Anemia

CHI Formulary Treatment algorithm

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Council of Health Insurance

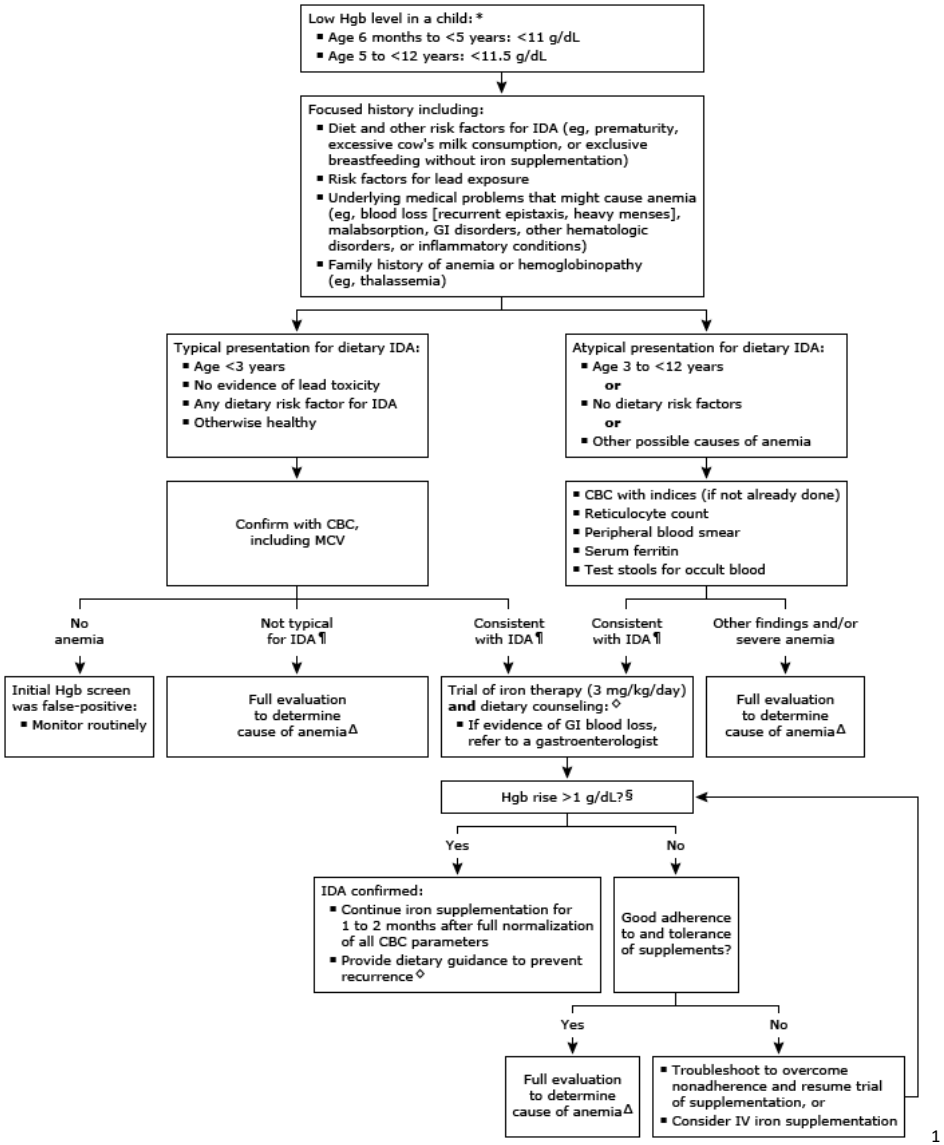
Treatment algorithm- February 2024

Supporting treatment algorithms for the clinical management of Anemia

Figures 1 to 7 outline a comprehensive treatment algorithm on the **management of Anemia**, respectively, aimed at addressing the different lines of treatment after thorough review of medical and economic evidence by CHI committees.

For further evidence, please refer to CHI **Anemia** full report. You can stay updated on the upcoming changes to our formulary by visiting our website at https://chi.gov.sa/AboutCCHI/CCHIprograms/Pages/IDF.aspx

Our treatment algorithm offers a robust framework for enhancing patient care and optimizing treatment outcomes across a range of treatment options, holding great promise for improving healthcare delivery.



[1]

Hgb: hemoglobin; IDA: iron deficiency anemia; GI; gastrointestinal; CBC: complete blood count; MCV: mean corpuscular volume; IV: intravenous; RDW: red cell distribution width; TIBC: total iron-binding capacity.

* Routine screening for IDA in children typically consists of measurement of a CBC or Hgb[1]. This approach to screening does not detect nonanemic iron deficiency. For children with risk factors for iron deficiency, we suggest measuring serum ferritin at the time of the initial screen.

¶ CBC findings typical for IDA are low hemoglobin (Hgb <11 g/dL), low MCV (microcytic anemia), elevated RDW, and, occasionally, thrombocytosis. These findings do not exclude some other causes of anemia, including anemia of chronic disease/inflammation, or thalassemia. A low serum ferritin level is always consistent with iron deficiency, but normal or elevated ferritin does not exclude iron deficiency.

Δ Evaluation may include an iron panel (serum iron, ferritin, TIBC), peripheral blood smear, Hgb electrophoresis, evaluation for gastrointestinal blood loss, assessment for inflammatory disease (eg, C-reactive protein), and review of newborn screening results to assess for alpha thalassemia trait (which cannot be diagnosed by Hgb electrophoresis). Anemia is severe if Hgb <7 g/dL. For details, refer to UpToDate content on approach to anemia in children. Depending on the type of concern, referral to a pediatric hematologist or gastroenterologist and/or IV iron supplementation may be appropriate.

◊ Dietary counseling includes measures to improve iron intake and avoid excessive cow's milk. Infants should not consume unmodified (nonformula) cow's milk. For children 12 months of age and older, cow's milk consumption should be limited to less than 20 oz (600 mL) daily. If occult blood is present in the stool, all milk products should be stopped and the patient should be evaluated to determine the cause of the GI blood loss.

§ In children with IDA, the Hgb rise (>1 g/dL) is expected within 4 weeks for those with mild or moderate anemia (baseline Hgb 7 to 11 g/dL) and within 2 weeks for those with severe anemia (baseline Hgb <7 g/dL).

Figure 1: Algorithm for evaluation of iron deficiency anemia in children 6 months to 12 years old

[1] *Evaluation of iron deficiency anemia in children*. (2023). UpToDate. https://www.uptodate.com/contents/image?rank=8~150&source=graphics_search&imageKey=PEDS%2F114480

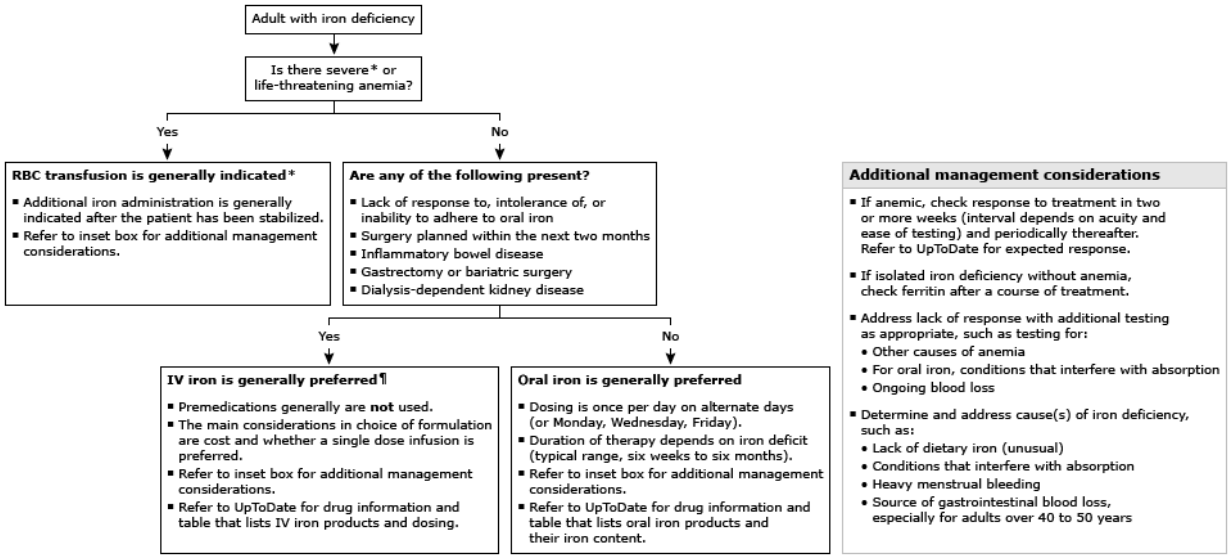


Figure 2: Treatment of iron deficiency in nonpregnant adults

This algorithm applies to individuals with iron deficiency, with or without anemia. We treat all individuals who have iron deficiency anemia and most who have iron deficiency without anemia. For oral iron, alternate-day dosing facilitates absorption and reduces adverse effects; however, some patients may reasonably take their dose daily rather than every other day if pr[2]eferred.

RBC: red blood cell; IV: intravenous.

* Severe anemia generally refers to a hemoglobin level of <7 to 8 g/dL or anemia with symptoms of hemodynamic compromise or cardiac ischemia. RBC transfusion is the fastest way to raise the hemoglobin level in these individuals, although some people may tolerate lower hemoglobin levels without transfusion and may reasonably decline transfusions for asymptomatic or mildly symptomatic anemia with a hemoglobin in this range. One unit of RBCs contains approximately 200 mg of iron, which is unlikely to completely replete body iron stores.

¶ Some experts will give a trial of oral iron first before using IV iron, especially if resources or facilities for administering IV iron are limiting. IV iron provides full replacement much more rapidly than oral iron and does not cause gastrointestinal side effects. IV iron can be given in the second and third trimesters of pregnancy but not the first trimester (due to lack of safety data in the first trimester). Concerns about anaphylaxis with IV iron mainly apply to a formulation that is no longer available. Minor infusion reactions such as flushing and myalgias occur in <1% of individuals and are generally treated by pausing the infusion.

[2] UpToDate. (2023). *Iron deficiency treatment (adults).* https://www.uptodate.com/contents/image?rank=1~150&source=graphics_search&imageKey=HEME%2F131023&search=Treatment%20of%20iron%20deficiency%20in%20nonpregnant%20adults

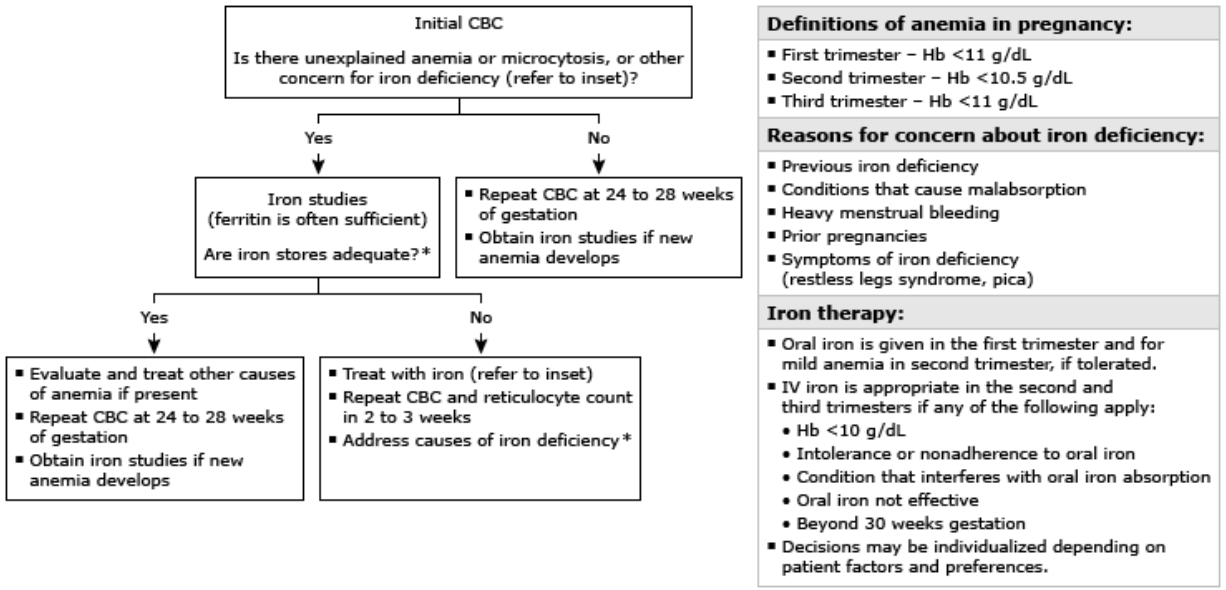


Figure 3: Evaluation and treatment of anemia in pregnancy

Iron deficiency is common in pregnancy and is associated with adverse maternal and fetal outcomes, although causation has not been demonstrated. Oral iron takes weeks to months to replete iron stores, depending on the degree of deficiency; this is unlikely to be effective beyond 30 weeks gestation. IV iron repletes stores much more rapidly; some individuals may reasonably choose to use oral iron if they have reasons to avoid IV iron. Transfusion is reserved for severe, symptomatic anemia (Hb <7 g/dL or acute anemia with hemodynamic or respiratory compromise).

Routine prenatal vitamins contain folic acid and may contain iron. The amount of iron in prenatal vitamins is helpful for preventing iron deficiency but is not sufficient for treating iron deficiency.[3]

CBC: complete blood count; IV: intravenous; Hb: hemoglobin.

* Ferritin <30 ng/mL (<30 mcg/L) confirms iron deficiency. Ferritin ≥30 ng/mL is sufficient to rule out iron deficiency in the absence of chronic illness. Refer to UpToDate for additional information on diagnosing iron deficiency and evaluating other causes of anemia in pregnancy.

[3] UpToDate. (2023). *Pregnancy anemia*. https://www.uptodate.com/contents/image?rank=4~76&source=graphics_search&imageKey=HEME%2F138445

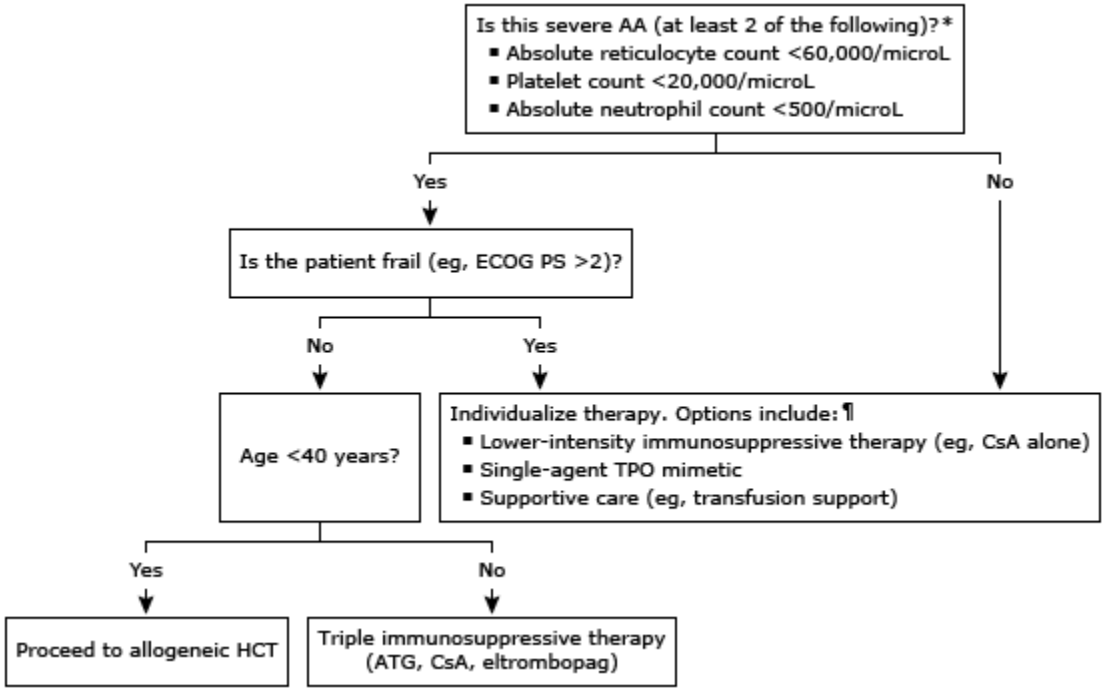


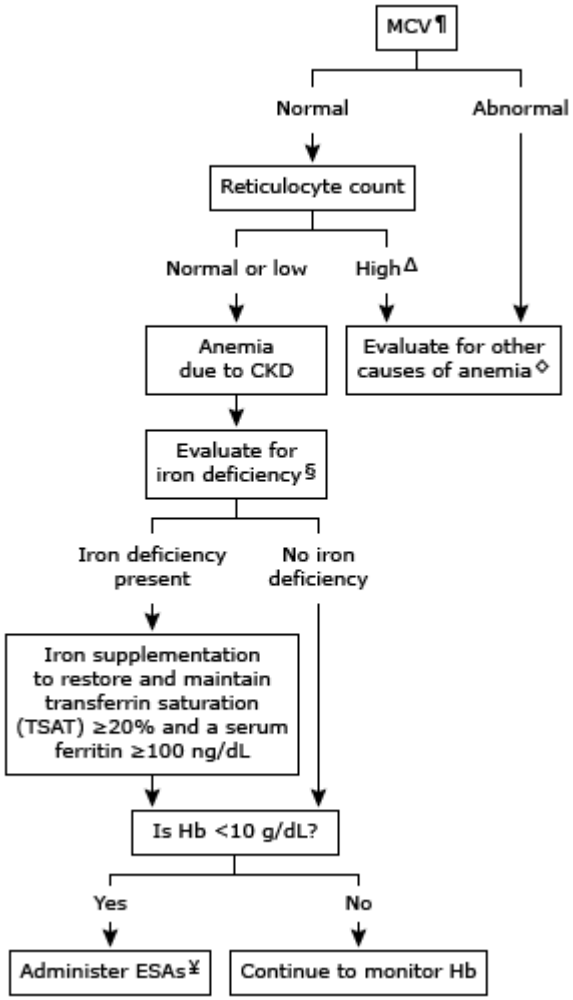
Figure 4: Management of aplastic anemia in adults

AA: aplastic anemia; ATG: anti-thymocyte globulin; CsA: cyclosporine A; ECOG PS: Eastern Cooperative Oncology Group performance status; HCT: hematopoietic cell transplantation; TPO: t[4]hrombopoietin.

* Criteria for severe AA may vary among centers. Some patients who do not strictly meet these criteria may be considered to have severe AA.

¶ Patients with moderate AA should be monitored for progression to severe AA; treatment is individualized and management should consider comorbid conditions.

[4] UpToDate. (2023). *Aplastic anemia: Management in adults*. https://www.uptodate.com/contents/image?rank=19~150&source=graphics_search&imageKey=HEME%2F139782



MCV: mean corpuscular volume; CKD: chronic kidney disease; Hb: hemoglobin; ESA: erythropoiesis-stimulating agents.
* This algorithm is intended for children with moderate to severe CKD defined as an estimated glomerular filtration rate <59 mL/min per 1.73 m^2 and anemia defined as an Hb <2.5th percentile based on the patient's age, sex, and race.

¶ MCV is measured directly by automated blood cell counters and represents the mean value (in femtoliters [fL]) of the volume of individual red blood cells in the blood sample. Normal values for MCV vary based upon age. sex, and race. Refer to UpToDate topics on the approach to the child with anemia.
Δ High reticulocyte count >3% is associated with an increased erythropoietic response to blood loss or hemolysis. Common causes of anemia with a high reticulocyte count include: hemorrhage, autoimmune hemolytic anemia, membranopathies (eg, hereditary spherocytosis), enzymopathies (eg, glucose-6-phosphate dehydrogenase [G6PD] deficiency). hemoglobinopathies (eg, sickle cell disease), and microangiopathic hemolytic anemia (eg, hemolytic uremic syndrome). Refer to UpToDate topic on the approach to the child with anemia.
◊ In some cases, anemia may be due to both CKD and iron deficiency resulting in microcytic anemia (low MCV). In this setting, anemia will persist with normalization of MCV after iron repletion demonstrating the underlying contribution of CKD.
§ Iron deficiency is diagnosed by laboratory testing including measuring serum iron, total iron binding capacity, percent transferrin saturation (TSAT), and serum ferritin. Refer to UpToDate topics on iron deficiency in children and adolescents.
¥ ESAs include recombinant human erythropoietin (rHuEPO) and darbepoetin alfa.

Figure 5: Evaluation and management of anemia in[5] children with CKD*

[5] UpToDate. (2023). *Evaluation and management of anemia in children with CKD*. https://www.uptodate.com/contents/image?rank=23~150&source=graphics_search&imageKey=PEDS%2F130059

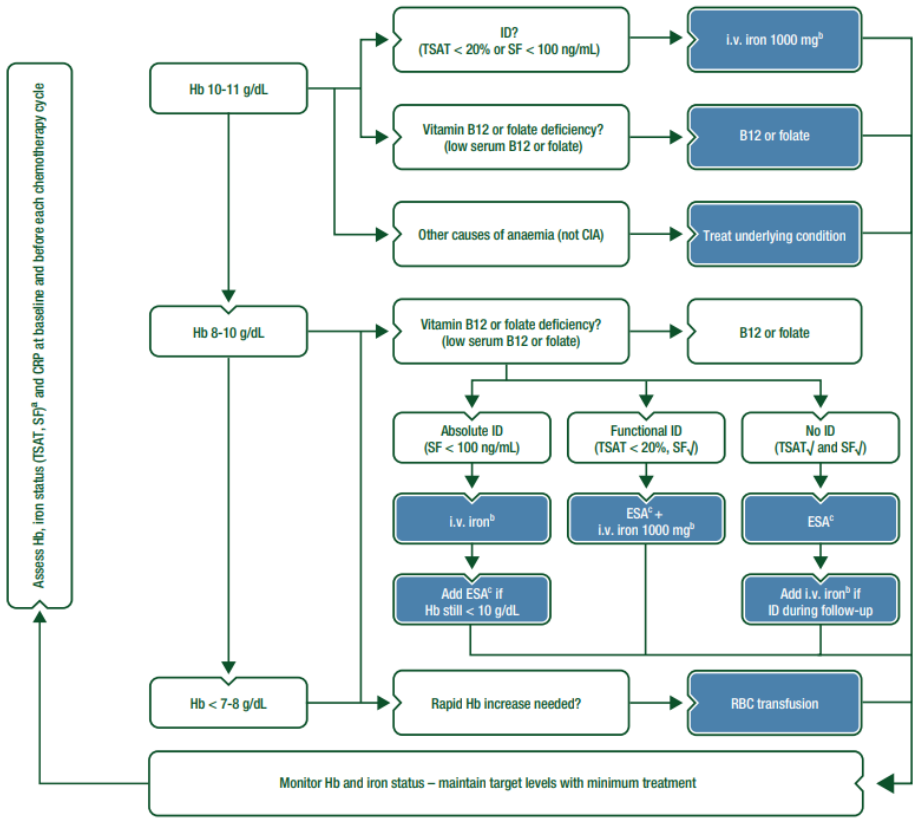


Figure 6: Management of chemotherapy-induced anemia in patients with solid or hematological malignancies

[a]Other parameters for impaired iron status: % hypochromic cells (%HYPO) > 5% and Hb content of reticulocytes (CHr) < 28 pg.

[b]i.v. iron given as a single dose of 1000 mg iron or an equivalent total dose in several infusions as feasible with available i.v. iron formulations. Oral iron to be considered only for patients with ferritin < 30 ng/mL and non-inflammatory conditions [CRP < 5 mg/L].

[c]ESA dosing should follow approved labels (i.e. ~ 450 IU/week/kg body weight for epoetins alpha, beta and zeta; 6.75 mg/kg body weight every 3 weeks or 2.25 mg/kg body weight weekly for darbepoetin alpha; 20 000 IU once weekly for epoetin theta which may be doubled after 4 weeks upon insufficient response). ESA dose escalations or a change to another ESA in patients who do not respond within 4–8 weeks are not recommended; ESA should be stopped in this case.

CIA, chemotherapy-induced anaemia; CRP, C-reactive protein; ESA, erythropoiesis-stimulating agent; Hb, haemoglobin; ID, iron deficiency; i.v., intravenous; RBC, red blood cell; SF, serum ferritin; TSAT, transferrin saturation

[6]

[6] Aapro, M., Beguin, Y., Bokemeyer, C., Dicato, M., Gascón, P., Glaspy, J., Hofmann, A., Link, H., Littlewood, T., Ludwig, H., Österborg, A., Pronzato, P., Santini, V., Schrijvers, D., Stauder, R., Jordan, K., & Herrstedt, J. (2018). Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. *Annals of Oncology*, *29*, iv96–iv110. https://doi.org/10.1093/annonc/mdx758

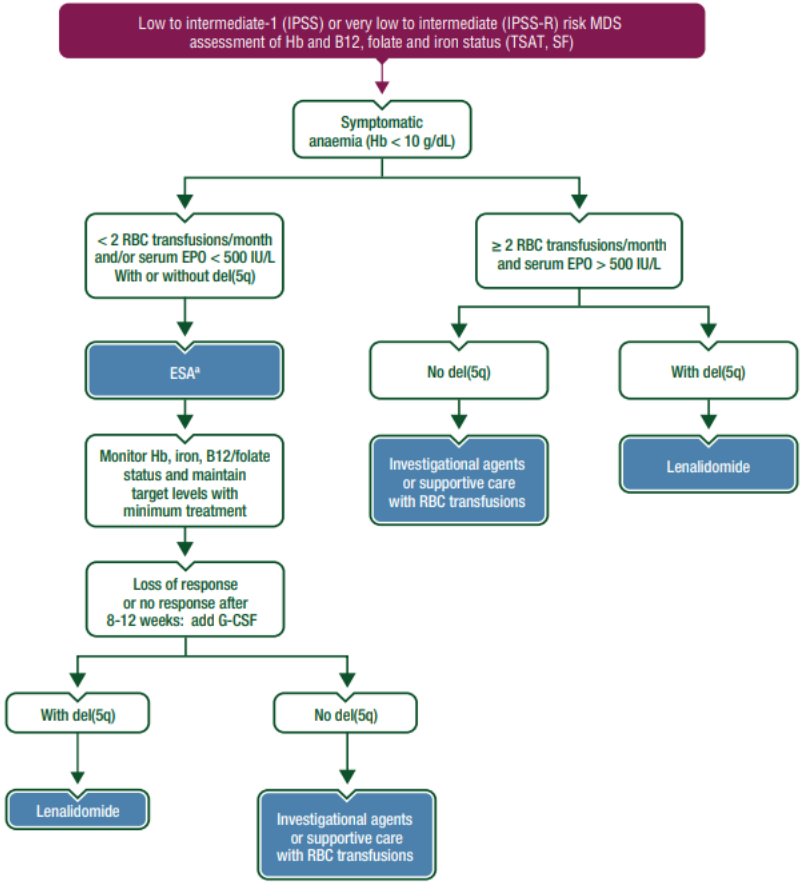


Figure 7: Management of anemia in patients with very low to intermediate-risk MDS

[a]ESA-treated patients who are iron deficient and transfusion independent may be considered for i.v. iron treatment.

EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; G-CSF, granulocyte colony-stimulating factor; Hb, haemoglobin; IPSS, International Prognostic Scoring System; IPSS-R, revised International Prognostic Scoring[7] System; i.v., intravenous; MDS, myelodysplastic syndrome; RBC, red blood cell; SF, serum ferritin; TSAT, transferrin saturation

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[7] Aapro, M., Beguin, Y., Bokemeyer, C., Dicato, M., Gascón, P., Glaspy, J., Hofmann, A., Link, H., Littlewood, T., Ludwig, H., Österborg, A., Pronzato, P., Santini, V., Schrijvers, D., Stauder, R., Jordan, K., & Herrstedt, J. (2018). Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. *Annals of Oncology*, *29*, iv96–iv110. https://doi.org/10.1093/annonc/mdx758