Policy Update

By Rachel Shaffer

ASN Discusses ESA Label Changes with FDA

When the Food and Drug Administration (FDA) changed the label on erythropoiesis-stimulating agents (ESAs) in July, ASN raised concerns about the modifications to the agency. FDA met with ASN this October to discuss the society's reservations.

FDA significantly revised the ESA label, most importantly by removing the recommended target hemoglobin range of 10–12 g/dL. The new label states that the dose of ESAs should be "reduced or interrupted" if hemoglobin levels exceed 11 g/dL. The label also states that "In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a hemoglobin level of greater than 11 g/dL." The revised label caused concern among nephrologists, including those on ASN's Public Policy Board, on multiple levels. First, no study has ever demonstrated that risk does in fact exist above the specific threshold of 11 g/dL, as stated on the label. Second, the label generates uncertainty about how ESAs should actually be administered. "Interrupting" a medication is not typical when treating patients with chronic disease and variable follow up. How low is it safe to let hemoglobin levels go? And would exceeding 11 g/dL generate risk of a malpractice lawsuit in the case of an adverse event?

Given the confusion and alarm among the nephrology community regarding the changes, ASN was pleased that FDA suggested an in-person meeting to discuss the already-published label—a rare move for the agency. ASN Public Policy Board chair Tom Hostetter, MD, and Public Policy Board member Wolfgang Winkelmayer, MD, ScD, FASN, represented the society at the FDA, along with ASN Manager of Policy and Government Affairs Rachel Shaffer. The key points ASN's contingent emphasized centered on the agency's assertion that hemoglobin levels above 11 g/dL have conclusively been proven to increase risk of adverse events.

ASN emphasized that since adverse events were consistently observed in randomization groups targeting only hemoglobin concentrations >13 g/dL, no scientific data are currently available that would either justify dropping the previous hemoglobin target of 10–12 g/dL, or substantiate the statement of risk at 11g/dL (Table 1). An accurate statement would instead read that "In controlled trials, patients experienced greater risks for death, serious adverse cardiovascular reactions, and stroke when administered ESAs to target a hemoglobin level of greater than **13 g/dL**."

"We recognize that FDA is doing its best to ensure patient safety in an area where evidence is sparse, and with a product that is known to increase safety risks when hemoglobins of 13 g/dL or more are aggressivley targeted," said Winkelmayer. "But it is fundamentally not true that evidence suggests those risks start at 11 g/dL. It would be more reasonable for the label to state that — based on available trial evidence—the risks of any treatment strategies targeting the range between 11 g/dL and 13 g/dL are currently unknown relative to lower or higher targets. That change would allow patients and their nephrologists to have a conversation about the potential risks and benefits."

ASN also pointed out the on-the-ground reality that the 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 changes to the ESRD Quality Incentive Program by the Centers for Medicare and Medicaid Services. The label change may place patients at increased risk of anemia and blood transfusions, which could adversely affect health and candidacy for transplantation.

The society also explained that physicians treating chronic disease rarely consider *interrupting* treatment as it may lead to adverse health outcomes. In the setting of anemia in CKD patients, interruption may place patients at increased risk of transfusions.

ASN's key request to FDA—a request shared by the Renal Physicians' Association, which also attended the meeting—is that FDA consider revising the label to reflect that studies actually show that greater risk exists when ESAs target a hemoglobin level of greater than 13 g/dL.

At press time (within a week of the meeting) FDA had not issued any formal responses to ASN. The society will keep members updated about additional communications with the FDA regarding the label. You may view ASN's letter to the FDA on this issue at www.asn-online.org.

Table 1

Available evidence from randomized controlled trials showing adverse cardiovascular outcomes in patients With CKD

	Target hemoglobin (g/dL)		Achieved hemoglobin (g/dL)	
	Low	High	Low	High
NHT	10	14	10.3	13.3
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. Adapted from *Sem in Dial*

Debt Committee Urged to Protect Kidney Disease Funding

The Joint Committee on Deficit Reduction, or the "super committee" is without question the most talked-about—and feared and revered—entity in Washington, DC, this fall. Tasked by the Budget Control Act of 2011 with developing a plan by November 23 to trim at least $1.2 trillion from the national debt over the next decade, the super committee's job is daunting. However, the committee possesses no shortage of options to meet that $1.2 trillion goal: everything is "on the table" for reductions. ASN is leading the way in making sure that funding affecting kidney patients and physicians is not among the reduced.

ASN identified the funding streams pertinent to kidney disease most likely to be endangered by the committee's search for programs to trim, and together with the American Society of Pediatric Nephrology (ASPN) and the Renal Physicians' Association (RPA), sent a letter to the super committee outlining the vital importance of their preservation for patient care, job preservation, and economic stability. "It's critical that the super committee recognize the significance of these programs, especially at this time," said ASN Public Policy Board chair Thomas H. Hostetter, MD. "Our letter emphasizes that it's not just doctors, or even just doctors and patients, who benefit—it is every American whose job, community or local economy is affected by these issues."

Discretionary workforce programs are considered to be among the most vulnerable. In the letter, ASN emphasized that decreasing federal support for physician training would result in a host of unintended consequences for patients and the nation's healthcare workforce. The society urged the super committee to avoid any cuts to physician training programs, which would exacerbate the problem of Americans' access to care, worsen the physician shortage already recognized by Congress, and endanger thousands of jobs. According to the economic consulting firm Tripp Umbach, cuts to graduate medical education at the nation's largest teaching hospitals alone would trigger the elimination of over 70,000 jobs and the loss of $10 billion to the U.S. economy.

Similarly, ASN highlighted the crucial role the research activities funded through the National Institutes of Health (NIH), Agency for Healthcare Research and Quality, and the Veterans' Administration play in maintaining the health of the U.S. population and the nation's economy. Besides enabling important medical discoveries, according to a 2010 study, investment in the NIH led to the creation of 487,900 new jobs and produced more than $68 billion in new economic activity.

The letter also urged the super committee to account for the needs of ESRD patients, the most vulnerable of all Medicare patient populations, by maintaining funding for ESRD care at current levels and not subjecting ESRD care to possible payment reductions. It further encouraged the super committee to consider incorporating the "Comprehensive Immunosuppressive Drug Coverage for Kidney Transplant Patients Act of 2011" into its recommendations to Congress, noting that this bipartisan legislation would save lives and protect Medicare's investment in kidney transplants. ASN, ASPN, and RPA also advocated that at this juncture in particular, repeal and replacement of the flawed sustainable growth rate (SGR) formula would be the most appropriate and fiscally responsible course of action in the effort to preserve Medicare beneficiary access to care.

Looking Ahead

Should the bipartisan group fail to reach agreement on a plan to reduce the deficit, or if Congress fails to enact the committee's recommendations, sequestration is automatically triggered. Spending cuts to the tune of 50 percent would be applied to all defense, non-defense discretionary, and mandatory spending. Exemptions exist for certain programs, including Social Security, Medicare, military retirement, unemployment insurance, and low-income programs. An across-the-board 2 percent cut to Medicare would go into effect. And as doubt grows regarding the committee's ability to reach a bipartisan consensus, the 2 percent cap is increasingly looking like a bright spot for the patients and physicians affected by the Medicare program.

For programs other than Medicare, failure to achieve a plan that Congress can agree upon would potentially be devastating. The good news is that several members of the super committee, including Rep. Max Baucus (D-MT) and Rep. Chris Van Hollen (D-MD)—whose district includes the NIH in Bethesda, MD—have voiced their continued support for the NIH. "It would be very short-sighted to make cuts to NIH because the history has [sic] that the discoveries that they've come up with have helped to reduce costs because they've developed treatments to various diseases, so I'm very hopeful that we'll be able to protect that very important national investment," said Rep. Van Hollen in a recent interview.

Finally, it is significant that if the super committee is unable to develop a plan that Congress supports, the actual automatic cuts would not be implemented until January 2013. Conceivably, Congress would still have another year to devise a different plan or otherwise prevent the automatic cuts—something it has proven adept at pulling off before. For the time being, ASN will continue to urge the committee to reach agreement while protecting certain key health training, research, and patient care programs. Join ASN in advocating for sensible protections for these programs by visiting ASN's Legislative Action Center at http://capwiz.com/asn/home.