MASAC RECOMMENDATIONS REGARDING THE TREATMENT OF VON WILLEBRAND DISEASE

The following recommendations were approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF) on October 23, 2016, and adopted by the NHF Board of Directors on November 3, 2016.

Von Willebrand disease (VWD) is the most common inherited bleeding disorder and affects males and females equally in up to 1% of the general population. (6,7) VWD is associated with mucous membrane bleeding, excessive bruising, and bleeding from cuts. It can result in excessive bleeding with invasive dental work, during surgical procedures, and after accident or injury. In women, excessive menstrual bleeding is often the major symptom. Women with VWD are also at risk of postpartum hemorrhage, particularly delayed postpartum hemorrhage.

Recently developed products have changed the treatment options for individuals with VWD. The following are current recommendations for treating bleeding in these individuals.

1. Persons with type 1 VWD should be treated with the synthetic agent desmopressin (DDAVP Injectable or Stimate Nasal Spray for Bleeding, 1.5 mg/ml), and their maximum response at first use should be documented for future reference (DDAVP trial). For surgery, trauma, or other serious bleeding episodes, if hemostasis is not achieved with DDAVP, a factor VIII concentrate rich in the high molecular weight multimers of von Willebrand factor (VWF) should be used (see #3 below).

2. Persons with type 2A, 2M, and 2N VWD should be treated with DDAVP if they have been shown by a DDAVP trial to be responsive.

3. Persons with type 2B and type 3 VWD, and those with type 1, 2A, 2M, and 2N who have been shown to be nonresponsive to DDAVP, should be treated with a factor VIII concentrate that is known to contain the higher molecular weight multimers of von Willebrand factor and that has been virally attenuated to eliminate transmission of HIV and hepatitis A, B, and C. Human plasma-derived products Alphanate, Humate P, and Wilate have been approved by the FDA for use in VWD. A recombinant VWF concentrate, Vonvendi, has also been approved. Another plasma-derived product, Koate DVI, may also be effective in these patients, but it has not been approved by the FDA for use in VWD. For further information, see MASAC Document #246, MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders Revised October, 2016.

4. Because of the increased risk of HIV and hepatitis A, B, and C transmission, cryoprecipitate should not be used except in an emergency situation when none of the above-mentioned products are available and delay of treatment would be life- or limb-threatening.
5. Desmopressin is a potent antidiuretic agent, and fluid retention is a potential complication of this drug. Both parenterally administered DDAVP and Stimate Nasal Spray have been associated with the development of hyponatremia and seizures. To minimize this risk, the following precautions should be observed when this drug is used at home and in the hospital:
   a. DDAVP and Stimate should be administered no more often than once every 24 hours.
   b. DDAVP and Stimate should be used for no more than three consecutive days unless directed to do so by Hemophilia Treatment Center medical staff.
   c. DDAVP and Stimate should not be used in children under the age of two years.
   d. DDAVP and Stimate should be used with caution in the elderly and in individuals with a history of heart disease, hypertension, or stroke.
   e. If a patient is treated with DDAVP before surgery, the anesthesiologist should be advised to avoid fluid overload and dilutional hyponatremia.
   f. DDAVP should be used with caution in pregnant women in the peripartum and immediate postpartum period, with careful attention to fluid management so as to avoid hyponatremia. (5)
   g. Oral fluids should be restricted to maintenance for 24 hours following treatment.

6. Adjunctive treatments for mucous membrane bleeding include the antifibrinolytic agents Amicar and tranexamic acid. These agents can be given orally or intravenously. (See MASAC Doc #246, MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and Other Bleeding Disorders Revised October, 2016.)

7. Prior to surgery in a patient with VWD, consultation should be obtained with a pediatric or adult hematologist who specializes in the management of individuals with inherited bleeding disorders. This consultation should cover such issues as the need for a DDAVP trial; type of fluid replacement or fluid restriction; dose and duration if DDAVP is to be used; appropriate dose, timing, and duration of factor replacement therapy; and use of adjunctive medications (Amicar).

References:

This material is provided for your general information only. NHF does not give medical advice or engage in the practice of medicine. NHF under no circumstances recommends particular treatment for specific individuals and in all cases recommends that you consult your physician or local treatment center before pursuing any course of treatment.

Copyright 2016 National Hemophilia Foundation. To facilitate the dissemination of these medical recommendations, reproduction of any material in this publication in whole or in part will be permitted provided: 1) a specific reference to the MASAC recommendation number and title is included and 2) the reproduction is not intended for use in connection with the marketing, sale or promotion of any product or service. NHF reserves the right to make the final determination of compliance with this policy. For questions or to obtain a copy of the most recent recommendations, please contact the NHF Director of Communications at 1-800-42-HANDI or visit the NHF website at www.hemophilia.org.