Epoetin and Darbepoetin

ACG: A-0301 (AC)
Link to Codes

MCG Health
Ambulatory Care
30th Edition

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Clinical Indications

- Epoetin and darbepoetin (recombinant) may be indicated for **1 or more** of the following(1)(2)(3)(4):
  - Anemia associated with chemotherapy, as indicated by **ALL** of the following(9)(10)(12):N
    - Anemia due to chemotherapy
    - Chemotherapy not being administered in anticipation of cure
    - Chemotherapy to be administered for 2 or more months
    - Hemoglobin 10 g/dL (100 g/L) or less(19)
    - No uncontrolled hypertension
    - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).(19)
    - Patient receiving myelosuppressive chemotherapy for metastatic nonmyeloid malignancy(47)
  - Anemia associated with myelodysplastic syndrome, as indicated by **1 or more** of the following[A](9)(10)(48)(51)(52):N
    - Initial course, as indicated by **ALL** of the following:
      - Endogenous serum erythropoietin level of 500 International Units per liter (IU/L) or less
      - Hemoglobin of 10 g/dL (100 g/L) or less
      - Less than 10% blasts in bone marrow[B]
      - No uncontrolled hypertension
      - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).
    - Subsequent course, with favorable response to prior administration of epoetin or darbepoetin
  - Anemia associated with myelofibrosis, as indicated by **1 or more** of the following(55)(56)(57)(58):N
    - Initial course, as indicated by **ALL** of the following:
      - Endogenous serum erythropoietin level of 500 International Units per liter (IU/L) or less
      - Hemoglobin of 10 g/dL (100 g/L) or less
      - No uncontrolled hypertension
      - No symptomatic splenomegaly(62)
      - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).
    - Subsequent course, with favorable response to prior administration of epoetin or darbepoetin

- Elective surgery, as indicated by **ALL** of the following[C](63)(64)(65):
  - Estimated blood loss of 2 units or more
  - No uncontrolled hypertension
  - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).(19)
  - Preoperative hemoglobin greater than 10 g/dL (100 g/L) and less than or equal to 13 g/dL (130 g/L)
  - Replacement for allogeneic transfusion desired
  - Surgical procedure elective, noncardiac, and nonvascular
- HIV/AIDS and **1 or more** of the following[D]:
  - Initial course, as indicated by **ALL** of the following:
    - Anemia has not improved after 6 months of highly active antiretroviral therapy.
    - Endogenous serum erythropoietin 500 International Units per liter (IU/L) or less
    - Hematocrit less than 30% (0.30)
    - HIV-infected patient receiving zidovudine treatment with dosage 4200 mg/week or less
    - No uncontrolled hypertension
    - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).(19)
  - Subsequent course, with favorable response to prior administration of epoetin or darbepoetin
- Kidney disease and **1 or more** of the following[E][F](69)(70)(71)(72)(73):
  - Initial course, as indicated by **ALL** of the following:
    - Anemia status is **1 or more** of the following(86):
      - For adult patient on dialysis, hemoglobin is less than 10 g/dL (100 g/L).(87)(88)(89)
      - For adult patient not on dialysis, **ALL** of the following:
        - Hemoglobin is less than 10 g/dL (100 g/L).
        - Rate of hemoglobin decline indicates likelihood of requiring blood transfusion.
        - Therapeutic goal is reduction of blood transfusion-related risks.
      - For pediatric patient with chronic kidney disease, hemoglobin is less than 10 g/dL (100 g/L).
    - Ferritin prior to therapy 100 ng/mL (mcg/L) or more(90)
    - Kidney disease, as indicated by **1 or more** of the following:
      - Chronic kidney disease, not on hemodialysis(91)
      - End-stage renal disease, on hemodialysis
      - Serum creatinine greater than 2 mg/dL (177 micromoles/L)
    - No uncontrolled hypertension
    - Patient has been evaluated and treated for other causes of anemia (eg, iron deficiency, hemolysis, vitamin B12 deficiency).(19)(92)
    - Transferrin saturation prior to therapy 20% or more(90)
  - Subsequent course, with favorable response to prior administration of epoetin or darbepoetin

Evidence Summary

Background

Epoetin and darbepoetin are erythropoiesis-stimulating agents; they are closely related recombinant human proteins similar to erythropoietin that stimulate production of erythrocytes.(1)(2)(3)(4)(5)(6) **(EG 2)**

Criteria

The evidence for the clinical indications found in this guideline includes 64 published peer reviewed articles, 6 specialty society or other evidence-based guidelines, and 13 Cochrane systematic reviews.

For anemia associated with chemotherapy, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Systematic reviews of randomized controlled trials and specialty society guidelines indicate that recombinant human erythropoietin is effective in reducing transfusion requirements in cancer patients undergoing chemotherapy, even though increased risks of death and thromboembolic events must always be considered.(11)(12)(43) **(EG 1)** Meta-analyses of patients receiving recombinant human erythropoietin during chemotherapy for lymphoproliferative, lung, and gynecologic malignancies confirmed incremental effectiveness in reducing transfusion requirements and no significant effects upon either mortality or disease progression.(44)(45) **(EG 1)** A phase III randomized noninferiority study of 2516 patients with stage IV non-small cell lung cancer (all of whom had anemia and were receiving myelosuppressive chemotherapy) compared treatment with either darbepoetin alfa or placebo and found that darbepoetin alfa was noninferior to placebo for overall survival and progression-free survival.(46) **(EG 1)**

For anemia associated with myelodysplastic syndrome, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A systematic review of 35 studies (6 randomized controlled trials, 18 single-arm investigations, and 11 observational reports) found that erythropoiesis-stimulating agents consistently improved erythroid response rates in up to 75% of patients with

anemia due to lower-risk myelodysplastic syndrome. Additionally, several studies showed that patients treated with erythropoiesis-stimulating agents had a reduced need for RBC transfusions and better health-related quality of life with no increased risk of progression to acute myeloid leukemia, when compared with pretreatment condition or placebo. The authors concluded that erythropoiesis-stimulating agents should be considered as first-line treatment for anemia in most patients with myelodysplastic syndrome who lack the 5q deletion.(53) **(EG 1)** Specialty society guidelines state that erythropoiesis-stimulating agents should not be used to treat anemia in patients with malignancy who are not receiving myelosuppressive chemotherapy; one exception is patients with lower-risk myelodysplastic syndrome in order to avoid transfusions.(10)(48)(54) **(EG 2)**

For anemia associated with myelofibrosis, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** Erythropoiesis-stimulating agents have been evaluated as a supportive care measure for patients with myelofibrosis and anemia in the setting of an inappropriately low endogenous serum erythropoietin level.(59)(60) **(EG 2)** Expert consensus guidelines recommend a trial of an erythropoiesis-stimulating agent in patients with myelofibrosis-associated anemia but note that response is typically limited to patients with moderate anemia without transfusion dependence and without significant splenomegaly.(56)(61) **(EG 2)** A specialty society guideline recommends consideration of erythropoiesis-stimulating agents for patients with myelofibrosis-associated anemia as an adjunct to targeted immunotherapy if a clinical trial is not available.(55) **(EG 2)**

For elective surgery, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** A systematic review and meta-analysis of 12 studies including 1880 adult patients with mild to moderate preoperative anemia (hemoglobin 10 to 12 g/dL (100 to 120 g/L)) undergoing noncardiac surgery found that administration of preoperative recombinant human erythropoietin plus iron reduced the need for RBC transfusion and, when given at higher doses, increased hemoglobin concentration compared with control (ie, no treatment, placebo, or standard of care with or without iron). No difference in adverse events or mortality within 30 days was evident; future well-designed randomized controlled trials were recommended.(63) **(EG 1)**

For HIV/AIDS patients with anemia due to zidovudine, evidence demonstrates a net benefit, but of less than moderate certainty, and may consist of a consensus opinion of experts, case studies, and common standard care. **(RG A2)** An analysis of pooled data from 4 randomized controlled trials with 255 patients with AIDS and zidovudine-related anemia found that for those with serum erythropoietin levels at or below 500 International Units per liter (IU/L), treatment with recombinant human erythropoietin decreased transfusion requirements by 40% and increased hematocrit levels by 3.9 percentage points compared with placebo. However, recombinant human erythropoietin did not provide hematologic benefit for patients with serum erythropoietin levels greater than 500 International Units per liter (IU/L).(66) **(EG 1)**

For kidney disease, evidence demonstrates at least moderate certainty of at least moderate net benefit. **(RG A1)** Systematic reviews and meta-analyses indicate that recombinant human erythropoietin is effective in stimulating erythropoiesis, improving anemia, increasing health-related quality-of-life measures, and reducing transfusion requirements in patients with chronic kidney disease, whether or not they are receiving dialysis.(68)(69)(70)(74) **(EG 1)** However, patients receiving these agents in controlled clinical trials have experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when the hemoglobin level target is greater than 11 g/dL (110 g/L).(75)(76)(77) **(EG 1)** Meta-analyses investigating the effectiveness of darbepoetin and epoetin for chronic kidney disease confirmed efficacy in reducing transfusion requirements but found no evidence of significant effects on either mortality or quality of life.(78)(79) **(EG 1)** A systematic review evaluating the efficacy of epoetin and darbepoetin in children with chronic kidney disease included 54 studies (6 randomized trials and 48 observational studies) with a total of 3895 children and found that treatment with either agent effectively increased hemoglobin levels. The authors noted that the analysis was limited by low-quality studies, different dosing regimens, and variable follow-up times among studies.(80) **(EG 1)** Systematic reviews and randomized trials indicate that erythropoietin administration directed at higher targeted hemoglobin levels in patients with chronic kidney disease also significantly increases risks for hypertension, vascular access thrombosis, and progression of end-stage renal disease.(81)(82)(83)(84)(85) **(EG 1)**

Inconclusive or Non-Supportive Evidence

For allogeneic stem cell transplant, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A randomized controlled trial with 131 patients found that erythropoietin administration significantly improved post-transplant erythroid recovery and hemoglobin restoration while significantly decreasing transfusion requirements, without concomitant worsening of thromboembolic events or other complications; the authors indicated that additional confirmatory study is required.(7) **(EG 1)**

For anemia associated with HIV other than due to zidovudine, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** A systematic review of randomized controlled trials concluded that erythropoiesis-stimulating agents for this indication do not improve quality of life, increase hemoglobin levels, reduce transfusion requirements, or reduce mortality.(8) **(EG 1)**

For anemia in cancer patients that is not directly related to current myelosuppressive chemotherapy of a nonmyeloid malignancy, evidence demonstrates potential harm that outweighs benefit; additional research is recommended. **(RG C2)** Practice guidelines and systematic reviews with meta-analyses indicate that erythropoiesis-stimulating agents may be ineffective in such settings and may contribute to higher mortality, with the exception of small cell lung cancer, for which there are trials that demonstrate no negative impact on survival or disease progression.(9)(10)(11)(12) **(EG 1)** Safety concerns regarding thromboembolic events,(13) cardiovascular events, tumor progression, and reduced survival(14) or increased mortality(15) have prompted guidelines that specify level of pretreatment hemoglobin,(9)(12) indicate lack of usefulness for myeloid malignancy, and assert lack of usefulness for anemia of cancer

related to surgery(16) or related to treatment with radiotherapy alone,(17)(18) or for treatment prior to chemotherapy.(10)(19) **(EG 2)** A meta-analysis concluded that erythropoietin and darbepoetin are not appropriate for managing cancer-related fatigue due to potential for these adverse effects.(20) **(EG 1)**

For anemia caused by ribavirin treatment for hepatitis C, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A systematic review and meta-analysis of 4 randomized trials including 257 patients found that patients who received erythropoietin in response to a drop in hemoglobin had a significantly higher probability of achieving a sustained virologic response as compared with those who underwent a ribavirin dose reduction due to anemia. However, the authors acknowledged that further study is required to determine safety for this indication.(21) **(EG 1)** A subsequent review article found limited data on this subject and indicated that ribavirin dose reduction should remain the primary strategy for anemia management.(22) **(EG 2)**

For aplastic anemia, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** A systematic review of the use of hematopoietic growth factors as adjunctive therapy to immunosuppression in patients ineligible for transplant found that there was no incremental improvement in mortality, infection rate, hematologic response, or relapse rate up to 5 years.(23) **(EG 1)**

For autologous stem cell transplant, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A randomized study assigned 72 patients undergoing autologous stem cell transplant to no darbepoetin, to darbepoetin every 2 weeks starting on day 28 after transplant, or to darbepoetin plus intravenous iron. Darbepoetin and intravenous iron were each significantly and independently associated with faster achievement of erythrocytic recovery, and were also associated with improved quality-of-life scores, but effects upon transfusion requirements were not significant; larger confirmatory studies are required.(24) **(EG 1)**

For carbon monoxide poisoning, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A randomized controlled study assigned 103 patients with carbon monoxide poisoning to administration of either erythropoietin or saline placebo. After 30 days, those in the active treatment group had significantly improved neurologic outcomes as compared with those in the placebo group, but the authors indicated that further studies are required to assess longer-term outcomes.(25) **(EG 1)**

For cardiac surgery, preoperative, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A systematic review and meta-analysis of 14 randomized studies (2294 patients) evaluating whether preoperative erythropoiesis-stimulating agents reduced the need for intraoperative RBC transfusion for patients undergoing open cardiac surgery found that, although there was low-certainty evidence that erythropoiesis-stimulating agents reduced the need for blood transfusion, there was moderate-certainty evidence that they increased the risk for postoperative acute myocardial infarction.(26) **(EG 1)**

For cerebrovascular accident, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A trial randomized 522 patients with acute ischemic stroke to either intravenous erythropoietin infusion or placebo. After 90 days, there was no difference between the groups in terms of any neurologic outcomes, but the mortality rate in the erythropoietin group was significantly higher, at 16.4%, as compared with the placebo group, at 9.0%.(27) **(EG 1)** For subarachnoid hemorrhage, a review article found some evidence that erythropoietin may improve both severity and outcome, but the authors concluded that larger confirmatory randomized trials are necessary.(28) **(EG 2)** A meta-analysis and systematic review on the use of erythropoietin in stroke found 3 trials, across which a significantly increased odds ratio of 1.98 was found for mortality; while erythropoietin significantly increased RBC count, there was no effect observed upon infarct volume.(29) **(EG 1)** A review article indicates that data are sparse as to the therapeutic effectiveness and safety of erythropoietin in stroke.(30) **(EG 2)**

For heart failure, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis of 11 randomized trials found that treatment of anemia in heart failure patients using erythropoiesis-stimulating agents was associated with improvement in quality of life, exercise capacity, and cardiac function, as well as a significant reduction in heart failure-related hospitalizations, but the authors stated that larger confirmatory trials are needed.(31) **(EG 1)** A meta-analysis of 13 randomized studies with 3172 patients found that while administration of erythropoiesis-stimulating agents was associated with subjective improvement in dyspnea and quality of life, there was no significant effect upon either all-cause mortality or rehospitalization; treatment with erythropoiesis-stimulating agents was associated with an increased risk of thromboembolic events.(32) **(EG 1)**

For myocardial ischemia, evidence demonstrates a lack of net benefit; additional research is recommended. **(RG C1)** A meta-analysis and systematic review concluded that short-term use of erythropoietin in the setting of acute myocardial infarction did not improve cardiac function, infarct size, or all-cause mortality.(33) **(EG 1)** A meta-analysis of 11 randomized controlled trials with data for 1564 patients reported that erythropoietin did not decrease infarct size, improve left ventricular ejection fraction, or reduce the risk of cardiovascular events or all-cause mortality.(34) **(EG 1)** A randomized study of 529 patients with acute ST-elevation myocardial infarction who received percutaneous coronary intervention assigned half of the patients to also receive a single bolus of erythropoietin at the time of intervention; after 1 year, there was no difference in occurrence of cardiovascular events between groups.(35) **(EG 1)** Similar lack of effectiveness with respect to infarct size was seen in a randomized study of 56 patients with acute ST-elevation myocardial infarction who received intracoronary instillation of either saline placebo or darbepoetin.(36) **(EG 1)**

For neurodegenerative diseases, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** Experimental observations that erythropoietin is present in the central nervous system and may have a role in neuronal protection and differentiation have led to optimism regarding its therapeutic potential; however, more robust clinical studies are still needed.(37)(38) **(EG 1)**

For postpartum iron deficiency anemia, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A meta-analysis and systematic review found 9 studies that evaluated the use of erythropoietin for postpartum iron deficiency anemia, but there was not sufficient high-quality evidence to make any conclusions as to its effectiveness.(39) **(EG 1)**

For renal transplant, evidence is insufficient, conflicting, or poor and demonstrates an incomplete assessment of net benefit vs harm; additional research is recommended. **(RG B)** A randomized controlled trial of 104 patients found that erythropoietin administration peri-transplant did not appear to prevent delayed or slow graft function after transplant.(40) **(EG 1)** A randomized study with 120 patients found positive results with darbepoetin, although the sole comparator was an erythropoietin receptor activator, without use of a true control group.(41) **(EG 1)** A meta-analysis found that the effects of darbepoetin on renal transplant recipients remain uncertain due to limited published evidence.(42) **(EG 1)**

Rationale

Use of this MCG care guideline helps the clinician determine if a particular treatment, medication, or service might be appropriate for a specific patient, taking into account their unique health complexities.

Use of these evidence-based clinical criteria to support decision making benefits the patient by identifying patient-specific complex clinical factors and conditions, promoting personalized treatment. Utilizing evidence-based clinical criteria promotes patient safety by helping ensure that potential patient benefits outweigh the risks. In addition, the use of evidence-based guidelines can increase consistency in treatment thresholds, leading to less variation in care and promoting equitable treatment among patients.

Related CMS Coverage Guidance

This guideline supplements but does not replace, modify, or supersede existing Medicare regulations or applicable National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs).

Code of Federal Regulations (CFR): 42 CFR 419.22(93); 42 CFR 422.101(94)

Internet-Only Manual (IOM) Citations: CMS IOM Publication 100-02, Medicare Benefit Policy Manual, Chapter 14 - Medical Devices(95); CMS IOM Publication 100-02, Medicare Benefit Policy Manual, Chapter 15 - Covered Medical and Other Health Services(96); CMS IOM Publication 100-02, Medicare Benefit Policy Manual, Chapter 16 - General Exclusions from Coverage(97)

Medicare Coverage Determinations: Medicare Coverage Database(98)

References

1. Epogen (epoetin alfa) for injection, for intravenous or subcutaneous use. Physician Prescribing Information [Internet] Amgen Inc. 2024 Dec Accessed at: https://www.epogen.com/. [created 1989; accessed 2025 Nov 12] [Context Link 1, 2, 3, 4, 5, 6, 7, 8, 9, 10]
2. Procrit (epoetin alfa) injection. Physician Prescribing Information [Internet] Janssen Products, LP. 2024 Apr Accessed at: https://www.procrit.com/. [created 1989; accessed 2025 Nov 10] [Context Link 1, 2, 3, 4, 5, 6, 7, 8, 9, 10]
3. Aranesp (darbepoetin alfa) injection, for intravenous or subcutaneous use. Physician Prescribing Information [Internet] Amgen Inc. 2024 Dec Accessed at: https://www.aranesp.com/professional/oncology. [created 2001; accessed 2025 Nov 06] [Context Link 1, 2, 3, 4, 5, 6]
4. Kidanewold A, Woldu B, Enawgaw B. Role of erythropoiesis stimulating agents in the treatment of anemia: a literature review. Clinical Laboratory 2021;67(4):Online. DOI: 10.7754/Clin.Lab.2020.200817. [Context Link 1, 2] View abstract...
5. Bunn HF. Erythropoietin. Cold Spring Harbor Perspectives in Medicine 2013;3(3):a011619. DOI: 10.1101/cshperspect.a011619. [Context Link 1] View abstract...
6. Jelkmann W. Erythropoietin. Frontiers of Hormone Research 2016;47:115-27. DOI: 10.1159/000445174. [Context Link 1] View abstract...
7. Jaspers A, et al. Erythropoietin therapy after allogeneic hematopoietic cell transplantation: a prospective, randomized trial. Blood 2014;124(1):33-41. DOI: 10.1182/blood-2014-01-546333. [Context Link 1] View abstract...
8. Marti-Carvajal AJ, Sola I, Pena-Marti GE, Comunian-Carrasco G. Treatment for anemia in people with AIDS. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD004776. DOI: 10.1002/14651858.CD004776.pub3. [Context Link 1] View abstract...
9. Aapro M, et al. Management of anaemia and iron deficiency in patients with cancer: ESMO Clinical Practice Guidelines. Annals of Oncology 2018;29(Suppliment_4):iv96-iv110. DOI: 10.1093/annonc/mdx758. (Reaffirmed 2025 Jul) [Context Link 1, 2, 3, 4, 5] View abstract...
10. Bohlius J, et al. Management of cancer-associated anemia with erythropoiesis-stimulating agents: ASCO/ASH clinical practice guideline update. Journal of Clinical Oncology 2019;37(15):1336-1351. DOI: 10.1200/JCO.18.02142. (Reaffirmed 2025 May) [Context Link 1, 2, 3, 4, 5] View abstract...
11. Tonia T, et al. Erythropoietin or darbepoetin for patients with cancer. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD003407. DOI: 10.1002/14651858.CD003407.pub5. [Context Link 1, 2] View abstract...

12. Griffiths EA, et al. Hematopoietic Growth Factors. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 1.2025; 2024 Oct 11 Accessed at: https://www.nccn.org/. [accessed 2024 Oct 15] [Context Link 1, 2, 3, 4]

13. Vansteenkiste J, et al. Benefits and risks of using erythropoiesis-stimulating agents (ESAs) in lung cancer patients: study-level and patient-level meta-analyses. Lung Cancer 2012;76(3):478-85. DOI: 10.1016/j.lungcan.2011.12.015. [Context Link 1] View abstract...

14. Untch M, et al. PREPARE trial: a randomized phase III trial comparing preoperative, dose-dense, dose-intensified chemotherapy with epirubicin, paclitaxel, and CMF versus a standard-dosed epirubicin-cyclophosphamide followed by paclitaxel with or without darbepoetin alfa in primary breast cancer--outcome on prognosis. Annals of Oncology 2011;22(9):1999-2006. DOI: 10.1093/annonc/mdq713. [Context Link 1] View abstract...

15. Ribatti D. Erythropoietin and tumor angiogenesis. Stem Cells and Development 2010;19(1):1-4. DOI: 10.1089/scd.2009.0402. [Context Link 1] View abstract...

16. Devon KM, McLeod RS. Pre and peri-operative erythropoietin for reducing allogeneic blood transfusions in colorectal cancer surgery. Cochrane Database of Systematic Reviews 2009, (verified by Cochrane 2010 Jan), Issue 1. Art. No.: CD007148. DOI: 10.1002/14651858.CD007148.pub2. [Context Link 1] View abstract...

17. Lambin P, et al. Erythropoietin as an adjuvant treatment with (chemo) radiation therapy for head and neck cancer. Cochrane Database of Systematic Reviews 2009, (verified by Cochrane 2010 Jan), Issue 3. Art. No.: CD006158. DOI: 10.1002/14651858.CD006158.pub2. [Context Link 1] View abstract...

18. Overgaard J, et al. DAHANCA 10 - Effect of darbepoetin alfa and radiotherapy in the treatment of squamous cell carcinoma of the head and neck. A multicenter, open-label, randomized, phase 3 trial by the Danish head and neck cancer group. Radiotherapy and Oncology 2018;127(1):12-19. DOI: 10.1016/j.radonc.2018.02.018. [Context Link 1] View abstract...

19. Decision Memo for Erythropoiesis Stimulating Agents (ESAs) for Non-Renal Disease Indications (CAG-00383N). Medicare Coverage Database [Internet] Centers for Medicare and Medicaid Services. 2007 Jul Accessed at: https://www.cms.gov/medicare-coverage-database/. [accessed 2025 Sep 09] [Context Link 1, 2, 3, 4, 5, 6]

20. Minton O, Richardson A, Sharpe M, Hotopf M, Stone P. Drug therapy for the management of cancer-related fatigue. Cochrane Database of Systematic Reviews 2010, (verified by Cochrane 2013), Issue 7. Art. No.: CD006704. DOI: 10.1002/14651858.CD006704.pub3. [Context Link 1] View abstract...

21. Alavian SM, Tabatabaei SV, Behnava B. Impact of erythropoietin on sustained virological response to peginterferon and ribavirin therapy for HCV infection: a systematic review and meta-analysis. Journal of Viral Hepatitis 2012;19(2):88-93. DOI: 10.1111/j.1365-2893.2011.01532.x. [Context Link 1] View abstract...

22. Hynicka LM, Heil EL. Anemia management in patients with chronic viral hepatitis C. Annals of Pharmacotherapy 2013;47(2):228-36. DOI: 10.1345/aph.1R513. [Context Link 1] View abstract...

23. Gurion R, et al. Hematopoietic growth factors in aplastic anemia patients treated with immunosuppressive therapy-systematic review and meta-analysis. Haematologica 2009;94(5):712-9. DOI: 10.3324/haematol.2008.002170. [Context Link 1] View abstract...

24. Beguin Y, et al. Darbepoetin-alfa and intravenous iron administration after autologous hematopoietic stem cell transplantation: a prospective multicenter randomized trial. American Journal of Hematology 2013;88(12):990-6. DOI: 10.1002/ajh.23552. [Context Link 1] View abstract...

25. Pang L, et al. Neuroprotective effects of erythropoietin in patients with carbon monoxide poisoning. Journal of Biochemical and Molecular Toxicology 2013;27(5):266-71. DOI: 10.1002/jbt.21484. [Context Link 1] View abstract...

26. Hakim SM, Ahmad AHM, Amer AM. Effect of preoperative recombinant human erythropoietin on the need for blood transfusion and surgical outcomes in adult patients undergoing cardiac surgery: a systematic review and meta-analysis with trial sequential analysis. Journal of Cardiothoracic and Vascular Anesthesia 2024;38(10):2402-2411. DOI: 10.1053/j.jvca.2024.06.013. [Context Link 1] View abstract...

27. Ehrenreich H, et al. Recombinant human erythropoietin in the treatment of acute ischemic stroke. Stroke 2009;40(12):e647-56. DOI: 10.1161/STROKEAHA.109.564872. [Context Link 1] View abstract...

28. Grasso G, Buemi M, Giambartino F. The role of erythropoietin in aneurysmal subarachnoid haemorrhage: from bench to bedside. Acta Neurochirurgica. Supplementum 2015;120:75-80. DOI: 10.1007/978-3-319-04981-6_13. [Context Link 1] View abstract...

29. Bath PM, Sprigg N, England T. Colony stimulating factors (including erythropoietin, granulocyte colony stimulating factor and analogues) for stroke. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD005207. DOI: 10.1002/14651858.CD005207.pub4. [Context Link 1] View abstract...

30. Souvenir R, Doycheva D, Zhang JH, Tang J. Erythropoietin in stroke therapy: friend or foe. Current Medicinal Chemistry 2015;22(10):1205-13. [Context Link 1] View abstract...

31. Kotecha D, Ngo K, Walters JA, Manzano L, Palazzuoli A, Flather MD. Erythropoietin as a treatment of anemia in heart failure: systematic review of randomized trials. American Heart Journal 2011;161(5):822-831.e2. DOI: 10.1016/j.ahj.2011.02.013. [Context Link 1] View abstract...

32. Kang J, Park J, Lee JM, Park JJ, Choi DJ. The effects of erythropoiesis stimulating therapy for anemia in chronic heart failure: A meta-analysis of randomized clinical trials. International Journal of Cardiology 2016;218:12-22. DOI: 10.1016/j.ijcard.2016.04.187. [Context Link 1] View abstract...

33. Ali-Hassan-Sayegh S, et al. Administration of erythropoietin in patients with myocardial infarction: does it make sense? An updated and comprehensive meta-analysis and systematic review. Cardiovascular Revascularization Medicine 2015;16(3):179-89. DOI: 10.1016/j.carrev.2015.01.008. [Context Link 1] View abstract...

34. Gao D, et al. Erythropoietin treatment in patients with acute myocardial infarction: a meta-analysis of randomized controlled trials. American Heart Journal 2012;164(5):715-727.e1. DOI: 10.1016/j.ahj.2012.07.031. [Context Link 1] View abstract...

35. Fokkema ML, et al. Long term effects of epoetin alfa in patients with ST- elevation myocardial infarction. Cardiovascular Drugs and Therapy 2013;27(5):433-9. DOI: 10.1007/s10557-013-6470-0. [Context Link 1] View abstract...

36. Roubille F, et al. Intracoronary administration of darbepoetin-alpha at onset of reperfusion in acute myocardial infarction: results of the randomized Intra-Co-EpoMI trial. Archives of Cardiovascular Diseases 2013;106(3):135-45. DOI: 10.1016/j.acvd.2012.12.001. [Context Link 1] View abstract...

37. Min K, et al. Umbilical cord blood therapy potentiated with erythropoietin for children with cerebral palsy: a double-blind, randomized, placebo-controlled trial. Stem Cells (Dayton, Ohio) 2013;31(3):581-91. DOI: 10.1002/stem.1304. [Context Link 1] View abstract...

38. Hemani S, Lane O, Agarwal S, Yu SP, Woodbury A. Systematic review of erythropoietin (EPO) for neuroprotection in human studies. Neurochemical Research 2021;46(4):732-739. DOI: 10.1007/s11064-021-03242-z. [Context Link 1] View abstract...

39. Jensen MCH, Holm C, Jorgensen KJ, Schroll JB. Treatment for women with postpartum iron deficiency anaemia. Cochrane Database of Systematic Reviews 2024, Issue 12. Art. No.: CD010861. DOI: 10.1002/14651858.CD010861.pub3. [Context Link 1] View abstract...

40. Martinez F, et al. High dose epoetin beta in the first weeks following renal transplantation and delayed graft function: Results of the Neo-PDGF Study. American Journal of Transplantation 2010;10(7):1695-700. DOI: 10.1111/j.1600-6143.2010.03142.x. [Context Link 1] View abstract...

41. Al-Otaibi T, et al. Long-acting erythropoietin stimulating agents for persistent anemia after kidney transplant: risk factors and outcome. Experimental and Clinical Transplantation 2014;12(3):220-6. [Context Link 1] View abstract...

42. Palmer SC, Saglimbene V, Craig JC, Navaneethan SD, Strippoli GF. Darbepoetin for the anaemia of chronic kidney disease. Cochrane Database of Systematic Reviews 2014, (verified by Cochrane 2014 Oct), Issue 3. Art. No.: CD009297. DOI: 10.1002/14651858.CD009297.pub2. [Context Link 1] View abstract...

43. Erythropoiesis-Stimulating Agents (Epoetin and Darbepoetin) for Treating Anaemia in People With Cancer Having Chemotherapy (Including Review of TA142). NICE Technology Appraisal Guidance TA323 [Internet] National Institute for Health and Care Excellence. 2014 Nov (NICE reviewed 2018) Accessed at: https://www.nice.org.uk/guidance/. [accessed 2024 Sep 24] [Context Link 1]

44. Hedenus M, Osterborg A, Tomita D, Bohac C, Coiffier B. Effects of erythropoiesis-stimulating agents on survival and other outcomes in patients with lymphoproliferative malignancies: a study-level meta-analysis. Leukemia and Lymphoma 2012;53(11):2151-8. DOI: 10.3109/10428194.2012.684347. [Context Link 1] View abstract...

45. Ohashi Y, et al. Meta-analysis of epoetin beta and darbepoetin alfa treatment for chemotherapy-induced anemia and mortality: Individual patient data from Japanese randomized, placebo-controlled trials. Cancer Science 2013;104(4):481-5. DOI: 10.1111/cas.12105. [Context Link 1] View abstract...

46. Gascon P, et al. A randomized, double-blind, placebo-controlled, phase III noninferiority study of the long-term safety and efficacy of darbepoetin alfa for chemotherapy-induced anemia in patients with advanced NSCLC. Journal of Thoracic Oncology 2020;15(2):190-202. DOI: 10.1016/j.jtho.2019.10.005. [Context Link 1] View abstract...

47. Esquerdo G, et al. Darbepoetin alfa administered once every three weeks for the treatment of anemia in elderly patients with non-myeloid tumors receiving chemotherapy. Tumori 2014;100(2):225-31. DOI: 10.1700/1491.16423. [Context Link 1] View abstract...

48. Greenberg PL, et al. Myelodysplastic Syndromes. NCCN Clinical Practice Guidelines in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2025; 2025 Jan 17 Accessed at: https://www.nccn.org/. [accessed 2025 Jan 17] [Context Link 1, 2, 3, 4]

49. Platzbecker U, et al. A phase 3 randomized placebo-controlled trial of darbepoetin alfa in patients with anemia and lower-risk myelodysplastic syndromes. Leukemia 2017;31(9):1944-1950. DOI: 10.1038/leu.2017.192. [Context Link 1] View abstract...

50. Seastone DJ, Gerds AT. Darbepoetin alfa for anemia with myelodysplastic syndrome. Expert Review of Hematology 2015;8(2):139-46. DOI: 10.1586/17474086.2015.1000854. [Context Link 1] View abstract...

51. Sekeres MA, Taylor J. Diagnosis and treatment of myelodysplastic syndromes: a review. Journal of the American Medical Association 2022;328(9):872-880. DOI: 10.1001/jama.2022.14578. [Context Link 1] View abstract...

52. Gascon P, Krendyukov A, Mathieson N, Aapro M. Epoetin alfa for the treatment of myelodysplastic syndrome-related anemia: A review of clinical data, clinical guidelines, and treatment protocols. Leukemia Research 2019;81:35-42. DOI: 10.1016/j.leukres.2019.03.006. [Context Link 1] View abstract...

53. Park S, et al. Clinical effectiveness and safety of erythropoietin-stimulating agents for the treatment of low- and intermediate-1-risk myelodysplastic syndrome: a systematic literature review. British Journal of Haematology 2019;184(2):134-160. DOI: 10.1111/bjh.15707. [Context Link 1] View abstract...

54. Fenaux P, et al. Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2021;32(2):142-156. DOI: 10.1016/j.annonc.2020.11.002. (Reaffirmed 2025 Jul) [Context Link 1] View abstract...

55. Gerds AT, et al. Myeloproliferative Neoplasms. NCCN Clinical Practice Guideline in Oncology [Internet] National Comprehensive Cancer Network (NCCN). v. 2.2025; 2025 Jul 08 Accessed at: https://www.nccn.org/. [accessed 2025 Jul 11] [Context Link 1, 2]

56. Reilly JT, et al. Guideline for the diagnosis and management of myelofibrosis. British Journal of Haematology 2012;158(4):453-471. DOI: 10.1111/j.1365-2141.2012.09179.x. [Context Link 1, 2] View abstract...

57. McMullin MF, et al. The use of erythropoiesis-stimulating agents with ruxolitinib in patients with myelofibrosis in COMFORT-II: an open-label, phase 3 study assessing efficacy and safety of ruxolitinib versus best available therapy in the treatment of myelofibrosis. Experimental Hematology & Oncology 2015;4:Online. DOI: 10.1186/s40164-015-0021-2. [Context Link 1] View abstract...

58. Cervantes F, et al. Darbepoetin-alpha for the anaemia of myelofibrosis with myeloid metaplasia. British Journal of Haematology 2006;134(2):184-186. DOI: 10.1111/j.1365-2141.2006.06142.x. [Context Link 1] View abstract...

59. Reynolds SB, Pettit K. New approaches to tackle cytopenic myelofibrosis. Hematology / the Education Program of the American Society of Hematology 2022;2022(1):235-244. DOI: 10.1182/hematology.2022000340. [Context Link 1] View abstract...

60. Ame S, et al. Advances in management of primary myelofibrosis and polycythaemia vera: Implications in clinical practice. eJournal of Haematology 2023;4(3):779-791. DOI: 10.1002/jha2.734. [Context Link 1] View abstract...

61. Vannucchi AM, et al. Philadelphia chromosome-negative chronic myeloproliferative neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2015;26 Suppl 5:v85-99. DOI: 10.1093/annonc/mdv203. (Reaffirmed 2025 Jun) [Context Link 1] View abstract...

62. Tefferi A. Primary myelofibrosis: 2023 update on diagnosis, risk-stratification, and management. American Journal of Hematology 2023;98(5):801-821. DOI: 10.1002/ajh.26857. [Context Link 1] View abstract...

63. Kaufner L, et al. Erythropoietin plus iron versus control treatment including placebo or iron for preoperative anaemic adults undergoing non-cardiac surgery. Cochrane Database of Systematic Reviews 2020, Issue 8. Art. No.: CD012451. DOI: 10.1002/14651858.CD012451.pub2. [Context Link 1, 2] View abstract...

64. Weber RS, Jabbour N, Martin RC. Anemia and transfusions in patients undergoing surgery for cancer. Annals of Surgical Oncology 2008;15(1):34-45. DOI: 10.1245/s10434-007-9502-9. [Context Link 1] View abstract...

65. Moonen AF, Thomassen BJ, Knoors NT, van Os JJ, Verburg AD, Pilot P. Pre-operative injections of epoetin-alpha versus post-operative retransfusion of autologous shed blood in total hip and knee replacement: a prospective randomised clinical trial. Journal of Bone and Joint Surgery. British Volume 2008;90(8):1079-83. DOI: 10.1302/0301-620X.90B8.20595. [Context Link 1] View abstract...

66. Henry DH, et al. Recombinant human erythropoietin in the treatment of anemia associated with human immunodeficiency virus (HIV) infection and zidovudine therapy. Overview of four clinical trials. Annals of Internal Medicine 1992;117(9):739-48. [Context Link 1] View abstract...

67. Silver MR, Agarwal A, Krause M, Lei L, Stehman-Breen C. Effect of darbepoetin alfa administered once monthly on maintaining hemoglobin levels in older patients with chronic kidney disease. American Journal of Geriatric Pharmacotherapy 2008;6(2):49-60. DOI: 10.1016/j.amjopharm.2008.05.002. [Context Link 1] View abstract...

68. Hahn D, Esezobor CI, Elserafy N, Webster AC, Hodson EM. Short-acting erythropoiesis-stimulating agents for anaemia in predialysis patients. Cochrane Database of Systematic Reviews 2017, Issue 1. Art. No.: CD011690. DOI: 10.1002/14651858.CD011690.pub2. [Context Link 1, 2] View abstract...

69. Hahn D, Cody JD, Hodson EM. Frequency of administration of erythropoiesis-stimulating agents for the anaemia of end-stage kidney disease in dialysis patients. Cochrane Database of Systematic Reviews 2014, (verified by Cochrane 2014 Nov), Issue 5. Art. No.: CD003895. DOI: 10.1002/14651858.CD003895.pub3. [Context Link 1, 2] View abstract...

70. Cody JD, Hodson EM. Recombinant human erythropoietin versus placebo or no treatment for the anaemia of chronic kidney disease in people not requiring dialysis. Cochrane Database of Systematic Reviews 2016, (verified by Cochrane 2016 Mar), Issue 1. Art. No.: CD003266. DOI: 10.1002/14651858.CD003266.pub3. [Context Link 1, 2] View abstract...

71. Ribeiro S, Belo L, Reis F, Santos-Silva A. Iron therapy in chronic kidney disease: Recent changes, benefits and risks. Blood Reviews 2016;30(1):65-72. DOI: 10.1016/j.blre.2015.07.006. [Context Link 1] View abstract...

72. Amato L, Addis A, Saulle R, Trotta F, Mitrova Z, Davoli M. Comparative efficacy and safety in ESA biosimilars vs. originators in adults with chronic kidney disease: a systematic review and meta-analysis. Journal of Nephrology 2018;31(3):321-332. DOI: 10.1007/s40620-017-0419-5. [Context Link 1] View abstract...

73. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney International. Supplement 2012;2(4):297-335. (Reaffirmed 2025 Jul) [Context Link 1]

74. Spinowitz B, et al. Economic and quality of life burden of anemia on patients with CKD on dialysis: a systematic review. Journal of Medical Economics 2019;1-12. DOI: 10.1080/13696998.2019.1588738. [Context Link 1] View abstract...

75. Amgen announces modifications to U.S. prescribing information for use of erythropoiesis-stimulating agents in chronic kidney disease. (press release detail) [Internet] Amgen Inc. 2011 Jun Accessed at: https://wwwext.amgen.com/. [accessed 2025 Sep 05] [Context Link 1]

76. Coyne DW. The health-related quality of life was not improved by targeting higher hemoglobin in the Normal Hematocrit Trial. Kidney International 2012;82(2):235-41. DOI: 10.1038/ki.2012.76. [Context Link 1] View abstract...

77. Bellinghieri G, et al. Erythropoiesis-stimulating agents: dose and mortality risk. Journal of Renal Nutrition 2015;25(2):164-8. DOI: 10.1053/j.jrn.2014.10.012. [Context Link 1] View abstract...

78. Collister D, et al. The effect of erythropoietin-stimulating agents on health-related quality of life in anemia of chronic kidney disease: a systematic review and meta-analysis. Annals of Internal Medicine 2016;164(7):472-8. DOI: 10.7326/M15-1839. [Context Link 1] View abstract...

79. Chung EY, Palmer SC, Saglimbene VM, Craig JC, Tonelli M, Strippoli GF. Erythropoiesis-stimulating agents for anaemia in adults with chronic kidney disease: a network meta-analysis. Cochrane Database of Systematic Reviews 2023, Issue 2. Art. No.: CD010590. DOI: 10.1002/14651858.CD010590.pub3. [Context Link 1] View abstract...

80. Bruce G, Schulga P, Reynolds BC. Use of erythropoiesis-stimulating agents in children with chronic kidney disease: a systematic review. Clinical Kidney Journal 2022;15(8):1483-1505. DOI: 10.1093/ckj/sfac058. [Context Link 1] View abstract...

81. Palmer SC, et al. Systematic review: erythropoiesis-stimulating agents in patients with chronic kidney disease. Annals of Internal Medicine 2010;153(1):23-33. DOI: 10.1059/0003-4819-153-1-201007060-00252. [Context Link 1] View abstract...

82. Solomon SD, et al. Erythropoietic response and outcomes in kidney disease and type 2 diabetes. New England Journal of Medicine 2010;363(12):1146-55. DOI: 10.1056/NEJMoa1005109. [Context Link 1] View abstract...

83. Inrig JK, et al. Effect of hemoglobin target on progression of kidney disease: a secondary analysis of the CHOIR (Correction of Hemoglobin and Outcomes in Renal Insufficiency) trial. American Journal of Kidney Diseases 2012;60(3):390-401. DOI: 10.1053/j.ajkd.2012.03.009. [Context Link 1] View abstract...

84. Vinhas J, Barreto C, Assuncao J, Parreira L, Vaz A. Treatment of anaemia with erythropoiesis-stimulating agents in patients with chronic kidney disease does not lower mortality and may increase cardiovascular risk: a meta-analysis. Nephron. Clinical Practice 2012;121(3-4):c95-c101. DOI: 10.1159/000345158. [Context Link 1] View abstract...

85. Ye Y, et al. Hemoglobin targets for the anemia in patients with dialysis-dependent chronic kidney disease: a meta-analysis of randomized, controlled trials. Renal Failure 2018;40(1):671-679. DOI: 10.1080/0886022X.2018.1532909. [Context Link 1] View abstract...

86. McMahon LP, MacGinley R, KHA-CARI. KHA-CARI guideline: biochemical and haematological targets: haemoglobin concentrations in patients using erythropoietin-stimulating agents. Nephrology 2012;17(1):17-9. DOI: 10.1111/j.1440-1797.2011.01535.x. (Reaffirmed 2025 Jun) [Context Link 1] View abstract...

87. Johansen KL, et al. Systematic review of the impact of erythropoiesis-stimulating agents on fatigue in dialysis patients. Nephrology, Dialysis, Transplantation 2012;27(6):2418-2425. DOI: 10.1093/ndt/gfr697. [Context Link 1] View abstract...

88. Zhang Y, Thamer M, Kaufman J, Cotter D, Hernan MA. Comparative effectiveness of two anemia management strategies for complex elderly dialysis patients. Medical Care 2014;52 Suppl 3:S132-9. DOI: 10.1097/MLR.0b013e3182a53ca8. [Context Link 1] View abstract...

89. Boyle SM, Jacobs B, Sayani FA, Hoffman B. Management of the dialysis patient with sickle cell disease. Seminars in Dialysis 2016;29(1):62-70. DOI: 10.1111/sdi.12403. [Context Link 1] View abstract...

90. Escudero-Vilaplana V, Martinez-Nieto C, Lopez-Gomez JM, Vega-Martinez A, Bellon-Cano JM, Sanjurjo-Saez M. Erythropoiesis-stimulating agents in anaemia due to chronic kidney disease: a cost-minimization analysis. International Journal of Clinical Pharmacy 2013;35(3):463-8. DOI: 10.1007/s11096-013-9774-z. [Context Link 1, 2] View abstract...

91. Iorember F, Aviles D. Anemia in nephrotic syndrome: approach to evaluation and treatment. Pediatric Nephrology 2017;32(8):1323-1330. DOI: 10.1007/s00467-016-3555-6. [Context Link 1] View abstract...

92. Roger SD, et al. Intravenous iron and erythropoiesis-stimulating agents in haemodialysis: A systematic review and meta-analysis. Nephrology 2017;22(12):969-976. DOI: 10.1111/nep.12940. [Context Link 1] View abstract...

93. Centers for Medicare and Medicaid Services. "Hospital services excluded from payment under the hospital outpatient prospective payment system." 42 CFR 419.22 Washington, DC 2023 Jul [accessed 2025 Jul 22] Accessed at: https://www.ecfr.gov/. [Context Link 1]

94. Centers for Medicare and Medicaid Services. "Requirements relating to basic benefits." 42 CFR 422.101 Washington, DC 2025 Jun 03 [accessed 2025 Jul 23] Accessed at: https://www.ecfr.gov/. [Context Link 1]

95. Centers for Medicare and Medicaid Services. Medicare Benefit Policy Manual. Chapter 14 - Medical Devices Rev. 198 [Internet] Centers for Medicare and Medicaid Services. 2014 Nov 06 Accessed at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/. [accessed 2025 Sep 09] [Context Link 1]

96. Centers for Medicare and Medicaid Services. Medicare Benefit Policy Manual. Chapter 15 - Covered Medical and Other Health Services Rev. 13108 [Internet] Centers for Medicare and Medicaid Services. 2025 Apr 11 Accessed at: https://www.cms.gov/manuals/. [accessed 2025 Sep 09] [Context Link 1]

97. Centers for Medicare and Medicaid Services. Medicare Benefit Policy Manual. Chapter 16 - General Exclusions From Coverage Rev. 198 [Internet] Centers for Medicare and Medicaid Services. 2014 Nov 06 Accessed at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/. [accessed 2025 Sep 09] [Context Link 1]

98. Medicare Coverage Database. [Internet] Centers for Medicare and Medicaid Services. Accessed at: https://www.cms.gov/medicare-coverage-database/search.aspx? Updated 2025 [accessed 2025 Oct 23] [Context Link 1]

Footnotes

[A] For anemia associated with myelodysplastic syndrome, expert consensus guidelines recommend that epoetin be administered as a once-weekly or twice-weekly subcutaneous injection or darbepoetin be administered every 1, 2, or 3 weeks as a subcutaneous injection.(9)(48)(49)(50) [A in Context Link 1]

[B] Risk factors for evolution to acute myelogenous leukemia include percentage of bone marrow blasts, number of cytopenias, chromosome anomalies, and cytogenetic subgroup.(48) [B in Context Link 1]

[C] For elective surgery, epoetin is administered as a subcutaneous injection, either daily for 10 days before surgery, on the day of surgery, and for 4 days after surgery, or as 4 weekly injections beginning 3 weeks before surgery and ending on the day of surgery.(1)(2) [C in Context Link 1]

[D] For HIV/AIDS, epoetin is administered as an intravenous or subcutaneous injection thrice weekly.(1)(2) Response should be evaluated, and dose adjusted if necessary, after 8 weeks and then every 4 to 8 weeks thereafter. If there is no response at the maximum dose, response at higher doses is unlikely.(1)(2) For responding patients, doses should be titrated to maintain the lowest possible hemoglobin below 12 g/dL (120 g/L) consistent with improvement in hemoglobin level and reduction of transfusion requirements.(1)(2) [D in Context Link 1]

[E] For kidney disease, epoetin is administered as a thrice-weekly subcutaneous or intravenous injection, the latter for patients on hemodialysis.(1)(2) Once-monthly doses also have been used successfully for patients not on dialysis.(67)(68) The goals are the lowest possible hemoglobin level for avoiding transfusion and a level below 11 g/dL (110 g/L) if the patient is an adult on dialysis, a level below 10 g/dL (100 g/L) if the patient is an adult not on dialysis, or a level below 12 g/dL (120 g/L) if the patient is a child.(1)(2) The rate of hemoglobin increase should not exceed 1 g/dL (10 g/L) every 2 weeks.(1)(2) Dosage increases should not be made more frequently than monthly.(1)(2) [E in Context Link 1]

[F] For chronic kidney disease, darbepoetin is administered as a single weekly or biweekly subcutaneous or, preferably, intravenous injection for patients on hemodialysis, or as a subcutaneous or intravenous injection every 4 weeks for other patients with chronic

kidney disease.(3) The goals are the lowest possible hemoglobin level for avoiding transfusion and a level below 11 g/dL (110 g/L) if the patient is an adult on dialysis, a level below 10 g/dL (100 g/L) if the patient is an adult not on dialysis, or a level below 12 g/dL (120 g/L) if the patient is a child.(3) The rate of hemoglobin increase should not exceed 1 g/dL (10 g/L) every 2 weeks.(3) Dosage increases should not be made more frequently than monthly.(3) [F in Context Link 1]

Codes

HCPCS: J0881, J0882, J0885, J0887, J0888, Q4081, S9537

Last Update: 1/25/2026 2:40:23 AM
Build Number: 30.0.2026012500524.025256