BLOOD FACTORS FOR IMPAIRED COAGULATION

2010 UPDATE: ADDITIONAL INFORMATION

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The information provided is intended as a general guide only. Consult additional references and product labeling for more detailed information.
The clinical implications of latex hypersensitivity and possible manufacturing changes present a challenge when administering products to latex-sensitive patients.
It is prudent to verify latex content with manufacturer prior to administration.

PRODUCT COMPARISON[a-l]

Infection Risk Comments:
The risk of transmission of infectious agents, including viruses and prions (such as the Creutzfeldt-Jakob disease [CJD] agent) cannot be totally eliminated with human plasma-derived products. Prions cannot be inactivated by any method.
When only one viral inactivation method is used, it should ideally inactivate viruses with or without lipid envelopes.
Heat treatment is generally effective against viruses with or without lipid envelopes, including Human Immunodeficiency Virus or Hepatitis A and Hepatitis C viruses.
Solvent/detergent does not inactivate Hepatitis A virus or other non-enveloped viruses.

Product Manufacturer	**Source** H=Human plasma R=Recombinant AHF=Antihemophilic factor vWF=von Willebrand factor	**Purity** (Factor content (IU)/mg total protein) L=Low I=Intermediate **VH=Very high**	**Viral Inactivation Method** DAC=Dual affinity chromatography IA=Immunoaffinity chromatography DH=Dry heat ST=Sodium thiocyanate NF=Nanofiltration UF=Ultrafiltration P=Pasteurization VF=Viral filtration SD=Solvent/detergent VH=Vapor heat	**FDA-approved indications**								**Approximate vial content** IU = International Unit F VIII=Factor VIII VWF=von Willebrand factor For most products, each vial labeled with the actual IU content	**Latex content** Devices, such as syringes or infusion sets, that are provided with blood factor products may or may not contain latex. Consult manufacturer for details.	**Storage instructions**		**Administration** • Prepare according to manufacturer instructions • Administer at room temperature • Use plastic syringes • Use within 3 hours
				Hemophilia A Factor VIII deficiency	**Hemophilia A with inhibitors**	**Acquired Factor VIII deficiency**	**Acquired Factor VIII inhibitors**	**von Willebrand disease (VWD)** von Willebrand factor deficiency	**Hemophilia B** Factor IX deficiency or Christmas disease	**Hemophilia B with inhibitors**	**Congenital FVII deficiency**			**Storage under refrigeration recommended 2-8°C (36-46°F)** • Avoid freezing • Use before expiration date on label	**Room temperature storage** • Use before expiration date on label	
New Product: **Wilate** Octapharma	H	L/I	SD, DH					✓				450 IU VWF:RCo and 450 IU FVII per 5 mL 900 IU VWF:RCo and 900 IU FVII per 10 mL Each vial labeled with VWF:RCo and FVIII activity	Latex free	Do not return to refrig after room temp storage	Up to 6 months not to exceed 25°C (77°F)	Administer by slow IV injection at 2-4 mL/min Reduce rate/ temporarily stop if marked increase in pulse rate

DISEASE MANAGEMENT [a,c,d,f,g,h,k,l,m]

Dosage and duration of therapy are guided by clinical response
Dosage must be individualized according to the needs of the patient (weight, severity, presence of inhibitors)
Whenever possible, serial assays should be performed at suitable intervals to confirm achievement and maintenance of adequate plasma factor levels

von Willebrand Disease-treatment with Wilate

von Willebrand Factor deficiency

Treatment of choice for von Willebrand Disease Type 1: Desmopressin (DDAVP)
Treatment of choice for Types 2 and 3, or when DDAVP is ineffective or contraindicated: Antihemophilic Factor/von Willebrand Factor (Humate-P, Alphanate)

Hemorrhage	Therapy	Product	Classification VWD	Dosage (units VWF:RCo/kg body weight) and frequency
Minor: • Epistaxis • Oral bleeding • Menorrhagia	AHF/vWF Human	Wilate	All types In VWD type 3 patients, especially in those with gastro-intestinal (GI) bleedings, higher doses may be required.	Loading dose 20-40 IU/kg then 20-30 IU/kg every 12-24 hours for 3 days to keep trough level VWF:RCo and FVIII activity trough levels of >30%
Major: • Severe or refractory epistaxis • GI bleeding • CNS trauma • Traumatic hemorrhage • Hemarthosis For major bleeds in all types of VWD where repeated dosing is required, monitor and maintain the patient's FVIII level according to the guidelines for hemophilia A therapy.	AHF/vWF Human	Wilate	All types In VWD type 3 patients, especially in those with gastro-intestinal (GI) bleedings, higher doses may be required.	Loading dose 40-60 IU/kg then 20-40 IU/kg every 12-24 hours for 3 days to keep trough level VWF:RCo and FVIII activity trough levels of >50%

Congenital Factor VII deficiency

Treatment of choice: Factor VIIa
Alternative treatment: Anti-inhibitor Coagulant Complex

Therapy	Product	Dose, Frequency, and Duration
Factor VIIa Recombinant	Novoseven RT	The recommended dose range for treatment of bleeding episodes or for prevention of bleeding in surgical interventions or invasive procedures in congenital Factor VII deficient patients is 15-30 micrograms per kg body weight every 4-6 hours until hemostasis is achieved. Effective treatment has been achieved with doses as low as 10 micrograms/kg. Dose and frequency of injections should be adjusted to each individual. The minimum effective dose has not been determined.

Acquired Hemophilia

Therapy	Product	Dose, Frequency, and Duration
Factor VIIa Recombinant	Novoseven RT For other agents indicated for acquired hemophilia, refer to hemophilia dosing above.	The recommended dose range for the treatment of patients with acquired hemophilia is 70-90 micrograms/kg repeated every 2-3 hours until hemostasis is achieved. The minimum effective dose in acquired hemophilia has not been determined. The majority of the effective outcomes were observed with treatment in the recommended dose range. The largest number of treatments with any single dose was 90 micrograms/kg; of the 15 treated, 10 (67%) were effective and 2 (13%) were partially effective.

RECOMMENDED RESOURCES

Organizations and Resources

Canadian Hemophilia Society. http://www.hemophilia.ca/en/

Hemophilia Federation of America. http://hemophiliafed.org/

Treatment Recommendations from Medical and Scientific Advisory Council (MASAC). National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=138

Publications. World Federation of Hemophilia. http://www.wfh.org/index.asp?lang=EN

UKHCDO Guidelines. United Kingdom Haemophlia Centres Doctors' Organisation. http://www.ukhcdo.org/UKHCDOguidelines.htm

Disease Management

Guidelines for the Management of Hemophilia. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/Guidelines_Mng_Hemophilia.pdf

Protocols for the Treatment of Hemophilia and von Willebrand Disase. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/VWD_WomenBleedingDisorders/TOH-14-Protocols-Hemophilia-VWD-Revised2008.pdf

MASAC Recommendation #186 (Replaces #173): MASAC Recommendations Regarding the Treatment of von Willebrand Disease. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac186.pdf

The Basic Diagnosis and Clinical Management of von Willebrand Disease; Treatment of Hemophilia monograph no. 35. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/VWD_WomenBleedingDisorders/TOH-35_VWD_%20Revision2008.pdf

The Diagnosis, Evaluation, and Management of von Willebrand Disease. National Heart, Lung, and Blood Institute. http://www.nhlbi.nih.gov/guidelines/vwd/vwd.pdf

von Willebrand Disease: An Introduction for the Primary Care Physician; Treatment of Hemophilia monograph no. 47. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/VWD_WomenBleedingDisorders/TOH-47-VWD-Intro.pdf

Keeling D, Tait C, Makris M. Guideline on the selection and use of theraputic products to treat haemophilia and other hereditary bleeding disorders. A United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline approved by the British Committee for Standards in Haematology. *Haemophilia.* 2008;14(4):671-684.

Inhibitors

Inhibitors in Hemophilia: A Primer. 4th ed. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Inhibitors/TOH-7%20Inhibitor-Primer-Revised2008.pdf

Management of Inhibitors to Factors VIII and IX: An Introductory Discussion for Physicians. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Inhibitors/TOH-34_English_Inhibitors.pdf

What Are Inhibitors? World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Inhibitors/Inhibitors_booklet_ENG.pdf

Hay CR, Brown S, Collins PW, Keeling DM, Liesner R. The diagnosis and management of factor VIII and IX inhibitors: a guideline from the United Kingdom Haemophilia Centre Doctors Organisation. *Br J Haematol.* 2006;133(6):591-605.

Clotting Factor Concentrates

Guide for the Assessment of Clotting Factor Concentrates. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Safety_and_Supply/GuideClottingFactor_Eng.pdf

MASAC Document #190: MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and other Bleeding Disorders. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=138

Key Issues in Hemophilia Treatment. Part 1: Products; Facts and Figures monograph no. 1. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Treatment_Products/Monographs/FF1_Part1_Products_ENG.pdf

Products Licensed in the US for Treatment of Hemophilia A, Hemophilia B, von Willebrand Disease, Inhibitors, and Rare Bleeding Disorders. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac190tables.pdf

Women's Health

Gynecological Complications in Women with Bleeding Disorders; Treatment of Hemophilia monograph no. 5. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/VWD_WomenBleedingDisorders/TOH-5_English_gynecological.pdf

MASAC Document # 192: MASAC Guidelines for Perinatal Management of Women with Bleeding Disorders and Carriers of Hemophlia A and B. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac192.pdf

MASAC Document #185 (Replaces #172): MASAC Recommendations Regarding Women with Inherited Bleeding Disorders. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac185.pdf

Pregnancy in Women with Inherited Bleeding Disorders; Treatment of Hemophilia monograph no. 29. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/VWD_WomenBleedingDisorders/TOH-29_English_Pregnancy.pdf

Treatment Centers

Hemophilia Treatment Center Directory. Centers for Disease Control. https://www2a.cdc.gov/ncbddd/htcweb/Main.asp

PATIENT ASSISTANCE PROGRAMS

Product	Program Details
Advate Feiba VH Hemofil M Recombinate	Baxter CARE Program 1-888-229-8379 http://www.thereforyou.com/patients/insurance/baxter-insurance-assistance/
Kogenate FS	Bayer Kogenate FS Patient Assistance Program (PAP) 1-800-288-8374 http://www.kogenatefs.com/patients/insurance-information.jsp
Novoseven RT	NovoNordisk SevenSECURE Support and Assistance program 1-877-NOVO-777 http://www.novonordisk-us.com/documents/article_page/document/patient_assistance_hemo.asp
Xyntha BeneFIX	Wyeth Factor Resource Program Patient Assistance Program 1-888-999-2349 (option 1, then option 2) http://www.hemophiliavillage.com/patient_assistance.html
Helixate FS Humate-P Monclate-P Mononine	CSL Behring Assurance 1-866-415-2164 http://www.cslbheringassurance.com
Alphanate Alpha Nine SD ProfilNine	Grifols PatientCare Program 1-888-325-8579 http://www.grifolspatientcare.com/pcProgram_more.html

REFERENCES

[a]Product prescribing information
[b]Personal communication with product manufacturer
[c]Guidelines for the Management of Hemophilia. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/Guidelines_Mng_Hemophilia.pdf
[d]Klasco RK, ed. DRUGDEX System. Greenwood Village, CO: Thomson MICROMEDEX,
[e]Products Licensed in the US for Treatment of Hemophilia A, Hemophilia B, von Willebrand Disease, Inhibitors, and Rare Bleeding Disorders. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac190tables.pdf
[f]Shord SS, Lindley CM. Coagulation products and their uses. Am J Health Syst Pharm. 2000; 57:1403-20.
[g]Drug Facts and Comparisons online. Saint Louis, MO: Wolters Kluwer Health, Inc; 2010.
[h]Lexi-Comp online. Hudson, OH: Lexi-Comp, Inc.; 2010.
[i]Gahart BL, Nazareno AR. Intravenous Medications: A Handbook for Nurses and Allied Health Professionals. 21st ed. St. Louis, MO: Mosby; 2010.
[j]BlackBoxRx.com. http://blackboxrx.com/index.php#F
[k]MASAC Document #190: MASAC Recommendations Concerning Products Licensed for the Treatment of Hemophilia and other Bleeding Disorders. National Hemophilia Foundation. http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=138
[l]Hereditary Plasma Clotting Factor Disorders and their Management; Treatment of Hemophilia monograph no. 4. World Federation of Hemophilia. http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/TOH-4-Hereditary-Plasma-Revised2008.pdf
[m]The Diagnosis, Evaluation, and Management of von Willebrand Disease. National Heart, Lung, and Blood Institute. http://www.nhlbi.nih.gov/guidelines/vwd/vwd.pdf