Thames Valley
Strategic Clinical Network

ANAGRELIDE

INDICATION

Reduction of elevated platelet counts in at risk essential thrombocythaemia (ET) patients who are

- 60 years of age or over, or
- a platelet count > 1000 x 10^9/L or
- a history of thrombo-haemorrhagic events

and are intolerant or refractory to first line therapy

TREATMENT INTENT

Disease Modification

PRE-ASSESSMENT

1. Investigations to include FBC, blood film and manual differential, coagulation screen, urea, creatinine, electrolytes, liver function tests, calcium, lipid profile, glucose, amylase, urate.
2. Ensure diagnosis is confirmed prior to commencing treatment by WHO or BSH criteria
3. Pregnancy Test - for all women of childbearing age unless they are postmenopausal, have been sterilised or undergone a hysterectomy.
4. ECG and consider echo in selected patients at risk of cardiac disease
5. Consider bone marrow trephine biopsy to assess for fibrosis
6. Record performance status (WHO/ECOG).
7. 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. Obtain written consent on the day of treatment.
8. Treatment should be agreed in the relevant MDT.

DRUG REGIMEN / CYCLE FREQUENCY

Staring Dose

ANAGRELIDE **0.5mg** oral **TWICE DAILY** (available as 0.5mg capsules)

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. Usual maintenance dose 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).

DOSE MODIFICATIONS

Use with caution in renal impairment. Avoid anagrelide in moderate to severe hepatic impairment.

CONTRAINDICATIONS

- Hypersensitivity to active substance or excipients.
- Pregnancy or Breastfeeding
- Moderate to severe hepatic impairment.
- Cardiac insufficiency and arrhythmias

INVESTIGATIONS

- FBC weekly until platelet count stable, then monthly.
- LFT, U&Es monthly
- Consider bone marrow biopsies every 3 years to assess for fibrosis particularly in patients with any features suggestive of bone marrow fibrosis such as anaemia, splenomegaly or blood film features.

CONCURRENT MEDICATION

Aspirin 75mg daily (Consider prescribing concomitant PPI if appropriate). Assess bleeding risk individually.

EMETIC RISK

Minimal

DRUG INTERACTIONS

(Consult with pharmacist and refer to SPC for full details)

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

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

(Consult with pharmacist and refer to SPC for full details)

Commonly reported: anaemia, fluid retention, headache, dizziness, hypertension, tachycardia, diarrhoea, vomiting, abdominal pain, flatulence, nausea, rash, fatigue. Side effects may subside after 2 weeks.

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

TREATMENT RELATED MORTALITY

Very low

REFERENCES

1. Takeda. Summary of Product Characteristics Xagrid 0.5mg hard capsules. Updated 27/11/2020. Accessed on 5/11/2021 via http://www.medicines.org.uk/emc
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-classidied essential thrombocythemia: the ANAHYDRET Study, a randomized controlled trial. Blood 121:1720-1728
4. Barosi et al (2013) Revised response criteria for polycythemia vera and essential thrombocythemia: an ELN and IWG-MRT consensus project. Blood 121(23):4778-4781.
5. Tefferi et al (2013) Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood 122(8):1395-1398

REVIEW

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung, Haematology Pharmacist. Dr Bethan Psaila, Consultant Haematologist NSSG Myeloid Group	New document. Annual protocol meeting	Oct 2019	1.0	Oct 2020
Yen Lim, Haematology Pharmacist NSSG Myeloid Group	Annual protocol meeting	Nov 2021	1.1	Nov 2023