Policy for the use of Erythropoietin's for Cancer Treatment Induced Anaemia in the Northern Cancer Alliance.

Scope

This policy applies to the use of erythropoiesis-stimulating agents (ESAs) for chemotherapy and/or radiotherapy induced anaemia for solid tumours and haematological malignancies in both children and adults.

The policy does not cover the use of ESAs for treatment of anaemia related to renal function (including cancers where renal function is impaired such as myeloma).

Background

Erythropoietin is a naturally occurring protein which is produced by the kidney and is responsible for regulating red cell production. Epoetin alfa (Eprex™) and epoetin beta (NeoRecormon™) are recombinant erythropoietin analogues with almost identical sequences to the native protein. Darbepoetin alfa (Aranesp™) is a derivative of epoetin with a longer half-life. More recently bio-similar erythropoietins, epoetin zeta and theta have been launched in the UK.

All four have marketing authorisations (with varying wording and detail/specific groups of patients) for treatment of anaemia in patients receiving chemotherapy. Erythropoietin is generally slow to increase haemoglobin, and so patients with acute symptoms will often require blood transfusion or other supportive treatments.

Evidence Base & Cost Effectiveness

The National Institute of Clinical Excellence (NICE) reviewed the use of erythpoietins for treatment of cancer treatment induced anaemia in May 2008[1] and has reviewed this guidance in November 2014[2] In its updated guidance NICE recommended:

> *1.1 ESAs(epoetin alfa, beta, theta and zeta, and darbepoetin alfa) are recommended, within their marketing authorisations, as options for treating anaemia in people with cancer who are having chemotherapy.*
>
> *1.2 If different ESAs are equally suitable, the product with the lowest acquisition cost for the course of treatment should be used.*

There is an increasing body of evidence published that suggests ESAs have a detrimental effect on overall survival in cancer patients[3]. NICE undertook its own review of this data and has concluded that the risk is greatest where the product is used outside of the current product licence. The mechanisms for this remain to be fully elucidated however they may be due to increased risk of thrombosis, the erythropoietin acting as a growth factor for tumours or preventing apoptosis.

None of the ESAs are licenced for use alongside chemotherapy in children or for radiotherapy in children or adults and therefore given the concerns that ESAs may impact on survival it would be difficult to recommend them in this setting

Recommended Uses

There is no requirement to use ESAs instead of blood transfusion, only that they can be considered as an option. When doing so the survival impacts for patients outside of the use described by the product licence must be taken into consideration, and therefore the product licence of the ESAs should be very carefully followed. All the product licences requires that:

- An individual patient's clinical course and condition is evaluated by a physician prior to commencing and during erythropoiesis-stimulating agents.
- ESAs should never be commenced in chemotherapy patients with a Hb (Haemoglobin) greater than 100g/l.
- ESAs should never be commenced in chemotherapy patients with a Hb less than 80g/l.
- The starting dose described in the SmPC must be followed. (This differs between erythropoiesis-stimulating agents)
- The dose must be adjusted to maintain the Hb in the range 100 to 120g/l, once therapeutic target is achieved dose reduction should be considered to maintain the Hb.
- Patients with a Hb above 120g/l should have their dose modified, if the Hb exceeds 130g/l treatment with an Erythropoiesis-stimulating agent must be suspended until the Hb is less that 120g/l and then only restarted at a reduced dose.
- Dose increases for patients who have had a rise in Hb of less than 10g/l over a 4 week period should only be considered where the reticulocyte count has not increased by 40,000 cells/microl. Darbopoetin doses should not be increased.
- ESAs should be discontinued after 8 weeks (9 weeks for darbopoetin) if therapeutic goals have not been reached.

Increasing Hb by 1g/l can take 4 to 8 weeks, if there is a pressing clinical need to increase Hb then ESAs are probably not appropriate, and blood transfusion would be more appropriate. Combining transfusion and ESAs will make dose adjustment for Hb difficult to interpret and increases the risk of raising Hb above 120g/l which increases the risk of adversely impacting survival.

ESAs clearly carry an additional risk, especially when used outside of product licence, with a significant impact on survival; their use should therefore be restricted to cases where the potential impact on survival is outweighed by the potential clinical advantages of use.

Where ESAs are used these should not normally continue for more than 4 weeks after discontinuing chemotherapy.

Where it is necessary to use erythropoietin, the one with the lowest acquisition cost should be used (individual trusts may have agreed prices locally).

References

1. National Institute of Clinical Excellence. TA142 Anaemia (cancer-treatment induced) - erythropoietin (alpha and beta) and darbepoetin: guidance. NICE. London, UK. 2008
2. National Institute of Clinical Excellence. TA323 Erythropoiesis-stimulating agents (epoetin and darbepoetin) for treating anaemia in people with cancer having chemotherapy (including review of TA142). NICE. London, UK. 2014
3. Bohlius J et al. Recombinant human erythropoiesis-stimulating agents and mortality in patients with cancer: a meta-analysis of randomised trials. Lancet. 2009 May 2; 373:1532-42

Document Control

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Summary of Changes	1.1a	Minor amendments per chemo group.	
	1.2	Added section on Jehovah's Witness following discussion at pharmacy group	
	1.3	Updated following expiry, reviewed named products and NICE status	
	1.4	Reviewed and reapproved, set new review date	
	1.5	Reviewed and Updated following revised NICE guidance	
	1.6	Reviewed and reissued (branding changed to Northern Cancer Alliance)	