Alphanate®

antihemophilic factor/von Willebrand factor complex (human)

Grifols is committed to safety before, during, and after ALPHANATE manufacturing

ALPHANATE is manufactured using a 10-steps-to-safety process, with full traceability from donor to patient.

Before: To guarantee all donations and donors are thoroughly screened and tested

STEP 1

Healthy Donor Selection

STEP 2

Plasma Donor Screening

STEP 3

Plasma Donation Identification and Testing

STEP 4

Inventory Hold and Look Back

STEP 5

Final Verification and Plasma Pool Testing

During: To enhance safety during manufacturing process

STEP 6

Specialized Quality Control Process

STEP 7

ALPHANATE Manufacturing and Purification Steps

STEP 8

Specific Safety Steps (SD/HT)

After: To uphold our commitment even after release to healthcare providers and patients

STEP 9

Laser-etched Identifier and Holographic Safety Seal

STEP 10

Pharmacovigilance

SD/HT, solvent detergent, heat-treated.

Plasma-derived products may carry a risk of transmitting infectious agents, such as viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, possibly, the Creutzfeldt-Jakob disease (CJD) agent. The risk that these products will transmit an infectious agent has been reduced by screening plasma donors for certain viruses, by testing for certain viral infections, and by stopping and/or removing certain viruses during manufacturing.

Please see Important Safety Information on page 4 and see accompanying full Prescribing Information for ALPHANATE.

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A closer look at the 10-steps-to-safety process

Step 1: Healthy donor selection
All potential plasma donors must:
- Provide valid identification and personal documentation
- Not be listed on the National Donor Deferral Registry
- Undergo and pass a thorough physical exam

Step 2: Plasma donor screening
Only plasma from qualified repeat donors is used to manufacture ALPHANATE. A qualified donor must take and pass a thorough health screening every time they donate plasma.

Step 3: Plasma donation identification and testing
Each plasma sample is tested for viruses. Any plasma sample that tests positive for viruses is not used in the manufacturing of ALPHANATE. Every unit of plasma that is donated has a unique barcode so it can be traced back to the donor.

Step 4: Inventory hold and look back
After the donated plasma passes all of the screening tests, it is held in inventory for at least 45 days. This is done because someone who has just been infected with a virus may not test positive during their health screening. Holding a donation for 45 days will help ensure that infected plasma can be identified and not used.

Step 5: Final verification and plasma pool testing
Following the 45-day inventory hold, the plasma is computer-verified before being sent to our manufacturing facility. All plasma is tested again for viruses before the manufacturing process begins.

Step 6: Specialized quality control process
All production facilities used to manufacture ALPHANATE are regularly inspected and regulated by the FDA in the United States and by the European health authorities. The Grifols staff members who manufacture ALPHANATE receive continuous training.

Step 7: ALPHANATE manufacturing and purification steps
During the process called fractionation, the proteins needed to manufacture ALPHANATE are separated from the rest of the plasma. Several purification steps are conducted to remove other proteins not needed in the final product.

Step 8: Specific safety steps
At this stage of manufacturing, additional safety steps are conducted to help ensure that ALPHANATE has the highest quality possible. These steps include specific and nonspecific virus inactivation and removal measures.

Please see Important Safety Information on page 4 and see accompanying full Prescribing Information for ALPHANATE.

Step 9: Laser-etched identifier and holographic safety seal
Each vial of ALPHANATE has a laser-etched lot number and a holographic seal on each package. These additional safety steps ensure that the ALPHANATE you are getting is an authentic Grifols product.

Step 10: Pharmacovigilance
Grifols works closely with healthcare providers to make sure immediate action is taken if a side effect related to ALPHANATE occurs. We provide continuous evaluation of the clinical effects of ALPHANATE to help ensure safety. This ongoing monitoring of ALPHANATE is called pharmacovigilance.

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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 accompanying full Prescribing Information for ALPHANATE or visit www.alphanate.com

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