Reconstitution: Use Aseptic Technique
1. Bring Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, (dry concentrate), and Sterile Water for Injection, USP, (30 mL) (diluent) to room temperature.
2. Remove caps from concentrate and diluent bottles to expose central portions of rubber stoppers.
3. Cleanse stoppers with germicidal solution.
4. Remove protective covering from one end of the double-ended needle and insert exposed needle through diluent stopper.
5. Remove protective covering from the other end of the double-ended needle. Invert diluent bottle over upright concentrate bottle. Vacuum in the concentrate bottle will draw in diluent. Do not shake vigorously.
6. Disconnect the two bottles by removing needle from the diluent bottle, then remove needle from concentrate bottle stopper. Swift or rotate the concentrate bottle until all material is dissolved. Do not shake vigorously. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

Note: Do not reaggregate after reconstitution.

Rate of Administration
It is recommended that Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, be infused initially at a rate of 2 mL/min. If infusion at this rate is well tolerated the administration rate may be gradually increased to 10 mL/min.

Administration: Use Aseptic Technique
When reconstitution of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is complete, its infusion should commence as soon as practical; however, it must be completed within 1 hour.

The reconstituted solution should be at room temperature during infusion.

A. Intravenous Drip Infusion
When a Hyland administration set is used, follow directions for use printed on the administration set container. When an administration set from another source is used, follow directions accompanying that set where necessary. The use of a Hyland administration set is recommended as it contains a suitable filter.

B. Intravenous Syringe Injection
1. Attach filter needle to syringe and draw back plunger to admit air into the syringe.
2. Insert needle into the reconstituted Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated.
3. Inject air into bottle and then withdraw the reconstituted material into the syringe.
4. Remove and discard the filter needle from the syringe; attach a suitable needle and inject intravenously as instructed under Rate of Administration.

If it is patient to receive more than one bottle of concentrate, the contents of two bottles may be drawn into the same syringe by drawing up each bottle with a separate unused filter needle. This practice lessens the loss of concentrate. Please note: filter needles are intended to filter the contents of a single bottle of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, only.

How Supplied
Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is packaged with 30 mL Sterile Water for Injection, USP, a double-ended needle; a filter needle; and a package insert.

Storage
Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, should be stored under ordinary refrigeration (2 - 8°C, 36 - 46°F). Avoid freezing to prevent damage to the diluent bottle.

References

Bibliography
Hawthorn G, Revin DR: Efficacy of viral clearance methods used in the manufacture of concentrates. Focus on AUTOPLEX® T. Haemophilia S (Supple 3): 19, 1999
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Distributed by:

Boca Raton, FL 33487 USA
NDC 59730-6059-7

Manufactured by:

Baxter Healthcare Corporation
Glenade, CA 92010 USA
U.S. License No. 140

Printed in USA
7279 Revised November 2000

Anti-Inhibitor Coagulant Complex
Heat Treated
Autoplex® T

Caution: This product is to be used only in patients with inhibitors to Factor VIII.

Warning: This is a potent drug with potential hazards. For maximal safety and efficacy, carefully read and follow directions below.

Description
Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is a sterile product prepared from pooled human plasma with subsequent alcohol fractionation to remove Factor IV. It contains, in concentrated form, variable amounts of activated and precursor vitamin K-dependent clotting factors. Factors of the kinin generating system are also present. The product is standardized to correct the clotting time of a patient deficient plasma or Factor VIII deficient plasma which contains inhibitors to Factor VIII.

When reconstituted, this product contains a maximum of 2 units per mL of heparin and a residual amount of polyethylene glycol (2 mg per mL, maximum). It also contains 0.02 M sodium citrate and the sodium content is 177 ± 15 milliequivalents per liter. Laboratory testing of several lots of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, has shown the presence of Factor VIII coagulant antigen (VIII:Ag). Although anamnestic response to this antigen following administration of the product was not observed during the clinical trials, the possibility of such a response does exist.

Each lot of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is assayed and labeled for units of Hyland Factor VIII corrective activity. Factor VIII corrective activity may not be exclusively related to the efficacious component(s). (See Clinical Pharmacology). During the manufacturing process, this product was heated for 6 days at 60°C. This heating step is designed to reduce the risk of transmission of hepatitis and other viral diseases. However, no procedure has been shown to be totally effective in removing hepatitis infectivity from Anti-Inhibitor Coagulant Complex.

Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, must be administered intravenously.

Clinical Pharmacology
The Factor VIII correcting activity of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is thought to be, in part, related to the Factor VIII content of the product. It is additionally hypothesized that the elevated Factor VIII:VIIa content of this product is also a contributing factor in the in vivo establishment of normal hemostasis by way of Factor X activation in conjunction with tissue factor, phospholipid and ionic calcium.

* This product and/or its manufacture covered by U.S. Patent Nos. 4,286,056, 4,287,180, 4,337,321, 4,380,581, 4,449,236, and 4,495,278. The “T” indicates that the product is heat treated.
Anti-Inhibitor Coagulant Complex, depending on the patient's clinical history and the severity of the bleeding episode.

Patients whose present Factor VIII inhibitor levels are between 2 and 10 Bethesda Units, as well as patients whose inhibitor levels are historically known to remain at 2 Bethesda Units or less following treatment with Antihemophilic Factor (Human), should be treated with Anti-Inhibitor Coagulant Complex.

Patients whose present Factor VIII inhibitor levels are greater than 10 Bethesda Units, or or AICC

Inhibitor INHIBITOR LEVEL PRESENT MAXIMUM

>10 B.U. AHFb or AICC AICCc

5.0 4.0 3.4 6.1 7.1 2.3 2.5

Concomitant Use Concomitant Use

epsilon-aminocaproic acid (EACA) or tranexamic acid,5 the concomitant use of prothrombin complex products together with antifibrinolytic agents such as epsilon-aminocaproic acid (EACA) or tranexamic acid is not recommended.

Contraindications

The following table is presented as a guide in determining the preferred control bleeding episodes in such patients.

Concomitantly with the administration of this product to the U.S. and foreign territories.

Other coagulation tests. Symptoms of DIC include changes in blood pressure and pulse rate, respiratory distress, chest pain and cough. Laboratory indications of DIC include prolonged thrombin time, prothrombin time and partial thromboplastin time. Levels of factors V, VII, X, and fibrinogen concentration, decreased platelet count and/or the presence of fibrinogen/fibrin degradation products. Special care should be taken in the use of this concentrate in newborns, where a high morbidity and mortality may be associated with hepatitis, and in individuals with pre-existing liver disease.

Laboratory Tests

In some cases, laboratory tests such as the activated partial thromboplastin time test may not correlate with clinical response. In that appearance of hemostatic improvement may occur without a reduction of partial thromboplastin time. However, the prothrombin time would be expected to be shortened.

In children, fibrinogen levels should be determined prior to the initial infusion and periodically during the course of the treatment.

Drug Interactions

Since only limited data are available on the administration of highly activated prothrombin complex products together with antifibrinolytic agents such as epsilon-aminocaproic acid (EACA) or tranexamic acid, the concomitant use of Autoplex® T, Anti-Inhibitor Coagulant Complex, with such agents is not recommended.

Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated. It is also not known whether Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, should be given to a pregnant woman only if clearly needed.

Adverse Reactions

As with all plasma protein preparations, reactions manifested by fever, chills or indications of protein sensitivity may be observed with the administration of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated. Signs and/or symptoms of prekallikrein deficiency such as changes in blood pressure or pulse rate may also be observed. It is advisable that appropriate medications be available for the treatment of acute allergic reactions or acute vascular reactions, should they occur.

A rate of infusion that is too rapid may cause headache, flushing, and changes in pulse rate and blood pressure. In such instances, stopping the infusion allows the symptoms to disappear promptly. With anaphylactic reactions, the reactive individuals, infusion may be resumed at a slower rate.

Dosage and Administration

Each bottle of Autoplex® T, Anti-Inhibitor Coagulant Complex, Heat Treated, is labeled with the initial of the Hyland Factor VIII Correctional Units that it contains. One Hyland Factor VIII Correctional Unit is that quantity of activated prothrombin complex which, upon addition to an equal volume of Factor VIII deficient or inhibitor plasma, will correct the clotting time (elicited acid-activated partial thromboplastin time) to 35 seconds (normal).

The recommended dosage range is 25 to 100 Hyland Factor VIII Correctional Units per kg of body weight, depending upon the severity of hemorrhage. If no hemostatic improvement is observed approximately 6 hours following the initial infusion, the infusion should be repeated. Subsequent dosage and administration intervals should be adjusted according to the patient's clinical response. (See Laboratory Tests.)