ASN and Recent ESA Label Changes

Thomas H. Hostetter, MD
Wolfgang C. Winkelmayer, MD, ScD

American Society of Nephrology

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ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

American Society of Nephrology

Representing more than 13,000 members—including physicians, scientists, and other health professionals—the American Society of Nephrology (ASN) leads the fight against kidney disease by educating health professionals, sharing new knowledge, advancing research, and advocating the highest quality care for patients.

ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

Issue #1: Inaccuracy of key statement in Boxed Warning

"[…] In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than **11** g/dL (5.1). […]"

- ✓ **Available trial evidence does not support this statement. No trial targeted a hemoglobin concentration >11 g/dL.**

Issue #1: Inaccuracy of key statement in Boxed Warning

	Target hemoglobin g/dL		Achieved hemoglobin g/dL	
	Low	High	Low	High
NHT	10	14	10.3	13.3
CREATE	*11-12.5*	*13-15*	*11.5*	*13.5*
CHOIR	11.3	13.5	11.4	12.8
TREAT	>9 *	13	10.6	12.5

* Not a hemoglobin target, but a threshold group; placebo group with darbepoetin rescue below a hemoglobin concentration of 9 g/dL.

Issue #1: Inaccuracy of key statement in Boxed Warning

An accurate statement would read as follows:

"[…] In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than **13** g/dL (5.1). […]"

Issue #2: Removal of the 10-12 g/dL Target Range

Since adverse events were consistently observed in randomization groups targeting hemoglobin concentrations >13 g/dL, no scientific data are currently available that would justify dropping the previous hemoglobin target of 10-12 g/dL.

Issue #3: Increased Risk of Anemia

New dosing recommendation terminology could result in overly conservative, more rigidly enacted ESA dosing practice patterns in some dialysis units, especially in light of recent coverage decisions by CMS. This change may place patients at increased risk of anemia and blood transfusions, which could adversely affect health and candidacy for transplantation.

Medicare Program; Changes to the End-Stage Renal Disease Prospective Payment System for CY 2012, End-Stage Renal Disease Quality Incentive Program for PY 2013 and PY 2014; Ambulance Fee Schedule; and Durable Medical Equipment

AGENCY: Centers for Medicare & Medicaid Services (CMS), HHS.

ACTION: Proposed rule.

Safety/ucm259639.htm. We have discussed with the FDA our proposal to retire the Hemoglobin Greater Than 10 g/dL measure starting in PY 2013. Since this measure encourages providers to keep hemoglobin above 10 g/dL in all patients, the FDA agrees that removing this measure is consistent with the new labeling for erythropoeisis stimulating agents approved by the FDA. The previous labeling recommendations to maintain hemoglobin levels between 10 and 12 g/dL are no longer appropriate and have been removed from the drug label. We, therefore, propose to retire the Hemoglobin Less Than 10g/dL measure from the ESRD QIP measure set, beginning with the PY 2013 program.

Issue #4: Dose interruptions

"[…] if the hemoglobin level approaches or exceeds 11 g/dL, reduce or **interrupt** the dose of epogen. […]"

In chronic treatments we rarely consider *interrupting* treatment as it may lead to adverse health outcomes. In the setting of anemia in CKD patients, this may place patients at increased risk of transfusions.

Issue #5: More research is needed

Further research examining ESA doses at various hemoglobin levels is needed to elucidate the optimal course of ESA therapy.

ASN Recommendations

1. Remove statement that "[…] In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered erythropoiesis-stimulating agents (ESAs) to target a hemoglobin level of greater than 11 g/dL (5.1). […]" or alternatively, correct the statement to reflect the correct threshold "[…] to target a hemoglobin level of greater than **13** g/dL […]"
2. Consider reinstating recommended 10-12 g/dL target hemoglobin range until the further research examining ESA doses at various hemoglobin levels elucidates the optimal course of ESA therapy (or proves conclusively that >10 g/dL is an inappropriate target).

ASN Recommendations

3. Consider removing the word “interrupt” from the statement “[…] if the hemoglobin level approaches or exceeds 11 g/dL, reduce or ***interrupt*** the dose of epogen. […]”
4. Continue to work with CMS to ensure consistency between the policies and goals of the agencies pertaining to ESAs.
5. Recognize that more scientific evidence is necessary to understand the most appropriate use of ESAs.

For More Information, Please Contact

Rachel Nell Shaffer
Policy and Government Affairs Manager
American Society of Nephrology
1510 H Street, NW
Suite 800
Washington, DC 20006
(202) 640-4659
rshaffer@asn-online.org