ANTIHEMOPHILIC FACTOR (HUMAN)
HT PROFILATE™
Dry Method

DESCRIPTION
Antihemophilic Factor (Human), HT Profilate is a stable freeze dried concentrate of Factor VIII (AHF, AHG) prepared from pooled plasma by cryoprecipitation of the active factor and its subsequent purification and concentration by chemical means. Antihemophilic Factor potency (Factor VIII) is expressed on the bottle label in International Units (I.U.). HT Profilate is a sterile preparation intended for intravenous administration. Each vial is a single dose container.

This product is prepared from units of human plasma which have been tested and found nonreactive for hepatitis B surface antigen (HBsAg) by an FDA required test. However, methods presently available are not sensitive enough to detect all units of potentially infectious plasma, and the risk of transmitting hepatitis is still present.

The process used in the manufacture of HT Profilate includes a dry heat-treatment step designed to reduce the risk of transmitting HTLV-III virus which has been suggested as the cause of Acquired Immunodeficiency Syndrome (AIDS). However, no method has been shown to be totally effective in completely eliminating the risk of AIDS infectivity from Antihemophilic Factor (Human).

CLINICAL PHARMACOLOGY
Antihemophilic Factor (Factor VIII) is a constituent of normal plasma required for clotting. The administration of Antihemophilic Factor (Human), HT Profilate temporarily increases the plasma level of this clotting factor, thus minimizing the hazards of hemorrhage[1,7] Following administration, the mean half-life of Factor VIII is approximately 12 hours.

A newly recognized retrovirus has been implicated as a possible causative agent of Acquired Immunodeficiency Syndrome (AIDS). This virus has been given several names, including human T-lymphotropic virus type III (HTLV-III), lymphadenopathy-associated virus (LAV), and AIDS-associated retrovirus (ARV) and has been commonly referred to in the literature as HTLV-III/LAV. The effectiveness of the heat-treatment step used in the manufacture of HT Profilate was assessed by an in-vitro inactivation study using live virus added to Antihemophilic Factor (Human), HT Profilate. When 4.47 logs of the virus was intentionally added to the product, the assay for HTLV-III/LAV virus after processing showed a zero result. However, since the limit of detection of the viral assay is 2.0 logs, it can only be said with certainty that at least 2.47 logs of HTLV-III/LAV virus is inactivated by the lyophilization and heat treatment process. It was also shown in the same study that the time to inactivate 1.0 Log of this virus under these conditions when added to HT Profilate was 39 minutes.

INDICATIONS AND USAGE
Antihemophilic Factor (Human), HT Profilate is indicated solely for the prevention and control of bleeding in patients with moderate or severe Factor VIII deficiency due to hemophilia A or acquired Factor VIII deficiency.[3] Antihemophilic Factor (Human), HT Profilate is not indicated in the management of bleeding in patients with von Willnbrand's disease.

CONTRAINDICATIONS
None known.

WARNINGS
Viral hepatitis may be transmitted by this product. Patients with mild deficiencies, who consequently have not received multiple transfusions of blood or blood products, are at greatest risk[4,7] In this situation, the benefits of Antihemophilic Factor (Human), HT Profilate administration must be carefully weighed against the risk of viral hepatitis.

The causal factors of Acquired Immunodeficiency Syndrome (AIDS) have not been fully defined, however, HTLV-III/LAV virus has been implicated as a possible causative agent of the disease. It is not presently known if other transmissible agents are involved. Alpha uses screening procedures to eliminate high risk plasma donors and a heat-treatment step in the manufacturing process to reduce the risk of transmitting AIDS. However, despite the careful selection of donors, it may be possible that the AIDS causative agents may still be present in and transmitted through this product.

PRECAUTIONS
GENERAL
Antihemophilic Factor (Human), HT Profilate should not be administered at a rate exceeding 10 ml/minute. Rapid administration may result in vasomotor reactions.

Some patients develop inhibitors to Factor VIII. These patients may show no response to Antihemophilic Factor (Human), HT Profilate or the response may be much less than would otherwise be expected and larger doses are often required[8,11,12] The management of patients with inhibitors requires careful monitoring, especially if surgical procedures are indicated. Patients with high inhibitor levels may not respond at all.

Nursing personnel and others who administer this material should exercise appropriate caution in handling because of the risk of exposure to viral hepatitis.

Discard any unused contents. Discard administration equipment after single use. Do not sterilize components.

PREGNANCY CATEGORY C
Animal reproduction studies have not been conducted with HT Profilate. It is also not known whether HT Profilate can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. HT Profilate should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS
Adverse reactions may include urticaria, fever, chills, nausea, vomiting, headache, somnolence or lethargy. Some patients may develop reactions of a mild nature following the administration of Antihemophilic Factor (Human), HT Profilate.[10] Adverse reactions may be on an allergic basis. If a reaction is noted and the patient requires additional Antihemophilic Factor (Human), product from a different lot should be administered.

Massive doses have rarely resulted in acute hemolytic anemia, increased bleeding tendency or hyperfibrinogenemia.[5]

Antihemophilic Factor (Human), HT Profilate contains blood group specific isoagglutinins and when large and/or frequent doses are required in patients of blood group A, B, or AB, the patient should be monitored for signs of intravascular hemolysis and falling hematocrit. Should this condition occur, thus leading to progressive hemolytic anemia, the administration of serologically compatible type O red blood cells should be considered.

DOSAGE AND ADMINISTRATION
Antihemophilic Factor (Human), HT Profilate must be administered intravenously within three hours following reconstitution with the diluent supplied. Antihemophilic Factor (Human), HT Profilate may be administered either by injection (plastic syringe only) or infusion.

After reconstitution, parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Antihemophilic Factor (AHF) activity is expressed in International Units (I.U.) on the product label. One unit approximates the activity in one ml of plasma. The following formula provides a guide of dosage.

$$\text{Number of AHF units required} = \frac{\text{Body weight in lbs}}{\text{x20x}} \times \text{Desired increase in Factor VIII percentage}$$

Example: $\frac{110\text{lbs}}{20} \times 0.30 = 660$ AHF units

or

$$\text{Number of AHF units required} = \frac{\text{Body weight in kg}}{\text{x44x}} \times \text{Desired increase in Factor VIII percentage}$$

Example: $\frac{50\text{kg}}{44} \times 0.30 = 660$ AHF units

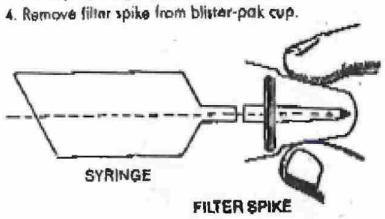
Mild to moderate hemorrhages may usually be treated with a single administration sufficient to raise the plasma AHF level to 20 or 30 percent. In the event of more serious hemorrhage the patient's plasma AHF level should be raised to 30 to 50 percent. Infusions are generally required at twice daily intervals over several days.[9]

Surgery in patients with Factor VIII deficiency requires that the AHF level be raised to 50 to 80 percent with the level maintained at or above 30 percent for approximately two weeks post-operatively. For dental extractions, the AHF level should be raised to 50 percent immediately prior to the procedure; additional Antihemophilic Factor (Human) may be administered if bleeding recurs.[9]

In patients with severe Factor VIII deficiency who experience frequent hemorrhages, Antihemophilic Factor (Human), HT Profilate may be administered prophylactically on a daily or every other day schedule to raise the AHF level to approximately 15 percent.[6]

RECONSTRUCTION
USE ASEPTIC TECHNIQUE
1. Warm diluent and concentrate bottles to at least room temperature but not above 37°C.
2. Remove plastic flip-off cap from the diluent bottle.
3. Swab the exposed rubber surface with alcohol. Do not leave excess cleaning agent in indentation on stopper.
4. Remove covering from one end of the double ended needle. Insert this exposed end of the needle through the depression in the center of the stopper in the bottle of diluent.
5. Remove plastic flip-off cap from the concentrate bottle. Tap bottle gently to dislodge concentrate from sides of bottle.
6. Swab the exposed rubber surface with alcohol. Do not leave excess cleaning agent in indentation on stopper.
7. Remove plastic cap from the upper end of the double ended needle now seated in the stopper of the diluent bottle. Hold concentrate bottle in one hand, invert the bottle of diluent in the other hand and push the exposed end of the needle through the depression in the center of the stopper, making certain that the diluent is always above the bottle of concentrate. There should be enough vacuum in the bottle to draw in all the diluent.
8. Disconnect the two bottles by removing the needle from the concentrate bottle stopper. Shake vigorously for ten seconds, then agitate or rotate concentrate bottle until all concentrate is dissolved. Reconstitution requires approximately five to ten minutes. When the reconstitution procedure is strictly followed a few small particles may occasionally remain. The filter spike will retain particles and the labeled potency will not be reduced.

ADMINISTRATION
By Syringe:
USE ASEPTIC TECHNIQUE
1. Peel cover from filter spike package.
2. Remove protective cover from a sterile disposable plastic syringe.
3. Securely install the syringe into the exposed inlet of the filter spike using slight twisting motion.
4. Remove filter spike from blister-pak cup.



FILTER SPIKE

5. Insert spike into reconstituted concentrate bottle perpendicular to stopper. If spike is not held perpendicular it may push stopper into bottle rendering contents unusable.
6. Remove and discard the filter spike from the syringe and attach syringe to an infusion set, expel air from syringe, perform venipuncture and administer slowly.
7. If the patient is to receive more than one bottle of concentrate, the infusion set will allow this to be performed with a single venipuncture.
8. Discard all administration equipment after use.

ADMINISTRATION
By Infusion Set:
USE ASEPTIC TECHNIQUE
1. Close clamp on administration set.
2. With bottle upright, insert piercing pin straight through stopper center. Do not twist or angle.
3. Immediately invert bottle to automatically establish proper fluid level in drip chamber (half full).
4. Attach infusion set, open clamp and allow solution to expel air from tubing needle, then close clamp.
5. Perform venipuncture and adjust flow.
6. Discard all administration equipment after use.

HOW SUPPLIED
Antihemophilic Factor (Human), HT Profilate is supplied in single dose bottles with suitable volume of diluent. AHF activity, expressed in International Units (I.U.), is stated on the label of each concentrate bottle.

STORAGE
Antihemophilic Factor (Human), HT Profilate should be stored at temperatures between 2°-8°C. Do not freeze.

CAUTION
Federal (U.S.A.) law prohibits dispensing without a prescription.

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08-R026 Printed in U.S.A. 10/85

TOTAL P.03

Antihemophilic Factor (Human)
HT Profilate™
Dry Method

Factor VIII indicated for the treatment of hemophilia A.

Manufacturing process designed to ensure patient safety.

- Contains no added preservative or stabilizer (such as heparin or albumin).
- Manufacturing process has been shown to inactivate 1 log of HTLV-111/LAV in approximately thirty minutes.
- Viral inactivation studies show dry process reduces the risk of transmitting human T-lymphotropic virus Type III/ lymphadenopathy-associated virus (HTLV-III/LAV), the virus implicated as a possible causative agent of Acquired Immunodeficiency Syndrome (AIDS).

In-vitro studies confirm the manufacturing method's effectiveness in viral inactivation.[1]

Virus	No. Logs Inactivated in Alpha Product
HTLV-III/LAV	2.47
Sindbis	7.40
Vesicular Stomatitis Virus (VSV)	6.98

1. It must, however, be pointed out that no manufacturing method has been shown to completely eliminate the risk of viral infectivity.

Reliable Performance

- Average in-vivo recovery 97.5%
- High specific activity.
- Wide range of assays: 250-1200 International Units per vial.
- Low isoagglutinin and blood group specific product also available.
- Average half-life 12.6 hours.
- High purity, low fibrinogen.
- Should be stored under refrigeration (2-8° C).