DOPTELET® ▼ (avatrombopag) - Abbreviated Prescribing Information

For further prescribing information and before prescribing, please consult DOPTELET® Summary of Product Characteristics (SPC)

DOPTELET®: Each film-coated tablet contains avatrombopag maleate equivalent to 20 mg of avatrombopag.

Indications: DOPTELET® is indicated for the treatment of severe thrombocytopenia in adult patients with chronic liver disease (CLD) who are scheduled to undergo an invasive procedure. DOPTELET® is indicated for the treatment of primary chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).

Dosage and Administration: Treatment should be initiated by and remain under the supervision of a physician who is experienced in the treatment of haematological diseases. Doses should be taken, at the same time of day, orally with food (including when taking less frequently than once daily). CLD: The recommended daily dose of DOPTELET® is based on the patient's baseline platelet count. For platelet count $<40x10^9$/L use 60mg once-daily dose (three 20mg tablets) for 5 days; for platelet count ≥40 to $<50x10^9$/L use 40mg once-daily dose (two 20mg tablets) for 5 days. Dosing should begin 10 to 13 days prior to the planned procedure. The patient should undergo their procedure 5 to 8 days after the last dose of DOPTELET®. Platelet count should be rechecked on the day of the procedure to ensure adequate increase. ITP: Use the lowest dose needed to achieve and maintain a platelet count ≥ 50 x 10^9/L as necessary to reduce the risk for bleeding. The recommended starting dose of is 20 mg (1 tablet) once daily with food. After initiating therapy, assess platelet counts at least once weekly until a stable platelet count ≥ 50 x 10^9/L and ≤ 150 x 10^9/L has been achieved. Twice weekly platelet count monitoring should be conducted during the first weeks of therapy in patients receiving DOPTELET® only once or twice weekly. Twice weekly monitoring should also be conducted after dose adjustments during the treatment. Due to the potential risk of platelet counts above 400 x 10^9/L within the first weeks of treatment patients should be carefully monitored for any signs or symptoms of thrombocytosis. After a stable platelet count has been achieved, obtain platelet counts at least monthly. After discontinuation of DOPTELET®, platelet counts should be obtained weekly for at least 4 weeks. Refer to SPC for dose adjustments in ITP patients and in special populations. Do not exceed a daily dose of 40 mg (2 tablets). Discontinue DOPTELET® if the platelet count does not increase to ≥ 50 x 10^9/L after 4 weeks of dosing at the maximum dose of 40 mg once daily. Discontinue if the platelet count is > 250 x 10^9/L after 2 weeks of dosing at 20 mg once weekly.

Contraindications: Hypersensitivity to avatrombopag or to any of the excipients.

Warnings and precautions: Thrombotic/thromboembolic events: Patients with CLD are known to be at increased risk for thromboembolic events. Portal vein thrombosis has been reported at an increased frequency in patients with CLD who had platelet counts > $200x10^9$/L receiving a thrombopoietin receptor agonist. In patients with ITP taking DOPTELET®, thromboembolic events (arterial or venous) occurred in 7% (9/128). Consider the potential increased thrombotic risk when administering to patients with known risk factors for thromboembolism. DOPTELET® should not be administered to patients with CLD or ITP in an attempt to normalise platelet counts. QTc prolongation with concomitant medications: At exposures similar to that achieved at the 40 mg and 60 mg dose, DOPTELET® did not prolong the QT interval to any clinically relevant extent. However, caution must be exercised when DOPTELET® is co-administered with moderate or strong dual CYP3A4/5 and CYP2C9 inhibitors, or with moderate or strong CYP2C9 inhibitors, as these medications can increase DOPTELET® exposures. Caution must also be exercised in patients with loss-of-function polymorphisms of CYP2C9, as these can increase DOPTELET® exposure. Reoccurrence of thrombocytopenia and bleeding after cessation of treatment in patients with ITP: Thrombocytopenia is likely to reoccur in ITP patients upon discontinuation of treatment. Patients should be closely monitored for a decrease in platelet count and medically managed to avoid bleeding upon discontinuation (refer to SPC). Increased bone marrow reticulin: Increased bone marrow reticulin is believed to be a result of TPO receptor stimulation, leading to an increased number of megakaryocytes in the bone marrow, which may subsequently release cytokines. Increased reticulin may be suggested by morphological changes in the peripheral blood cells and can be detected through bone

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marrow biopsy. Therefore, examinations for cellular morphological abnormalities using peripheral blood smear and complete blood count (CBC) prior to and during treatment with DOPTELET® are recommended. Progression of existing myelodysplastic syndrome (MDS): The effectiveness and safety of DOPTELET® have not been established for the treatment of thrombocytopenia due to MDS. DOPTELET® should not be used outside of clinical studies for the treatment of thrombocytopenia due to MDS. Severe hepatic impairment: There is limited information on the use of DOPTELET® in patients with severe hepatic impairment. DOPTELET® should only be used in such patients if the expected benefit outweighs the expected risks. Use in patients with chronic liver disease undergoing invasive procedures: The objective of treatment with DOPTELET® is to increase platelet counts. While the benefit-risk profile for procedures that were not specifically included in the clinical studies is likely to be comparable, the efficacy and safety of DOPTELET® have not been established in major surgeries like laparotomy, thoracotomy, open-heart surgery, craniotomy or excision of organs. Retreatment for patients with chronic liver disease undergoing invasive procedures: There is limited information on the use of DOPTELET® in patients previously exposed to DOPTELET®. Co-administration with interferon preparations: Interferon preparations have been known to reduce platelet counts, therefore, this should be considered when co-administering DOPTELET® with interferon preparations. Lactose: Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Refer to SPC section 4.4 for full warnings and precautions.

Interactions: P-gp inhibitors: Concomitant use of DOPTELET® with P-gp inhibitors resulted in alterations in exposure that were not clinically significant. No dose adjustment is recommended. CYP3A4/5 and CYP2C9 inhibitors: Concomitant use of DOPTELET® with moderate or strong CYP3A4/5 and CYP2C9 dual inhibitors increases DOPTELET® exposure. Concomitant use of DOPTELET® with moderate or strong CYP2C9 inhibitors is expected to increase DOPTELET® exposure. CLD: The increase in DOPTELET® exposure is not expected to have a clinically important effect on platelet counts due to the 5-day treatment duration, and no dose adjustment is recommended. These patients should be evaluated on day of procedure for unexpectedly high increase in platelet count. ITP: Reduce the starting dosage of DOPTELET® when used concomitantly with a moderate or strong dual inhibitor of CYP2C9 and CYP3A4/5. Reduction of the starting dose should also be considered for patients receiving a moderate or strong CYP2C9 inhibitor. Monitor platelet count and adjust dose as necessary. CYP3A4/5 & CYP2C9 inducers: Concomitant use of moderate or strong CYP3A4/5 and CYP2C9 dual inducers reduces DOPTELET® exposure and may result in a decreased effect on platelet counts. Concomitant use of DOPTELET® with moderate or strong CYP2C9 inducers is expected to reduce DOPTELET® exposure. CLD: The decrease in DOPTELET® exposure is not expected to have a clinically important effect on platelet counts due to the 5-day treatment duration. No dose adjustment is recommended. ITP: Increase the recommended starting dosage of DOPTELET® when used concomitantly with a moderate or strong dual inducer of CYP2C9 and CYP3A4/5. An increase in the starting dose should also be considered for patients receiving a moderate or strong CYP2C9 inducer. Monitor platelet count and adjust dose as necessary. Medicinal products for treatment of ITP: Platelet counts should be monitored when combining DOPTELET® with other medicinal products for the treatment of ITP in order to avoid platelet counts outside of the recommended range.

Pregnancy and lactation: Not recommended during pregnancy and in women of childbearing potential not using contraception. A decision must be made whether to discontinue breast-feeding or discontinue DOPTELET® during lactation, taking into account the relative benefits for the woman and child.

Undesirable Effects: Consult SPC section 4.8 for full details. The adverse reactions at least possibly related to treatment are listed below as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100) or not known (cannot be estimated from the available data). CLD: A common adverse reaction was fatigue; uncommon were anaemia, portal vein thrombosis, bone pain, myalgia and pyrexia; not known was hypersensitivity. ITP: Very Common adverse reactions were headache, fatigue. Common adverse reactions were thrombocytopenia, anaemia, splenomegaly, hyperlipidaemia, decreased appetite, dizziness, head discomfort,

migraine, paraesthesia, hypertension, epistaxis, dyspnoea, nausea, diarrhoea, vomiting, abdominal pain upper, flatulence, rash, acne, petechiae, pruritis, arthralgia, back pain, pain in extremity, myalgia, musculoskeletal pain, asthenia, blood glucose increased, platelet count increased, blood glucose decreased, blood triglycerides increased, blood lactate dehydrogenase increased, platelet count decreased, alanine aminotransferase increased, blood gastrin increased; not known was hypersensitivity. For uncommon adverse reactions consult the SPC section 4.8.

Legal Category: Prescription Only Medicine (POM). **Marketing Authorisation No**.: PLGB 30941/0021 (Great Britain) and EU/1/19/1373/001-003 (Republic of Ireland and Northern Ireland) **Pack size:** Each carton contains one blister of 10 or 15 film-coated tablets or two blisters of 15 film-coated tablets. **Price**: NHS List Price £640 per pack of 10 tablets, £960 per pack of 15 tablets, £1,920 per pack of 30 tablets. Eire List Price available on request. **Marketing Authorisation Holder**: Swedish Orphan Biovitrum AB (publ), SE-112 76 Stockholm, Sweden. **Further Information Available From:** Swedish Orphan Biovitrum (UK) Ltd, Suite 2, Riverside 3, Cambridgeshire, CB21 6AD. **Date of Preparation**: December 2022. **Company Reference**: PP-11219

▼ **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard (for United Kingdom) and www.hpra.ie (for Republic of Ireland). Adverse events should also be reported to Swedish Orphan Biovitrum Ltd at medical.info.uk@sobi.com or Telephone +44 (0) 800 111 4754**

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