NOVARTIS

REVOLADE®(eltrombopag olamine)

25 mg, 50 mg Film-coated tablets

Basic Succinct Statement (BSS)

Code: BSS RD 17 JUN 2019; APPR 16 APR 2020

This material is only meant for Healthcare Professionals

REVOLADE®

Important note: Before prescribing, consult full prescribing information.

Presentation: ♦Film-coated tablets containing eltrombopag olamine equivalent to 25 mg or 50 mg of eltrombopag free acid.

Indications: ♦Indicated for the treatment of patients aged 6 years and above with primary immune thrombocytopenic (ITP) lasting 6 months or longer from diagnosis and who are refractory to other treatments (e.g. corticosteroids, immunoglobulins). ♦Indicated in adult patients with chronic hepatitis C virus (HCV) infection for the treatment of thrombocytopenia, where the degree of thrombocytopenia is the main factor preventing the initiation or limiting the ability to maintain optimal interferon-based therapy. ♦Indicated in adult patients with acquired severe aplastic anemia (SAA) who were either refractory to prior immunosuppressive therapy or heavily pretreated and are unsuitable for hematopoietic stem cell transplantation.

Dosage and administration: ♦Dosing regimens individualized based on platelet counts. ♦Dose regimen for ITP, HCV and SAA: Starting dose between 25 to 50 mg once daily. Maintenance doses with maximum daily doses between 75 to 150 mg depending on patient population and indication.

Special populations: ♦**Renal impairment**: Caution, close monitoring. ♦**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. Caution and close monitoring, starting dose 25 mg once daily (ITP, HCV, SAA). ♦**Pediatric age group**: The safety and efficacy of Revolade have not been established in paediatric ITP patients younger than one year. In paediatric clinical trials, subjects between 1 to 5 years of age were administered Revolade as a powder for oral suspension formulation. Revolade is only available as tablets and cannot be used in patients who are unable to swallow Revolade tablets whole. The safety and efficacy of Revolade in paediatric patients with chronic HCV related thrombocytopenia or SAA have not been established. ♦**Elderly**: No clinically significant differences in safety.

Contraindications: ♦ Hypersensitivity to Revolade or to any of the excipients.

Warnings and precautions: ♦**Hepatoxicity**: Can cause hepatobiliary abnormalities, severe hepatotoxicity, which might be life-threatening. ALT, AST, bilirubin measurement prior initiation, every 2 weeks during dose adjustment and monthly following establishment of stable dose. Discontinuation if ALT ≥3 x ULN in patients with normal liver function, or ≥3 x baseline (or >5 x ULN, whichever is the lower) in patients with elevations in transaminases before treatment and if progressive, persistent for ≥4 weeks, accompanied by increased direct bilirubin, or accompanied by symptomatic liver injury/evidence for hepatic decompensation. Cautious administration to patients with hepatic disease. Lower starting dose in ITP and SAA patients with hepatic impairment. ♦**Hepatic decompensation (use with interferon)**: Chronic HCV patients with cirrhosis may be at risk for hepatic decompensation, some with fatal

outcomes, when receiving alpha interferon therapy. Greater risk in patients with low albumin levels (<35 g/l) or with MELD score ≥10 at baseline. Close monitoring of such patients for signs and symptoms of hepatic decompensation. Treatment stop at discontinuation of antiviral therapy. ♦**Thrombotic/thromboembolic complications**: Cautious use in patients with risk factors for thromboembolism (e.g., Factor V Leiden, ATIII deficiency, antiphospholipid syndrome). Monitoring of platelet counts and potentially dose reduction or discontinuation if platelet count exceeds target level. Not indicated for the treatment of thrombocytopenia in patients with chronic liver disease in preparation for invasive procedures. ♦**Increased bleeding risk after discontinuation of treatment**: Following discontinuation, platelet counts return to baseline levels within 2 weeks in the majority of patients. Increased bleeding risk; bleeding in some cases. Monitoring weekly for 4 weeks following discontinuation. ♦**Malignancies and progression of malignancies**: Theoretical concern of stimulation of progression of existing hematological malignancies such as myelodysplastic syndrome (MDS) by TPO-R agonists. Effectiveness and safety not established for treatment of thrombocytopenia due to MDS. Not to be used outside of clinical trials for treatment of thrombocytopenia due to MDS. ♦**Cataracts**: Routine monitoring. ♦**Interference with serological testing:** Potential to interfere with some laboratory tests. Serum discoloration and interference with total bilirubin/creatinine testing reported. Re-testing using another method may help in determining the validity of the result.

Adverse drug reactions (by highest reporting frequency of any subpopulation):

Adult ITP study population: ♦ Very common (≥10%): Nausea, alanine aminotransferase increased ♦**Common (1 to 10%):** 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, mouth ulceration, vomiting, abdominal pain, mouth haemorrhage, flatulence, aspartate aminotransferase 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, chest pain, asthenia, blood alkaline phosphatase increased.
Pediatric ITP study population (1 to 17 years of age)- Additional Adverse drug reactions: Very common (≥10%): Nasopharyngitis, upper respiratory tract infection, cough, diarrhoea, abdominal pain, pyrexia. **Common (1 to 10%):** Rhinorrhoea, toothache.
HCV study population: ♦Very common (≥10%): Anemia, decreased appetite, headache, cough, nausea, diarrhea, pruritus, myalgia, fatigue, pyrexia, influenza like illness, chills, asthenia. ♦**Common (1 to 10%):** Urinary tract infection, upper respiratory tract infection, bronchitis, nasopharyngitis, influenza, oral herpes, hepatic neoplasm malignant, lymphopenia, hyperglycaemia, abnormal loss of weight, depression, anxiety, sleep disorder, dizziness, disturbance in attention, dysgeusia, hepatic encephalopathy, lethargy, memory impairment, paraesthesia, cataract, retinal exudates, dry eye, ocular icterus, retinal haemorrhage, vertigo, palpitations, dyspnoea, oropharyngeal pain, dyspnoea exertional, productive cough, vomiting, ascites, abdominal pain, abdominal pain upper, dyspepsia, dry mouth, constipation, abdominal distension, toothache, stomatitis, gastrooesophagal reflux disease, haemorrhoids, abdominal discomfort, varices oesophageal, hyperbilirubinaemia, jaundice, drug-induced liver injury, rash,

dry skin, eczema, rash pruritic, erythema, hyperhidrosis, pruritus generalised, alopecia, arthralgia, muscle spasms, back pain, pain in extremity, musculoskeletal pain, bone pain, irritability, pain, malaise, injection site reaction, non-cardiac chest pain, oedema, oedema peripheral, blood bilirubin increased, weight decreased, white blood cell count decreased, haemoglobin decreased, neutrophil count decreased, international normalised ratio increased, activated partial thromboplastin time prolonged, blood glucose increased, blood albumin decreased.

SAA study population: ♦Very common (≥10%): Headache, dizziness, cough, oropharyngeal pain, rhinorrhoea, diarrhoea, nausea, gingival bleeding, abdominal pain, transaminases increased, arthralgia, muscle spasms, pain in extremity, fatigue, pyrexia, chills. **♦Common (1 to 10%):** Neutropenia, splenic infarction, iron overload, decreased appetite, hypoglycaemia, increased appetite, anxiety, depression, syncope, dry eye, cataract, ocular icterus, vision blurred, visual impairment, vitreous floaters, epistaxis, oral mucosal blistering, oral pain, vomiting, abdominal discomfort, constipation, abdominal distension, dysphagia, faeces discoloured, swollen tongue, gastrointestinal motility disorder, flatulence, blood bilirubin increased (hyperbilirubinemia), jaundice, petechiae, rash, pruritus, urticaria, skin lesion, rash macular, back pain, myalgia, bone pain, chromaturia, asthenia, oedema peripheral, malaise, blood creatine phosphokinase increased. **For a complete list of ADRs, consult full prescribing information.**