

## Anemia Management Protocols: Providing Consistent Hemoglobin Outcomes

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Numerous studies have documented the benefits of managing anemia in patients on dialysis to maintain hemoglobin (Hb) levels in the target range of 11.0 to 12.0 g/dL recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI™) (NKF, 2001). The processes for achieving this goal have been compartmentalized in anemia management protocols to provide consistent, evidence-based guidance for managing the wide range of factors that can affect anemia-related outcomes. Since the late 1990s, most dialysis facilities have empowered nurses to coordinate the assessment and management of anemia protocols on a day-to-day basis. This article provides an overview of major protocol components, with a focus on how these data can be used to guide current and future clinical interventions.

### Components of an Anemia Management Protocol

#### Defining Target Hb Levels

Anemia management protocols have been refined over the past decade to provide a stepwise and focused method of assessing and managing anemia (see Table 1). The first component of the anemia management protocol is to define the desired outcome based on Hb levels. Achieving and maintaining in the Hb target range of 11 to 12 g/dL as suggested by the NKF-K/DOQI™ guidelines is widely accepted as the

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*Anemia management protocols encourage a consistent therapeutic approach that can increase the likelihood of patients achieving and maintaining stable hemoglobin levels within the target range of 11 to 12 g/dL recommended by the National Kidney Foundation. This article provides an overview of current concepts of anemia management that can be integrated into protocol development and refinement.*

standard of care for patients on dialysis, and trend analyses of mean Hb levels indicate significant progress in attaining this goal. At the time the NKF-K/DOQI™ anemia guidelines were released in 1997, the mean Hb level for prevalent patients on dialysis was below 11.0 g/dL (USRDS, 2003). In contrast, data from the 2004 Clinical Performance Measurement Project (CPM) show a nationwide mean Hb level of about 11.9 g/dL (CMS, 2004).

While mean Hb levels among prevalent patients on dialysis have improved, data also indicate that a significant percentage of patients continue to have Hb levels below 11 g/dL. The CPM analysis, for example, found that 20% of patients on hemodialysis had Hb levels less than 11 g/dL (ranging from 17% to 23% by Network). Further, subanalyses showed that some patients had significantly poorer outcomes, with Hb levels below 11 g/dL observed in 43% of patients on dialysis for less than 5 months, 39% of patients with mean albumin levels less than 3.5 g/dL, 30% of patients with mean spKt/V levels less than 1.2, and 28% of patients who were dialyzing with a catheter (CMS, 2004).

Another topic that has been the focus of recent clinical attention is whether patients with mean Hb levels of 11 to 12 g/dL experience periodic or prolonged decreases in Hb to levels below 11 g/dL. That is, what percentage of the time is a patient's Hb within the recommended range compared with the time below the range? This issue was addressed in a recent analysis that was presented at the European Renal Association/European Dialysis and Transplant

Nurses' Association's 2005 Congress. In this U.S.-based study, 41,919 patients on dialysis were followed to determine the percentage of time their Hb levels were below 11 g/dL over a 6-month period. Results showed that 53% of patients had Hb levels below 11 g/dL 20% of the time or more, and 29% of patients had Hb levels below 11 g/dL 40% of the time or greater during the study period (Ofsthun et al., 2005).

Results from these two data sources suggest that a significant percentage of patients continue to have Hb levels below the NKF-K/DOQI™ target range—either chronically or periodically. Data from the CPM report highlight several specific factors that may increase the risk for low Hb levels, while the results from Ofsthun et al. (2005) point to the possibility that evaluation of mean Hb levels may not provide a qualitative assessment of the quality of care that is being provided. Most dialysis facilities (including ours) are still evaluating mean Hb levels as the primary method of evaluating anemia outcomes. However, these recent data imply that, in the future, clinicians may have to re-examine the way that Hb levels are assessed and reported to account for both interpatient population-based differences, as well as inpatient variations that may unknowingly place patients at risk for poorer outcomes.

#### Epoetin alfa Dosing

The second step of the anemia management protocol is to define parameters for use of Epoetin alfa (see Table 2). On the basis of clinical trials,

**Table 1**  
**Primary Components of Anemia Management Protocols**

Step 1:	Select a target Hb level
Step 2:	Define parameters for use of Epoetin alfa
Step 3:	Define parameters for use of iron
Step 4:	Define and correct causes of hyporesponse
Step 5:	Document assessments, interventions, and outcomes

the recommended starting dose of Epoetin alfa is 50 to 100 units/kg intravenously three times a week (TIW). Once therapy has been initiated, the protocol should provide guidance on how to adjust doses to achieve desired outcomes. Clinical trials have shown that maintenance dose requirements can vary widely (from 12.5 to 525 units/kg TIW—median of 75 units/kg TIW), depending on individual bone marrow response and the presence of underlying comorbid conditions (Eschbach, Abdulhadi, Browne, & DeLano, 1989; Eschbach, Egrie, Downing, Browne, & Adamson, 1987; Eschbach, Varma, & Stivelman, 2002). Therefore, individualized titration of Epoetin alfa doses is a vital component of successful therapy.

At Central Florida Kidney Centers, parameters for Epoetin alfa dose adjustments outline methods for monitoring Hb response, as well as maintaining, increasing, or decreasing Epoetin alfa doses. The protocol stresses the importance of maintaining Hb levels above 11 g/dL for all patients, while ensuring an appropriate response if levels exceed 12 g/dL. The algorithm is used in conjunction with trend analyses to provide a method of evaluating both long-term response and current clinical parameters, thereby ensuring that clinical interventions are guided by the most accurate data available.

**Parameters for monitoring Hb response.** The NKF-K/DOQI™

**Table 2**  
**Principles for Epoetin alfa Dosing**

- Calculate initial dose based on weight to provide 50 to 100 Units/kg TIW
- Monitor Hb every 2 to 4 weeks
- Increase or decrease the dose in increments of approximately 25%, as clinically indicated
- Decrease the dose if Hb rises more than 1 g/dL in any 2-week period
- If high Hb levels necessitate temporarily holding the dose, monitor Hb frequently to determine trends and restart Epoetin alfa at an approximate 25% lower dose when the Hb has decreased to within the target range

guidelines recommend monitoring Hb every 1 to 2 weeks following the initiation of Epoetin alfa therapy or a change in the dose, and then every 2 to 4 weeks once a stable Hb has been achieved (National Kidney Foundation, 2001). We have adopted the practice of checking Hb levels every 2 weeks when patients are in the initiation or dose titration phase of therapy, and every 2 to 4 weeks in patients with stable Hb levels. This approach allows a standardized Hb monitoring schedule and encourages long-term trend analysis.

**Parameters for increasing or decreasing Epoetin alfa doses.** Incremental modifications may be required either at the onset of therapy as Hb levels are titrated into the target range or during the maintenance phase in response to changes in clinical status. Our protocol calls for an incremental increase of 25%, depending on the rate of change in Hb and the predicted final level. Similarly, dose reductions or temporary holding of Epoetin alfa doses may be required because of Hb levels that continually exceed the recommended range, and/or a sudden increase in Hb level. Our protocol calls for a 25% reduction in the Epoetin alfa dose if the Hb exceeds 12 g/dL and the patient does not require higher levels for medical reasons. It is important to note that any holding of the dose is accompanied by increased assessment (once a week) to ensure that Hb levels do not decline precipitously. Epoetin alfa therapy is automatically restarted

with a 25% dose reduction as soon as Hb levels decrease to below 12 g/dL. Our protocol also calls for a decrease in the Epoetin alfa dose if Hb levels rise by more than 1.0 g/dL in any 2-week period—a practice that is in accordance with the safety recommendations in the NKF-K/DOQI™ guidelines (NKF, 2001).

### Managing Iron Parameters

The next step in anemia management protocol development is to define parameters for iron assessment and supplementation (see Table 3). Although iron is not an erythropoietic stimulant, it is an essential ingredient in the formation of Hb, and adjuvant iron therapy is therefore required to support Epoetin alfa-stimulated erythropoiesis. While clinicians agree that supplemental iron is required for virtually all patients receiving Epoetin alfa therapy, there is an ongoing debate regarding optimal levels for ferritin and transferrin saturation. The ultimate goal of iron therapy is to support Epoetin alfa-stimulated erythropoiesis and maintain target Hb levels, not to achieve a particular level of serum ferritin or transferrin saturation. As such, there is no single level of transferrin saturation or serum ferritin that is optimal for all patients. To provide enough iron to support erythropoiesis, the NKF-K/DOQI™ guidelines recommend that transferrin saturation be maintained at greater than 20% and serum ferritin at over 100 ng/mL.

Clinical studies suggest that maintaining ferritin between 100 and 800 ng/mL and transferrin saturation between 20% and 50% can avert iron deficiency and benefit most patients. Similarly, the guidelines recommend temporary ceiling levels of 50% for transferrin saturation and 800 ng/mL for serum ferritin, and discontinuing IV iron administration when levels exceed these ceilings (based on unknown safety risks at higher iron levels and no additional clinical benefits) (NKF, 2001). Protocols should be designed to allow both flexibility and individualization of iron supplementation, while ensuring that enough iron is available to support erythropoiesis.

Since Epoetin alfa and iron work synergistically to achieve and maintain Hb levels, the ideal approach is to integrate both components of therapy into a single protocol. A unified protocol helps ensure that anemia treatments are assessed and modified in concert on the basis of each patient's current status.

### Defining Processes for Evaluating Hyporesponse

We define hyporesponse as chronic Hb levels below 11.0 g/dL despite ongoing Epoetin alfa therapy. When hyporesponse occurs, clinicians often focus on several well-defined factors that are known to affect Hb response during Epoetin alfa therapy, including Epoetin alfa dosing practices, iron deficiency, infection or inflammation, blood loss, secondary hyperparathyroidism, and coexisting medical conditions (see Table 4). As previously discussed, the 2004 CPM report revealed several other factors that can significantly increase the risk for low Hb levels, including protein malnutrition, inadequate dialysis, and use of catheters (CMS, 2004). Whenever possible, the underlying cause for low Hb levels should be corrected. In some cases—for example, when patients present with low Hb levels when returning to the dialysis facility following hospitalization—it may be appropriate to temporarily increase

**Table 3**  
Principles for Iron Supplementation

- Maintain transferrin saturation  $\geq 20\%$  but less than 50%
- Maintain ferritin  $\geq 100$  ng/mL but less than 800 ng/mL
- Most patients on hemodialysis will require IV iron

the dose of Epoetin alfa to ensure that patients receive the benefits associated with Hb levels maintained in the NKF-K/DOQI™ target range. In cases where the underlying comorbidity is permanent and not correctable, a patient may still be able to achieve target Hb levels with progressive incremental increases in the Epoetin alfa dose. Similarly, in patients with consistently low Hb levels who do not have discernable comorbidities affecting response, incremental dose increases (e.g., 25%) can be given until the target level is reached.

### Documenting Clinical Interventions/Rationale for Therapy

The final component of the anemia management protocol is to define methods for proper documentation of clinical outcomes and interventions. The documentation process starts with the approval of the protocol, signed by participating physicians. On an ongoing basis, nursing and physician documentation should include current progress notes that address patient assessments and interventions, especially the following: (a) individual patient target Hb levels, (b) the most recent Hb level, (c) the rationale for the target Hb, (d) the current Epoetin alfa dose, (e) the new Epoetin alfa dose (if required), (f) the rationale for any dose changes, and (g) the physician's signature.

For patients with Hb levels higher than 12 g/dL, additional documentation is required to show how the Epoetin alfa dose is being titrated

**Table 4**  
Factors Contributing to Hyporesponse

- New to dialysis or Epoetin alfa therapy
- Inadequate Epoetin alfa dose
- Post-hospitalization
- Iron deficiency
- Infection or inflammation
- Blood loss
- Secondary hyperparathyroidism
- Coexisting medical conditions
- Medications causing anemia
- Protein malnutrition
- Inadequate dialysis/use of catheters
- Vitamin deficiency
- Hemolysis
- Aluminum toxicity

to maintain levels between 11 and 12 g/dL. (Medical justification is required when higher target Hb levels are dictated by patient need.) Similarly, medical justification may be requested for those who require an Epoetin alfa dose of 10,000 Units or more per administration (Messana, 2003).

### Nurse-Directed Anemia Management

A nurse-directed anemia management protocol provides an excellent method of focusing attention on the importance of attaining the global goals of anemia management. The anemia manager is responsible for achieving desired outcomes, as defined by the members of the quality improvement team (team members include a physician, a nurse anemia manager, registered nurses, and a dietitian). This individual needs to have broad theoretical knowledge of anemia and the practical experience to manage aspects of care that affect outcomes. The anemia manager is empowered to work in conjunction with physicians to ensure consistent execution of the protocol and appropriate documentation, to analyze Hb outcomes, and to educate both staff and patients. Each component of the protocol should be designed to

achieve this objective by focusing the actions of both staff members and patients on the importance of maintaining Hb levels in the NKF-K/DOQI™ target range to achieve improved individual and system-wide outcomes.

### Conclusions

Using an anemia management protocol that incorporates an Epoetin alfa administration algorithm can help provide consistent clinical interventions that allow individual patients to maintain stable Hb levels between 11 and 12 g/dL. Protocol development should be guided by an ongoing review of the clinical literature to ensure that current data are being incorporated into assessment techniques and management procedures. Nurses are often empowered as the anemia manager responsible for serial measurements that evaluate both individual patient response and facility-wide improvements in mean Hb levels. Ultimately, the success of any anemia management protocol is determined by its ability to help guide clinical interventions that will ensure that all patients have the opportunity to maintain targeted Hb levels.

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