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PRODUCT LICENCE HOLDER

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DATA SHEET

Koāte®

Antihaemophilic Factor (Human)

PRESENTATION

A stable, purified, dried concentrate of Human Antihaemophilic Factor (Factor VIII; AHF; AHG). It is in the form of a white lyophilised powder for reconstitution with Water for Injection U.S.P.
Each vial contains a nominal 250 or 500 units of Antihaemophilic Factor. The assayed amount of activity is stated on the label. (One unit is approximately equivalent to the antihaemophilic activity of 1 ml of average normal plasma.)

USES

Koāte provides a means of temporarily replacing the missing or deficient coagulation Factor VIII and restoring levels to normal or near normal values without overloading the circulatory system. It is indicated in the management and control of classical haemophilia (Haemophilia A); von Willebrand's disease and in patients with inhibitors to Factor VIII.

DOSAGE AND ADMINISTRATION

Dosage required for controlling haemostasis should be calculated to the need of the patient. The dose is dependent upon the weight of the patient, the severity of the deficiency, the severity of the haemorrhage, the presence of inhibitors and on the Factor VIII level desired.
For each unit of Antihaemophilic Factor administered per Kg of body weight a 2% rise in Factor VIII activity has been observed. The following formulae can be used as a guide to dosage.

$$\text{Expected increase in Factor VIII (\% of normal)} = \frac{2{\cdot}0 \times \text{units administered}}{\text{body weight in Kg.}}$$

Units required = body weight in Kg × desired increase in Factor VIII (% normal) × 0·5.
The following generalised dosage schedule is suggested for various clinical situations:

1. *Joint haemorrhages*

If aspiration is not carried out, 10 units/Kg body weight should be administered at eight to twelve hour intervals for a period of one or more days depending on severity and patient response.
The latter may be measured by relief of pain, swelling and restriction of joint movement. Early joint bleeds (associated with mild pain and minimal swelling), if treated promptly, may respond to a single dose of 10 units/Kg.
If aspiration is carried out, 10 units/Kg should be administered just prior to aspiration with a similar dose given six to eight hours later and repeated

as necessary. Fully developed haemarthrosis also may be treated with a single dose of 25 units/Kg aimed at achieving a Factor VIII level of 50%.

2. *Muscle haemorrhages*

A. Minor haemorrhages in the muscles of the extremities or trunk (non-vital areas). A dose of 10 units/Kg should be administered every eight to twelve hours until pain and swelling are relieved.

B. Massive haemorrhages in non-vital areas

A dose of 10 units/Kg should be infused at eight to twelve hour intervals for two days or more, depending on relief of pain, improvement in haematocrit if this has fallen, and relief of other symptoms depending on the area of haemorrhage.

C. Haemorrhages near vital organs (neck, throat, subperitoneal, etc.)

A 20 unit/Kg dose should be administered initially, followed by 10 units/Kg every eight hours for 48 hours. Then half the dose should be administered at those time intervals for another 48 hours or more.

3. *Overt Bleeding*

The initial dose should be 20 units/Kg followed by 10 units/Kg every eight hours for the first 24 hours then every twelve hours for three to four days as necessary.

4. *Massive wounds*

Koāte should be infused until the bleeding stops. Then a maintenance dose of 20 units/Kg should be administered every eight hours. Levels of Factor VIII should be obtained and enough Koāte infused to maintain a minimum Factor VIII level of 40% in the patient.

5. *Surgery*

Factor VIII levels of at least 40% are required for surgery. For surgery in the central nervous system even higher levels are recommended.

Thirty to forty units/Kg body weight should be administered prior to surgery followed by 20 units/Kg every eight hours after surgery. This should be done with laboratory control, and the dosage should be increased if the Factor VIII level falls below 30% just prior to the next infusion. The postinfusion level should be approximately 60% and it has been suggested that the Factor VIII level be raised to 30 to 40% of normal for at least ten days postoperatively.

6. *Dental Extractions*

The dosage required depends on the severity of the haemophilia and the number of teeth extracted. Usually 10 to 20 units/Kg should be given as an initial dose followed by 10 units/Kg every eight hours for up to ten days. Factor VIII levels should not be allowed to fall below 10% of normal values.

7. *Prophylaxis*

In the prophylactic treatment of Haemophilia A a dosage of 250 units of Koāte per day in the morning for patients weighing less than 50 kg, 500 units of Koāte per day for heavier patients. If bleeding episodes still occur too frequently, the daily dose should be progressively increased until a satisfactory degree of protection is obtained.

The clinical effect of Factor VIIIon the patient is the most important element in evaluating the effectiveness of treatment.

Koāte is rapidly soluble in Water for Injection U.S.P. The concentrate should be administered intravenously, immediately after reconstitution at room temperature (not above 37°C). It may be given as a single intravenous injection or in the case of larger volumes by infusion. Any reconstituted concentrate not used at the same time should be discarded.

CONTRA-INDICATIONS AND WARNINGS

There are no known contra-indications to Koāte.

Hepatitis – Koāte is prepared from units of human plasma, each donation of which has been found non-reactive for hepatitis B antigen (Hb_sAg) when tested by radioimmunoassay. In addition, each batch has also been tested against hepatitis by radioimmunoassay. However, despite these tests and the precautions taken in selecting donors, the risk of transmitting serum hepatitis cannot be excluded.

Allergic Reactions – As with the administration of all human plasma derivatives these are possible. If they occur, they are usually of a mild nature.

Factor VIII inhibitors – if the Factor VIII levels, following administration of Koāte, fail to reach the expected levels or if bleeding is not controlled after adequate calculated dosage the presence of circulating inhibitors should be suspected. By appropriate laboratory procedures the presence of inhibitors can be substantiated and quantified thus allowing calculation of the amount of Factor VIII for neutralisation.

Whilst circulating inhibitors to Factor VIII can be detected, their appearance cannot be predicted, nor does it relate to the amount or frequency of Factor VIII administered. The management of patients with inhibitors requires careful monitoring and in such cases the dose of Koāte required to control haemostasis may be much higher than usual.

PHARMACEUTICAL PRECAUTIONS

Koāte should be stored at temperatures between 2°C and 6°C and protected from light. Under such conditions it has a shelf life of one and a half years.

LEGAL CATEGORY

T.S.A.

PACKAGE QUANTITY

250 and 500 unit vials of Antihaemophilic Factor (Human) together with either 10ml or 20ml vials of Water for Injection U.S.P. and a sterile filter needle.

FURTHER INFORMATION

The total amount of protein in each vial is stated on the label enabling precise calculation of the protein to be administered. The rapid and simple reconstitution of Koāte in a small volume of Water for Injection U.S.P. (10ml or 20ml) make it especially suitable for syringe administration facilitating home treatment and high dosage therapy, e.g. surgery.