Trombola

Eltrombopag Olamine INN

Composition:
Trombola 25 Tablet: Each film coated tablet contains Eltrombopag Olamine INN equivalent to Eltrombopag 25 mg.
Trombola 50 Tablet: Each film coated tablet contains Eltrombopag Olamine INN equivalent to Eltrombopag 50 mg.

Pharmacology:
Eltrombopag is an orally bioavailable, small-molecule TPO-receptor agonist that interacts with the transmembrane domain of the human TPO-receptor and initiates signaling cascades that induce proliferation and differentiation of megakaryocytes from bone marrow progenitor cells.

Indications:
Eltrombopag is indicated for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who has had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. Eltrom should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding. Eltrom should not be used in an attempt to normalize platelet counts.

Dose & administration:
Eltrombopag dosing requirements must be individualized based on the patient's platelet counts. The objective of treatment with Eltrombopag should not be to normalise platelet counts.

Chronic immune (idiopathic) thrombocytopenia
The lowest dose of Eltrombopag to achieve and maintain a platelet count ≥ 50,000/µl should be used. Dose adjustments are based upon the platelet count response.
Adults and paediatric population aged 6 to 17 years

The recommended starting dose of Eltrombopag is 50 mg once daily.

Paediatric population aged 1 to 5 years
The recommended starting dose of Eltrombopag is 25 mg once daily.

Table 1: Dose adjustments of Eltrombopag in ITP patients

Platelet count	Dose adjustment or response
< 50,000/µl following at least 2 weeks of therapy	Increase daily dose by 25 mg to a maximum of 75 mg/day.
≥ 50,000/µl to ≤ 150,000/µl	Use lowest dose of Eltrombopag and/or concomitant ITP treatment to maintain platelet counts that avoid or reduce bleeding.
> 150,000/µl to ≤ 250,000/µl	Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments.
> 250,000/µl	Stop Eltrombopag; increase the frequency of platelet monitoring to twice weekly. Once the platelet count is ≤ 100,000/µl, reinitiate therapy at a daily dose reduced by 25 mg.

Severe aplastic anaemia
Initial dose regimen
Eltrombopag should be initiated at a dose of 50 mg once daily. The treatment should not be initiated when the patients have existing cytogenetic abnormalities of chromosome 7.

Table 2: Dose adjustments of Eltrombopag in patients with severe aplastic anaemia

Platelet count	Dose adjustment or response
< 50,000/µl following at least 2 weeks of therapy	Increase daily dose by 50 mg to a maximum of 150 mg/day. For patients taking 25 mg once daily, increase the dose to 50 mg daily before increasing the dose amount by 50 mg.
≥ 50,000/µl to ≤ 150,000/µl	Use lowest dose of Eltrombopag to maintain platelet counts.
> 150,000/µl to ≤ 250,000/µl	Decrease the daily dose by 50 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments.
> 250,000/µl	Stop Eltrombopag; for at least one week. Once the platelet count is ≤ 100,000/µl, reinitiate therapy at a daily dose reduced by 50 mg.

Chronic hepatitis C (HCV) associated thrombocytopenia
Initial dose regimen
Eltrombopag should be initiated at a dose of 25 mg once daily. No dosage adjustment is necessary for HCV patients of East Asian ancestry or patients with mild hepatic impairment.

Table 3: Dose adjustments of Eltrombopag in HCV patients during antiviral therapy

Platelet count	Dose adjustment or response
< 50,000/µl following at least 2 weeks of therapy	Increase daily dose by 25 mg to a maximum of 100 mg/day.
≥ 50,000/µl to ≤ 100,000/µl	Use lowest dose of Eltrombopag as necessary to avoid dose reductions of peg interferon.
> 100,000/µl to ≤ 150,000/µl	Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments.
> 150,000/µl	Stop Eltrombopag; increase the frequency of platelet monitoring to twice weekly.Once the platelet count is ≤ 100,000/µl, reinitiate therapy at a daily dose reduced by 25 mg.

Route of administration: Oral

Contra-indication:
Hypersensitivity to Eltrombopag or to any of the excipients.

Warning and precaution:
Combination with direct acting antiviral agents
Safety and efficacy have not been established in combination with direct acting antiviral agents approved for treatment of chronic hepatitis C infection.

Risk of hepatotoxicity
Eltrombopag administration can cause abnormal liver function. In the controlled clinical studies in chronic ITP with Eltrombopag, increases in serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin were observed. Hepatic decompensation (use with interferon) Hepatic decompensation in patients with chronic hepatitis C: Monitoring is required in patients with low low albumin levels (≤ 35 g/L) or with MELD score ≥ 10 at baseline.
In Eltrombopag clinical trials in ITP thromboembolic events were observed at low and normal platelet counts. Caution should be used when administering Eltrombopag to patients with known risk factors for thromboembolism.

Side effects:
The most common adverse reactions occurring in at least 10% of patients included: headache, dizziness, insomnia, cough, dyspnoea, oropharyngeal pain, rhinorrhoea, nausea, diarrhoea, abdominal pain, transaminases increased, ecchymosis, arthralgia, muscle spasms, pain in extremity, fatigue, febrile neutropenia, and pyrexia.

Special populations:

Renal impairment
No dose adjustment is necessary in patients with renal impairment.

Hepatic impairment
Eltrombopag 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 for ITP patients with hepatic impairment the starting dose must be 25 mg once daily. After initiating the dose of Eltrombopag in patients with hepatic impairment an interval of 3 weeks should be observed before increasing the dose.

Paediatric population:
Eltrom is not recommended for use in children under the age of one year with chronic ITP due to insufficient data on safety and efficacy.

Use in pregnancy & lactation:
Pregnancy: Eltrombopag is not recommended during pregnancy.
Women of childbearing potential / Contraception in males and females
Eltrom is not recommended in women of childbearing potential not using contraception.
Lactation: To discontinue breast-feeding or to continue/abstain from Eltrom therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Drug interaction:
HMG Co-A reductase inhibitors
Administration of Eltrombopag HMG Co-A reductase inhibitors, plasma concentration of HMG Co-A inhibitors increased. When co-administered with Eltrombopag, a reduced dose of statins should be considered and careful monitoring for statin adverse reactions should be undertaken.

Ciclosporin
Platelet count should be monitored at least weekly for 2 to 3 weeks when Eltrombopag is co-administered with ciclosporin. Eltrombopag dose may need to be increased based on these platelet counts.

Polyvalent cations (chelation)
Eltrombopag chelates with polyvalent cations such as iron, calcium, magnesium, aluminium, selenium and zinc. Administration of a single dose of Eltrombopag 75 mg with a polyvalent cation-containing antacid decreased plasma Eltrombopag. 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.

Lopinavir/ritonavir
Co-administration of Eltrombopag with lopinavir/ritonavir (LPV/RTV) may cause a decrease in the concentration of Eltrombopag. Platelet count should be closely monitored in order to ensure appropriate medical management of the dose of Eltrombopag when lopinavir/ritonavir therapy is initiated or discontinued.

Overdose:
In the event of overdose, platelet counts may increase excessively and result in thrombotic/thromboembolic complications. In case of an overdose, consideration should be given to oral administration of a metal cation-containing preparation, such as calcium, aluminium, or magnesium preparations to chelate Eltrombopag and thus limit absorption. Platelet counts should be closely monitored.

Storage:
Do not store above 25° C. Protect from light. Keep out of the reach of children.

Packaging:
Trombola 25 Tablet: Each box contains 3 x 10's tablets in blister strips.
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Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh

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