Avatropag 20

Avatrombopag Maleate INN

Composition:

Each film coated tablet contains Avatrombopag Maleate INN eqv. to Avatrombopag 20 mg.

Pharmacology:
Avatrombopag is an orally bioavailable, small molecule TPO receptor agonist that stimulates proliferation and differentiation of megakaryocytes from bone marrow progenitor cells, resulting in an increased production of platelets. The median time to maximal concentration (Tmax) occurred at 5 to 6 hours post-dose. Avatrombopag has an estimated mean volume of distribution (%CV) of 180 L (25%). Avatrombopag is greater than 96% bound to human plasma proteins. The mean plasma elimination half-life (%CV) of avatrombopag is approximately 19 hours (19%). The mean (%CV) of the clearance of avatrombopag is estimated to be 6.9 L/hr (29%). Avatrombopag is primarily metabolized by cytochrome P450 CYP2C9 and CYP3A4. Fecal excretion accounted for 88% of the administered dose, with 34% of the dose excreted as unchanged avatrombopag. Only 6% of the administered dose was found in urine.

Indications:
Treatment of Thrombocytopenia in Patients with Chronic Liver Disease (CLD): It is indicated for the treatment of thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
Treatment of Thrombocytopenia in Patients with Chronic Immune Thrombocytopenia (ITP): It is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia who have had an insufficient response to a previous treatment.

Dosage and administration: Recommended Dosage for Patients with Chronic Liver Disease: Table 1: Recommended Dose and Duration in Patients with Chronic Liver Disease Scheduled to Undergo a Procedure

Platelet Count	Once Daily Dose	Duration
Less than 40 X 10^9/L	60 mg (3 tablets)	5 days
40 to less than 50 10^9/L	40 mg (2 tablets)	5 days

Recommended Dosage for Patients With Chronic Immune Thrombocytopenia: Initial Dose Regimen: Begin Avatrombopag at a starting dose of 20mg (1tablet) once daily with food. Table 2: Avatrombopag Dose Adjustments for Patients with Chronic Immune Thrombocytopenia

Platelet Count	Dose Adjustment or Action
Less than 50 after at least 2 weeks of Avatrombopag x 10^9/L	Increase One Dose Level per Table 3. Wait 2 weeks to assess the effects of this regimen and any subsequent dose adjustments.
Between 200 and 400 x 10^9/L	Decrease One Dose Level per Table 3. Wait 2 weeks to assess the effects of this regimen and any subsequent dose adjustments.
Greater than 400 x 10^9/L	Stop Avatrombopag. Increase platelet monitoring to twice weekly. When platelet count is less than 150 x10^9/L, decrease One Dose Level per Table 3 and reinitiate therapy.
Less than 50 after 4 weeks of Avatrombopag 40 mg once daily x 10^9/L	Discontinue Avatrombopag.
Greater than 400 after 2 weeks of Avatrombopag 20 mg weekly x 10^9/L	Discontinue Avatrombopag.

Table 3: Avatrombopag Dose Levels for Titration in Patients with Chronic Immune Thrombocytopenia

Dose	Dose Level
40 mg Once Daily	6
40 mg Three Times a Week AND 20 mg on the Four Remaining Days of Each Week	5
20 mg Once Daily*	4
20 mg Three Times a Week	3
20 mg Twice a Week OR 40 mg Once Weekly	2
20 mg Once Weekly	1
*Initial dose regimen for all patients except those taking Moderate or Strong Dual Inducers or Moderate or Strong Dual Inhibitors of CYP2C9 and CYP3A4.	

Table 4: Avatrombopag Recommended Starting Dose for Patients with Chronic Immune Thrombocytopenia Based on Concomitant Medications

Concomitant Medications	Recommended Starting Dose
Moderate or strong dual inhibitors of CYP2C9 and CYP3A4	20 mg (1 tablet) three times a week 40 mg (2 tablets) once daily
Moderate or strong dual inducers of CYP2C9 and CYP3A4	

Or, as directed by the registered physician.

Contraindacations:
It is contraindicated in patients with hypersensitivity to Avatrombopag or any component of this product.

Precautions:
Thrombotic/Thromboembolic Complications : Avatrombopag is a thrombopoietin (TPO) receptor agonist and TPO receptor agonists have been associated with thrombotic and thromboembolic complications in patients with chronic liver disease or chronic immune thrombocytopenia. Monitor platelet counts and for thromboembolic events and institute treatment promptly.

Side effects:
In patients with chronic liver disease, the most common adverse reactions were pyrexia, abdominal pain, nausea, headache, fatigue, and edema peripheral. In patients with chronic immune thrombocytopenia, the most common adverse reactions were headache, fatigue, confusion, epistaxis, upper respiratory tract infection, arthralgia, gingival bleeding, petechiae and nasopharyngitis.

Use in Pregnancy and Lactation:
Pregnant women should be advised of the potential risk to a fetus. Females of reproductive potential should be advised to inform their prescriber of a known or suspected pregnancy.
Nursing Mother: Women should be advised not to breastfeed during treatment with Avatrombopag and for at least 2 weeks after the final dose.
Use in Child: There is no data available.

Drug interactions:
In patients starting moderate or strong dual inhibitors of CYP2C9 and CYP3A4 while receiving Avatrombopag, monitor platelet counts and adjust Avatrombopag dose as necessary.

Overdose:
There is no data available.

Storage:
Do not store above 30º C. Protect from light. Keep out of reach of children.

Packing:
Each box contains 3x10's tablets in blister pack.

Manufactured by:
ZISKA PHARMA **Ziska Pharmaceuticals Ltd.**
Kaliakoir, Gazipur, Bangladesh
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