**Antithemophilic Factor (Human)**

**Factor VIII:C P熟悉**

**Monoclonal Antibody Purified**

**Monoclate-P®**

**ZLB Behring**

**Is only DESCRIPTION**

**Antithemophilic Factor (Human), Monoclate-P®, Factor VIII:C P熟悉, Monoclonal Antibody Purified,** is a ster-ile, lyophilized concentrate of Factor VIII:C with reduced amounts of WNV-Ag and purified of extraneous plasma proteins. The concentrate has been shown to contain no detectable antibodies to HIV-1, HIV-2, and hepatitis C virus, and no detectable antibody to viral Hepatitis B. The concentrate is for use in the treatment of classical hemophilia (Hemophilia A). It is the only concentrate available currently that contains a specific albumin (Human) as a stabilizer, resulting in a concentrate with a specific activity of 4 and 10 units of total protein. In the absence of this added albumin (Human) stabilizer, specific activity has been determined to exceed 3000 units/mg of protein. Monoclate-P® has been prepared from pooled human plasma and is intended for use in therapy of classical hemophilia (Hemophilia A).

The plasma used in the manufacture of this product has been tested and found negative for HIV-1, HBV, and HCV; and is the investigational test procedure referred to as Nucleic Testing (NAT) using Polymerase Chain Reaction (PCR) Technology. Investigational testing is being performed to determine the effectiveness of NAT to detect low levels of viral material. The significance of a negative result is unclear since the effectiveness of the test has not been established.

This concentrate has been pasteurized by heating at 60°C for 10 hours in aqueous solution for duration of its manufacture in order to further reduce the risk of viral transmission. However, no procedure has been shown to be totally effective in removing viral infectivity from concentrate factors (see CLINICAL PHARMACOL- OGY and WARNINGS). Monoclate-P®, being a highly purified preparation of Factor VIII:C. When stored as directed, it will maintain its labeled potency at least through the control expiration dates shown on the container and vial. Upon reconstitution of the 250, 500 and 1000 U.U. concentrates, a clear, colorless solution is obtained, containing 50 to 150 times as much Factor VIII:C as does an equal volume of plasma.

Upon reconstitution of the 1500 U.U. concentrate, a clear, colorless solution is obtained, containing 120 to 180 times as much Factor VIII:C as does an equal volume of plasma.

Each vial contains the labeled amount of antithrombic factor (AHF) activity as expressed in terms of International Units (IU) of antihemophilic activity. One unit of antihemophilic activity is equivalent to the quantity of AHF activity required to correct one ml of normal human plasma. When reconstituted as recommended, the resulting solution contains approximately 450 to 450 millimoles of sodium ions per liter and has 2 to 3 times the tonicity of saline. It contains approximately 2.5 millimoles of calcium ions per liter, contributed as calcium chloride, approximate 3.8% mannitol), and 1.2% sodium phosphate, monobasic acid and sodium hydroxide. Monoclate-P® also contains trace amounts (50 ng per 100 U.U. of AHF) of the murine monoclonal antibody (see CLINICAL PHARMACOLOGY). Monoclate-P® is to be administered only intravenously.

**CLINICAL PHARMACOLOGY**

Factor VIII:C is the coagulant portion of the Factor VIII complex circulating in plasma. It is a nonoxonol assiated glycoprotein whose expression is encoded by a gene on chromosome 12. Factor VIII_C acts as a cofactor for Factor IX to activate factor X in the intrinsic pathway of blood coagulation. Hemophilia A, a hereditary condition characterized by absence or decreased levels of Factor VIII:C in plasma, results in inability to bleeding into muscles or internal organs as a result of a trauma. Monoclate-P® provides an increase in plasma levels of AHF thereby enabling temporary correction of Hemophilia A bleeding.

Clinical evaluation of Monoclate-P® concentrate for its half-life characteristics in hemophilic patients showed it to be comparable to other commercially available Antithemophilic Factor (Human) concentrates. The mean half-life obtained from six patients was 17.5 hours with a mean recovery of 1.9 from each unit/kg.

The purification process used in the manufacture of this concentrate has demonstrated in vivo inactivation of human immunodeficiency virus (HIV) and several model viruses. In two separate studies, HIV was reduced by 2.0-2.1 log10 to an undetectable level by 10.5 log10, respectively. In addition to HIV studies were also performed using hepatitis B virus, hepatitis C virus, and West Nile virus. A single log10 reduction of HIV was observed. These data indicate that the purification and preparative steps of the manufacturing process are capable of providing a non- specific, viral reduction of approximately 5 to 6 logs, independent of the purification process. Monoclate-P® concentrates contain trace amounts of mouse protein (50ng per 100 U.U. of AHF). In a study using an earlier lot that did not undergo purification (Monoclate), a number of patients seropositive for Anti-HIV-1 were monitored to determine whether they would develop antibody or experience adverse reactions as a result of repeated exposure. These patients were treated on multiple occasions. Pre-study serum measurements at 2 patients for anti-human m-1gG showed that, prior to treatment, 6 of the 10 had either detectable antibody to mouse proteins or cross-reactive proteins. These patients continued to demonstrate similar antibody profiles even after as many as 34 doses. Of the remaining 21 patients, 6 were shown to have low anti-body levels on one or more occasions. In no case was there evidence of low antibody level associated with an anamnestic response or any with clinical adverse reaction. Patients were observed for time periods ranging from 2 to 30 months.

The safety of Monoclate-P® has been evaluated in two open-label studies using patients (aged 1 day to 20 years) with moderate to severe hemophilia A previously exposed to blood or blood products. Thirty patients received Monoclate-P® vials of 1500 U.U. and were monitored to determine whether they would develop antibody or experience adverse reactions as a result of repeated exposure. These patients were treated on multiple occasions. Pre-study serum measurements at 2 patients for anti-human m-1gG showed that, prior to treatment, 6 of the 10 had either detectable antibody to mouse proteins or cross-reactive proteins. These patients continued to demonstrate similar antibody profiles even after as many as 34 doses. Of the remaining 21 patients, 6 were shown to have low antibody levels on one or more occasions. In no case was there evidence of low antibody level associated with an anamnestic response or any with clinical adverse reaction. Patients were observed for time periods ranging from 2 to 30 months. indus-
5 micron filter needle and contained in a separate blister pack, and an all plastic 5 micron vented filter spike which is supplied with the four-item administration components blister pack, either of which may be used to withdraw the reconstituted product for administration. The withdrawal directions specific for each of these alternate devices must be followed exactly for whichever device is chosen for use as described below. Product loss or inability to withdraw product will result if the improper instructions are followed.

A. Administration using the stainless steel filter needle for withdrawal
   (This item is individually packaged in a separate, labeled blister pack.)

   **Intravenous Injection**
   Plastic disposable syringes are recommended with Antihemophilic Factor (Human), Monoclate-P® solution. The ground glass surfaces of all-glass syringes tend to stick with solutions of this type.
   1. Using aseptic technique, attach the vented filter spike to a sterile disposable syringe.
   2. Draw air into the syringe equal to or greater than the contents of the vial.
   3. Insert the filter needle into the stopper of the Monoclate-P® vial, invert the vial, position the filter needle above the level of the liquid and inject all of the air into the vial.
   4. Pull the filter needle back down below the level of the liquid until the tip is at the inside edge of the stopper.
   5. Withdraw the reconstituted solution into the syringe being careful to always keep the tip of the needle below the level of the liquid.
   **CAUTION:** Failure to inject air into the vial, or allowing air to pass through the filter needle while filling the syringe with reconstituted solution, may cause the needle to clog.
   6. Discard the filter needle. Perform venipuncture using the enclosed winged needle with microbore tubing. Attach the syringe to the luer end of the tubing.
   **CAUTION:** Use of other winged needles without microbore tubing, although compatible with the concentrate, will result in a larger retention of solution within the winged infusion set.
   7. Administer solution intravenously at a rate (approximately 2 mL/minute) comfortable to the patient.

B. Administration using the all plastic vented filter spike for withdrawal
   (This spike is supplied in the four-item Administration Components pack.)

   **Intravenous Injection**
   Plastic disposable syringes are recommended with Monoclate-P® solution. The ground glass surfaces of all-glass syringes tend to stick with solutions of this type.
   1. Using aseptic technique, attach the vented filter spike to a sterile disposable syringe.
   **CAUTION:** DO NOT INJECT AIR INTO THE MONOCLOATE-P® VIAL. The self-venting feature of the vented filter spike precludes the need to inject air in order to facilitate withdrawal of the reconstituted solution. The injection of air could cause partial product loss through the vent filter.
   **CAUTION:** The use of other non-vented filter needles or spikes without the proper procedure may result in an air lock and prevent the complete transfer of the concentrate.
   2. Insert the vented filter spike into the stopper of the Monoclate-P® vial, invert the vial, and position the filter spike so that the orifice is at the inside edge of the stopper.
   3. Withdraw the reconstituted solution into the syringe.
   4. Discard the filter spike. Perform venipuncture using the enclosed winged needle with microbore tubing. Attach the syringe to the luer end of the tubing.
   **CAUTION:** Use of other winged needles without microbore tubing, although compatible with the concentrate, will result in a larger retention of solution within the winged infusion set.
   5. Administer solution intravenously at a rate (approximately 2 mL/minute) comfortable to the patient.

**STORAGE**
When stored at refrigerator temperature, 2-8°C (36-46°F), Monoclate-P® is stable for the period indicated by the expiration date on its label. Within this period, Monoclate-P® may be stored at room temperature not to exceed 25°C (77°F), for up to 6 months. Avoid freezing which may damage container for the diluent.

**HOW SUPPLIED**
Monoclate-P® is supplied in a single dose vial with diluent, double-ended needle for reconstitution, vented filter spike for withdrawal, filter needle for withdrawal, winged infusion set and alcohol swabs. I.U. activity is stated on the label of each vial.

The following strengths are available:
- NDC 0053-7655-01 in 10 mL vials containing approximately 250 I.U.
- NDC 0053-7655-02 in 10 mL vials containing approximately 500 I.U.
- NDC 0053-7656-04 in 20 mL vials containing approximately 1000 I.U.
- NDC 0053-7656-05 in 20 mL vials containing approximately 1500 I.U.

**REFERENCES**
5. B. Spire, D. Dormont, E. Barre-Sinoussi, L. Montagnier, and J.C. Chermann, Inactivation of Lymphadenopathy Associated Virus by Heat, Gamma Rays, and Ultraviolet Light, Lancet, Jan. 26, 1985, p. 188.

**BIBLIOGRAPHY**

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