Avatrombopag

INDICATIONS

Chronic immune thrombocytopenia (ITP) refractory to standard treatment.
Blueteq required

TREATMENT INTENT

- 80% of patients will reach a platelet count of 50 x10^9/L or more
- 66% patients reach a platelet count of 50 x10^9/L or more by day 8 after starting avatrombopag
- 20-30% likely to have a durable response when avatrombopag is discontinued

PRE-ASSESSMENT

1. Blood tests – FBC, U&E, LFT, blood film
2. Record height and weight.
3. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given.
4. Treatment should be agreed with a consultant with experience of managing ITP

DRUG REGIMEN

	Starting dose
AVATROMBOPAG	20mg once a day with food.

Available as 20mg tablets

DOSE FREQUENCY

Once a day to start, then according to tables below

MONITORING

Check platelet count once a week and adjust frequency until the platelet count is stable at 50 x10^9/L or more, then monitor every 2-4 weeks. If frequency of medication is adjusted, platelet monitoring is required more often (e.g. at least 2 weeks following dose change).

DOSE ADJUSTMENTS

Dose levels for titration

Dose	Dose level
40mg once DAILY	6
40mg three times a WEEK (Mon / Wed / Fri) and 20mg on each of the four remaining days (Tues / Thurs / Sat / Sun)	5
20mg once DAILY	4
20mg three times a WEEK (Mon / Wed / Fri)	3
20mg twice a WEEK **or** 40mg once a WEEK	2
20mg once a WEEK	1

For precise haematological control, it may be necessary to adjust dosing in a way that falls in-between the recommended dose levels above.

Haematological

Platelet count	Dose adjustment or response
Less than 50 x 10^9/L following at least 2 weeks of therapy	Increase by one level dose (see table below)
50 x 10^9/L to 150 x 10^9/L	Continue same dose
151 x 10^9/L to 250 x 10^9/L	Decrease by one level dose and check in 2 weeks
More than 250 x 10^9/L	Stop avatrombopag and increase the frequency of platelet monitoring to twice weekly. Once the platelet count is < 100 x10^9/L, reinitiate therapy at a daily dose reduced by one level
If < 50 x 10^9/L after 4 weeks of 40mg daily	Discontinue as assume treatment failure
If > 250 x 10^9/L after 2 weeks of 20mg once weekly	Discontinue as assume treatment hypersensitivity

Renal and Hepatic impairment

No dose adjustments necessary, however use with caution in severe liver disease.

DISCONTINUATION

Avatrombopag should be stopped if a platelet count sufficient to prevent bleeding has not been reached 4 weeks after reaching a dose of 40mg once a day.

Avatrombopag should be stopped if a platelet count is over 250 x 10^9/L for more than 2 weeks of 20mg once weekly (i.e.over sensitivity)

Consider weaning and stopping avatrombopag if platelet count stable for four to six months

Avatrombopag may cause reticulin deposition within the bone marrow and should be stopped if a leukoerthroblastic picture develops on a blood film.

SPECIAL PRECAUTIONS

Caution for patients with preexisting MDS (theoretical concern that avatrombopag may stimulate haematological malignancies

Potential increased risk of thrombosis, approx. 7% shown in studies– advise general antithrombotic measures

---

ADVERSE EFFECTS

Common side effects include fever, abdominal pain, nausea, headache, fatigue and swelling of extremities

---

DRUG INTERACTIONS

Itraconazole, fluconazole, rifampicin, cyclosporine, verapamil

QTc prolongation with concomitant medications such as P-gp inhibitors (due to CYP3A4/5 and CYP2C9 inhibition)

PREGNANCY and BREASTFEEDING

Potential risks to a fetus
Breastfeeding is not recommended until 2 weeks after the final dose

---

References

1. Swedish Orphan Biovitrum Ltd. Doptelet 20 mg film-coated tablets. Summary of Product Characteristics. Last updated: 21 Oct 2021. Available at: https://www.medicines.org.uk/emc/product/11837/smpc#gref
2. Provan et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. Blood Advances 2019;3(22):3780-17
3. Jurczak et al. Phase 3 randomised study of avatrombopag, a novel thrombopoietin receptor agonist for the treatment of chronic immune thrombocytopenia. Br J Haematol 2018;183:479-90

DOCUMENT REVIEW

Name	Revision	Date	Vers	Review date
Immunohaematology group	New document	Jan 2023	1.2	Jan 2025
Donna Constantine Advanced Cancer Pharmacist	Updated funding mechanism (no longer CCG IFR). Format adjustment and logo update.	Jan 2025	1.3	March 2025