

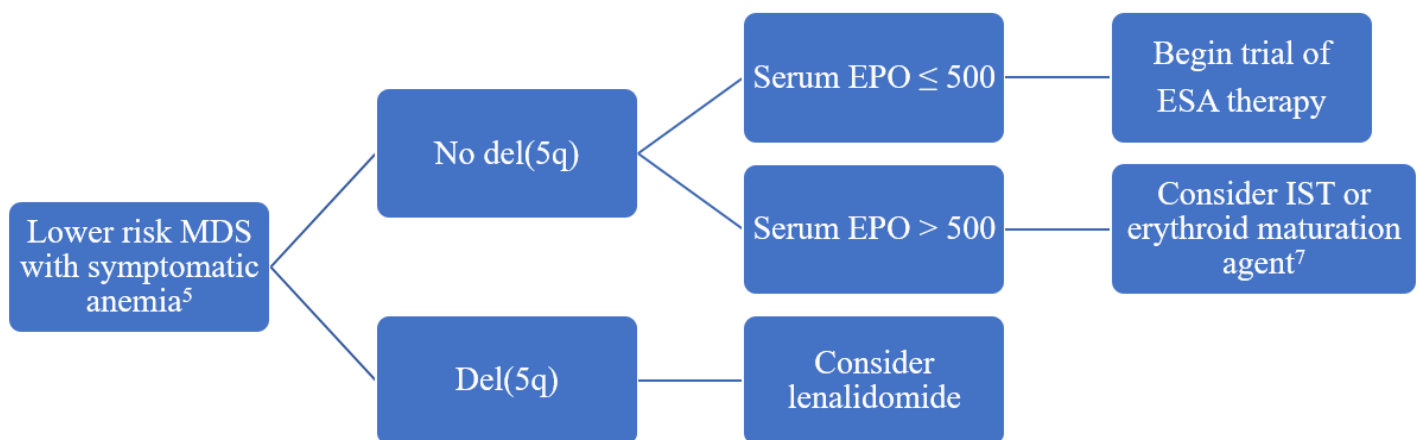
Positive Quality Intervention: Erythropoietin Stimulating Agent (ESA) Ineligibility in Myelodysplastic Syndromes (MDS)

Description: This PQI is centered on erythropoietin stimulating agent (ESA) ineligibility in patients suffering from myelodysplastic syndromes (MDS), as well as understanding when an MDS patient fails ESA treatment or has a suboptimal ESA response.

Background: MDS are chronic disorders of clonal hematopoiesis leading to peripheral cytopenias, primarily anemia, which can ultimately progress to bone marrow failure and acute myeloid leukemia. Patients suffering from MDS are stratified by the revised International Prognostic Scoring System (IPSS-R) into risk groups ranging from very low to very high risk (Tables 1 and 2 in Supplemental Information).^{4,5} The treatment of lower risk MDS is typically focused on optimizing patients' quality of life and providing support for symptomatic anemia. ESA agents, including epoetin and darbepoetin, are commonly used to treat MDS-associated anemia in lower risk disease to avoid chronic transfusions and the risk of iron overload, but patient response to these agents can be variable and impermanent.³⁻⁶ Generally, administration of ESAs yields an erythroid response, i.e., at least 1.5 g/dL increase in hemoglobin or decrease in need for RBC transfusion, in 20-60% of MDS patients with anemia.^{4,6} Factors considered to be predictive of favorable response of MDS anemia to ESA agents include low baseline endogenous erythropoietin (EPO) levels (< 500 mU/mL, but preferably < 200 mU/mL), low (< 2 per month) or no RBC unit transfusion requirement, and disease cytogenetics, namely absence of del(5q) and less than 2 somatic mutations.^{2,4,6,8} Conversely, patients with del(5q) disease, serum EPO levels > 500 mU/mL, or heavy transfusion dependence would commonly be considered ineligible for a trial of ESA therapy.^{2,10} Primary resistance to ESA agents is possible, and, even if these patients do have an initial response to ESA therapy, in up to 70% of cases this response tends to wane within 18 to 24 months.⁶⁻⁷

PQI Process:

- Upon diagnosis or clinical review of a MDS patient, patient should be assessed for symptomatic anemia
- If symptomatic anemia present proceed through following stepwise treatment algorithm:



EPO: erythropoietin; ESA: erythropoietin stimulating agent; IST: immunosuppressive therapy

Important Notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional. *Updated 10.6.22*

- Recommended starting dose of ESA⁷:
 - Epoetin alfa or biosimilar 40,000–60,000 units subcutaneously 1–2 times per week
 - Or
 - Darbepoetin alfa 150–300 mcg subcutaneously weekly to every other week
- Assessment for ESA response by 6 to 8 weeks of treatment⁶:
 - 1.5 g/dL rise in hemoglobin
 - And/or
 - Decrease in RBC transfusion requirement
- Target hemoglobin range 10 to 12 g/dL; not to exceed 12 g/dL^{1,4,7,9,11}
- If desired response not reached can consider add on therapy with agent such as lenalidomide or granulocyte-colony stimulating factor^{2,4,6}
- Avoid use of ESAs in patients who also have concomitant diagnosis of solid tumor malignancy and are undergoing active treatment. ESAs shortened overall survival and/or increased the risk of tumor progression or recurrence in clinical studies of patients with solid tumor malignancy. ESAs are not indicated for patients receiving myelosuppressive chemotherapy when the anticipated outcome is cure.⁹

Patient Centered Activities:

- If patient to start on ESA for treatment of MDS anemia:
 - Advise patient of risk of increased blood pressure with ESAs especially if patient has baseline history of hypertension^{1,9}
 - Advise patient on signs/symptoms of venous thromboembolism, stroke, and myocardial infarction and when to contact healthcare provider or proceed to ER for evaluation
 - Counsel patient to notify team of any upcoming surgical procedures as DVT prophylaxis is recommended in perisurgery patients
 - Counsel patient that response to ESA therapy typically takes at least 6 to 8 weeks but can take up to 12 weeks
 - Counsel patient regarding risk of cutaneous reactions including rash but also severe reactions such as erythema multiforme and Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN)

References:

1. [Aranesp \(darbepoetin alfa\) \[prescribing information\]](#)
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3. Fenaux P, et al. Luspatercept in Patients with Lower-Risk Myelodysplastic Syndromes. *N Engl J Med*. 2020 Jan 9;382(2):140-151. doi: 10.1056/NEJMoa1908892. PMID: 31914241.
4. Fenaux P, Adès L. How we treat lower-risk myelodysplastic syndromes. *Blood*. 2013 May 23;121(21):4280-6. doi: 10.1182/blood-2013-02-453068. Epub 2013 Apr 10.
5. Greenberg PL, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012 Sep 20;120(12):2454-65. doi: 10.1182/blood-2012-03-420489. Epub 2012 Jun 27.
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7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myelodysplastic Syndromes V.3.2022. ©
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9. [Procrit® \(epoetin alfa\) \[prescribing information\]](#)
10. Santini V. Treatment of low-risk myelodysplastic syndromes. *Hematology Am Soc Hematol Educ Program*. 2016 Dec 2;2016(1):462-469. doi: 10.1182/asheducation-2016.1.462.
11. Carraway, H. E., & Saygin, C. (2020, December 4). Therapy for lower-risk MDS. *American Society of Hematology*. Retrieved October 6, 2022, from <https://ashpublications.org/hematology/article/2020/1/426/474325/Therapy-for-lower-risk-MDS>.

Supplemental Information:

Table 1. Revised international prognostic scoring system (IPSS-R) in myelodysplastic syndrome⁵

Prognostic variable	Score						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics	Very good		Good		Intermediate	Poor	Very poor
Bone marrow blast	≤ 2		>2 to <5		5 to 10	>10	

(percent)							
Hemoglobin (g/dL)	≥10		8 to <10	<8			
Platelets (cells/microL)	≥100	50 to 100	<50				
Absolute neutrophil count (cells/microL)	≥0.8	<0.8					

Table 2. IPSS-R myelodysplastic syndrome risk groups and prognosis⁵

Risk group	IPSS-R score	Median overall survival (years)	Median time to 25 percent AML evolution (years)
Very low	≤1.5	8.8	>14.5
Low	>1.5 to 3.0	5.3	10.8
Intermediate	>3 to 4.5	3.0	3.2
High	>4.5 to 6	1.6	1.4
Very high	>6	0.8	0.7