MDS UK
Supporting Patients with Bone Marrow Failure
www.mdspatientsupport.org.uk

What are ESAs?

Information and advice on EPO and GCSF

Fact sheet for Myelodysplastic Syndrome (MDS) Patients

Symptoms of MDS may place extra physical and mental demands on you. We produce Factsheets, to help you understand care and treatment options. Join us for more help, if you have not yet done so.

Erythropoiesis stimulating agents (ESAs) in MDS

More than two thirds of patients with myelodysplastic syndromes (MDS) are anaemic at the time of diagnosis. About the same proportion have the lower-risk form of MDS, as defined by the Revised International Prognostic Scoring System criteria (IPSS-R).

Anaemia can be a significant burden and may impair a person's ability to perform normal tasks due to exhaustion or fatigue. It may also worsen other medical conditions, like heart disease or respiratory conditions. Measures taken to optimise or improve **haemoglobin** levels are vitally important, particularly in low-risk MDS where anaemia may persist for many years.

In MDS, **red cell blood transfusions** are the most frequent way in which anaemia is managed. However, regular transfusions may cause iron overload, which consequently may then need to be controlled. Additionally, regular red cell transfusion schedules are time-consuming and carry the inconvenience and burden of travel to and from the hospital.

ESAs are drugs that improve haemoglobin levels, may reduce the frequency or need for red cell transfusions, and may improve or maintain **your quality of life**.

What is Erythropoietin?

Erythropoietin (usually referred to as EPO) is a naturally occurring hormone produced by specific cells in the kidneys. It plays a vital role in red cell production (erythropoiesis) by the bone marrow. When EPO is administered by a simple injection under the skin (subcutaneous injection) it can lead to an increase in haemoglobin levels which may result in improved wellbeing.

There are data to suggest that starting ESA therapy early may delay the need for regular red cell blood transfusion and **improve quality of life.**

Since the 1990s clinical trials demonstrated that EPO can be safely used to improve haemoglobin levels in patients with low-risk MDS. Better responses to EPO have been reported in MDS patients with baseline EPO levels of less than 200 U/L (with the exception of MDS with ring sideroblasts (MDS-RS)). However, other factors influence response to EPO in MDS, including shorter time from diagnosis to treatment, low transfusion requirement before starting EPO treatment and low-risk disease defined as IPSS-R very low to intermediate.

Erythropoietin and granulocyte colony-stimulating factor

Granulocyte colony-stimulating factor (G-CSF) is a growth protein that stimulates the production of neutrophils (a type of white blood cell) in the bone marrow. Like EPO, it is administered as a subcutaneous injection.

Several clinical studies have demonstrated that EPO and G-CSF work together to enhance haemoglobin levels.

How will my haematologist decide if I need an ESA?

You may be a candidate for ESA therapy, if you have:

- low-risk MDS (IPSS-R score= very low, low or intermediate)
- symptoms of anaemia with haemoglobin level of less than 100g/L

Your haematologist will use a scoring system, based on your monthly red cell blood transfusion requirement, and baseline serum EPO levels prior to starting ESA, to calculate if ESA therapy is likely to work for you.

With a score of 0 or 1.0: the predicted response level will vary between 74% and 23% respectively.
You may be offered EPO if you are anaemic.

With a score of 2.0: generally, there is a low chance of responding to ESA (less than 10%).
EPO is therefore generally not recommended.

Dosing of ESA

Typically**, if you have a low-risk form of MDS** (with the exception of MDS-RS) the initial start dose of EPO is 30,000 units/week.
For patients with impaired kidney function, lower doses may be recommended.
If the treatment does not produce a response after 8 weeks, your dose may be increased to 30,000 units twice weekly or 60,000 units/week for a further 8 weeks.
If you have been prescribed the ESA Darbopoietin, the starting dose should be 150 micrograms/week or 300 micrograms every 2 weeks. In case of non-response, after 8 weeks, the dose can be increased to 300 micrograms/week.

If the treatment is not producing a response to EPO alone, you may be prescribed G-CSF as an additional treatment. The typical starting dose of G-CSF in this setting is 300 micrograms once weekly with the aim of increasing the neutrophil count to no more than 6 to $10x10^9$/L. Doses of G-CSF should generally not exceed 300 micrograms three times per week.

How will I know if the treatment is working?

Your haematologist will assess your response to ESA assessed after a maximum period of 4 months of therapy.
Clinical responses are usually assessed by documenting improvement in haemoglobin levels, and/or reduction in red cell transfusion requirement. Response (efficacy) can be defined as:

- **Partial response/efficacy**
  - In red cell transfusion dependent patients: Stable anaemia without need for transfusions
  - In patients with stable anaemia: Increase in haemoglobin of at least 15g/L but haemoglobin less than 115g/L
- **Complete response/efficacy**
  - Stable haemoglobin of at least 115g/L and transfusion independence.

If the treatment produces a sustained complete response, your haematologist may slowly reduce the ESA dose to the lowest level that sustains the response.
If the response to ESA becomes weaker, it may be necessary to reassess your MDS disease status with a bone marrow biopsy, full blood count and blood film examination in order to exclude the possibility of progression of the MDS.

Side effects

ESAs are generally well tolerated by most patients. However, you **may** experience:

- mild but temporary discomfort at the site of injection particularly with the first dose, as well as redness at the injection site
- a rise in blood pressure. Your blood pressure should be measured before starting ESA treatment and should be assessed whilst on treatment. This is particularly important if you have a history of high blood pressure.
- headaches
- cough
- muscle and joint pain
- fever

The use of ESAs has been associated with thrombosis (blood clot) but this risk is very low and ESA treatment will usually be stopped if your haemoglobin rises above 120 g/L, or rises too rapidly.

Always report health issues or side-effects to your medical team, even if not necessarily linked to any new treatment

References and further reading

This MDS patient Factsheet on ESAs is an abridged version of a full article by Dr Chris Dalley, Consultant Haematologist, (University Hospital Southampton NHS Foundation Trust, Southampton General Hospital) and reviewed by Dr Sally Killick (Consultant Haematologist at University Hospitals Dorset, The Royal Bournemouth Hospital) and MDS UK Patient Support Group. The full article, with full references can be found on the MDS UK website:
https://mdspatientsupport.org.uk/epo-erythropoietin-other-erythropoiesis-stimulating-agents-esas-in-the-treatment-of-mds/
The article follows the July 2021 updated BSH Treatment Guidelines for MDS:
https://b-s-h.org.uk/guidelines/guidelines/guidelines-for-the-management-of-adult-myelodysplastic-syndromes/
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Please note this fact sheet is a guide and should not replace the advice of your clinical team.

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