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FEIBA IMMUNO™

Characteristics and Composition

FEIBA IMMUNO is a human plasma fraction with Factor VIII inhibitor bypassing activity shortening the activated PTT of plasma containing a Factor VIII inhibitor. The FEIB-activity is measured by determining the shortening of the activated PTT of a standard Factor VIII inhibitor plasma, and is expressed in FEIBA-units*. FEIBA IMMUNO is prepared from the plasma of donors meeting the requirements of the British Pharmacopoeia 1980, Vol. II, p.845 described under items (a) to (d) of Albumin. Donors who are HBs-Ag-positive by radioimmunoassay are permanently excluded from the programme.

Tests on FEIBA IMMUNO also include absence of pyrogens, sterility and innocuity.

Indications

FEIBA's most important indication is the control of bleeding episodes in haemophilia A patients with Factor VIII inhibitors and in patients with acquired Factor VIII inhibitors. FEIBA IMMUNO can also be used in patients with inhibitors to Factor IX and Factor XIa.

Administration

FEIBA IMMUNO must be dissolved immediately before injection using the amount of solvent provided.

Directions for Reconstitution of a Solution for Injection

1. Warm solvent to room temperature.

2. Remove the protective caps (fig. 1) and disinfect the rubber stoppers of both bottles.

3. Transfer of the solvent into the bottle containing the lyophilisate is done with the help of the transer needle. For this purpose first remove the protective cap of the transfer needle and insert it into the rubber stopper of the bottle containing the solvent (fig. 2).
   Then remove the protective tube of the transfer needle. Turn the solvent bottle with the inserted transfer needle upside-down and insert the latter into the rubber stopper of the lyophilisate bottle leaving a free needle length of 1 cm outside the bottle (fig. 3). Caution: do not touch the needle!
   Because of the vacuum in the lyophilisate bottle the solvent will then run in.

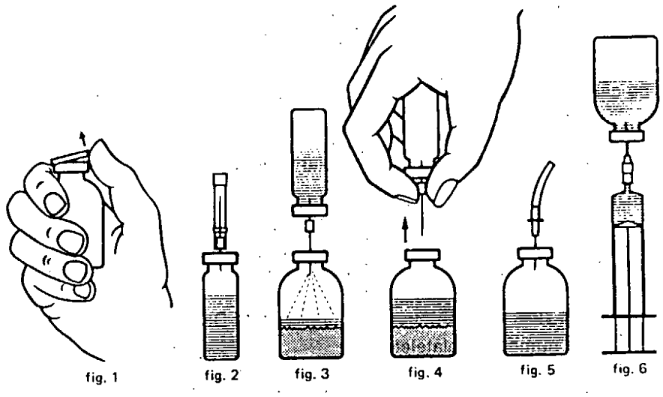
* 1 FEIBA unit is defined as the FEIB-activity shortening the activated PTT of a high titre Factor VIII Inhibitor Reference Plasma (IMMUNO House Standard) to 50 per cent of the blank value.

4. Remove the solvent bottle with the transfer needle from the lyophilisate bottle (fig. 4). Gently agitate the latter in order to accelerate solution.

5. Insert the provided aeration needle and any foam will collapse (fig. 5). Remove the aeration needle.

6. Fit the enclosed filter needle onto the disposable syringe and draw up the solution into the syringe (fig. 6).

7. Separate the syringe from the filter needle and fit the enclosed disposable needle (or winged adapter needle). Slowly inject the solution intravenously at a maximum rate of 2 U/kg/min.



Do not exceed the maximum injection rate of 2 U/kg/min.

The solution must be injected through a filter if a different method of reconstitution is used.

Dosage and Frequency of Application

A. Factor VIII-Inhibitor Patients

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.

The determination of the Whole Blood Clotting Time (WBCT) according to Lee White and/or the calculation of the r-value in the thrombelastogram (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 bodyweight given 8-hourly, a combined therapy with 40 units per kg bodyweight 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.

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 bodyweight.

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 bodyweight).

For checking effectiveness, the following tests should be carried out:

Whole Blood Clotting Time (WBCT) according to Lee White
r-value of the thrombelastogram (TEG).

When a 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**

** Fibrin-Fibrinogen Degradation Products

Caution

Before each individual application of FEIBA IMMUNO with Factor VIII inhibitor patients it is advisable to count the patient's platelets, since some investigators (VERMYLEN, ENGLISH) 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.

B. Factor XIa Inhibitor Patients

In one patient who had an aorto-coronary bypass a single application of approximately 40 units of FEIBA/kg bodyweight resulted in a normalisation of the Cephalin Clotting Time (CCT) which persisted for several days.

Concerning effectiveness and side effects, the same control tests should be carried out as with Factor VIII inhibitor patients.

C. Factor IX Inhibitor Patients

Recently a few cases with Factor IX inhibitor in Haemophilia B were reported where bleeding was controlled with infusion of FEIBA IMMUNO in a dose of 50 - 100 units/kg bodyweight. Concerning effectiveness and side effects, the same control tests should be carried out as with Factor VIII inhibitor patients.

Contraindications

Presence of disseminated intravascular coagulation (DIC).

Side Effects

In the application of extremely high doses, i.e. 200 units of FEIBA per kg bodyweight or more, occasionally signs of DIC have been seen. For this reason patients receiving FEIBA IMMUNO must continually be checked for signs of accelerated coagulation.

In order to determine the possible presence of DIC

the number of platelets
fibrinogen and
fibrin-fibrinogen degradation products (FDP)

should be checked repeatedly.

Caution is necessary if

the Activated Partial Thromboplastin Time (APTT) or
Prothrombin Time

are prolonged after administration of FEIBA IMMUNO™.

If this is the case, it is absolutely necessary to carry out the three obligatory tests mentioned above. If the results point to DIC (platelet drop, fibrinogen decrease, rise in FDP) the application of FEIBA must be interrupted.

With the application of human plasma derivatives any kind of allergic reaction may be observed, ranging from mild, short-term, urticarial rashes to anaphylactic shock. In these cases the application of FEIBA IMMUNO must be discontinued immediately. Allergic reactions should be treated with antihistamines and gluco-corticoids. Shock should be treated in the usual way.

Despite continuous donor tests it is impossible to completely exclude the risk of transmission of viral hepatitis in the use of human coagulation-factor preparations.

Anamnestic reactions showing raised inhibitor titres may not be totally excluded after the application of FEIBA IMMUNO. However, some of the patients treated with FEIBA IMMUNO show lowered inhibitor titres, while the titres of the majority remain unchanged.

Shelf Life and Storage

Two years at a temperature between +2° and +8°C.

Packs

FEIBA IMMUNO

500 FEIBA-units
dried substance + 20 ml of Water for Injections B.P.
1000 FEIBA-units
dried substance + 20 ml of Water for Injections B.P.

All packages contain equipment for reconstitution and injection.

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