Effective Health Care

Inhibitor Antibody Production in Previously Untreated Hemophilia Patients Nomination Summary Document

Results of Topic Selection Process & Next Steps

- *The topic, Inhibitor Antibody Production in Previously Untreated Hemophilia Patients,* was found to be addressed by a number of systematic reviews, including a 2012 systematic review titled, *Cumulative inhibitor incidence in previously untreated patients with severe hemophilia A treated with plasma derived versus recombinant factor VIII concentrates: a critical systematic review.*
  - Franchini M, Tagliaferri A, Mengoli C, Cruciani M. Cumulative inhibitor incidence in previously untreated patients with severe hemophilia A treated with plasma derived versus recombinant factor VIII concentrates: a critical systematic review. Critical Reviews in Oncology/Hematology.2012;81(1):82 93.
- Although this topic is currently covered by existing systematic reviews, the topic could potentially be considered for new research in comparative effectiveness.

Topic Description

Nominator(s): Individual

Nomination Summary: The nominator is interested in the use of fresh frozen plasma (FFP) and cryoprecipitate (plasma-derived) clotting factor versus specifically licensed clotting factor replacement agents (recombinant) to reduce the risk of inhibitor antibody development in previously untreated patients. The scope of the nomination was expanded to include all plasma-derived clotting factors.

Staff-Generated PICO
Population(s): Previously untreated patients diagnosed with hemophilia
Intervention(s): Fresh frozen plasma (FFP) and cryoprecipitate (plasma-derived) clotting factor
Comparator(s): Recombinant clotting factor replacement agents
Outcome(s): Avoidance of or reduction in the rate of development of inhibitory antibodies in previously untreated patients.

Key Questions from Nominator: What is the comparative effectiveness of plasma-derived, recombinant agents and plasma-derived versus recombinant clotting agents for the prevention or risk reduction of inhibitor development?

Considerations

- The topic meets Effective Health Care (EHC) Program appropriateness and importance criteria. (For more information, see http://effectivehealthcare.ahrq.gov/index.cfm/submit-a-suggestion-for-research/how-are-research-topics-chosen/.)
- Patients with hemophilia have a deficiency of functional clotting factor VIII or IX (<0.01 IU per milliliter) and have bleeding in the joints and muscles. To prevent joint destruction, the current standard of care for children with severe hemophilia A is primary prophylaxis which includes regular infusions of recombinant factor VIII, which are initiated at the time of the first episode of bleeding in a joint or earlier aiming at the prevention of joint damage. However, in about 30% of children, inhibitory antibodies to infused factor VIII products develop, making usual treatment with factor VIII and prophylaxis impossible.
- A recent systematic review by Franchini et al., concluded that there are limitations to the available evidence, including conflicting results across studies, the lack of RCTs, and small study populations. Based on these findings, there is a need for additional research to address these limitations.