MASAC Recommendation Regarding the Use of Recombinant Clotting Factor Replacement Therapies

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on November 11, 2000 and adopted by the NHF Board of Directors on November 12, 2000.

While current plasma-derived concentrates employed in the treatment of hemophilia A and B, von Willebrand disease, and related bleeding disorders are very safe with respect to transmission of HIV, hepatitis B, hepatitis C, and hepatitis A, these products may be capable of transmitting nonenveloped viruses such as parvovirus B19. In addition, these products are potentially capable of transmitting the unknown agents of Creutzfeldt-Jakob disease (CJD) and new variant CJD (nvCJD), which are not eliminated by current viral inactivation and product purification techniques. No known cases of transmissible spongiform encephalopathy have resulted from the use of plasma-derived products in the past 30 years during which they have been in use. However, parvovirus B19 and the agent for CJD or nvCJD may be markers for as yet undiscovered or unrecognized blood-borne infectious agents.

Recombinant proteins including clotting factor products are produced in well-characterized hamster cell lines. Thousands of patients have been treated with several different recombinant proteins over the last ten years. To date, there have been no known instances of animal virus transmission by any therapeutic recombinant proteins.

Recombinant clotting factor concentrates are much safer than plasma-derived products because they are either completely free of plasma derivatives (BeneFIX) or else use pasteurized human serum albumin in the cell culture medium (Helixate FS, Kogenate FS, ReFacto) and as a stabilizer in the vial (Bioclate, Recombinate). This pasteurized human serum albumin has a 50-year safety record. Bovine serum proteins are used in the cell culture medium in the production of Bioclate and Recombinate. However, the bovine material comes from non-bovine spongiform encephalitis-endemic areas.

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.

Therefore, MASAC makes the following recommendations:

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

2. The recombinant factor IX product BeneFIX is the safest factor IX product available with respect to viral transmission and should be considered the treatment of choice for individuals with hemophilia B.

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

4. Manufacturers of the recombinant products are strongly encouraged to avoid using human and animal proteins in manufacturing their products. Development, regulatory review, and licensure of these concentrates should be expedited.

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