Systemic Anti-Cancer Therapy Protocol

Anagrelide
Essential Thrombocythaemia

PROTOCOL REF: MPHAANETHA
(Version No: 1.0)

Approved for use in:

Essential thrombocythaemia (ET) with a high risk of thrombosis who are one of:

- > 60 years of age
- > platelet count 1000 x 10^9/L
- History of thrombo-haemorrhagic events

AND

Intolerant or refractory to first line therapy.

Blueteq registration not required

Dosage:

Drug	Dose	Route	Frequency
Anagrelide	500 micrograms	PO	Twice daily continuous

Titrate dose at weekly intervals to achieve the lowest effective dose required to maintain a platelet count between 150 x 10^9/L and 400 x 10^9/L. Increase or reduce dose by 0.5mg/day at each interval. The recommended maximum single dose should not exceed 2.5 mg. The usual maintenance dose is 1-3mg/day. During clinical development doses of 10 mg/day have been used. Responses are usually achieved within 8-16 weeks of therapy in about 90% (PR) and 70% of patients (CR).

Administration:

- Anagrelide is available as 500 microgram capsules
- Capsules should not be crushed or the contents diluted in liquid
- Can be taken on an empty stomach or with food

Anti-emetic risk:

Minimal

Supportive treatments:

- Allopurinol 300mg once daily until counts are controlled
- Aspirin or equivalent if no existing anticoagulation therapy (ask GP to prescribe, consider addition of gastro-protection where appropriate)

Dosing in renal and hepatic impairment:

Renal	Hepatic
Limited clinical experience in patients with CrCl <50ml/min – use with caution	There is limited pharmacokinetic data on treating patients with hepatic impairment. Company recommends avoiding if Child-Pugh score B or C.

Interactions:

Avoid CYP1A2 inducers (e.g. omeprazole) or inhibitors (e.g. fluvoxamine)

Please refer to the relevant SPC for more drug-drug interaction information

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2 onwards	Ongoing
Informed Consent	X			
Clinical Assessment	X	X	X	
SACT Assessment (including toxicity assessment and PS)		X	X	
ECG + ECHO	X			If at risk of cardiac disease
FBC	X	X	X	Prior to every cycle. A cycle may extend to three months in length once patients are stable on treatment. FBC should be taken within 7 days of prescribing but may be taken up to 14 days prior to prescription at clinician's discretion. **Prescribers must check FBC prior to prescribing and document that this check has taken place in the medical notes. SACT assessment will not include checking of this parameter in this instance.**
U&E & LFTs	X			Must have had within 6 months of prescription. **Prescribers must check U+E & LFT prior to prescribing and document that these checks have taken place in the medical notes. SACT assessment will not include checking of these parameters in this instance.**
Height	X			
Weight	X	X	X	Prior to every cycle
Pregnancy test	X			If clinically indicated

Dose Modifications and Toxicity Management:

Main toxicities:

- Drowsiness – dose reduction or consider dosing at night only. Affected patients should be counselled on taking more care when driving
- Anagrelide is contraindicated in patients with marked bone marrow depression, or severe anaemia; or in patients who have demonstrated a previous hypersensitivity to anagrelide or any other component or its formulation.
- Anagrelide is contraindicated in patients with cardiac insufficiency and arrhythmias.
- Breast feeding is contra-indicated.
- When appropriate both male and female patients should be counselled concerning the use of contraceptive measures before and during treatment with anagrelide.

Side effects

Common: anaemia, fluid retention, headache, dizziness, hypertension, tachycardia, diarrhoea, vomiting, abdominal pain, flatulence, nausea, rash, fatigue.

Rare: Some studies have suggested an association between Anagrelide treatment and increased risk of progression in reticulin fibrosis. This may be reversible in some cases on cessation of anagrelide. Anagrelide should be used with caution in patients with baseline fibrosis pre-treatment

Please refer to the relevant SPC for more information on toxicities.

Haematological toxicity:

- Anagrelide causes macrocytic red cell indices and may mask iron, B12 or folic acid deficiency.
- Consider reducing the dose/ interrupting therapy if the patient develops leukopenia < 2.5 x10^9/L, neutropenia < 1.5 x 10^9/L or thrombocytopenia < 100 x 10^9/L.

- Patients with ET may have differing platelet / WCC treatment targets. It may be helpful to document these targets in the patient's medical notes to ensure continuity of care.

References:

1. Harrison et al (2010) Guideline for investigation and management of adults and children presenting with a thrombocytosis. BJH 149:352-375

2. Harrison CN (2005) Hydroxyurea compared with anagrelide in High-Risk Essential Thrombocythemia. NJEM 353:33-45

3. Gisslinger H (2013) Anagrelide compared with hydroxyurea in WHO-classified essential thrombocythemia: the ANAHYDRET Study, a randomized controlled trial. Blood 121:1720-1728

4. Summary of Product Characteristics Xagrid 0.5mg hard capsule © updated 18/9/2019 https://www.medicines.org.uk/emc/product/271/smpc