

# 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<sup>a-l</sup>

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 NF=Nanofiltration P=Pasteurization SD=Solvent/detergent ST=Sodium thiocyanate UF=Ultrafiltration VF=Viral filtration 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	
<b>New Product:</b> 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 refrigeration after room temperature 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
<b>Minor:</b> <ul style="list-style-type: none"> <li>• Epistaxis</li> <li>• Oral bleeding</li> <li>• Menorrhagia</li> </ul>	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%
<b>Major:</b> <ul style="list-style-type: none"> <li>• Severe or refractory epistaxis</li> <li>• GI bleeding</li> <li>• CNS trauma</li> <li>• Traumatic hemorrhage</li> <li>• Hemarthosis</li> </ul> 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 Haemophilia 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](http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/Guidelines_Mng_Hemophilia.pdf)

Protocols for the Treatment of Hemophilia and von Willebrand Disease. World Federation of Hemophilia. [http://www.wfh.org/2/docs/Publications/VWD\\_WomenBleedingDisorders/TOH-14-Protocols-Hemophilia-VWD-Revised2008.pdf](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](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](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 therapeutic 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](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](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](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](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](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 Hemophilia 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](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 <a href="http://www.thereforeyou.com/patients/insurance/baxter-insurance-assistance/">http://www.thereforeyou.com/patients/insurance/baxter-insurance-assistance/</a>
Kogenate FS	Bayer Kogenate FS Patient Assistance Program (PAP) 1-800-288-8374 <a href="http://www.kogenatefs.com/patients/insurance-information.jsp">http://www.kogenatefs.com/patients/insurance-information.jsp</a>
Novoseven RT	NovoNordisk SevenSECURE Support and Assistance program 1-877-NOVO-777 <a href="http://www.novonordisk-us.com/documents/article_page/document/patient_assistance_hemo.asp">http://www.novonordisk-us.com/documents/article_page/document/patient_assistance_hemo.asp</a>
Xyntha BeneFIX	Wyeth Factor Resource Program Patient Assistance Program 1-888-999-2349 (option 1, then option 2) <a href="http://www.hemophiliavillage.com/patient_assistance.html">http://www.hemophiliavillage.com/patient_assistance.html</a>
Helixate FS Humate-P Monclate-P Mononine	CSL Behring Assurance 1-866-415-2164 <a href="http://www.cslbheringassurance.com">http://www.cslbheringassurance.com</a>
Alphanate Alpha Nine SD ProfilNine	Grifols PatientCare Program 1-888-325-8579 <a href="http://www.grifolspatientcare.com/pcProgram_more.html">http://www.grifolspatientcare.com/pcProgram_more.html</a>

## REFERENCES

<sup>a</sup>Product prescribing information

<sup>b</sup>Personal communication with product manufacturer

<sup>c</sup>Guidelines for the Management of Hemophilia. World Federation of Hemophilia. [http://www.wfh.org/2/docs/Publications/Diagnosis\\_and\\_Treatment/Guidelines\\_Mng\\_Hemophilia.pdf](http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/Guidelines_Mng_Hemophilia.pdf)

<sup>d</sup>Klasco RK, ed. DRUGDEX System. Greenwood Village, CO: Thomson MICROMEDEX,

<sup>e</sup>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>

<sup>f</sup>Shord SS, Lindley CM. Coagulation products and their uses. Am J Health Syst Pharm. 2000; 57:1403-20.

<sup>g</sup>Drug Facts and Comparisons online. Saint Louis, MO: Wolters Kluwer Health, Inc; 2010.

<sup>h</sup>Lexi-Comp online. Hudson, OH: Lexi-Comp, Inc.; 2010.

<sup>i</sup>Gahart BL, Nazareno AR. Intravenous Medications: A Handbook for Nurses and Allied Health Professionals. 21st ed. St. Louis, MO: Mosby; 2010.

<sup>j</sup>BlackBoxRx.com. <http://blackboxrx.com/index.php#f>

<sup>k</sup>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>

<sup>l</sup>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](http://www.wfh.org/2/docs/Publications/Diagnosis_and_Treatment/TOH-4-Hereditary-Plasma-Revised2008.pdf)

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