NATIONAL HEMOPHILIA FOUNDATION
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MASAC Document #226
(Replaces #169)

MASAC RECOMMENDATION REGARDING THE USE OF RECOMBINANT CLOTTING FACTOR PRODUCTS WITH RESPECT TO PATHOGEN TRANSMISSION

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on April 13, 2014, and adopted by the NHF Board of Directors on May 6, 2014.

Recombinant clotting factor concentrates differ from plasma-derived products in that they are either completely free of human plasma derivatives (Advate, Alprolix, BeneFIX, Rixubis, Tretten, Xyntha) or else use human plasma protein solution (Helixate FS, Kogenate FS) or newborn calf serum (NovoSeven) in the cell culture medium and pasteurized bovine serum albumin as a stabilizer in the vial (Recombinate). Current plasma-derived concentrates employed in the treatment of hemophilia A and B, von Willebrand disease, and other inherited bleeding disorders are very safe with respect to transmission of HIV, hepatitis B, hepatitis C, and hepatitis A. However, these products may be capable of transmitting nonenveloped viruses such as parvovirus B19. In addition, these products are potentially capable of transmitting prions, the agents causing Creutzfeldt-Jakob disease (CJD) and variant CJD (vCJD), which are not eliminated by current viral inactivation and product purification techniques. While vCJD has now been transmitted by RBC transfusion, no known cases have been reported from the use of plasma-derived factor products in the past over 35 years of use. However, parvovirus B19 and prions may be markers for as yet undiscovered or unrecognized blood-borne infectious agents. This possibility suggests a potentially improved safety profile for recombinant products over plasma-derived products with respect to pathogen transmission.

In April 1998, the Public Health Service's Advisory Committee on Blood Safety and Availability recommended the following:

"Every effort should be made to make recombinant clotting factors available to all who would benefit from them, and all barriers to conversion from human plasma-derived concentrates to recombinant clotting factors should be removed."

MASAC fully endorses this recommendation and calls on industry and the Food and Drug Administration to carry out the Committee's recommendation for all bleeding disorders.

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Therefore, MASAC makes the following recommendations:

1. The recombinant factor VIII products Advate, Helixate FS, Kogenate FS, Recombinate, and Xyntha are potentially the safest factor VIII products available with respect to pathogen transmission and should be considered the treatment of choice for individuals with hemophilia A.

2. The recombinant factor IX products Alprolix, BeneFIX, and Rixubis are potentially the safest factor IX products available with respect to pathogen transmission and should be considered the treatment of choice for individuals with hemophilia B.

3. The recombinant factor VIIa product NovoSeven is potentially the safest factor VII product available with respect to pathogen transmission and should be considered the treatment of choice for individuals with congenital factor VII deficiency.

4. The recombinant factor XIII-A subunit product Tretten is potentially the safest factor XIII-A subunit product available with respect to pathogen transmission and should be considered the treatment of choice for individuals with congenital factor XIII-A subunit deficiency.

5. For hemophilia A and B patients with inhibitors, there are often overriding concerns about efficacy that supersede those of potentially increased safety with respect to pathogen transmission.

6. In all patients, including patients with inhibitors, the issue of potential pathogen transmission must be weighed against the issue of efficacy.

7. Manufacturers should endeavor to make the cost of their recombinant clotting factor products more competitive with plasma-derived products.

8. Manufacturers of the recombinant products are strongly encouraged to avoid using human and animal proteins in manufacturing their products.