NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT

Shared care guidelines for Anagrelide for Adults with Essential Thrombocythaemia
Monitoring level Amber 0 – Prescribe drug and perform basic monitoring eg annual review

Generic and Proprietary/Brand Name
Anagrelide / Xagrid®
Indications for shared care
The reduction of elevated platelet counts in 'at risk' patients with essential thrombocythaemia who intolerant of or poorly controlled on hydroxycarbamide.

Specialist Prescribing and Monitoring Responsibilities – summary. Full details in main body of document	GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities – summary. Full details in main body of document
Prescribing: • To initiate treatment. • Discuss benefits and side effects of treatment with the patient. • Titrate the dose of anagrelide according to the patient's condition. • Prompt communication with the GP of any changes in treatment and on cessation of treatment. • Undertake monitoring of blood counts together with if relevant electrolytes and liver function tests frequency depending on patients' stability. • Inform GP of treatment plan and when to cease treatment. **Monitoring:** • FBC with differential initially weekly. The frequency will reduce as the condition is stabilised generally 3 to 4 monthly. • LFTs and renal function at review. • Emergence of any side-effects. • Review of need for continued treatment every two to three months.	**Prescribing:** • Prescribing anagrelide once patient stabilised on treatment. • Adjust dose or discontinue anagrelide as recommended by haematologist. • Alert/inform haematologist if deterioration of illness, development of intolerable side effects or signs of Adverse Drug Events. **Monitoring:** • Compliance and tolerability. • No routine blood or clinical monitoring by the GP is required. • If the patient presents with any potential side effects (see below), alert / inform the haematologist.

Patient Information
Patient information booklet available from Consultant / Specialist.
Specialist Contact Details
• **On Call Haematologist** via NNUH switchboard • **Clinical Nurse Specialist:** 01603 286286 ext 6753 or bleep 0579

GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment
Anagrelide is an inhibitor of cyclic AMP phosphodiesterase III. However, the specific mechanism of action whereby anagrelide lowers platelet counts is unknown. Following oral administration, at least 70% is absorbed by GI tract. The plasma half-life is approximately 1.3 hours.
Licensed use and agreed local off-label use
Xagrid® is indicated for the reduction of elevated platelet counts in at risk essential thrombocythaemia (ET) patients who are intolerant to their current therapy or whose elevated platelet counts are not reduced to an acceptable level by their current therapy.
Criteria for Patient Selection
'At risk' patients with essential thrombocythaemia who intolerant of or poorly controlled on hydroxycarbamide. For the latter patients, anagrelide can be used alone or in combination with hydroxycarbamide. 'At risk' is defined as having at least one of the following (1): • >60 years of age • platelet count >1500 x109/L • a history of thrombo-haemorrhagic events
Form and strength of preparation
500mcg capsule
Side Effects and Management
Link to BNF Link to SPC
Drug Interactions
Link to BNF Link to SPC • Concomitant use of anagrelide with other phosphodiesterase (PDE III) inhibitors such as milrinone, enoximone, olprinone and cilostazol is not recommended. • Caution in using in those taking theophylline and antiplatelet drugs. • If anagrelide causes GI disturbances, caution in patients taking hormonal oral contraceptives.
Cautions and Contraindications
Link to BNF Link to SPC Hypersensitivity to anagrelide.

- **The SPC recommends that patients with moderate or severe hepatic impairment are not treated with anagrelide:**
  - Severe hepatic impairment (serum transaminases >5 times upper limit normal/ Child-Pugh classification C).
  - Moderate or severe renal impairment (creatinine clearance < 50 ml/min).
  - Pregnancy or lactation.

Anagrelide should be used with caution in patients of any age with known or suspected heart disease, and only if the potential benefits of therapy outweigh the potential risks.

Initiation of therapy and ongoing dose regimen

Initiation by Consultant Haematologist:

- 500 micrograms twice daily orally. Starting dose should be maintained for at least one week.

Maintenance dose:

- After one week, the dose should be titrated to maintain the platelet count below 600 x109/L, and ideally between 150-400 x109/L.
- The dosage increment must not exceed 500 micrograms/day in any one week.
- The recommended maximum single dose should not exceed 2.5mg.

Administration Information

Anagrelide is normally given continuously.

Baseline assessment and ongoing monitoring – by Specialist

- FBC with differential initially weekly. The frequency will reduce as the condition is stabilised generally 3 to 4 monthly.
- LFTs and renal function at review.
- Emergence of any side-effects.
- Review of need for continued treatment every two to three months.

GP / Community Team or other Primary Care monitoring responsibilities

- Compliance and tolerability.
- No routine blood or clinical monitoring by the GP is required.
- If the patient presents with any potential side effects (see below), alert / inform the haematologist.

Consultant / Specialist prescribing responsibilities

- To initiate treatment.
- Discuss benefits and side effects of treatment with the patient.
- Titrate the dose of anagrelide according to the patient's condition.
- Prompt communication with the GP of any changes in treatment and on cessation of treatment.
- Undertake monitoring of blood counts together with if relevant electrolytes and liver function tests frequency depending on patients' stability.
- Inform GP of treatment plan and when to cease treatment.

GP prescribing responsibilities

- Prescribing anagrelide once patient stabilised on treatment.
- Adjust dose or discontinue anagrelide as recommended by haematologist.
- Alert/inform haematologist if deterioration of illness, development of intolerable side effects or signs of Adverse Drug Events.

Pregnancy, Paternal Exposure and Breastfeeding

As per BNF, effective contraception is required during treatment.

Indications for referral back to Specialist
Deterioration of illness, development of intolerable side effects or signs of Adverse Drug Events.
Further information and supporting documents
• Refn: Guideline for investigation and management of adults and children presenting with thrombocytosis – Claire Harrison et al. British Journal Haematology 2010, 149, 352-375 http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2010.08122.x/full • See also Xagrid® (anagrelide) SPC available via www.medicines.org.uk/emc/

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Document history:

Version	Date	Author / Editor	Status	Comment
1.	Nov 2006	Dr Jane Parker / Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	Review due Nov 2008
2.	July 2008	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	No changes to previous version. Supported by the TAG. Review due July 2008
3.	Sept 2010	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	No changes from previous version. Review due Sept 2012
4.	Sept – Oct 2012	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona	Superseded	**Revisions to specialist monitoring:** "Every clinic appointment initially, then every 2 to 3 months if LFTs

		Marshall TAG Lead Pharmacist		remain stable" changed to "FBC with differential initially weekly. The frequency will reduce as the condition is stabilised, generally 3 to 4 monthly". "Renal function at every clinic appointment initially, then every 2 to 3 months if U&Es remain normal / stable" changed to "LFTs and renal function at review." Platelet level revised to 1500 $x10^9$/L in line with current NNUH treatment protocol and national guidance. Version 4 supported by N&W Drugs & Therapeutics Commissioning Group Oct 2012 and the TAG Nov 2012.
5.1	July 2014	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	NEL CSU logos added. General principles of shared care prescribing added to the top of the document. Sent for review by the author.
5.2	Sept 2014	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	Title amended to reflect use in adults. Clarification regarding Licensed use verse Criteria for patient selection. Request review of cautions regarding hepatic and renal function. Side effects; updated as per current SPC Drug Interactions: SPC indicates caution regarding co-use of anagrelide with theophylline Link to current version of Anagrelide treatment protocol to be checked
5.3 (5 Final)	Oct 2014	Dr Jennie Wimperis, Consultant Haematologist, Norfolk & Norwich University Hospital NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	Link to haematology protocol removed as no longer published on Knowledge Anglia. Criteria for Patient Selection: Platelet count confirmed – Refn and link to BSH guideline inserted. Supported by the TAG November 2014

6.0	May – Sept 2017	TBC / Fiona Marshall TAG Lead Pharmacist	Current	Updated in line with current SPC. For consideration by local specialists – request sent to Dr Matthew Lawes, NNUH. No recommendations for further changes received from the NNUH after a follow-up message. Amended version supported by the TAG September 2017 in the interim.
7.0	Aug 2021	Jen Carroll, TAG Lead Technician	FINAL	Discussed at August 2021 TAG meeting. Review dates extended for a year from meeting due to covid pressures
8.0	March 2024	Jen Carroll, TAG Lead Technician	Final	SCA moved to new template ready for publication on KNoW. Content not yet reviewed but remains current