



AMERICAN SOCIETY OF CLINICAL ONCOLOGY



ASCO's National Audioconference on CMS' NCD for ESAs

**September 27, 2007
4:00 PM ET**

Today's Topics

- Detail the chain of events related to ESAs
- Outline specific covered and non-covered indications under the NCD
- Guidance on when to refer to local coverage decisions (LCDs)
- Review of the Centers for Medicare & Medicaid Services' (CMS) National Coverage Determination (NCD) on Erythropoiesis Stimulating Agents (ESAs)
- Update on the current status of ASCO's involvement on ESA issue
- Ongoing challenges

Timeline of Events

- In 1989 epoetin alfa was approved
 - Indicated for the treatment of anemia associated with chronic renal failure
 - In 1993 the indication was expanded to include the treatment of anemia associated with cancer chemotherapy
 - Since approval, the FDA expressed concern about potential tumor promotion
- In 2001 darbepoetin was approved
 - Indicated for the treatment of anemia associated with chronic renal failure
 - In 2002 the indication was expanded to include the treatment of anemia associated with cancer chemotherapy

Timeline of Events

- Subsequent trials for both drugs continued after their approval
- Some of these published trials showed negative effects
- In 2004, the FDA convened an Oncologic Drugs Advisory Committee (ODAC) meeting in response to those published reports
 - Purpose of the meeting was to re-assess the safety of ESAs
 - May 2004 - product label for epoetin alfa was revised to include information on response rates, time to progression and overall survival in patients with solid tumors
 - December 2004 – product label for darbepoetin was revised to include information on thrombotic events and tumor promotion

Timeline of Events

- February 2007, preliminary data released in some ongoing trials prompted the FDA to review safety of ESAs
- March 2007 a Congressional committee began an inquiry on the marketing and regulation of these drugs.
- March 2007, the FDA revised the labels for both epoetin alfa and darbepoetin to include a “black box” warning.
 - Warning provided expanded information on safety, tumor progression, and survival
 - Warning also stated that ESAs are not indicated for cancer/active malignant disease patients who are not receiving chemotherapy or radiotherapy

Timeline of Events

- March/April 2007 – One of the recognized CMS compendia changed its indication status for epoetin alfa
 - The “treatment of anemia of cancer” indication was changed from accepted to unaccepted
 - Because one of the compendia lists the use/indication as unaccepted, Medicare is no longer required to cover it
- March/April 2007 – Many Medicare carriers changed or updated their LCDs following the “black box” warnings
 - NOTE: This was the first noticeable change physicians and offices encountered relating to the ESA issue

Timeline of Events

- In May 2007 the FDA convened another ODAC meeting to re-assess safety and efficacy of ESAs
 - ODAC recommended the FDA
 - Set a “baseline” hemoglobin level to initiate ESA treatment
 - Provide a reassessment of anemia post-chemotherapy regimen
 - Place a restriction on use of ESAs in certain malignancies
 - Provide further restrictions on indications in the product labels
 - Conduct further clinical trials on survival and collect data on adverse events
 - * The FDA has not yet acted on these recommendations
- May 2007, CMS published a “Proposed Decision Memo” on coverage of ESAs in non-renal indications
 - The proposed decision memo went beyond the ODAC recommendations and placed more restrictions on the coverage of ESA treatment

Timeline of Events

- July 2007, CMS published its final national coverage determination on “The Use of Erythropoiesis Stimulating Agents in Cancer and Related Neoplastic Conditions”
 - NOTE: This was the next noticeable coverage change physicians and practices encountered
- August 2007, ASCO files a formal reconsideration request on CMS’ NCD on ESAs
- Fall 2007, the updated ASCO/American Society of Hematology (ASH) guideline on the use of epoetin/darbepoetin in patients with cancer will be published

Covered vs. Non-covered Indications

- CMS lists specific indications in the NCD which are considered either reasonable and necessary or not reasonable and necessary
 - If reasonable and necessary – the ESA treatment is covered
 - If not reasonable and necessary – the ESA treatment is not covered
- If a particular indication is not discussed in the NCD, the local Medicare carrier has coverage discretion
- Confusion around Myelodysplastic Syndrome (MDS)
 - MDS was mentioned in CMS' proposed decision memo
 - CMS made NO coverage decision on ESA treatment in the NCD; therefore,
 - Local Medicare carriers will have coverage discretion for this indication

Non-covered Indications for ESA Treatment

- Acute and Chronic Myelogenous Leukemias
 - NCD states that ESA treatment for the anemia associated with the treatment of AML & CML are not covered
- Anemia in cancer not related to cancer treatment
- ESA treatment for prophylactic use to prevent chemotherapy-induced anemia
- Anemia due to cancer treatment if patients have uncontrolled hypertension
- Anemia due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis in cancer patients or patients receiving cancer treatment
- Anemia associated only with radiotherapy
- ESA treatment for patients with erythropoietin resistance due to neutralizing antibodies
- ESA treatment for prophylactic use to reduce tumor hypoxia

Covered Indications for ESA Treatment

- Anemia that is secondary to myelosuppressive anticancer chemotherapy given in
 - Solid tumors
 - Multiple myeloma
 - Lymphoma
 - Lymphocytic leukemia

Overview of NCD

- On July, 30 CMS published its final national coverage determination on ESA treatment
- Effective date of NCD is July 30, 2007
- Coverage guidelines outlined in NCD should be followed as of the July 30th effective date
- Scope of NCD is restricted to the use of ESAs in cancer and other related neoplastic conditions
- CMS, like the FDA, considers all ESAs to be equivalent
- Coverage set forth in the NCD would overrule local Medicare policies
 - For indications not addressed in NCD, the local policy should be consulted

Overview of NCD

- The NCD specifies an initiation and maintenance period
 - Initiation period – first four weeks of treatment and starts with first dose
 - Maintenance period – the fifth week and ongoing weeks of treatment
 - These periods have been arbitrarily defined CMS
- The NCD outlines coverage for dosing
 - Epoetin alfa starting dose - weight-based at no more than 150 U/kg three times a week (same as product label)
 - Darbepoetin starting dose – weight-based at 2.25 mcg/kg weekly (same as product label)
 - Maximum dose of ESA is 25% above of the allowable dose
 - NCD specifically states that other “equivalent doses may be given over other approved time periods”
 - CMS informed ASCO that FDA approved dosing will be covered

Overview of NCD

- CMS sets a “baseline” hemoglobin level for initiating and continuing treatment
 - Hemoglobin must be <10 g/dL immediately prior to initiation
 - Hemoglobin must be <10 g/dL immediately prior to the maintenance period (the 5th week)
 - Maintenance doses of ESAs can continue if hemoglobin remains <10 g/dL
 - Documentation of hemoglobin should be made prior to first dose and before each dose in maintenance period
 - NCD does not specifically state that documentation must be made; however, ASCO’s interpretation is that there must be some documentation of the hemoglobin level to support treatment

Overview of NCD

■ Monitoring the hemoglobin level

- CMS does not specifically state that the hemoglobin be tested during the first four weeks (initiation period)
- If hemoglobin is checked during any two week period during the

Initiation phase

- And the rise is less than 1 g/dL, the ESA treatment can continue
- And it has risen more than or equal to 1 g/dL, the hemoglobin must be below 10 to continue treatment, and the ESA dose must be decreased by 25%
- And the rise is more than or equal to 1 g/dL and the hemoglobin is greater than 10, the ESA treatment is no longer covered (If the hemoglobin subsequently falls below 10, the ESA can be provided but at a 25% dose reduction)

Overview of NCD

■ Monitoring the hemoglobin level (cont.)

- If hemoglobin is checked during any two week period during the **Maintenance phase**
 - And the rise is less than 1 g/dL and the hemoglobin remains below 10, the ESA treatment can continue
 - And it has risen more than or equal to 1 g/dL, the hemoglobin must be below 10 to continue treatment, and the ESA dose must be decreased by 25%
 - And the rise is more than or equal to 1 g/dL and the hemoglobin is greater than 10, the ESA treatment is no longer covered (If the hemoglobin subsequently falls below 10, the ESA can be provided but at a 25% dose reduction)

Overview of NCD

- CMS outlines coverage of a dose increase
 - The only approved dose increase is 25%
 - Only one dose increase is allowed during each course of chemotherapy
 - A 25% increase can be provided after the initiation period if the hemoglobin is less than 10 and the hemoglobin rise is less than 1 from the baseline
 - The dose increase can only happen at week 5 (beginning of maintenance period)
- CMS outlines coverage of a dose reduction
 - The only approved dose reduction is 25%
 - A 25% dose reduction can occur if during any two week period there is a hemoglobin rise greater than or equal to 1 and the hemoglobin is less than 10

Overview of NCD

- The NCD defines treatment timeframes
 - Each full course of chemotherapy is considered to be eligible for ESA treatment
 - The 8 weeks following the final dose of chemotherapy are also eligible for ESA treatment
 - NOTE: The hemoglobin and dosing requirements must be followed

Overview of NCD

- Under the NCD, the ESA treatment is not covered if
 - The hemoglobin is greater than or equal to 10
 - NOTE: The hemoglobin can exceed 10 during the initiation period (first 4 weeks)
 - If during any two week period, the hemoglobin rise is greater than or equal to 1 and the hemoglobin is greater than or equal to 10
 - If after 8 weeks (the initiation and maintenance period) the hemoglobin rise is less than 1

ASCO Activities

- Since CMS released the Proposed Decision Memo, ASCO has:
 - Taken part in multiple meetings and conference calls with CMS
 - Met with administration officials on this issue
 - Met with the FDA
 - Provided CMS with multiple written comments based on the best available evidence

ASCO Activities

- Most recently, in a letter dated August 30, 2007, ASCO requested that CMS re-open the NCD
 - Request addresses specific issues within the NCD
 - Material misinterpretation of clinical evidence (hemoglobin level and consideration of blood transfusions)
 - Dose escalation and timing are inconsistent with FDA-approved labeling
- CMS responded to ASCO on September 24, asking us to answer six questions related to the evidence on ESA use
- ASCO is in the process of drafting a response to this letter
- ASCO will continue to work with government agencies to maintain awareness of this issue and to advocate for change to these coverage restrictions

ASCO Activities

- Many Medicare carriers are starting to update their local coverage policies based on the NCD
 - ASCO is reviewing local policies and will be compiling changes
 - Summary of changes will be disseminated and posted to website

Challenges in Today's Environment

- ASCO feels that the CMS NCD is not based on a comprehensive assessment of the best available evidence
- However, CMS currently has restricted coverage in place
- Many private payers intend to follow the ASCO/ASH Clinical Practice Guidelines for ESA use, and do not intend to implement the NCD restrictions for private patients
 - ASCO sent letters to major private carriers outlining our concerns about the CMS policy
- The result: a “two-tiered” system of care, one for Medicare beneficiaries, one for patients with private insurance

Challenges in Today's Environment

- How to handle patients who are/were on ESA treatment when NCD was released
 - Determine what phase the patient is/was in (initiation vs. maintenance)
 - Follow the guidelines set forth in the NCD
- How to handle patients who have received transfusions, have comorbid conditions, or reside in high-altitude areas
 - ASCO has strongly encouraged CMS to issue carrier instructions regarding the NCD
- Building awareness between patient and physician - communicate ESA treatment and coverage changes
- As of January 1, 2008, physicians will be required to report the hemoglobin or hematocrit on each claim
 - New CMS requirement separate from NCD

Ongoing Updates and Information

- Latest information and updates can be found on ASCO's website
 - Cancer Policy Today & Cancer Policy Alerts
 - Journal of Oncology Practice (JOP)
- ASCO staff available for questions
 - Coding & Reimbursement Hotline, 703-299-1054
 - practice@asco.org
- ESA Audioconference page: www.asco.org/ESAaudiocall
 - Slides are available for download
 - ASCO FAQs on ESAs
 - MP3 downloadable version of audiocall available within a week