NATIONAL HEMOPHILIA FOUNDATION
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MASAC Document #211

MASAC RECOMMENDATIONS REGARDING INHIBITOR RISK AND RECOMBINANT FACTOR VIII CONCENTRATES

The following recommendation was approved by the Medical and Scientific Advisory Council (MASAC) on May 6, 2012, and adopted by the NHF Board of Directors on June 22, 2012.

Inhibitor formation is the single most important complication of clotting factor concentrate usage, especially for patients with severe hemophilia A. Based on the total body of current knowledge and emerging data available at this time, any FVIII preparation can be associated with alloantibody inhibitor formation; however, this risk appears to be small in previously treated patients who have over 150 exposure days to FVIII products. (1-4)

There are a number of ongoing national and international studies to identify the potential risks for inhibitor formation related to genetic, environmental, and product-specific factors. It is critical that patients participate in surveillance studies of existing products and in clinical studies of new products and therapies, including those that utilize bioengineered technologies including B-domain-deleted recombinant Factor VIII (BDD-rFVIII) constructs, in order to answer these important questions about inhibitor formation. When more data become available from these ongoing studies, they will be reviewed by MASAC and disseminated to the broader hemophilia community.

MASAC therefore recommends that

1. Physicians, individuals with hemophilia, insurance companies, and formulary benefits managers who are making decisions about clotting factor selection or purchase should consider the available data when making decisions about which rFVIII product to recommend for an individual patient. Interpretation of data utilized to support marketing claims and medical care decisions should be based on broad literature review and knowledge of study limitations.
2. There should be a concerted effort on the part of industry to monitor for the development of new inhibitors in research studies of all new and existing products, including those using BDD-rFVIII technology. Ideally these studies should be adequately powered, randomized clinical trials to allow for meaningful interpretation of the results.
3. MASAC encourages individuals with hemophilia A to consider participation in surveillance studies of existing products, in clinical trials employing innovative replacement products derived from recombinant technologies, and in gene therapy studies.

116 West 32nd Street · 11th floor
New York, NY · 10001
(800) 42.HANDI · (212) 328.3700 · fax (212) 328.3777
www.hemophilia.org · info@hemophilia.org

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