

**Frequently Asked Questions on July 30, 2007 Medicare National Coverage Decision
On Use of Erythropoiesis Stimulating Agents (ESAs) in
Cancer and Related Neoplastic Conditions**

IMPLEMENTATION AND EFFECTIVE DATES

Q1. When does the ESA coverage decision take effect?

The coverage decision became effective on the date of its publication, July 30, 2007. The Centers for Medicare & Medicaid Services (CMS) has stated that physicians are expected to follow the new coverage guidelines immediately.

Q2. If the coverage decision became effective July 30, then what does a September 30, 2007 implementation date mean?

The September 30, 2007 implementation date is the deadline by which local Medicare contractors will be required to process and review Medicare claims in accordance with the new policy.

Q3. My Medicare Part B carrier issued a local coverage determination (LCD) on ESAs earlier this year. Should I follow the NCD or the LCD?

NCD requirements supersede LCD requirements. You should follow the NCD where there are issues addressed by both decisions.

SCOPE OF NATIONAL COVERAGE DECISION

Q4. Does the National Coverage Decision (NCD) address the use of ESAs in patients with anemia of chronic diseases associated with non-cancer diagnoses such as inflammatory bowel disease and rheumatoid arthritis?

No, the NCD is restricted to use of ESAs in cancer and related neoplastic conditions. Uses in these other chronic diseases are outside the scope of the July 30 NCD. CMS is pursuing a separate national coverage decision on the use of ESAs in patients with end-stage renal disease. You are encouraged to check with your local carrier for guidance on the use of ESAs for all non-cancer diagnoses.

Q5. Does the NCD address the use of ESAs in myelodysplastic syndrome (MDS)?

No. Although CMS had originally proposed restrictions to coverage for ESAs used in patients with MDS, the final decision states that MDS has been excluded from the scope of this coverage determination. Local carriers will continue to have discretion over coverage of ESAs in patients with MDS.

Q6. I heard that the NCD will restrict coverage for use of ESAs in conjunction with certain drugs such as bevacizumab? Is that true?

No. While CMS did propose non-coverage earlier this year, CMS has ultimately decided not to restrict coverage for use of ESAs in conjunction with specific drug categories.

PATIENT ELIGIBILITY FOR TREATMENT

Q7. CMS specifies that coverage policy will differ between the “initiation” period and the “maintenance” period. How are “initiation” and “maintenance” being defined?

A patient on myelosuppressive chemotherapy becomes “eligible” for ESA therapy starting with the first dose of chemotherapy within a course of chemotherapy (i.e., a planned chemotherapy regimen). Each full course of chemotherapy counts as one eligibility period. The “initiation” phase starts with the first dose of an ESA within a course of chemotherapy, and must be accompanied by documentation of a hemoglobin level of <10 g/dL prior to that first dose. This initiation phase continues for 4 weeks from the first dose of an ESA. Starting with week 5, the patient enters the “maintenance” phase.

Q8. At what point does a patient’s eligibility for ESA treatment end?

Eligibility for ESA coverage ends at 8 weeks following the administration of the last dose of chemotherapy within a course of chemotherapy.

Q9. Are patients with anemia associated with acute and/or chronic myelogenous leukemias (AML, CML) eligible for treatment under this coverage decision?

No, CMS announces in this final coverage decision that it does not consider ESA treatment as reasonable and necessary for patients with anemia associated with the treatment of CML and AML.

Q10. Is it true that I will not be able to initiate ESA treatment for patients unless their hemoglobin level is below 10 g/dL?

Yes, a patient’s hemoglobin level must be <10g/dL (or hematocrit <30%) to receive ESA treatment.

Q11. At the beginning of this course of chemotherapy, my patient received ESA therapy, but it was discontinued after eight weeks because his hemoglobin rose by less than 1 g/dL, despite a 25% dose increase after the first 4 weeks. His hemoglobin continues to drop throughout this course of chemotherapy, and I would like to try another round of an ESA before considering transfusion. May I?

No. Your patient would no longer be considered “eligible” for ESA coverage during this course of chemotherapy. Medicare will cover only one dose escalation by 25% and does not

consider additional rounds of ESAs within this same course of chemotherapy “reasonable and necessary” if the hemoglobin rises less than 1 g/dL (hematocrit rise less than 3%).

Q12. Isn't the NCD's restriction on coverage whenever a patient's hemoglobin goes above 10 g/dL inconsistent with FDA labeling?

Yes, this restriction is inconsistent with both FDA-approved labeling and national guidelines. The FDA-approved label for Epogen (epoetin alfa) states, “The dose of Epogen should be titrated for each patient to achieve and maintain the lowest hemoglobin level sufficient to avoid the need for blood transfusion and not to exceed 12 g/dL.” The FDA-approved label for Aranesp (darbepoetin alfa) states, “For both dosing schedules, the dose should be adjusted for each patient to maintain the lowest hemoglobin level sufficient to avoid the need for RBC transfusion and not to exceed 12 g/dL.” The ASCO and American Society of Hematology (ASH) joint clinical practice guidelines recommend consideration of ESA therapy when the hemoglobin falls below 10 (for most patients); the hemoglobin with ESA treatment should not exceed 12. ASCO has urged CMS to revisit this decision so that coverage would be permitted as long as the dosage is being titrated to maintain a hemoglobin level less than 12, consistent with FDA labeling and the ASCO/ASH guidelines.

HEMOGLOBIN MONITORING

Q13. What are the requirements for hemoglobin monitoring in order to ensure coverage during the initiation and maintenance phases?

After the initial documentation of a hemoglobin level <10 g/dL, during the first 4 weeks (initiation) of ESA therapy, CMS does not require submission of documentation of a hemoglobin level less than 10. The hemoglobin may, in fact, go above 10 during these first 4 weeks, and CMS will still provide coverage for ESA therapy (*with the exception of patients for whom hemoglobin levels increase by more than 1 g/dL in a two week period is detected – see Q16 below*). At the 5th week, however (the beginning of the maintenance phase), CMS does require documentation of a hemoglobin level <10 g/dL immediately prior to that dose of an ESA, and for every subsequent dose.

Q14. If I check my patient's hemoglobin at any point during the first four weeks, and it's above 10 g/dL, do I need to discontinue ESA therapy?

No, see above discussion regarding hemoglobin monitoring.

Q15. Do I need to provide documentation of a hemoglobin level below 10 g/dL after the first 4 weeks of therapy?

Yes, for every single dose of an ESA given after the first 4 weeks, there must be a hemoglobin level below 10 g/dL immediately preceding that dose.

Q16. During the first 4 weeks of ESA therapy, if the hemoglobin increases more than 1 g/dL in any 2 week period, will ESA therapy then be non-covered?

The answer depends on the hemoglobin level. If you check the hemoglobin level during the four week initiation period and the patient's hemoglobin has risen more than 1 g/dL in 2 weeks, then the hemoglobin must be below 10 for coverage to continue. If the hemoglobin level remains below 10, you may continue ESA therapy, but the dose must be decreased by 25%.

Q17. If my patient was taken off standard-dose ESA therapy at any point because he had a hemoglobin level rise of more than 1 g/dL within 2 weeks and his hemoglobin was over 10 g/dL, once the hemoglobin falls below 10 again, should I restart ESA dosing using standard doses?

No. In this situation, CMS will only cover ESAs at a dose reduction of 25% from the previously administered dose. If the previous dose was a standard dose, you must decrease that dose by 25%. If the previous dose was different than the standard dose, the next dose must reflect a 25% dose decrease from the actual previous dose.

Q18. My patient received an ESA for four weeks shortly after beginning chemotherapy, and I discontinued the ESA at the end of this time because her hemoglobin was 10.3 g/dL. A few weeks have passed, she is receiving the same course of chemotherapy, and now her hemoglobin is below 10 g/dL. Do I have to document a hemoglobin level below 10 g/dL before every dose of an ESA from this point forward?

Yes. Once the initial 4 week "initiation" period has passed, within any one course of chemotherapy, every ESA dose given after that counts as a "maintenance" dose, and you must document that dose was immediately preceded by a hemoglobin level of less than 10 g/dL.

Q19. We understand that CMS will start requiring practices to document hematocrit/hemoglobin in conjunction with administration of ESAs starting January 1, 2008. Is there any additional information available about how this requirement will be implemented?

CMS is required by the Tax Relief and Health Care Act of 2006 to implement a requirement that all Medicare claims for ESAs include information on hemoglobin or hematocrit levels. CMS has not yet finalized its regulations for reporting and has not proposed guidance or instructions as to the timeframe in which the hemoglobin reported must be drawn (i.e., how it relates temporally to the ESA dose). ASCO will urge CMS to make sure the requirement is clinically appropriate but not unduly burdensome on practices.

DOSING & DOSE ESCALATION

- Q20. The NCD describes only weight-based dosing for epoetin and darbepoetin, and then says “Equivalent doses may be given over other approved time periods.” What does this mean?**

CMS has clarified in communications with ASCO that all FDA-approved dosing regimens for ESAs are covered under the NCD. Therefore, Medicare will cover the alternative flat dose weekly dosing schedule listed in the FDA-approved label for epoetin, and the alternative flat dose every three weeks dosing schedule listed in the FDA-approved label for darbepoetin.

- Q21. We understand that for a patient who does not respond to initial doses, the dose may be increased by 25%. In this scenario, if a patient’s hemoglobin goes from 8 to 9 with the initial dose increase, will ESA therapy be covered if the physician increases the dose by an additional 25% in order to get the hemoglobin closer to 10?**

No, CMS has clarified that there is a one-time limit on the 25% dose escalation.

- Q22. For hypo- or non-responders (patients with a rise in hemoglobin of less than 1 g/dL over 4 weeks of treatment), the new policy allows for a one-time dose escalation of 25%. Isn’t this inconsistent with the FDA-approved label?**

Yes, this is inconsistent with the FDA label. The weight-based starting dose for darbepoetin is 2.25 mcg/kg (weekly) and for epoetin it is 150 U/kg (three times a week). The FDA label states that, for hypo- or non-responders, weight-based dosing can be increased by 100% (i.e., up to 4.5 mcg/kg for darbepoetin, and to 300 U/kg for epoetin). The ASCO/ASH clinical practice guideline makes similar recommendations. ASCO plans to appeal this decision to CMS.

- Q23. If my patient initially responded very quickly to ESA therapy and needed to have a 25% dose reduction, but then needs a higher dose later on due to the cumulative effects of myelosuppressive chemotherapy, am I limited to raising the dose by 25% (i.e., back to the “standard” dose)?**

No. If a patient is on a “standard” dose of ESA therapy, the maximum allowable dose is 25% above that. However, if a patient is on a lower than standard dose (whether due to hyper-response or started on a lower dose due to clinician judgment), you are allowed to escalate that patient’s dose to standard dose plus 25%.

- Q24. I started my patient on an ESA 4 weeks ago, and his hemoglobin has risen by less than 1 g/dL, and is still below 10. May I increase the dose?**

Yes, by 25%. Note that this dose escalation allowance applies only to week 5 (see Q25 below).

Q25. My patient has been receiving ESA therapy for 8 weeks, and she is no longer responding as well to the ESA as she did initially, due to the cumulative effects of myelosuppressive chemotherapy. May I increase the dose?

No. The CMS rule allows for one trial of dose escalation (25%) only at the 5th week of ESA treatment within any one course of chemotherapy (i.e., the first week after the “initiation” phase).

ADDITIONAL RESOURCES

Q26. Has ASCO developed any tools to help members understand the new NCD?

Yes, in addition to this FAQ ASCO has developed an overview of the NCD requirements. That overview can be found at the end of this document. We will continue to develop tools and resources that will help members understand Medicare coverage policy on ESAs.

Q27. Where can I read the final NCD and instructions from CMS?

To view and download the entire NCD, go to:
<https://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=203>

CMS also issued a Q & A document on July 31. To view and download the Q & A, go to:
http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=12

Q28. How can I access the ASCO/ASH guidelines on use of ESAs in patients with cancer?

The guideline can be accessed at www.asco.org/guidelines. Please note that ASCO and ASH are developing an update to the guideline and expect to release it this fall.

QUESTIONS AND CONCERNS

Q29. I am very concerned that the requirements set forth in the National Coverage Decision will impair my ability to continue providing ESAs to patients. Is ASCO concerned that the NCD may have a deleterious effect on access?

Yes, ASCO has been in frequent communication with CMS to express concerns that the NCD inappropriately limits coverage and will be extremely difficult to implement in clinical practice. ASCO is appealing a number of these decisions to CMS and has recommended that CMS reopen portions of the NCD to address specific, unresolved problems.

Q30. To whom should I address additional questions that I would like to see included in this FAQ?

Please direct additional questions to practice@asco.org or call (703) 299-1050.

Overview of ESA National Coverage Decision

Initiate ESA when Hgb <10

After 4 weeks		After 8 weeks	
If:	Then:	If:	Then:
Hgb <10 AND Hgb rise from baseline >1	Continue ESA at same dose		
Hgb ≥10	ESA no longer covered ESA may be resumed if Hgb again drops below 10		
Hgb <10 AND Hgb rise from baseline <1	Increase ESA dose by 25%	Hgb rise ≥1	Continue ESA at same dose
		Hgb rise <1	ESA no longer covered

During ANY 2-week period	
If:	Then:
Hgb rise <1	Continue ESA and re-assess Hgb
Hgb rise ≥1 AND Hgb <10	Reduce ESA dose by 25%
Hgb rise ≥1 AND Hgb ≥10	ESA no longer covered If Hgb again falls below 10, may reinstitute ESA with a 25% dose reduction

The maximum dose for the first 4 weeks is 1,800 U/kg for epoetin and 9 mcg/kg for darbepoetin. ESA treatment meeting the above requirements may be continued for 8 weeks following the completion of the final dose of myelosuppressive chemotherapy in a chemotherapy regimen. Following the first 4 weeks of ESA treatment, a hemoglobin level of <10 g/dL must be documented immediately prior to each dose of an ESA.