treatment of overdosage:

Extremely high doses of FEIBA IMMUNO may cause laboratory and/or clinical signs and symptoms of disseminated intra-vascular coagulation. In these cases treatment with FEIBA IMMUNO should be discontinued promptly.

pharmaceutical precautions: FEIBA IMMUNO must be stored between +2° and +8°C when it will have a shelf life of 2 years.

legal category: P.O.M.

package quantities: FEIBA IMMUNO is supplied in packs containing 500 and 1000 FEIBA units together with a separate vial containing 20 ml Water for Injections B.P. as solvent. All packs contain sufficient equipment for reconstitution and administration.

further information:

1) **Effect on laboratory tests.**

Inherent in its mechanism of action FEIBA IMMUNO causes a shortening of the following clotting times: activated partial thromboplastin time (APTT), whole blood clotting time (WBCT), activated clotting time (ACT), thromboelastogram (TEG).

Coagulation tests measuring the extrinsic coagulation system such as the prothrombin time, which is usually normal in haemophiliacs, remained unchanged after treatment with FEIBA IMMUNO. Overdosage of the product may result in laboratory signs of DIC; as are the presence of fibrinopeptide A, fibrin/fibrinogen degradation products, a fall in fibrinogen, a prolonged APTT, thrombin time and prothrombin time.

2) FEIBA IMMUNO is only available to Haemophilia Treatment Centres.

product licence numbers, name and address: 0215/0021-22

Product Licence Holder:
Immuno Limited,
Arctic House,
Rye Lane,
Dunton Green,
Sevenoaks, Kent TN14 5HB

Tel. No: Sevenoaks (0732) 458101
Telex No: 95413

date of preparation: January 1986.

FEIBA IMMUNO®
Heat Treated

IMMUNO

DATA SHEET

name of product: FEIBA IMMUNO (Factor VIII Inhibitor Bypassing-Fraction Human) Heat-Treated.

presentation:

FEIBA IMMUNO in its lyophilised form is an amorphous powder. After reconstitution with Water for Injections B.P. it is a clear yellowish solution. It is prepared from the plasma of suitable human donors as described in the British Pharmacopoeia 1980 Vol. II under Albumin, whose donations are shown by RIA to be free from HBsAg. Pooled plasma and the final product are also tested for freedom from HBsAg.

During production FEIBA IMMUNO is heated for 10 hours at 80°C to reduce the risk of transmission of infectious agents.

It is presented in vials each containing 500 or 1000 FEIBA units; 1 FEIBA unit being defined as the FEIB activity which shortens the activated partial thromboplastin time of a high titre Factor VIII Inhibitor Reference Plasma to 50% of the blank value.

A separate vial containing Water for Injections B.P. is provided for reconstitution.

uses: FEIBA IMMUNO is mainly used to control bleeding episodes in haemophilia A patients with Factor VIII Inhibitors and also in patients with acquired Factor VIII Inhibitors.

dosage and administration: FEIBA IMMUNO should only be administered intravenously.

On the basis of available clinical trial results obtained in the treatment of Factor VIII inhibitor patients it is possible that FEIBA's effectiveness may vary between patients, this may be due to varying inhibitor titres and other, as yet unknown, factors. As a result larger doses may be necessary if the inhibitor titres are high, but this is not a general rule.

The determination of the whole blood clotting time (WBCT) according to Lee White and/or the calculation of the r-value in the thromboelastogram (TEG) help to determine the most effective dose and to check the success of therapy.

Care must be taken to distinguish between the following indications.

Spontaneous bleeding episodes.

A dosage of 50 to 100 units per kg bodyweight administered in 8- to 12-hourly intervals is recommended and should be continued until clear signs of therapeutic improvement appear. This means, in the case of exterior bleeding, healing of the bleeding site, or in the case of internal bleeding, a lessening of pain, reduction in swelling or mobilisation of the joint. If there are no signs of therapeutic improvement despite the administration of 100 units of FEIBA per kg given 8-hourly, combined therapy with 40 units per kg of a Factor VIII concentrate (KRYOBULIN or FACTOR VIII CONCENTRATE HUMAN IMMUNO) is recommended. The Factor VIII must be administered after each individual dose of FEIBA IMMUNO.

In home treatment of bleeding complications up to 150 U/kg bodyweight have been administered, the effective dose very likely depending on the extent of bleeding. In some cases a kind of maintenance prophylaxis was successfully undertaken in home treatment with three applications weekly of approximately 30 units of FEIBA IMMUNO per kg bodyweight followed by approximately 60 units of Factor VIII concentrate per kg.

Minor surgery

Basically, the same kind of therapy should be followed as in the case of spontaneous bleeding episodes. It is, however, necessary to check the substitution effect before the operation and, if necessary, increase the dose or give consideration to combined treatment with Factor VIII Concentrate (40 units per kg).

For checking effectiveness, the following tests should be carried out: whole blood clotting time (WBCT) according to Lee White; r-value of the thromboelastogram (TEG).

When combination therapy with Factor VIII concentrate is used the activated partial thromboplastin time (APTT) may be shortened to normal values.

Since disseminated intravascular coagulation (DIC) cannot be totally excluded in the course of this treatment, it is advisable to carry out repeated tests on platelets, fibrinogen and FDP.

use in the elderly:

No specific precautions have to be taken into account when using the drug in the elderly, attention is, however, drawn to the fact that in patients with a tentative or definitive diagnosis of coronary heart disease the use of FEIBA IMMUNO is only indicated in life-threatening bleeding events.

use in pregnancy:

Animal reproduction studies have not been conducted with FEIBA IMMUNO. It is also not known, whether FEIBA IMMUNO can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. FEIBA IMMUNO should only be given to a pregnant woman if clearly needed.

contra-indications, warnings etc:

Contra-indications:
Presence of disseminated intravascular coagulation (DIC).

Precautions and warnings:

1. Before each individual application of FEIBA IMMUNO with Factor VIII inhibitor patients it is advisable to count the patient's platelets, since some investigators have found that FEIBA's effectiveness depends on the presence of a normal number of platelets. If the number of platelets is below 100,000/mm^3 this should be normalised by giving platelet-concentrate before administering FEIBA IMMUNO. In this connection special attention must be drawn to the platelet drop which follows the use of animal AHG, which may render FEIBA IMMUNO ineffective.

2. Caution is also necessary if the APTT or prothrombin time is prolonged after the administration of FEIBA IMMUNO. If prolongation is found, it is essential to carry out the 3 obligatory tests mentioned above. Should the results point to DIC, (platelet drop, fibrinogen decrease, FDP increase), the administration of FEIBA IMMUNO must be interrupted.

3. All forms of allergic reaction ranging from mild short term urticarial rashes to anaphylactic shock are possible following the administration of human plasma derivatives. If such reactions occur, the administration of FEIBA IMMUNO must be immediately discontinued. Allergic reactions should be treated with antihistamines. Shock should be treated in the usual way.

4. Despite the measures taken to reduce the risk, the transmission of viral hepatitis or other viral infections cannot be ruled out.

5. The occurrence of an anamnestic reaction giving a raised inhibitor titre cannot be totally excluded after administration of FEIBA IMMUNO. Experience shows, however, that some patients treated with FEIBA IMMUNO show lowered inhibitor titres whilst in the majority of patients, the titre remains unchanged.

1. Use in the Elderly

Use in the elderly is normally limited to the prevention of sensitisation following incompatible transfusion. Under these circumstances no special precautions or dosage amendments need to be observed in the elderly.

2. Use in Pregnancy

PARTOBULIN is not licensed for use in pregnancy. However, the administration of anti-D immunoglobulin during pregnancy has been described for prevention of antenatal sensitisation. This does not usually produce antibody titres in the maternal circulation that might threaten the fetus. Exceptions are possible, for example if anti-D immunoglobulin is given repeatedly at short intervals. In general the antibody titre in the maternal blood should not exceed 1:2 (Coombs Test).

3. Treatment of Overdosage*

In rhesus negative individuals overdosage need not be expected to lead to more frequent or more severe adverse reactions than the normal dose. It has been observed that even an accidental injection of the preparation into the newborn does not necessarily lead to adverse reaction.

4. Effect on Laboratory Tests

Passively introduced Rh_o(D)-antibodies may be detected in the blood of the mother several weeks and even months after an injection of PARTOBULIN. Therefore, any previous administration of PARTOBULIN must be taken into account when examining maternal blood for its content of Rh_o(D)-antibody and when evaluating these tests.

The presence of additional antibodies (e.g. Rubella) in PARTOBULIN may lead to false positive reactions in tests for such antibodies.

Note: Do you have a suggested text for overdosage or accidental administration in Rh positive individuals?

RN/BSH/VIENNA
28.9.89