ANAGRELIDE

Second-line use in Essential Thrombocythaemia where initial treatment (usually hydroxycarbamide or interferon) has failed or patient cannot tolerate.
For high risk patients only: age > 60 years and/or platelet count > 1000 x 10^9/L and/or history of thrombo-haemorrhagic events
Anagrelide should not be used in any patient who is pregnant or considering pregnancy

Drugs/Dosage: **Anagrelide** initial dose 500 micrograms (0.5mg) po bd for at least 7 days, then increase dose according to the following guidelines:

Adjust the dose on an individual basis to reduce / maintain a platelet count below 600 x 10^9/L, and ideally at levels between 150 x 10^9/L and 400 x 10^9/L.

Each dosage increment must not exceed more than 500 micrograms/day in any one-week period - i.e. first dose increase will be to 1mg mane and 500 micrograms nocte for at least 7 days, second increase will be to 1mg bd for at least 7 days.

Note that it typically takes 14 – 21 days from the start of treatment for a fall in platelet count to be observed.

For most patients, response will be achieved with a maintenance dose of 0.5mg to 1.5mg bd. The maximum single dose should not exceed 2.5mg, and the maximum daily dose should not exceed 10mg.

Administration: Available as 500 microgram (0.5mg) capsules, which should be swallowed whole with a glass of water. They can be taken with or after food, or on an empty stomach.
Anecdotally, patients report less gastric side-effects if anagrelide is taken with or after a meal, and it may be particularly helpful to recommend this for patients who are also on low-dose aspirin[1].
Grapefruit juice or grapefruit pieces should be avoided while on anagrelide.

If morning and evening doses are not equal, it is recommended that the higher of the two doses is given in the morning, as this minimises the risk of patients complaining of palpitations at rest.

Frequency: continuous treatment (indefinitely) according to platelet count.
If platelets remain > 400 x 10^9/L after 3 months, anagrelide should be discontinued.

Main Toxicities: anaemia (transient); palpitations, fluid retention, tachycardia, heart failure and other cardiac side effects (see Comments); headache; rash

Anti- emetics: none routinely required

Regular Investigations:		
	FBC	weekly until a stable maintenance dose is achieved, then reduce to monthly, then 3 monthly, then up to 6 monthly only in suitable stable patients, as approved by Consultant
	LFTs	baseline, then 3 - 6 monthly as indicated
	U&Es	baseline, then 3 - 6 monthly as indicated

Reason for Update: review of frequency of monitoring FBC and biochem	Approved by Chair of Alliance TSSG: Dr A Laurie
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Supersedes: Version 3	Review date: Sept 2017
Prepared by: S Taylor	Checked by: C Tucker

Comments:	Anagrelide should be used with caution in patients with a history of heart failure. All patients should be monitored regularly throughout treatment for evidence of cardiovascular effects that may require further investigation.

Dose Modifications

Haematological Toxicity:	The platelet count will increase within 4 days of stopping treatment with anagrelide and will return to pre-treatment levels within 10 to 14 days.
Renal Impairment:	The Xagrid SPC states that anagrelide is contra-indicated in patients with CrCl < 50ml/min. The manufacturer has no pharmacokinetic data from patients with CrCl < 50ml/min. However, it is primarily metabolised in the liver and patients with mild to severe renal impairment have been treated with anagrelide at doses consistent with those used in patients without impairment. The potential risks and benefits of anagrelide should therefore be carefully considered before treatment is commenced in any patient with renal impairment, and anagrelide must only be used with caution and close monitoring in such patients.
Hepatic Impairment:	Hepatic metabolism represents the major route of anagrelide clearance. The potential risk versus benefit of anagrelide therapy in a patient with mild hepatic impairment should be assessed before treatment is commenced. It is contra-indicated in patients with moderate or severe hepatic impairment. It is not recommended in patients with elevated transaminases > 5 x ULN.
Patient Information:	Xagrid Patient Handbook produced by Shire Pharmaceuticals
References:	London New Drugs Group DTC Anagrelide Briefing Document Jan 2005 [1]Shire Pharmaceuticals