Avatrom™

Avatrombopag Maleate INN

Jenphar Bangladesh | جنفار بنغلاديش

Composition:

Avatrom™ 20 Tablet: Each film coated tablet contains Avatrombopag Maleate INN equivalent 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. Avatrombopag does not compete with TPO for binding to the TPO receptor and has an additive effect with TPO on platelet production.

Indications:

Avatrombopag is indicated for the treatment of:

- Thrombocytopenia in adult patients with chronic liver disease who are scheduled to undergo a procedure.
- 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:* Avatrombopag dose based upon platelet count prior to procedure, orally for 5 days beginning 10 to 13 days before procedure.
- *Chronic Immune Thrombocytopenia:* Initiate Avatrombopag at 20 mg (1 tablet) once daily. Adjust the dose or frequency of dosing to maintain platelet count greater than or equal to 50×10^9/L. Do not exceed 40 mg per day.

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 x 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 20 mg (1 tablet) once daily with food.

Table 2: Avatrombopag dose adjustments for Patients with Chronic Immune Thrombocytopenia

Platelet Count	Dose Adjustment or Action
Less than 50 x 10^9/L after at least 2 weeks of Avatrombopag	• Increase one dose level per (Table 3) • Wait 2 weeks to assess the effects of this regimen & 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 x 10^9/L after 4 weeks of Avatrombopag 40 mg once daily	Discontinue Avatrombopag.
Greater than 400 x 10^9/L after 2 weeks of Avatrombopag 20 mg weekly	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 & 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
Moderate or strong dual inducers of CYP2C9 and CYP3A4	40 mg (2 tablets) once daily

Contraindications:

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

Warning and precaution:

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.

Adverse Effect:

In patients with chronic liver disease, the most common adverse reactions (≥ 3%) were pyrexia, abdominal pain, nausea, headache, fatigue, and edema peripheral. In patients with chronic immune thrombocytopenia, the most common adverse reactions (≥ 10%) were headache, fatigue, confusion, epistaxis, upper respiratory tract infection, arthralgia, gingival bleeding, petechiae and nasopharyngitis.

Use in Pregnancy and Lactation:

Pregnancy: Based on findings from animal reproduction studies, Avatrombopag may cause fetal harm when administered to a pregnant woman.
Lactation: Women should be advised not to breastfeed during treatment with Avatrombopag and for at least 2 weeks after the final dose.
Pediatric population: Safety and effectiveness in pediatric patients have not been established.

Drug interactions:

Moderate or Strong Dual Inhibitors of CYP2C9 and CYP3A4
Concomitant use with a moderate or strong dual inhibitor of CYP2C9 and CYP3A4 increases Avatrombopag AUC, which may increase the risk of Avatrombopag toxicities. Reduce the starting dosage of Avatrombopag when used concomitantly with a moderate or strong dual inhibitor of CYP2C9 and CYP3A4. In patients starting moderate or strong dual inhibitors of CYP2C9 and CYP3A4 while receiving Avatrombopag, monitor platelet counts and adjust Avatrombopag dose as necessary.
Moderate or Strong Dual Inducers of CYP2C9 and CYP3A4
Concomitant use with a moderate or strong dual inducer of CYP2C9 and CYP3A4 decreases Avatrombopag AUC, which may reduce Avatrombopag efficacy. Increase the recommended starting dosage of Avatrombopag when used concomitantly with a moderate or strong dual inducer of CYP2C9 and CYP3A4. In patients starting moderate or strong dual inducers of CYP2C9 and CYP3A4 while receiving Avatrombopag, monitor platelet counts and adjust Avatrombopag dose as necessary.

Overdose:

In the event of overdose, platelet count may increase excessively and result in thrombotic or thromboembolic complications. Closely monitor the patient and platelet count. Treat thrombotic complications in accordance with standard of care. No antidote is known for Avatrombopag overdose.

Storage:

Store in a cool & dry place below 30° C, protect from light. Keep out of the reach of children.

Packing:

Avatrom™ 20 Tablet: Each box contains 10 Tablets and one packet silica gel in a sealed HDPE container.

Manufactured by:
Jenphar Bangladesh Ltd.
Sreepur, Gazipur, Bangladesh.

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