Alphanate®
antihemophilic factor/von Willebrand factor complex (human)

Inhibitors are the greatest challenge in hemophilia A treatment[1,2]

What is an inhibitor?

Inhibitors are the most serious and challenging hemophilia A treatment complication.[1,2] Inhibitors develop when the body stops accepting the factor VIII (FVIII) treatment product as a normal part of blood. The body thinks the FVIII treatment product is a foreign substance and tries to destroy it. An inhibitor stops the FVIII treatment product from working, which makes it more difficult to stop a bleeding episode.[3]

The risk of inhibitor development in hemophilia A is significant[4]

- All patients with hemophilia A are at risk for developing inhibitors, regardless of age and disease severity[5]
- Up to 35% of patients with hemophilia A will develop inhibitors[4]
- 25% of patients who develop inhibitors will have them for life[6]

Risk factors for inhibitors are genetic and environmental

Genetic	Environmental
Severity of hemophilia A[7]	Intensive FVIII treatment at peak treatment moments[7]
Large mutation of FVIII gene[7]	Early intensive exposure to FVIII treatment[8]
Family history of inhibitors[7]	Immunologic/inflammatory/infectious events (eg, vaccination, surgery, illness)[8]
Ethnicity[7]	Type of FVIII product used[4]

What is the impact of an inhibitor?

- Inhibitors may increase the risk of uncontrollable bleeding, disability, and premature death[9]
- Inhibitors double the likelihood a patient will be hospitalized for a bleeding complication[5]
- Treatment costs for a person with an inhibitor are on average 2 to 10 times higher than costs for a person without inhibitors, and can exceed $1,000,000 annually[5,10]
- Inhibitors increase the odds of death by 70% compared with patients without an inhibitor in severe hemophilia[11]

When FVIII and von Willebrand factor (VWF) are together, VWF may prevent inhibitors from binding to FVIII.[12]

References 1. Kempton CL, White GCII. *Blood*. 2009;113(1):11-17. **2.** Leissinger CA. *Am J Hematol*. 2004;77:187-193. **3.** Inhibitors. Centers for Disease Control and Prevention Website. https://www.cdc.gov/ncbddd/hemophilia/inhibitors.html. Updated December 7, 2016. Accessed February 28, 2017. **4.** Oldenburg J, Lacroix-Desmazes S, Lillicrap D. *Haematologica*. 2015;100(2):149-156. **5.** Soucie JM, Miller CH, Kelly FM, et al. *Haemophilia*. 2014;20(2):230-237. **6.** Valentino LA, et al; the International Immune Tolerance Induction Study Investigators. *Haemophilia*. 2015:1-9. doi: 10.1111/hae.12730. **7.** DiMichele DM. *Inhibitors in Hemophilia: A Primer*. 4th ed. World Federation of Hemophilia, 2008. http://www1.wfh.org/publications/files/pdf-1122.pdf. Accessed January 3, 2017. **8.** Carcao M, Re W, Ewenstein B. *Haemophilia*. 2016;22(1):22-31. **9.** Srivastava A, Brewer AK, Mauser-Bunschonten EP, et al; Treatment Guidelines Working Group. Inhibitors. In: *Guidelines for the Management of Hemophilia*. 2nd ed. World Federation of Hemophilia; 2012. http://www1.wfh.org/publications/files/pdf-1472.pdf. Accessed January 3, 2017. **10.** Ullman M, Hoots WK. *Haemophilia*. 2006; 12(Suppl. 6):74–80. **11.** Walsh CE, et al; the United States Hemophilia Treatment Center Network. *Am J Hematol*. 2015;90(5):400-405. **12.** Franchini M, Lippi G. *Thromb Haemost*. 2010;104:931-940.

Please see Important Safety Information on page 2 and see full Prescribing Information available at www.alphanate.com.

Alphanate®

antihemophilic factor/von Willebrand factor complex (human)

Indications

ALPHANATE® (antihemophilic factor/von Willebrand factor complex [human]) is indicated for:

- Control and prevention of bleeding episodes and perioperative management in adult and pediatric patients with factor VIII (FVIII) deficiency due to hemophilia A
- Surgical and/or invasive procedures in adult and pediatric patients with von Willebrand disease (VWD) in whom desmopressin (DDAVP) is either ineffective or contraindicated. It is not indicated for patients with severe VWD (type 3) undergoing major surgery

Important Safety Information

ALPHANATE is contraindicated in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components.

Anaphylaxis and severe hypersensitivity reactions are possible with ALPHANATE. Discontinue use of ALPHANATE if hypersensitivity symptoms occur, and initiate appropriate treatment.

Development of procoagulant activity-neutralizing antibodies (inhibitors) has been detected in patients receiving FVIII-containing products. Carefully monitor patients treated with AHF products for the development of FVIII inhibitors by appropriate clinical observations and laboratory tests.

Thromboembolic events have been reported with AHF/VWF complex (human) in VWD patients, especially in the setting of known risk factors.

Intravascular hemolysis may occur with infusion of large doses of AHF/VWF complex (human).

Rapid administration of a FVIII concentrate may result in vasomotor reactions.

Because ALPHANATE is made from human plasma, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, despite steps designed to reduce this risk.

Monitor for development of FVIII and VWF inhibitors. Perform appropriate assays to determine if FVIII and/or VWF inhibitor(s) are present if bleeding is not controlled with expected dose of ALPHANATE.

The most frequent adverse drug reactions reported with ALPHANATE in >1% of infusions were pruritus, headache, back pain, paresthesia, respiratory distress, facial edema, pain, rash, and chills.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1.800.FDA.1088.

Please see full Prescribing Information available at www.alphanate.com.

GRIFOLS

©2017 Grifols All rights reserved May 2017 BN/A8/0317/0267