Enerplat™

Eltrombopag Olamine INN Film Coated Tablet

DESCRIPTION

Enerplat™ is a preparation of Eltrombopag Olamine, a small-molecule thrombopoietin (TPO) receptor agonist. Thrombopoietin (TPO) is the main cytokine involved in regulation of megakaryopoiesis and platelet production, and is the endogenous ligand for the TPO-R (Thrombopoietin Receptor). Eltrombopag interacts with the transmembrane domain of the human TPO-R and initiates signaling cascades that induce the proliferation and differentiation of megakaryocytes and bone marrow progenitor cells, leading to increased platelet production.

INDICATIONS

Enerplat™ is indicated:

- For the treatment of thrombocytopenia in adult and pediatric patients 1 year and older with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy. **Enerplat**™ should be used only in patients with ITP whose degree of thrombocytopenia and clinical condition increases the risk for bleeding.
- For the treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation and maintenance of interferon-based therapy. **Enerplat**™ should be used only in patients with chronic hepatitis C whose degree of thrombocytopenia prevents the initiation of interferon-based therapy or limits the ability to maintain interferon-based therapy.
- In combination with standard immunosuppressive therapy for the first-line treatment of adult and pediatric patients 2 years and older with severe aplastic anemia.
- For the treatment of patients with severe aplastic anemia who have had an insufficient response to immunosuppressive therapy.

DOSAGE AND ADMINISTRATION

Enerplat™ may be taken either without a meal or with a meal that contains low calcium (50 mg or less). It should be taken at least 2 hours before or 4 hours after any medications or products that contain polyvalent cations, such as antacids, calcium-rich foods, and mineral supplements.

- Persistent or Chronic ITP: Initiate **Enerplat**™ at a dosage of 50 mg once daily for most adult and pediatric patients aged 6 years and older, and at 25 mg once daily for pediatric patients aged 1 to 5 years. Dose reductions are necessary for patients with hepatic impairment and for some patients of East and Southeast Asian ancestry. Adjust the dosage to maintain a platelet count of at least 50 x 109/L. Do not exceed a daily dose of 75 mg.
- Chronic Hepatitis C-associated Thrombocytopenia: Initiate **Enerplat**™ at 25 mg once daily for all patients. Adjust to achieve the target platelet count required to initiate antiviral therapy. Do not exceed a daily dose of 100 mg.
- First-line Severe Aplastic Anemia: Initiate **Enerplat**™ once daily at 2.5 mg/kg (in pediatric patients aged 2 to 5 years old), 75 mg (pediatric patients aged 6 to 11 years old), or 150 mg for patients aged 12 years and older concurrently with standard immunosuppressive therapy. Reduce initial dose in patients of East-/Southeast-Asian ancestry. Modify dosage for toxicity or elevated platelet counts.
- Refractory Severe Aplastic Anemia: Initiate **Enerplat**™ at 50 mg once daily. Reduce initial dose in patients with hepatic impairment or patients of East-/Southeast-Asian ancestry. Adjust to maintain the platelet count greater than 50 x 109/L. Do not exceed 150 mg per day.

CONTRAINDICATIONS

Hypersensitivity to Eltrombopag.

SIDE EFFECTS

The most common side effects of Eltrombopag include anemia, nausea, pyrexia, increased alanine aminotransferase, cough, fatigue, headache, and diarrhea.

PRECAUTIONS AND WARNINGS

- *Hepatotoxicity:* Monitor liver function before and during therapy with Eltrombopag.
- *Increased Risk of Death and Progression of Myelodysplastic Syndromes to Acute Myeloid Leukemia.*
- *Thrombotic/Thromboembolic Complications:* Portal vein thrombosis has been reported in patients with chronic liver disease receiving Eltrombopag. Monitor platelet counts regularly.

USE IN PREGNANCY AND LACTATION

Available data from a small number of published case reports with Eltrombopag use in pregnant women are insufficient to assess any drug-associated risks for major birth defects, miscarriage, or adverse maternal or fetal outcomes. Studies in animals have shown reproductive toxicity. Eltrombopag is not recommended during pregnancy and in women of childbearing potential not using contraception.

It is not known whether Eltrombopag/metabolites are excreted in human milk. Studies in animals have shown that Eltrombopag is likely secreted into milk; therefore a risk to the suckling child cannot be excluded. A decision must be made whether to discontinue breast-feeding or to continue/abstain from Eltrombopag therapy, taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

It is not known whether Eltrombopag is excreted in human milk. Eltrombopag is not recommended for nursing mothers unless the expected benefit justifies the potential risk to the infant.

PEDIATRIC USE

The safety and efficacy of Eltrombopag have been established in pediatric patients 1 year and older with persistent or chronic ITP and in pediatric patients 2 years and older with IST-naïve severe aplastic anemia (in combination with h-ATG and cyclosporine). Safety and efficacy in pediatric patients below the age of 1 year with ITP have not been established. Safety and efficacy in pediatric patients with thrombocytopenia associated with chronic hepatitis C and refractory severe aplastic anemia have not been established.

DRUG INTERACTION

Eltrombopag interacts with various cations found in foods, including iron, calcium, aluminum, magnesium, selenium, and zinc, as well as in mineral supplements and antacids. Eltrombopag should be taken at least 2 hours before or 4 hours after any medications or products containing polyvalent cations, such as antacids, dairy products, and mineral supplements to avoid significant reduction in absorption of Eltrombopag due to chelation. Caution must be exercised when concomitantly administering Eltrombopag and drugs that are substrates of OATP1B1 (e.g., atorvastatin, bosentan, ezetimibe, fluvastatin, glyburide, olmesartan, pitavastatin, pravastatin, rosuvastatin, repaglinide, rifampin, simvastatin acid, SN-38 [active metabolite of irinotecan], valsartan) or breast cancer resistance protein (BCRP) (e.g., imatinib, irinotecan, lapatinib, methotrexate, mitoxantrone, rosuvastatin, sulfasalazine, topotecan).

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. Treatment with Eltrombopag should be reinitiated in accordance with dosing and administration recommendations.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C temperature. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Enerplat™ **50mg Tablet:** Each box contains 1 strip of 7 tablets. Each film coated tablet contains Eltrombopag Olamine INN equivalent to Eltrombopag 50 mg.

SK+F ONCOLOGY
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
TONGI, GAZIPUR, BANGLADESH
TM TRADEMARK
PM10684 V01