## UK Prescribing Information

## Revolade® (eltrombopag) 25 mg, 50 mg and 75 mg film-coated tablets.

**Important note: Before prescribing, consult Summary of Product Characteristics (SmPC).**

Each tablet contains eltrombopag olamine equivalent to 25 mg, 50 mg and 75 mg eltrombopag respectively. **Indication:** Revolade is indicated for patients aged 1 year and above with primary immune thrombocytopenia (ITP) lasting 6 months or longer from diagnosis and who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). **Dosage and administration:** Treated by physician experienced in treatment of haematological diseases. Dosing must be individualised based on the patient's platelet counts, aiming to achieve and maintain a platelet count ≥50,000/µl as necessary to reduce the risk for bleeding. *Paediatric population aged 1 to 5 years.* The recommended starting dose of eltrombopag is 25 mg once daily. *Adults and paediatric population aged 6 to 17 years:* Recommended starting dose is 50 mg once daily, for patients of Asian Ancestry, initiate at a reduced dose of 25 mg once daily. After initiation, dose should be adjusted to achieve and maintain a platelet count ≥50,000/µl as necessary. Wait for at least 2 weeks to see effect of dose adjustment on patient's platelet response prior to considering another dose adjustment. Dose is not to exceed 75 mg/day. Clinical haematology and liver tests should be monitored regularly. Full blood counts should be assessed weekly until a stable platelet count (at least 4 weeks) is achieved and monthly thereafter. *Food interaction:* Eltrombopag should be taken at least two hours before or four hours after any products such as antacids, dairy products or mineral supplements containing polyvalent cations, to avoid significant reduction in eltrombopag absorption due to chelation. *Hepatic Impairment:* Should not be used in ITP patients with hepatic impairment (Child-Pugh score ≥5) unless the expected benefit outweighs the identified risk of portal venous thrombosis. If the use of eltrombopag is deemed necessary the starting dose must be 25 mg once daily. After initiating the dose of eltrombopag wait 3 weeks before increasing the dose. *Paediatric Population <1 year old:* Revolade is not recommended for use in children under the age of one year with ITP due to insufficient data on safety and efficacy. **Contraindications:** Hypersensitivity to eltrombopag or to any of the excipients. **Warnings /Precautions:** *Hepatic effects:* Can cause abnormal liver function and severe hepatotoxicity, which might be life-threatening. Clinical studies show mostly mild (Grade 1-2), reversible increase in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin. Serum ALT, AST and bilirubin should be measured prior to eltrombopag initiation, every 2 weeks during dose adjustment and monthly on a stable dose. Abnormal serum liver tests should be repeated within 3-5 days and patients monitored until abnormalities resolve, stabilise, or return to baseline levels. Use a lower starting dose of eltrombopag and monitor closely when administering eltrombopag to patients with hepatic impairment. *Thrombotic/thromboembolic complications:* Caution should be used for patients with known risk factors for thromboembolism. Dose should be reduced or discontinued if platelet count exceeds target levels. Risk of thromboembolic events (TEEs) has been found to be increased in patients with chronic liver disease treated with 75 mg/day for 2 weeks in preparation for invasive procedures. TEEs might be expected in patients with severe aplastic anaemia. *Bleeding following discontinuation of eltrombopag:* On discontinuation of eltrombopag, platelet counts return to baseline levels in the majority of patients within 2 weeks, increasing the risk of bleeding. This risk is increased if discontinued in the presence of anticoagulants or anti-platelet agents. If discontinued, patients should restart therapy according to current treatment guidelines. *Bone marrow reticulin formation and risk of bone marrow fibrosis:* Increased risk. *Progression of existing Myelodysplastic Syndromes (MDS):* There is a concern that thrombopoietin receptor agonists (TPO-RAs) may stimulate existing haematopoietic malignancies such as MDS. In clinical studies with a TPO-RA in patients with MDS, cases of transient increases in blast cell counts were observed and cases of MDS disease progression to acute myeloid leukaemia were reported. Diagnosis of ITP should be confirmed by exclusion of other clinical entities presenting with thrombocytopenia, in particular MDS. *Cataracts:* Routine monitoring recommended. *Loss of response:* Search for causative factors. *Interference with laboratory tests:* Eltrombopag is highly coloured. Serum discolouration and interference with total bilirubin and creatinine testing have been reported. If the laboratory results and clinical observations are inconsistent, re-testing using another method may help in determining the validity of the result. **Interactions:** *Effects of eltrombopag on other medicinal products: ciclosporin - platelet count should be monitored at least weekly for 2 to 3 weeks; boceprevir* – monitor for HCV suppression; *rosuvastatin* and other *HMG-CoA reductase inhibitors:* interactions expected; *OATP1B1 and BCRP substrates:* co-administer with caution; *Cytochrome P450 substrates:* no clinically significant interactions. *Effects of other medicinal products on eltrombopag: lopinavir/ritonavir:* co-administer with caution. *Medicinal products for treatment of ITP:* platelet counts should be monitored when co-administered with other ITP treatments. **Pregnancy:** Not recommended during pregnancy and in women of childbearing potential not using contraception. Eltrombopag has negligible influence on the ability to drive and use machines. **Undesirable effects:** *Very common:* Nasopharyngitis, upper respiratory tract infection Cough, Nausea, Diarrhoea, ALT increased,. *Common:* Pharyngitis, Influenza, Oral herpes, Pneumonia, Sinusitis, Tonsillitis, Respiratory tract infection, Gingivitis, Anaemia, Eosinophilia, Leukocytosis, Thrombocytopenia, Haemoglobin decreased, White blood cell count decreased, Hypokalaemia, Decreased appetite, Blood uric acid increased, Sleep disorder, Depression, Paraesthesia, Hypoaesthesia, Somnolence, Migraine, Dry eye, Vision blurred, Eye pain, Visual acuity reduced, Ear pain, Vertigo, Deep vein thrombosis, Haematoma, Hot flush, Oropharyngeal pain, Rhinorrhoea, Mouth ulceration, Toothache, Vomiting, Abdominal pain *(very common in paediatric ITP)*, Mouth haemorrhage, Flatulence, AST increased, Hyperbilirubinaemia, Hepatic function abnormal, Rash, Alopecia, Hyperhidrosis, Pruritus generalised, Petechiae, Myalgia, Muscle spasm, Musculoskeletal pain, Bone pain, Back pain, Proteinuria, Blood creatinine increased, thrombotic microangiopathy with renal failure, Menorrhagia, Pyrexia *(very common in paediatric ITP)*, Chest pain, Asthenia, Blood alkaline phosphatase increased. *Uncommon:* Skin infection, Rectosigmoid cancer, Anisocytosis, Haemolytic anaemia, Myelocytosis, Haemoglobin increased, Band neutrophil count increased, Myelocyte present, Platelet count increased, Hypersensitivity, Anorexia, Gout, Hypocalcaemia, Apathy, Mood altered, Tearfulness, Tremor, Balance disorder, Dysaesthesia, Hemiparesis, Migraine with aura, Neuropathy peripheral, Peripheral sensory neuropathy, Speech disorder, Toxic neuropathy, Vascular headache, Lenticular opacities, Astigmatism, Cataract cortical, Lacrimation increased, Retinal haemorrhage, Retinal pigment epitheliopathy, Visual impairment, Visual acuity tests abnormal, Blepharitis and Keratoconjunctivitis sicca, Tachycardia, Acute myocardial infarction, Cardiovascular disorder, Cyanosis, Sinus tachycardia, Electrocardiogram QT prolonged, Embolism, Thrombophlebitis superficial, Flushing, Pulmonary embolism, Pulmonary infarction, Nasal discomfort, Oropharyngeal blistering, Sinus disorder, Sleep apnoea syndrome, Dry mouth, Glossodynia, Abdominal tenderness, Faeces discoloured, Food poisoning, Frequent bowel movements, Haematemesis, Oral discomfort, Cholestasis, Hepatic lesion, Hepatitis, Drug-induced liver injury, Urticaria, Dermatosis, Cold sweat, Erythema, Melanosis, Pigmentation disorder, Skin discolouration, Skin exfoliation, Muscular weakness, Renal failure, Leukocyturia, Lupus nephritis, Nocturia, Blood urea increased, Urine protein/creatinine ratio increased, Feeling hot, Vessel puncture site haemorrhage, Feeling jittery, Inflammation of wound, Malaise, Sensation of foreign body, Blood albumin increased, Protein total increased, Blood albumin decreased, pH urine increased, Sunburn, Prescribers should consult the summary of product characteristics for information on other adverse reactions. **Overdose:** Platelet counts may increase excessively resulting in thrombotic/thromboembolic complications. In case of overdose, oral administration of a metal cation-containing preparation, such as calcium, aluminium, or magnesium preparations to chelate eltrombopag can limit absorption.

**Legal classification:** POM

**Marketing Authorisation (MA) number, quantities and NHS price:**

EU/1/10/612/002 – 25 mg x 28 tablet pack £770

EU/1/10/612/005 – 50 mg x 28 tablet pack £1540

EU/1/10/612/008 – 75 mg x 28 tablet pack £2310

**Date of last revision of prescribing information**: May 2020

**Full Prescribing Information available from**: Novartis Pharmaceuticals UK Ltd, 2nd Floor, The WestWorks Building, White City Place, 195 Wood Lane, London, W12 7FQ. Tel: 01276 692255.

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**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 Novartis via uk.patientsafety@novartis.com or online through the patient safety information (PSI) tool at https://psi.novartis.com**

**If you have a question about the product, please contact Medical Information on 01276 698370 or by email at medinfo.uk@novartis.com**