Myeloma UK Organisation Statement
NICE Health Technology Appraisal: Anaemia (cancer treatment-induced) – Erythropoiesis-stimulating agents (epoetin and darbepoetin) including a review of NICE TA142

Sources of evidence for inclusion in the statement

The patient perspective outlined in this submission is gathered from the day-to-day contact that Myeloma UK has with patients across the UK participating in and using our programmes and services.

These programmes and services include the Myeloma UK freephone Infoline, an 'Ask the Nurse' email service, Patient and Family Myeloma Infodays, Myeloma Support Group meetings, as well as regular user involvement questionnaires and evaluations.

Myeloma UK has conducted our own review of relevant published literature and has interpreted this very much from the perspective of patients.

We also work closely with a broad range of healthcare professionals involved in the treatment and care of myeloma patients, nationally and internationally, informally and more formally, via a number of advisory boards and committees. We have sought input and opinions from these professionals in relation to this appraisal, in particular using a brief survey on access to erythropoietin across England and Wales, the results of which we outlined in our earlier response to the draft scope.

If you have any questions or require any further information to assist with this appraisal, please contact [redacted] by emailing [redacted] or by calling [redacted].

General comments

In the Myeloma UK response to the NICE draft scope, we argued that due to reported issues with accessing erythropoiesis-stimulating agents (ESAs) for myeloma patients with cancer-related anaemia (i.e. anaemia relating to myeloma) across England and Wales, the remit of appraisal could either be expanded to assess the use of ESAs in this setting, or that they could be assessed separately by NICE. ESA treatment in patients with cancer-related anaemia, a particularly chronic form of the condition. is currently a major area of unmet need.

In response to this, NICE stated they "can only appraise the technologies within their marketing authorisation. The technologies are currently licensed for people receiving chemotherapy; therefore an appraisal of cancer-related anaemia is beyond the remit for this appraisal" (Appendix D – Page 6).

Whilst we acknowledge that this issue is beyond the remit of NICE in this appraisal, we do consider the lack of discussion about the wider use of ESAs to treat patients with cancer-related anaemia as short-sighted, particularly given the problems clinicians may sometimes face accurately determining the cause of anaemia and the impact both types of anaemia can have on a patients overall quality of life and experience.

Despite these general comments, the evidence provided below relates to cancer treatment-related anaemia.

About myeloma

Myeloma is an incurable, complex and debilitating cancer of the plasma cells. Across the UK there are approximately 4,000 people diagnosed with myeloma each year, with around 14,000 patients living with myeloma at any one time. Myeloma occurs mostly in older people, with 70% of patients over the age of 65.

In myeloma, whilst the survival rates have historically been poor, the introduction of 'novel' drugs such as thalidomide, bortezomib and lenalidomide administered in combination with traditional chemotherapy treatments and/or steroids have transformed the treatment of myeloma. Recent statistics show that the ten-year survival rates for myeloma have increased from just 5% in 1970 to

over 17% in 2011.[1] The Office for National Statistics (ONS) in 2010 also showed that five-year survival rates in myeloma are increasing at one of the fastest paces among all cancer types in the UK with over one-third of myeloma patients surviving for at least five years.[2]

Whilst the survival rates of myeloma are on the increase, the complications of myeloma and the associated treatment toxicities continue to impact on patients' overall quality of life, their experience of treatment and care and on their ability to 'live-well' with myeloma.

The complications of myeloma and its treatment include mild to severe anaemia, varying levels of fatigue, peripheral neuropathy, nausea, hypercalcaemia, bone destruction, bone fractures, frequent infection and kidney failure.

It is therefore very important that alongside direct anti-myeloma treatment, appropriate supportive treatments and interventions are available for patients to manage their complications and side-effects and to ensure that they are able to continue to lead a 'normal', good quality of life whilst living with myeloma – both whilst receiving treatment and during treatment-free intervals.

Anaemia and myeloma

In myeloma, anaemia is normochromic and normocytic and attributed to either the myeloma itself (a more chronic form) and/or the myelosuppressive effect of the chemotherapy (a more acute form, relating to this appraisal).

The British Committee for Standards in Haematology Guidelines for Supportive Care in Myeloma suggests that approximately 75% of myeloma patients present with anaemia[3] and a European-wide survey in patients with myeloma suggested that the prevalence of anaemia during chemotherapy is around 85%[4].

Anaemia is one of many complications patients may face as a result of treatment with chemotherapy and novel therapies and can impact severely on quality of life. Anaemia in myeloma patients receiving chemotherapy can range from a moderate form, which requires little to no medical intervention, through to severe anaemia where patients require frequent blood transfusions and treatment with ESAs.

Patients who experience symptomatic anaemia report varying levels of fatigue (ranging from mild tiredness to being physically unable to get out of bed), breathlessness, weakness throughout the body and the inability to carry out everyday tasks (such as walking or even boiling the kettle).

In a Myeloma UK survey conducted in 106 patients, 95% of patients reported that fatigue impacted on their personal and family life and on their emotional wellbeing. When asked about the tasks that became the most difficult with fatigue: 62% stated walking, 62% stated taking exercise, 46% stated concentrating and 49% stated cleaning the house.

Consensus of clinical opinion

Whilst anaemia can severely impact upon a patient who is receiving chemotherapy, it is also a side effect that is relatively easy to manage and can dramatically improve the experience of a patient.

Whilst the normal range for haemoglobin is 13.0 g/dL– 18.0 g/dL in adult males and 11.5 g/dL – 16.5 g/dL in females, the decision to treat anaemia is usually made depending on how symptomatic a patient is rather than on low haemoglobin levels. The British Committee for Standards in Haematology states that in most myeloma patients with symptomatic anaemia it can be adequately controlled through the use of blood transfusions. In patients who have anaemia that is less severe

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[1] **Cancer Research UK (2011)** http://www.cancerresearchuk.org/cancer-info/news/archive/pressrelease/2010-07-12-deadly-cancer-survival-doubles

[2] **Office for National Statistics** - Five-year age-standardised relative survival (%) for adults (15-99 years) diagnosed during 2003-2007 and followed up to 2008: England, 21 common cancers, by sex, 16 April 2010

[3] **British Society for Standards in Haematology in conjunction with the UK Myeloma Forum (2010)** – Guidelines for Supportive Care in Myeloma

[4] **Birgegard et al (2006)** – Evaluation of anaemia in patients with multiple myeloma and lymphoma: findings of the European Cancer Anaemia Survey. European Journal of Haematology 147, 22-42

(minimally or asymptomatic individuals) should be observed and do not necessarily require treatment.

The overall recommendations from the BCSH and UKMF state 'a therapeutic trial of ESA should be considered in a patient with persistent symptomatic anaemia (typically haemoglobin concentration of less than 10.0 g/dl) in whom haematinic deficiency has been excluded[5]'.

It is therefore important that ESAs are made available through NICE guidance for myeloma patients in the setting covered by the appraisal so that haematologists have access to them and can use their clinical discretion whether or not to use them in their individual patient.

Current use of ESAs in clinical practice

ESAs are mostly used in myeloma patients with kidney failure, as this is a setting approved by NICE.

As NICE has restricted the use of EPO in patients with cancer treatment-related anaemia, it is not routinely used in this setting for myeloma except in cases where a patient is unable to start or continue having blood transfusions or where a patient has experienced extremely severe symptoms of anaemia. However, the use of ESAs has been increasing due to their decreasing cost and to home delivery schemes operated in some areas of the UK, although access has been patchy.

Appraisal Technology Treatment Setting

Myeloma UK welcomes the opportunity presented by this appraisal to assess the new ESA products on the market, including biosimilars, and to the review the previous decision of NICE TA142 in light of new evidence on clinical effectiveness and the reduction in the price of ESAs.

Below we provide a brief outline of the clinical and cost-effectiveness of ESAs and the potential advantages and disadvantages of the technology. We consider the advantages of providing access to ESAs for myeloma patients with cancer treatment-related anaemia to far outweigh the potential disadvantages.

Clinical effectiveness

There is a wide range of published evidence to support the use of ESAs in the treatment of symptomatic anaemia in patients with cancer treatment-related anaemia which has been built upon since the last appraisal of ESAs. This evidence demonstrates that ESAs are both safe and effective in the treatment of myeloma and other cancer patients with moderate to severe anaemia who are receiving chemotherapy.

Since the previous NICE assessment a number of updated clinical guidelines have been published demonstrating consensus on the use of ESAs in myeloma. The American Society for Haematology (ASH) and the American Society of Clinical Oncology (ASCO) and the British Committee for Standards in Haematology (BCSH) and the UK Myeloma Forum (UKMF) all recommend the use of ESAs in symptomatic patients with cancer treatment-related anaemia. More specifically, the ASH and ASCO guidelines recommend that ESAs should be considered for patients undergoing myelosuppressive chemotherapy and who have haemoglobin of less than 10.0 g/dL[6].

In the UK, myeloma clinicians have also had extensive experience of using ESAs in clinical practice, particularly in patients with kidney failure, demonstrating their clinical effectiveness in the NHS real-world setting. Myeloma UK has also heard directly from myeloma patients who report the dramatic affect that ESAs can have on their quality of life after experiencing anaemia. We hope that this information will be taken into account in the appraisal.

Cost effectiveness

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[5] **British Society for Standards in Haematology in conjunction with the UK Myeloma Forum (2010)** – Guidelines for Supportive Care in Myeloma

[6] **ASCO-ASH (2010) -** Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin in Adult Patients with Cancer, Journal of Clinical Oncology, Volume 28, Issue 33 (November), 2010: 4996-5010

The introduction of a range of new ESA products and biosimilars onto the market has paved the way for a reduction in the price of ESAs and the relative cost it has to blood transfusions, making it more affordable for the NHS to provide for patients.

We welcome the introduction of biosimilars onto the market as a way of improving patient access to treatments and increasing market competition. There is currently no evidence to suggest ESA biosimilars are any less effective or safe than the generic versions of the treatments.

Myeloma UK has worked directly with patients who have received access to ESAs through home delivery schemes and contracts in place across different health authorities in England and Wales. Whilst these are not in place across all health authorities, they have made ESAs a lot cheaper and more convenient for patients in these areas and have also added to the reduction in price for these products.

(a) Potential advantages

Quality of life

The main advantage that the use of ESAs has in patients with cancer treatment-related anaemia is the dramatic impact they can have on improving their experience of chemotherapy and novel therapy treatment and their quality of life. ESAs can help to relieve fatigue and improve a patient's ability to carry out normal function and everyday tasks. This should not be underestimated by the NICE appraisal committee, particularly as the QALY does not adequately account for factors relating to quality of life.

ESA vs. Blood transfusion

There are a number of benefits that ESAs have over the use of continuous blood transfusion in patients with cancer treatment-related anaemia:

- Whilst blood transfusions may be able to improve anaemia in a patient with cancer treatment-related more quickly, ESAs can help a patient's anaemia recover on a longer and more permanent basis.
- The cost difference between ESAs and blood transfusions is also narrowing due to the increase of generics and biosimilars on the market making wider provision of ESAs more viable on the NHS
- As ESAs can now be provided in the home, this is easier and more convenient for patients and removes the necessity of continual treatments to hospital for repeat blood transfusions

Improved treatment outcomes

In patients with cancer treatment-related anaemia, if blood transfusions are not working appropriately and ESAs are not provided to a patient then this could result in below optimum treatment for patients as in severe cases patients may have to have the dose of their cancer treatment reduced to counter for their side-effects. Ultimately, this could affect their long term outcomes from their treatment.

(b) Potential disadvantages

Thrombotic events

The BCSH and UKMF state that there is an increase risk of thrombotic events in patients with cancer who are treated with ESAs. However, these can be offset by a thorough assessment of the benefits and risks of an individual patient prior to prescribing the use of ESAs.

Summary

Myeloma UK believes there is a very strong case to support the approval of ESAs in the treatment of cancer treatment-related anaemia in myeloma. Myeloma clinicians should have the option to prescribe ESAs to patients in this setting where it is clinically relevant.

The supporting information on the clinical and cost-effectiveness of ESAs is compelling and the potential advantages to patients significantly outweigh any disadvantages.