Eltrombopag is indicated for chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients aged 1 year and above who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).
Your practical guide

CONTENTS

4 Supporting your eltrombopag patients
6 What is eltrombopag?
8 Prescribing eltrombopag
10 Dosing with eltrombopag
13 Regular monitoring
14 Interactions with foods, drinks and other medicines
25 Identifying adverse events
26 Consultation checklist
28 Follow-up conversations
Supporting your eltrombopag patients

So you’ve decided that eltrombopag is the appropriate treatment option for your patients with chronic immune thrombocytopenic purpura (chronic ITP).

Support for you
This booklet is a practical guide to eltrombopag and is provided in addition to the Safety Guide for eltrombopag which is already available to you.

This guide provides information on the initiation and ongoing management of eltrombopag, from how eltrombopag works and essential dosing information, to monitoring your patient and managing side effects. It also offers useful advice on helping patients conveniently integrate eltrombopag into their daily routine. For full safety information, please refer to the eltrombopag SmPC and Safety Guide for eltrombopag.*

Support for your chronic ITP patient
The eltrombopag patient guide is designed to support your patients with chronic ITP. When provided by you, it hopes to equip your patients with practical information they need to improve their engagement with treatment and manage eltrombopag on a daily basis.

When taken correctly, eltrombopag can help your patients manage their chronic ITP

* If you do not have access to a copy of the Safety Guide for eltrombopag, please contact your local Novartis office.
What is eltrombopag?

Eltrombopag is an oral thrombopoietin-receptor (TPO-R) agonist, indicated for chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients aged 1 year and above who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).

How does eltrombopag work?

Eltrombopag increases platelet production to maintain haemostatic platelet levels by uniquely binding to the transmembrane domain of the TPO receptor. This stimulates differentiation and proliferation of cells in the megakaryocyte lineage, as shown in the diagram opposite.
TPO-R activation leading to increased platelet production

- Eltrombopag binds to the TPO receptor
- Megakaryocyte differentiation and proliferation
- Increased platelet production
Prescribing eltrombopag

The objective of treatment with eltrombopag is to maintain a platelet count greater than or equal to 50,000/µL, above the level for haemorrhagic risk, rather than to normalise platelet counts.

**Dosing**

Eltrombopag is a once-daily oral therapy, and should be taken at the same time every day.

The lowest dose of eltrombopag needed to achieve and maintain a platelet count ≥50,000/µL should be used.

**Formulations and strengths**

In Ireland eltrombopag is available in 2 tablet strengths: 25 mg and 50 mg.

- For paediatric patients aged 1 to 5 years, eltrombopag is also available as a 25 mg sachet of powder for oral suspension.

**Eltrombopag is not recommended:**

- For use in infants less than 1 year of age
- During pregnancy and in women of childbearing potential not using contraception
- In ITP patients with hepatic impairment (Child-Pugh score ≥5) unless the expected benefit outweighs the identified risk of portal venous thrombosis
- In patients who are allergic to eltrombopag or any of its ingredients

For more information, refer to the Safety Guide for eltrombopag.
Dosing with eltrombopag

The recommended starting dose of eltrombopag is 50 mg in most patients. In patients aged 1 to 5 years, the recommended starting dose is 25 mg.

Dose adjustment

- Dosing should be individualised based on the patient’s platelet counts.
- If required, the dose may be adjusted by increasing by 25 mg to a maximum dose of 75 mg to manage platelet counts or decreasing by 25 mg.
- The lowest effective dosing regimen should be used as clinically indicated. See the table opposite.
- In a few patients, a combination of different film-coated tablet strengths on different days may be required.

In patients of East Asian ancestry (such as Chinese, Japanese, Taiwanese, Korean or Thai):

- Initiate eltrombopag at a reduced dose of 25 mg once daily.
- Platelet counts should continue to be monitored and the standard criteria for further dose modification followed. Refer to the table opposite outlining monitoring requirements.

In patients with 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 chronic 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, wait 3 weeks before increasing the dose.

Concomitant ITP medicinal products

Eltrombopag can be administered in addition to other ITP medicinal products. Modify the dose regimen of concomitant ITP medicinal products, as medically appropriate, and monitor platelet counts to avoid excessive increases during therapy with eltrombopag.
The dosing requirements for eltrombopag must be individualised based on the patient’s platelet counts.

```
Recommended starting dose

≥50,000/µL
50 mg once daily (patients aged 6+)

25 mg once daily (patients aged 1-5)

<50,000/µL
Wait 2 weeks

≥50,000/µL to ≤ 150,000/µL
MAINTAIN

≥ 150,000/µL to ≤ 250,000/µL
DECREASE

>250,000/µL
STOP

INCREASE
Increase daily dose by 25 mg to a maximum of 75 mg/day.

Use lowest dose of eltrombopag and/or concomitant ITP treatment to maintain platelet counts that avoid or reduce bleeding.

Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments.

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.

Wait 2 weeks to reassess
```

^ For patients taking 25 mg eltrombopag once every other day, increase dose to 25 mg once daily.

* For patients taking 25 mg eltrombopag once daily, consideration should be given to dosing at 12.5 mg once daily or alternatively a dose of 25 mg once every other day.

Please note the starting dose of eltrombopag in special populations:
In patients with 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, in which case the starting dose of eltrombopag must be 25 mg once daily.
In patients of East Asian ancestry: initiate eltrombopag at initial dose of 25 mg once daily.
In patients aged 1 to 5 years: initiate eltrombopag at 25 mg daily.
The table below outlines the monitoring requirements for eltrombopag during the dose-adjustment phase, and the stable-dose phase:

<table>
<thead>
<tr>
<th>Phase</th>
<th>Prior-treatment phase</th>
<th>Dose-adjustment phase</th>
<th>Stable-dose phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver*</td>
<td></td>
<td>CBC (weekly)</td>
<td>CBC (monthly)</td>
</tr>
<tr>
<td>Peripheral blood smears</td>
<td></td>
<td>Liver (every two weeks)</td>
<td>Liver (monthly)</td>
</tr>
</tbody>
</table>

*Liver: Serum ALT, AST and bilirubin. CBC = complete blood count including platelets and white blood cells.

It may take up to 2 weeks for patients to respond to eltrombopag.

Additional monitoring may be required, including routine ophthalmologic monitoring and bone marrow aspirates. For more information refer to the Safety Guide for eltrombopag.
INTERACTIONS with foods, drinks and other medicines

Eltrombopag is known to interact with polyvalent cations in certain foods, drinks and medicines. This interaction can significantly impair the absorption of eltrombopag into the body.

Polyvalent cations to be avoided include calcium, aluminium, iron, magnesium, selenium and zinc as these can significantly reduce the absorption of eltrombopag.

Eltrombopag must be administered at least 2 hours before or 4 hours after polyvalent cation-containing antacids, dairy products (or any foods, drinks, or medicines containing ≥50 mg calcium) and other products containing polyvalent cations, such as mineral supplements.

For information on interactions with other medicines, please see Other drug considerations on page 23.
To get the full benefit from THEIR TREATMENT, remind patients to...

... take eltrombopag

at least 2 hours before...

... or 4 hours after certain foods, drinks or medicines
HELP your patients INTEGRATE eltrombopag conveniently into their daily routine.

Eltrombopag may be taken at any time of the day or night provided patients remember to take eltrombopag at least 2 hours before or 4 hours after certain foods, drinks, and medicines. However, patients may find it easier to remember if they take it at the same time every day.

Because certain foods, drinks and medicines affect the absorption of eltrombopag, it can be useful to help patients think about when they eat and whether they might need to adjust their mealtimes, so they take eltrombopag at least 2 hours before or 4 hours after certain foods, drinks, and medicines.

Patients should take eltrombopag at a time that suits their lifestyle:
• Taking it in the evening – what adjustments might they need to make to their routine?
• Taking it in the morning – how will this affect what they eat for breakfast?

The following pages give some practical guidance on how you can help patients make eltrombopag part of their daily routine.
Remind your patients to use the MEAL PLANNER to remember to take eltrombopag at least 2 hours before or 4 hours after certain foods, drinks, and medicines.
PATIENTS can take eltrombopag before they go to bed

If patients feel that they want to take their eltrombopag earlier than 10pm, here are some foods they could eat for their evening meal:

- Meats such as chicken, lean ham or beef
- White fish e.g., cod or haddock
- Non-leafy vegetables
- Potatoes, brown rice, pasta
- Fruit
- Unfortified (no added minerals) fruit juice
- Black coffee/tea
REMEMBER…

Eltrombopag should be taken at least 2 hours before or 4 hours after certain products:

- Foods, drinks or medicines that are high in calcium*
- Mineral supplements or fortified foods, i.e. those with added calcium, iron, magnesium, aluminium, selenium or zinc

* Foods, drinks and medicines containing 50 mg or more of calcium are considered high in calcium. Help patients think about the foods they can eat and encourage them to check nutritional information on food packaging.
PATIENTS can take eltrombopag as soon as they wake up

Things patients could eat for breakfast are:

- Porridge oats
- Unfortified soy milk
- Cold meats such as lean ham
- Fruit
- Small portion of nuts or raisins
- Black coffee/tea
- Unfortified fruit juice
REMEMBER…

Eltrombopag should be taken at least 2 hours before or 4 hours after certain products:

- Foods, drinks or medicines that are high in calcium*
- Mineral supplements or fortified foods, i.e. those with added calcium, iron, magnesium, aluminium, selenium or zinc

* Foods, drinks and medicines containing 50 mg or more of calcium are considered high in calcium. Help patients think about the foods they can eat and encourage them to check nutritional information on food packaging.
Take eltrombopag at least 2 hours before or 4 hours after these medicines:

Antacids containing calcium, aluminium, iron, magnesium, selenium or zinc:

Medicines and supplements that contain calcium, aluminium, iron, magnesium, selenium or zinc (including multivitamins and protein shakes):

It’s important to help patients understand which foods, drinks and medicines they should avoid when taking eltrombopag.
OTHER drug considerations

- **Statins**: in clinical studies with eltrombopag, reducing statin dose by 50% was recommended

- **OATP1B1 and BCRP substrates (e.g. topotecan and methotrexate)**: co-administration of eltrombopag should be undertaken with caution

- **Contraceptive pill and hormone therapy**: caution should be taken when administering eltrombopag owing to the observed risk of thromboembolic events in clinical trials

- **Lopinavir/ritonavir (LPV/RTV)**: caution should be taken, as the concentration of eltrombopag may be decreased when co-administered with LPV/RTV

- **Ciclosporin**: co-administration of eltrombopag may decrease eltrombopag exposure. Eltrombopag dose adjustment is permitted, but platelet count should be closely monitored

- **Other medicinal products for the treatment of ITP**: platelet counts should be monitored when eltrombopag is co-administered with other medicinal products for the treatment of ITP such as corticosteroids, danazol or azathioprine
Identifying ADVERSE EVENTS

Adverse events of special interest include:
- Hepatotoxicity
- Thrombotic/thromboembolic complications
- Bone marrow reticulin formation and risk for bone marrow fibrosis
- Haematological malignancies
- Post-therapy thrombocytopenia
  - Patients should be informed of the risk of bleeding and platelet count should be monitored weekly for 4 weeks following discontinuation of eltrombopag

You should make patients aware of the most common side effects, such as:
- Headache
- Nausea
- Diarrhoea
- Anaemia
- Decreased appetite
- Insomnia
- Cough
- Alopecia
- Pruritus
- Myalgia
- Pyrexia
- Fatigue
- Influenza like illness
- Asthenia
- Chills
- Peripheral oedema

Paediatric patients have also commonly experienced the following side effects
- Nasopharyngitis
- Upper respiratory tract infection
- Rhinitis
- Abdominal pain
- Diarrhea
- Rash
- Toothache
- Cough
- Oropharyngeal pain
- Rhinorrhea
- Pyrexia
- Abnormal liver values

For full safety information, please refer to the eltrombopag SmPC and the Safety Guide for eltrombopag.*

The eltrombopag practical guide for patients contains practical tips to help patients best manage the most common side effects.

*If you do not have access to a copy of the Safety Guide for eltrombopag, please contact your local Novartis office.

This guidance does not replace other safety information about eltrombopag.
Consultation CHECKLIST

You could use this suggested checklist during a consultation to ensure the key points about taking eltrombopag have been discussed.

Have you talked about…

✓ Dosing?
  • Eltrombopag is taken in one daily dose.
  • Patients will find it easier to take eltrombopag at the same time every day. Help your patient decide on the best time of day to take eltrombopag (morning or evening?).
  • The starting dose is 50 mg/day in most patients. In patients of East-Asian origin, patients with hepatic impairment, and patients aged 1 to 5 years, the starting dose is 25 mg/day.

✓ Adverse events?
  • Is your patient aware of the potential adverse events associated with eltrombopag?

✓ Meal planning?
  • Some minerals in certain foods, drinks or medicines may prevent eltrombopag from being properly absorbed.

• Explain that this interaction can reduce the effect of eltrombopag.
• Help your patients remember to take eltrombopag at least 2 hours before or 4 hours after certain foods, drinks, and medicines and integrate eltrombopag conveniently into their daily routine.

✓ Dose adjustment and monitoring?
  • The objective of treatment with eltrombopag is to maintain a platelet count greater than or equal to 50,000/µL, above the level for haemorrhagic risk, rather than to normalise platelet counts.
  • The dose of eltrombopag should be adjusted to the lowest effective dosing regimen.
  • Liver enzymes and peripheral blood smears need to be monitored before and during treatment with eltrombopag.

Please note that additional monitoring may be required, including routine ophthalmologic monitoring and bone marrow aspirates. Please refer to the Safety Guide for eltrombopag for more information.
Follow-up CONVERSATIONS

To ensure that patients are getting the full benefit from eltrombopag, here are some sample questions you could use to find out how your patients are getting on.

General questions:
• Is your patient taking their eltrombopag at the same time every day?
• Has your patient been missing any doses, and why?
• What are your patient’s additional needs or concerns?

Tolerability:
• Is your patient experiencing any nausea or diarrhoea?
• Has your patient experienced any other adverse events? If so, does this require action on your part?

Food and drug interactions:
If your patient is not responding, or has a sub-optimal response to eltrombopag, this may be a result of interactions with foods, drinks or other medicines:
• Does your patient understand the interactions with foods, drinks and other medicines with eltrombopag?
• Has your patient been taking their eltrombopag less than 2 hours before or 4 hours after foods or other products that contain polyvalent cations?
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine. Adverse events should also be reported to Novartis Ireland by calling 01-2080612 or by email to drugsafety.dublin@novartis.com. If you use email please write “reporting of adverse event” in the mail heading.