night blindness, eye inflammation, corneal thickening. Measure hepatic enzymes 4 months after initiation of treatment and at least annually thereafter. Cases of liver transplant rejection have been reported in patients treated with Inotersen. Patients should be monitored for signs and symptoms of transplant rejection during treatment with Inotersen. Discontinuation of Inotersen should be considered in patients who develop liver transplant rejection. Prior to initiation, measure platelet count, eGFR, UPCR and hepatic enzymes. Contains sodium.

Interactions: Use with caution with antithrombotics, antiplatelet products, products that may lower platelet count, nephrotoxic products and other products that may impair renal function.

Pregnancy and lactation: Not to be used in pregnancy, unless required by clinical condition of the woman. Exclude pregnancy before initiation. Effective contraception should be in place. Tegsedi and vitamin A supplementation should be discontinued and vitamin A levels should have returned to normal before conception is attempted. In event of unplanned pregnancy, discontinue Tegsedi. A vitamin A deficit may develop after cessation of treatment. No recommendation can be given whether to continue/discontinue vitamin A supplementation during the first trimester. If 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. Decision to be made whether to discontinue breastfeeding or discontinue Tegsedi 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, anaemia, platelet count decreased, headache, vomiting, nausea, pyrexia, chills, injection-site reactions, peripheral oedema. Common (≥ 1/100 to < 1/10): 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.

Legal Category: POM

Package Quantities and Basic NHS Price: £5,925

Marketing Authorisation Holder:
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Marketing Authorisation Number: EU/1/18/1296/001, EU/1/18/1296/002

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Date of preparation: October 2019

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
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