Approved Patient Information Leaflet

Amended Patient Information Leaflet
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Amended Patient Information Leaflet
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Feiba Immuno
Factor VIII Inhibitor Bypassing Activity
Vapour Heated

What does Feiba (Factor VIII Inhibitor Bypassing Activity) Contain?

Active ingredient:			
Human Plasma Protein with a Factor Eight Inhibitor Bypassing Activity of	200 - 600mg 500 units	or or	400 - 1200mg 1000 units
Other ingredients:			
Sodium Chloride	160mg	or	160mg
Sodium Citrate	80 mg	or	80mg

Feiba (Factor VIII Inhibitor Bypassing Activity) also contains factors II, IX and X mainly in non-activated form as well as activated factor VII; factor VIII coagulant antigen (F VIII C:Ag) is present in a concentration of up to 0.1 U/l U Feiba. Other factors naturally occurring in the blood may be present in trace amounts.

How is Feiba (Factor VIII Inhibitor Bypassing Activity) Supplied?

Feiba (Factor VIII Inhibitor Bypassing Activity) is supplied as a dried substance together with a bottle of Water for Injections BP to make a solution.

Feiba (Factor VIII Inhibitor Bypassing Activity) is available in sizes of 500 and 1000 units, to be dissolved in 20ml of Water for Injections BP. Each pack also includes a kit of needles and syringes to help to make and inject the solution.

How does Feiba (Factor VIII Inhibitor Bypassing Activity) work?

Feiba (Factor VIII Inhibitor Bypassing Activity) is a coagulation (blood clotting) factor concentrate. It contains an anti-inhibitor coagulant complex with standardised FEIB-activity (Factor Eight Inhibitor Bypassing Activity) for use in patients who have developed inhibitors (antibodies) to Factor VIII. Factor VIII is a component of the blood, essential for normal blood clotting processes and if you have inhibitors your blood will not clot properly.

Licence Holder

Immuno Ltd., Caxton Way, Thetford, Norfolk, IP24 3SE, United Kingdom.

Product Licence No 0215/0021-22

Manufacturer

Österreichisches Institut für Haemoderivate Ges.m.b.H.
Production Division of
IMMUNO AG Vienna Austria

Who should receive Feiba (Factor VIII Inhibitor Bypassing Activity)?

Feiba (Factor VIII Inhibitor Bypassing Activity) is used for the treatment of bleeding episodes in Haemophilia A patients with inhibitors to their usual Factor VIII Concentrate.

In addition, Feiba (Factor VIII Inhibitor Bypassing Activity) may be used for treating non-haemophiliacs who have developed inhibitors to factor VIII.

When should Feiba (Factor VIII Inhibitor Bypassing Activity) not be given?

Feiba (Factor VIII Inhibitor Bypassing Activity) should not be given if you are suffering from:

1. a) Disseminated Intravascular Coagulation (DIC) - an excessive activation of the blood clotting system

   b) liver damage

NOTE DIC usually occurs in connection with severe disease, injury, or a major operation and will be diagnosed by your doctor using laboratory tests.

2. Heart attack, severe clot formations or clots in the lung (embolism).

Feiba (Factor VIII Inhibitor Bypassing Activity) should not be given in the above cases with the exception of life threatening bleeding episodes where no other form of treatment is likely to work.

Precautions when taking Feiba (Factor VIII Inhibitor Bypassing Activity)

Please see side effects.

Significance of Platelet Count

If there is an inadequate or reduced response to treatment with Feiba, your doctor may carry out a platelet count, since a sufficient number of functionally intact platelets is considered necessary for Feiba (Factor VIII Inhibitor Bypassing Activity) to work.

Do other medicines affect the action of Feiba (Factor VIII Inhibitor Bypassing Activity)?

It is not recommended to use fibrinolytic drugs such as epsilon-aminocaproic acid (which break down blood clots) in combination with Feiba (Factor VIII Inhibitor Bypassing Activity).

If treatment with drugs such as epsilon-aminocaproic acid and Feiba (Factor VIII Inhibitor Bypassing Activity) is to be carried out, the time interval between the giving of either product should be at least 6 hours.

Is Feiba (Factor VIII Inhibitor Bypassing Activity) safe to use when you are pregnant or breast feeding?

The safety of Feiba (Factor VIII Inhibitor Bypassing Activity) Immuno for use in human pregnancy or breastfeeding has not been established. Because of the increased risk of clotting during pregnancy Feiba Immuno should only be used if no alternative treatment is available.

Special Warnings

As Feiba (Factor VIII Inhibitor Bypassing Activity) Immuno is prepared from human plasma (the liquid part of blood) it is not possible to exclude the theoretical risk that an unknown infectious agent such as a virus might be transmitted to you as a result of the injection. All the blood donors used for the production of Feiba Immuno are very strictly selected and tested to ensure that they are healthy. In addition their blood is tested to ensure we cannot find any evidence of the viruses that cause Hepatitis B, Hepatitis C or HIV (the virus that causes AIDS) in their blood. The blood is collected in the USA and some European countries but not in the UK. (Further information is provided at the end of this leaflet.)

How much Feiba (Factor VIII Inhibitor Bypassing Activity) do you need?

This product is for intravenous administration. As a general guide a dose of 50 to 100 units of Feiba (Factor VIII Inhibitor Bypassing Activity) per kg body weight (b.w.) is recommended, however, not exceeding a daily dose of 200 U/kg b.w.

The dose does not depend on your inhibitor titre. Since the response to treatment may differ from patient to patient the dosage recommendations are only guidelines.

1. Spontaneous Bleeding

Joint, muscle and soft tissue bleeding

For minor to moderate bleeds a dose of 50-75 U/kg b.w. is recommended at 12-hour intervals. Treatment should be continued until clear signs of improvement appear, such as relief of pain, reduction of swelling or movement of the joint.

For major muscle and soft tissue bleeds, such as retroperitoneal bleeding, doses of 100 U/kg b.w. at 12-hour intervals are recommended.

Mucous Membrane Bleeding

A dose of 50 U/kg b.w. is recommended to be given every 6 hours with careful monitoring of the patient (visible bleeding site, repeated measurements of haematocrit). Again, if the bleeding does not stop, the dose may be increased to 100 U/kg b.w. taking care not to exceed the maximum daily dose of 200 U/kg b.w.

Other Severe Bleeding

Severe bleeding, such as central nervous system bleeds, have been effectively treated with doses of 100 U/kg b.w. at 12 hour intervals. In individual cases Feiba (Factor VIII Inhibitor Bypassing Activity) may be given at intervals of 6 hours until clear clinical improvement is achieved. (Do not exceed the maximum daily dose!).

2. Surgery

Taking care not to exceed the maximum daily dose, 50-100 U/kg b.w. should be given at intervals of up to 6 hours.

The dosage given above applies equally to children and the elderly.

What happens if you receive too much Feiba (Factor VIII Inhibitor Bypassing Activity)?

Occasionally laboratory tests and symptoms indicating DIC have been observed following the use of high doses of Feiba (Factor VIII Inhibitor Bypassing Activity).

In such cases your treatment should be stopped quickly and your doctor will take further actions as appropriate.

How to dissolve and inject Feiba (Factor VIII Inhibitor Bypassing Activity)

Feiba (Factor VIII Inhibitor Bypassing Activity) is to be made up immediately before use only. The solution should then be used promptly.
Any unused solution must be discarded appropriately.

Reconstitution of dried substance:

1. Warm the unopened vial containing solvent (Water for Injection B.P.) to room temperature (max. +37°C).

2. Remove protective caps from the concentrate vial and solvent vial (Fig. A) and disinfect the rubber stoppers of both.

3. Remove protective covering from one end of the enclosed "transfer needle" by twisting and pulling (Fig. B). Insert the exposed needle through the rubber stopper of the solvent vial (Fig.C).

4. Remove protective covering from the other end of the transfer needle taking care not to touch the exposed end.

5. Invert the solvent vial over the concentrate vial, and insert the free end of the transfer needle through the rubber stopper of the concentrate vial (Fig. D). The solvent will be drawn into the concentrate vial by vacuum.

6. Disconnect the two vials by removing the needle from the concentrate vial (Fig. E). Gently agitate or rotate the concentrate vial to accelerate dissolution.

7. Upon complete reconstitution of the concentrate, insert the enclosed "aeration needle" (Fig. F) and any foam will collapse. Remove aeration needle.

Injection/Infusion:

1. Remove protective covering from the enclosed "filter needle" by twisting and pulling and fit the needle onto a sterile disposable syringe. Draw the solution into the syringe (Fig. G).

2. Disconnect the filter needle from the syringe and slowly inject the solution into a vein with the enclosed "winged infusion set" (or the enclosed disposable needle).

If administered by infusion, a disposable infusion set with adequate filter is to be used.

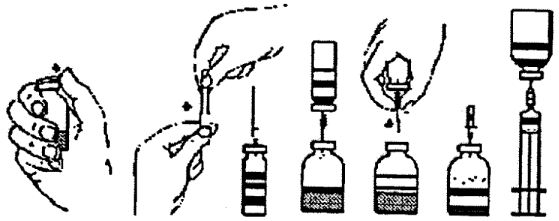

fig. A fig. B fig. C fig. D fig. E fig. F fig. G

Monitoring of Therapy

Single doses of 100 units Feiba per kg body weight and daily doses of 200 units Feiba (Factor VIII Inhibitor Bypassing Activity) per kg body weight should not be exceeded. Patients given single doses of 100 units Feiba per kg body weight should be monitored for the development of DIC e.g. pains in the chest or arm, or symptoms of heart attack. High doses of Feiba should be given only as long as is absolutely necessary to stop bleeding.

Should changes in blood pressure, pulse rate, breathing problems, chest pain or cough occur, the infusion should be stopped immediately and appropriate medical tests carried out.

Side Effects

If minor allergic reactions such as rashes, fever or nausea occur during the administration of Feiba (Factor VIII Inhibitor Bypassing Activity), the infusion should be stopped and your doctor will prescribe antihistamines.

In the rare case of severe hypersensitivity reactions your doctor will follow the current guidelines of shock treatment.

If you have experienced allergic reactions to plasma derivatives in the past then your doctor may prescribe antihistamines as a preventative measure.

In the course of treatment with preparations such as Feiba blood clots may occur, particularly after high doses and/or in patients with other risk factors for developing clots.

After administration of high doses (single doses of more than 100 units Feiba (Factor VIII Inhibitor Bypassing Activity) per kg b.w. and daily doses of more than 200 units per kg body weight) excessive activation of the blood clotting system (Disseminated Intravascular Coagulation) was observed in a few cases.

In very rare cases myocardial infarction (heart attack) occurred after high doses and/or prolonged administration in the presence of risk factors predisposing to cardiovascular disease.

Please tell your doctor or pharmacist of any suspected undesirable effect that is not mentioned in this leaflet.

Shelf Life and Storage

Feiba (Factor VIII Inhibitor Bypassing Activity) is stable for two years when stored between +2°C and +8°C.

Within the shelf life the product may be stored at room temperature (max. 25°C) for a period of up to 6 months. The dates between which the product is not stored at refrigerator temperature should be noted on the package.

Feiba (Factor VIII Inhibitor Bypassing Activity) must not be used beyond the expiry date printed on the label.

Store out of the reach of children.

Date of revision November 1998

Further Information

Only plasma from healthy donors which has been tested with negative results for antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and -2) and hepatitis C virus (HCV) as well as hepatitis B virus surface antigen (HBsAg) is used for the manufacture of Feiba Immuno. The liver enzyme value (ALT) must not exceed the accepted threshold value (twice the upper limit of normal). Further measures include Non-Returning Donor-Applicant Exclusion, Inventory Hold for each plasma donation (minimum three months) and the Lookback Program.

Each plasma pool is tested for HIV and HCV antibodies as well as for HBsAg. In addition a test for virus genome sequences of HIV-1, HBV and HCV with the polymerase chain reaction (IQ-PCR[1]) is carried out. The polymerase chain reaction (PCR) is a highly sensitive method with which, in contrast to antibody testing, direct identification of virus genomes is possible. Only plasma pools in which no genomes of these viruses are detectable are released for further processing.

In prospective international safety studies with coagulation factor concentrates virus inactivated by vapour heat treatment, none of the patients, who were all previously untreated, showed any evidence of a transmission of hepatitis viruses or HIV. Pharmaco-epidemiological surveillance of Feiba Immuno has shown no product-related transmission of the above mentioned agents.

[1] IQ-PCR (IMMUNO Quality-Assured Polymerase Chain Reaction) is a quality-assured assay system for the detection of genomic sequences of HIV-1, HBV, and HCV. With the highest degree of probability this assay system allows for the detection of 500 genome equivalents of each of the above viruses per ml, its sensitivity being below this limit. Also test results ranging below 500 genome equivalents per ml are considered positive leading to exclusion of the respective donation from further processing.

Feiba Immuno
Factor VIII Inhibitor Bypassing Activity Fraction Human
Vapour Heated

What does Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Contain?

Active ingredient:			
Human Plasma Protein with a Factor Eight Inhibitor Bypassing Activity Fraction Human of	200 - 600mg 500 units	or or	400 - 1200mg 1000 units
Other ingredients:			
Sodium Chloride	160mg	or	160mg
Sodium Citrate	80 mg	or	80mg

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) also contains factors II, IX and X mainly in non-activated form as well as activated factor VII; factor VIII coagulant antigen (F VIII C:Ag) is present in a concentration of up to 0.1 U/l U Feiba. Other factors naturally occurring in the blood may be present in trace amounts.

How is Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Supplied?

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is supplied as a dried substance together with a bottle of Water for Injections BP to make a solution.

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is available in sizes of 500 and 1000 units, to be dissolved in 20ml of Water for Injections BP. Each pack also includes a ~~kit of needles and syringes to help to make and inject the solution.~~ transfer needle, an aeration needle and a filter needle.

How does Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) work?

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is a coagulation (blood clotting) factor concentrate. It contains an anti-inhibitor coagulant complex with standardised FEIB-activity (Factor Eight Inhibitor Bypassing Activity Fraction Human) for use in patients who have developed inhibitors (antibodies) to Factor VIII. Factor VIII is a component of the blood, essential for normal blood clotting processes and if you have inhibitors your blood will not clot properly.

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Manufacturer

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In addition, Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) may be used for treating non-haemophiliacs who have developed inhibitors to factor VIII.

When should Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) not be given?

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) should not be given if you are suffering from:

1. a) Disseminated Intravascular Coagulation (DIC) - an excessive activation of the blood clotting system

   b) liver damage

NOTE DIC usually occurs in connection with severe disease, injury, or a major operation and will be diagnosed by your doctor using laboratory tests.

2. Heart attack, severe clot formations or clots in the lung (embolism).

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) should not be given in the above cases with the exception of life threatening bleeding episodes where no other form of treatment is likely to work.

Precautions when taking Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)

Please see side effects.

Significance of Platelet Count

If there is an inadequate or reduced response to treatment with Feiba, your doctor may carry out a platelet count, since a sufficient number of functionally intact platelets is considered necessary for Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) to work.

Do other medicines affect the action of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)?

It is not recommended to use fibrinolytic drugs such as epsilon-aminocaproic acid (which break down blood clots) in combination with Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human).

If treatment with drugs such as epsilon-aminocaproic acid and Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is to be carried out, the time interval between the giving of either product should be at least 6 hours.

Is Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) safe to use when you are pregnant or breast feeding?

The safety of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Immuno for use in human pregnancy or breastfeeding has not been established. Because of the increased risk of clotting during pregnancy Feiba Immuno should only be used if no alternative treatment is available.

Special Warnings

As Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Immuno is prepared from human plasma (the liquid part of blood) it is not possible to exclude the theoretical risk that an unknown infectious agent such as a virus might be transmitted to you as a result of the injection. All the blood donors used for the production of Feiba Immuno are very strictly selected and tested to ensure that they are healthy. In addition their blood is tested to ensure we cannot find any evidence of the viruses that cause Hepatitis B, Hepatitis C or HIV (the virus that causes AIDS) in their blood. The blood is collected in the USA and some European countries but not in the UK. (Further information is provided at the end of this leaflet.)

How much Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) do you need?

This product is for intravenous administration. As a general guide a dose of 50 to 100 units of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) per kg body weight (b.w.) is recommended, however, not exceeding a daily dose of 200 U/kg b.w.

The dose does not depend on your inhibitor titre. Since the response to treatment may differ from patient to patient the dosage recommendations are only guidelines.

1. Spontaneous Bleeding

Joint, muscle and soft tissue bleeding

For minor to moderate bleeds a dose of 50-75 U/kg b.w. is recommended at 12-hour intervals. Treatment should be continued until clear signs of improvement appear, such as relief of pain, reduction of swelling or movement of the joint.

For major muscle and soft tissue bleeds, such as retroperitoneal bleeding, doses of 100 U/kg b.w. at 12-hour intervals are recommended.

Mucous Membrane Bleeding

A dose of 50 U/kg b.w. is recommended to be given every 6 hours with careful monitoring of the patient (visible bleeding site, repeated measurements of haematocrit). Again, if the bleeding does not stop, the dose may be increased to 100 U/kg b.w. taking care not to exceed the maximum daily dose of 200 U/kg b.w.

Other Severe Bleeding

Severe bleeding, such as central nervous system bleeds, have been effectively treated with doses of 100 U/kg b.w. at 12 hour intervals. In individual cases Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) may be given at intervals of 6 hours

until clear clinical improvement is achieved. (Do not exceed the maximum daily dose!).

2. Surgery

Taking care not to exceed the maximum daily dose, 50-100 U/kg b.w. should be given at intervals of up to 6 hours.

The dosage given above applies equally to children and the elderly.

What happens if you receive too much Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)?

Occasionally laboratory tests and symptoms indicating DIC have been observed following the use of high doses of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human).

In such cases your treatment should be stopped quickly and your doctor will take further actions as appropriate.

How to dissolve and inject Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is to be made up immediately before use only.
The solution should then be used promptly.
Any unused solution must be discarded appropriately.

Reconstitution of dried substance:

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2. Remove protective caps from the concentrate vial and solvent vial (Fig. A) and disinfect the rubber stoppers of both.

3. Remove protective covering from one end of the enclosed "transfer needle" by twisting and pulling (Fig. B). Insert the exposed needle through the rubber stopper of the solvent vial (Fig.C).

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7. Upon complete reconstitution of the concentrate, insert the enclosed "aeration needle" (Fig. F) and any foam will collapse. Remove aeration needle.

Injection/Infusion:

1. Remove protective covering from the enclosed "filter needle" by twisting and pulling and fit the needle onto a sterile disposable syringe. Draw the solution into the syringe (Fig. G).

2. Disconnect the filter needle from the syringe and slowly inject the solution into a vein with ~~the enclosed "winged infusion set" (or the enclosed disposable needle).~~ a winged infusion set or disposable needle.

If administered by infusion, a disposable infusion set with adequate filter is to be used.

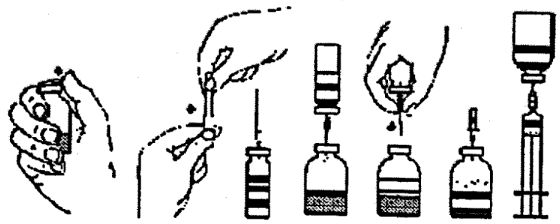

fig. A fig. B fig. C fig. D fig. E fig. F fig. G

Monitoring of Therapy

Single doses of 100 units Feiba per kg body weight and daily doses of 200 units Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) per kg body weight should not be exceeded. Patients given single doses of 100 units Feiba per kg body weight should be monitored for the development of DIC e.g. pains in the chest or arm, or symptoms of heart attack. High doses of Feiba should be given only as long as is absolutely necessary to stop bleeding.

Should changes in blood pressure, pulse rate, breathing problems, chest pain or cough occur, the infusion should be stopped immediately and appropriate medical tests carried out.

Side Effects

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In the rare case of severe hypersensitivity reactions your doctor will follow the current guidelines of shock treatment.

If you have experienced allergic reactions to plasma derivatives in the past then your doctor may prescribe antihistamines as a preventative measure.

In the course of treatment with preparations such as Feiba blood clots may occur, particularly after high doses and/or in patients with other risk factors for developing clots.

After administration of high doses (single doses of more than 100 units Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) per kg b.w. and daily doses of more than 200 units per kg body weight) excessive activation of the blood clotting system (Disseminated Intravascular Coagulation) was observed in a few cases.

In very rare cases myocardial infarction (heart attack) occurred after high doses and/or prolonged administration in the presence of risk factors predisposing to cardiovascular disease.

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Shelf Life and Storage

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is stable for two years when stored between +2°C and +8°C.

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Date of revision November 1998

Further Information

Only plasma from healthy donors which has been tested with negative results for antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and -2) and hepatitis C virus (HCV) as well as hepatitis B virus surface antigen (HBsAg) is used for the manufacture of Feiba Immuno. The liver enzyme value (ALT) must not exceed the accepted threshold value (twice the upper limit of normal). Further measures include Non-Returning Donor-Applicant Exclusion, Inventory Hold for each plasma donation (minimum three months) and the Lookback Program.

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Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) should not be given in the above cases with the exception of life threatening bleeding episodes where no other form of treatment is likely to work.

Precautions when taking Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)

Please see side effects.

Significance of Platelet Count

If there is an inadequate or reduced response to treatment with Feiba, your doctor may carry out a platelet count, since a sufficient number of functionally intact platelets is considered necessary for Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) to work.

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Is Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) safe to use when you are pregnant or breast feeding?

The safety of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Immuno for use in human pregnancy or breastfeeding has not been established. Because of the increased risk of clotting during pregnancy Feiba Immuno should only be used if no alternative treatment is available.

Special Warnings

As Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) Immuno is prepared from human plasma (the liquid part of blood) it is not possible to exclude the theoretical risk that an unknown infectious agent such as a virus might be transmitted to you as a result of the injection. All the blood donors used for the production of Feiba Immuno are very strictly selected and tested to ensure that they are healthy. In addition their blood is tested to ensure we cannot find any evidence of the viruses that cause Hepatitis B, Hepatitis C or HIV (the virus that causes AIDS) in their blood. The blood is collected in the USA and some European countries but not in the UK. (Further information is provided at the end of this leaflet.)

How much Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) do you need?

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For major muscle and soft tissue bleeds, such as retroperitoneal bleeding, doses of 100 U/kg b.w. at 12-hour intervals are recommended.

Mucous Membrane Bleeding

A dose of 50 U/kg b.w. is recommended to be given every 6 hours with careful monitoring of the patient (visible bleeding site, repeated measurements of haematocrit). Again, if the bleeding does not stop, the dose may be increased to 100 U/kg b.w. taking care not to exceed the maximum daily dose of 200 U/kg b.w.

Other Severe Bleeding

Severe bleeding, such as central nervous system bleeds, have been effectively treated with doses of 100 U/kg b.w. at 12 hour intervals. In individual cases Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) may be given at intervals of 6 hours

until clear clinical improvement is achieved. (Do not exceed the maximum daily dose!).

2. Surgery

Taking care not to exceed the maximum daily dose, 50-100 U/kg b.w. should be given at intervals of up to 6 hours.

The dosage given above applies equally to children and the elderly.

What happens if you receive too much Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)?

Occasionally laboratory tests and symptoms indicating DIC have been observed following the use of high doses of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human).

In such cases your treatment should be stopped quickly and your doctor will take further actions as appropriate.

How to dissolve and inject Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human)

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is to be made up immediately before use only.
The solution should then be used promptly.
Any unused solution must be discarded appropriately.

Reconstitution of dried substance:

1. Warm the unopened vial containing solvent (Water for Injection B.P.) to room temperature (max. +37°C).

2. Remove protective caps from the concentrate vial and solvent vial (Fig. A) and disinfect the rubber stoppers of both.

3. Remove protective covering from one end of the enclosed "transfer needle" by twisting and pulling (Fig. B). Insert the exposed needle through the rubber stopper of the solvent vial (Fig.C).

4. Remove protective covering from the other end of the transfer needle taking care not to touch the exposed end.

5. Invert the solvent vial over the concentrate vial, and insert the free end of the transfer needle through the rubber stopper of the concentrate vial (Fig. D). The solvent will be drawn into the concentrate vial by vacuum.

6. Disconnect the two vials by removing the needle from the concentrate vial (Fig. E). Gently agitate or rotate the concentrate vial to accelerate dissolution.

7. Upon complete reconstitution of the concentrate, insert the enclosed "aeration needle" (Fig. F) and any foam will collapse. Remove aeration needle.

Injection/Infusion:

1. Remove protective covering from the enclosed "filter needle" by twisting and pulling and fit the needle onto a sterile disposable syringe. Draw the solution into the syringe (Fig. G).

2. Disconnect the filter needle from the syringe and slowly inject the solution into a vein with a winged infusion set or disposable needle.

If administered by infusion, a disposable infusion set with adequate filter is to be used.

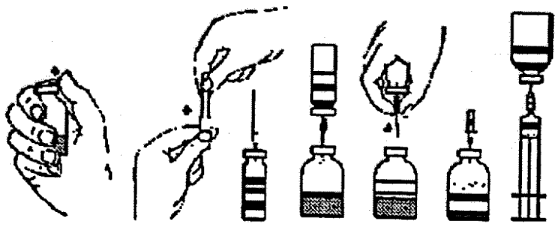

fig. A fig. B fig. C fig. D fig. E fig. F fig. G

Monitoring of Therapy

Single doses of 100 units Feiba per kg body weight and daily doses of 200 units Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) per kg body weight should not be exceeded. Patients given single doses of 100 units Feiba per kg body weight should be monitored for the development of DIC e.g. pains in the chest or arm, or symptoms of heart attack. High doses of Feiba should be given only as long as is absolutely necessary to stop bleeding.

Should changes in blood pressure, pulse rate, breathing problems, chest pain or cough occur, the infusion should be stopped immediately and appropriate medical tests carried out.

Side Effects

If minor allergic reactions such as rashes, fever or nausea occur during the administration of Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human), the infusion should be stopped and your doctor will prescribe antihistamines.

In the rare case of severe hypersensitivity reactions your doctor will follow the current guidelines of shock treatment.

If you have experienced allergic reactions to plasma derivatives in the past then your doctor may prescribe antihistamines as a preventative measure.

In the course of treatment with preparations such as Feiba blood clots may occur, particularly after high doses and/or in patients with other risk factors for developing clots.

After administration of high doses (single doses of more than 100 units Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) per kg b.w. and daily doses of more than 200 units per kg body weight) excessive activation of the blood clotting system (Disseminated Intravascular Coagulation) was observed in a few cases.

In very rare cases myocardial infarction (heart attack) occurred after high doses and/or prolonged administration in the presence of risk factors predisposing to cardiovascular disease.

Please tell your doctor or pharmacist of any suspected undesirable effect that is not mentioned in this leaflet.

Shelf Life and Storage

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) is stable for two years when stored between +2°C and +8°C.

Within the shelf life the product may be stored at room temperature (max. 25°C) for a period of up to 6 months. The dates between which the product is not stored at refrigerator temperature should be noted on the package.

Feiba (Factor VIII Inhibitor Bypassing Activity Fraction Human) must not be used beyond the expiry date printed on the label.

Store out of the reach of children.

Date of revision November 1998

Further Information

Only plasma from healthy donors which has been tested with negative results for antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and -2) and hepatitis C virus (HCV) as well as hepatitis B virus surface antigen (HBsAg) is used for the manufacture of Feiba Immuno. The liver enzyme value (ALT) must not exceed the accepted threshold value (twice the upper limit of normal). Further measures include Non-Returning Donor-Applicant Exclusion, Inventory Hold for each plasma donation (minimum three months) and the Lookback Program.

Each plasma pool is tested for HIV and HCV antibodies as well as for HBsAg. In addition a test for virus genome sequences of HIV-1, HBV and HCV with the polymerase chain reaction (IQ-PCR[1]) is carried out. The polymerase chain reaction (PCR) is a highly sensitive method with which, in contrast to antibody testing, direct identification of virus genomes is possible. Only plasma pools in which no genomes of these viruses are detectable are released for further processing.

In prospective international safety studies with coagulation factor concentrates virus inactivated by vapour heat treatment, none of the patients, who were all previously untreated, showed any evidence of a transmission of hepatitis viruses or HIV. Pharmaco-epidemiological surveillance of Feiba Immuno has shown no product-related transmission of the above mentioned agents.

[1] IQ-PCR (IMMUNO Quality-Assured Polymerase Chain Reaction Fraction Human) is a quality-assured assay system for the detection of genomic sequences of HIV-1, HBV, and HCV. With the highest degree of probability this assay system allows for the detection of 500 genome equivalents of each of the above viruses per ml, its sensitivity being below this limit. Also test results ranging below 500 genome equivalents per ml are considered positive leading to exclusion of the respective donation from further processing.