

## **PACKAGE LEAFLET: INFORMATION FOR THE USER**

### **FEIBA 50 U/ml**

#### **Powder and solvent for solution for infusion**

**Active substance:** Factor VIII Inhibitor Bypassing Activity

**Read all of this leaflet carefully before you start using this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

#### **In this leaflet:**

1. What FEIBA 50 U/ml is and what it is used for.
2. What you need to know before you use FEIBA 50 U/ml.
3. How to use FEIBA 50 U/ml.
4. Possible side effects.
5. How to store FEIBA 50 U/ml.
6. Content of the pack and other information.

### **1. WHAT FEIBA 50 U/ML IS AND WHAT IT IS USED FOR**

FEIBA is a preparation made from human plasma which allows hemostasis, even when individual coagulation factors are reduced or absent.

FEIBA is used for the treatment of bleedings in inhibitor hemophilia A patients.

FEIBA is used for the treatment of bleedings in inhibitor haemophilia B patients, if no other specific treatment is available.

FEIBA is also used for prophylaxis of bleeding in inhibitor hemophilia A patients who have experienced a significant bleed or are at high risk of significant bleeding.

Furthermore, FEIBA may be used for the treatment of bleedings in non-hemophilic patients who have acquired inhibitors to factor VIII.

## **2. WHAT YOU NEED TO KNOW BEFORE YOU USE FEIBA 50 U/ML.**

Please inform your doctor if you have a known allergy.

Please inform your doctor if you are on a low-sodium diet.

### **Do not use FEIBA**

In the following situations FEIBA should only be used if - for example due to a very high inhibitor titre - no response to treatment with the appropriate coagulation factor concentrate can be expected.

- if you are allergic (hypersensitive) to any of the components of FEIBA.
- if a disseminated intravascular coagulation (DIC) exists. (DIC = consumption coagulopathy, a life-threatening condition in which excessive blood coagulation with pronounced blood clot formation in the blood vessels occurs. This then leads to a consumption of the coagulation factors in the entire body.)
- in case of myocardial infarction, acute thrombosis and/or embolism: FEIBA should only be used in life threatening bleeding episodes.

### **Warnings and precautions**

Talk to your doctor before using FEIBA, because hypersensitivity reactions may occur, as is the case with all intravenously administered plasma products. To be able to recognize an allergic reaction as soon as possible, you should be aware of potential early symptoms of a hypersensitivity reaction such as

- erythema (reddening of the skin)
- skin rash
- occurrence of hives on the skin (nettle rash/urticaria)
- itching over the entire body
- swelling of lips and tongue
- breathing difficulties/dyspnoea
- tightness of the chest
- general indisposition
- dizziness
- drop of blood pressure

Other symptoms of hypersensitivity reactions to plasma-derived products include lethargy and restlessness.

If you notice one or more of these symptoms, stop the infusion immediately and contact your doctor straight away. The above mentioned symptoms may be early indications of an anaphylactic shock. Severe symptoms require prompt emergency treatment.

Your doctor will only re-use FEIBA in patients with suspected hypersensitivity to the product or any of its components after careful weighing of the expected benefit and the risk of re-exposure and/or no reaction with another preventative therapy or alternative therapeutic agents is to be expected.

- if you experience major changes in blood pressure or pulse rate, breathing difficulties, coughing or chest pain, stop the infusion immediately and contact your doctor. Your doctor will initiate the appropriate diagnostic and therapeutic measures.
- in patients with inhibitor hemophilia or acquired inhibitors to coagulation factors. Under treatment with FEIBA, these patients may have an increased bleeding tendency and an increased risk of thrombosis at the same time.

Thrombotic and thromboembolic events, including disseminated intravascular coagulation (DIC), venous thrombosis, pulmonary embolism, myocardial infarction, and stroke, have occurred in the course of treatment with FEIBA. Concomitant use of recombinant Factor VIIa likely increases the risk of developing a thromboembolic event. Some of the thromboembolic events have occurred in case of treatment with high doses of FEIBA.

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and the testing of each donation and pools of plasma for signs of virus/ infections. Manufacturers of these products also include steps in the processing of the blood and plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus and hepatitis C virus, and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly or repeatedly receive human plasma-derived Factor VIII inhibitor products.

After administration of high doses of FEIBA, the transitory rise of passively transferred Hepatitis B surface antibodies may result in misleading interpretation of positive results in serological testing.

It is strongly recommended that every time you receive a dose of FEIBA the name and batch number of the product are recorded in order to maintain a record of the batches used.

### **Other medicines and FEIBA**

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

No adequate and well-controlled studies of the combined or sequential use of FEIBA and recombinant Factor VIIa or antifibrinolytics have been conducted. The possibility of thrombotic events should be considered when systemic antifibrinolytics such as tranexamic acid and aminocaproic acid are used during treatment with FEIBA. Therefore, antifibrinolytics should not be used for approximately 6 to 12 hours after the administration of FEIBA.

In cases of concomitant rFVIIa use a potential drug interaction cannot be excluded according to available in vitro data and clinical observations, potentially resulting in a thromboembolic event. As in all blood coagulation preparations, FEIBA should not be mixed with other medicinal products before administration, as the efficacy and tolerance of the preparation may be impaired. It is advisable to rinse a common venous access with a physiological saline solution before and after the administration of FEIBA.

### **Pregnancy, breast-feeding and fertility**

Your doctor will decide if FEIBA may be used during pregnancy and breast-feeding. Due to the increased risk of thrombosis during pregnancy, FEIBA should be administered only under careful medical monitoring and only if absolutely necessary. Information about parvovirus B19 infection is given in section warnings and precautions.

### **Driving and using machines**

There are no signs that FEIBA may affect the ability to drive or to use machines.

### **Important information about some of the ingredients of FEIBA**

FEIBA 50 U/ml contains approximately 4 mg sodium (calculated) per ml, it is approx. 40 mg sodium for the presentation 500 U FEIBA, approx. 80 mg sodium for the presentation 1000 U FEIBA and approx. 200 mg sodium for the presentation 2500 U FEIBA. This is to be taken into consideration for patients on low sodium diet.

### **3. HOW TO USE FEIBA 50 U/ml.**

Reconstitute the freeze-dried FEIBA powder with the enclosed solvent and administer the solution intravenously.

Always use FEIBA exactly as your doctor has told you. You should check with your doctor or pharmacist, if you are not sure.

Taking into consideration the severity of your blood coagulation disorder, the location and extent of the hemorrhage, and your general condition and response to the preparation, your doctor has determined the dose and dosage intervals required for you personally. Do not change the dosage established by your doctor and do not discontinue the application of the preparation independently.

Please talk to your doctor or pharmacist if you have the impression that the effect of FEIBA is too strong or too weak.

Warm the product to room or body temperature prior to administration if necessary.

FEIBA is to be reconstituted immediately prior to administration. The solution should be used immediately (as the preparation does not contain preservatives).

Swirl gently until all material is dissolved. Ensure that FEIBA is completely dissolved; otherwise, less FEIBA Units will pass through the device filter.

Solutions, which are cloudy or have deposits, are to be disposed of appropriately.

Do not reuse opened containers.

Use only the enclosed Water for Injections and the enclosed device set for reconstitution.

If devices other than those enclosed are used, ensure use of a suitable filter with at least 149 µm pore size.

Do not use the product if its sterile barrier has been breached, its package damaged or if it shows signs of deterioration.

Any unused product or waste material should be disposed of in accordance with local requirements.

**Reconstitution of the powder for preparing a solution for infusion with the BAXJECT II Hi-Flow:**

1. Warm the unopened solvent vial (Water for Injections) to room temperature or max + 37°C if necessary, for example by using a water bath for several minutes.
2. Remove the protective caps from the powder vial and solvent vial and disinfect the rubber stoppers of both vials. Place the vials on an even surface.
3. Open the packaging of the BAXJECT II Hi-Flow by pulling off the protective foil without touching the contents of the package (Fig. a). Do not remove the transfer system from the package at this point.
4. Turn the package around and press the transparent plastic pin through the rubber stopper of the solvent vial (Fig. b). Now remove the packaging from the BAXJECT II Hi-Flow (Fig. c). Do not remove the blue protective cap from the BAXJECT II Hi-Flow at this point.
5. Now turn the system, consisting of the BAXJECT II Hi-Flow and the solvent vial, in such a way that the solvent vial is on top. Press the purple pin of the BAXJECT II Hi-Flow through the FEIBA vial. The solvent is drawn into the FEIBA vial by vacuum (Fig. d).
6. Swirl, but do not shake the entire system gently until the powder is dissolved. Make sure that the FEIBA has been dissolved completely, as active material may otherwise be retained by the filter in the system.

Fig. a



Fig. b



Fig. c



## Infusion

Use aseptic techniques throughout the entire procedure!

- 1) Remove the blue protective cap from the BAXJECT II Hi-Flow. Tightly connect the syringe to the BAXJECT II Hi-Flow. **DO NOT DRAW AIR INTO THE SYRINGE.** (Fig. e). In order to ensure tight connection between syringe and BAXJECT II Hi-Flow, the use of a luer lock syringe is highly recommended (turn syringe in clockwise direction until stop position when mounting).
- 2) Invert the system so that the dissolved product is on top. Draw the dissolved product into the syringe by pulling the plunger back **SLOWLY** and ensure that the tight connection between BAXJECT II Hi-Flow and the syringe is maintained throughout the whole pulling process (Fig. f).
- 3) Disconnect the syringe.
- 4) If foaming of the product in the syringe occurs, wait until the foam is collapsed. Slowly administer the solution intravenously with the enclosed infusion set (or disposable needle).

Fig. d



Fig. e

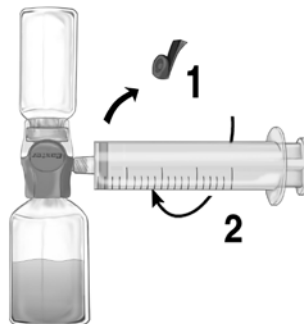
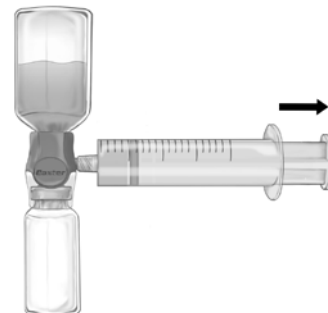


Fig. f



**Do not exceed an infusion rate of 2 U FEIBA/kg body weight per minute.**

### **If you use more FEIBA than you should:**

Please inform your doctor immediately. Overdosage of FEIBA may increase the risk of undesired events, such as thromboembolism (formation of a blood clot with flushing into the blood vessels), consumption coagulopathy (DIC) or myocardial infarction. Some of the reported thromboembolic events occurred with doses above 200 U/kg or with patients with other risk factors for thromboembolic events. If signs or symptoms of thrombotic and thromboembolic events are observed, the infusion should be stopped immediately and appropriate diagnostic and therapeutic measures initiated.

#### 4. POSSIBLE SIDE EFFECTS

Like all medicines, FEIBA can cause side effects although not everybody gets them.

**Common side effects** (may affect up to 1 in 10 people)

Hypersensitivity, Headache, Dizziness, Hypotension, Rash, Hepatitis B surface antibody positive.

**Side effects with unknown frequency** (the frequency cannot be estimated on the basis of the available data)

**Blood and lymphatic system disorders:** Consumption coagulopathy (DIC), Increase of inhibitor titer

**Immune system disorders:** Anaphylactic reactions, Nettle-rash on the entire body (Urticaria)

**Nervous system disorders:** Feeling of numbness in the limbs (hypoesthesia), Abnormal or reduced sensation (Paresthesia), Stroke (Thrombotic stroke, Embolic stroke), Sleepiness (Somnolence), Altered sense of taste (Dysgeusia)

**Cardiac disorders:** Heart attack (Myocardial infarction), Palpitation of the heart (Tachycardia)

**Vascular disorders:** Blood clot formation with flushing into the vessels (thromboembolic events, venous and arterial thrombosis), Increase of blood pressure (Hypertension), Flushing

**Respiratory, Thoracic, and Mediastinal disorders:** Obstruction of the pulmonary artery (Pulmonary embolism), Constriction of the air passages (Bronchospasm), Wheezing, Cough, Breathlessness (Dyspnea)

**Gastrointestinal disorders:** Vomiting, Diarrhea, Abdominal discomfort, Feeling of sickness (Nausea)

**Skin and subcutaneous tissue disorders:** Feeling of numbness in the face, Swelling of face, tongue and lips (Angioedema), Nettle-rash on the entire body (Urticaria), Itching (Pruritus)

**General disorders and complaints at the injection site:** Pain at injection site, general feeling of being unwell, feeling hot, chills, fever, chest pain, chest discomfort

**Investigations:** Drop in blood pressure,

Rapid intravenous infusion can cause stabbing pain and a sensation of numbness in face and limbs, as well as a decrease in blood pressure.

Myocardial infarctions were observed after the administration of doses above the maximum daily dose and/or prolonged application and/or the presence of risk factors for thromboembolism.

#### Reporting of side effects



If you get any side effect, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: [www.hpra.ie](http://www.hpra.ie); e-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie).

By reporting side effects you can help provide more information on the safety of this medicine.

## 5. HOW TO STORE FEIBA 50 U/ml.

Keep out of the sight and reach of children.

Do not store above 25°C. Do not freeze.

Store in the original package in order to protect from light.

Do not use FEIBA after the expiry date which is stated on the label and the carton. The expiry date refers to the last day of that month.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

### What FEIBA 50 U/ml contains

#### Powder

- The active substance per vial is factor VIII inhibitor bypassing activity.
  - 1 ml contains 50 U factor VIII inhibitor bypassing activity.
  - FEIBA 50 U/ml is available in ~~two~~three different presentations:
    - The presentation 500 U FEIBA contains 500 U (Units) factor VIII inhibitor bypassing activity in 200 – 600 mg human plasma protein
    - The presentation 1000 U FEIBA contains 1000 U (Units) factor VIII inhibitor bypassing activity in 400 – 1,200 mg human plasma protein
    - The presentation 2500 U FEIBA contains 2500 U (Units) factor VIII inhibitor bypassing activity in 1,000 – 3,000 mg human plasma protein.
- FEIBA also contains factors II, IX and X, mainly in non-activated form as well as activated factor VII. Factor VIII coagulation antigen (F VIII C:Ag) as well as the factors of the kallikrein-kinin system are present only in trace amounts, if at all.
- The other ingredients are sodium chloride and sodium citrate.

#### Solvent

- Water for Injections

### **What FEIBA 50 U/ml looks like and contents of the pack**

The product is presented as freeze-dried powder or friable solid of white to off-white or pale green color. The pH-value of the ready to use solution is between 6.8 and 7.6.  
Powder and solvent are supplied in vials made of glass and are closed with rubber stoppers.

**Presentation:** 1 x 500 U  
1 x 1000 U  
1 x 2500 U

Not all presentations may be marketed.

#### **Content of package:**

- 1 vial with 500 U / 1000 U / 2500 U FEIBA powder for solution for infusion
- 1 vial with 10 ml / 20 ml / 50 ml Water for Injections
- 1 BAXJECT II Hi-Flow for reconstitution
- 1 disposable syringe
- 1 disposable needle
- 1 butterfly needle with clamp

#### **Marketing authorisation holder and manufacturer:**

##### **Marketing authorisation holder:**

Baxalta Innovations GmbH  
Industriestrasse 67  
A-1221 Vienna  
Austria

##### **Manufacturer:**

Baxter AG  
Industriestrasse 67  
A-1221 Vienna  
Austria

#### **This medicinal product is authorised in the Member states of the EEA under the following names:**

Austria  
FEIBA 50 E./ml Pulver und Lösungsmittel zur Herstellung einer Infusionslösung

Bulgaria

FEIBA 50 U/ml powder and solvent for solution for infusion

Croatia

FEIBA 50 U/ml prašak i otapalo za otopinu za infuziju

Cyprus

FEIBA 50 U/ml κόνις και διαλύτης για διάλυμα προς έγχυση

Denmark

Feiba

Estonia

FEIBA

Finland

Feiba

Greece

FEIBA 50 U/ml κόνις και διαλύτης για διάλυμα προς έγχυση

Ireland

FEIBA 50 U/ml powder and solvent for solution for infusion

Norway

~~FEIBA~~ Feiba

Romania

FEIBA 50 U/ml pulbere și solvent pentru soluție injectabilă

Slovenia

FEIBA 50 e./ml prašek in vehikel za raztopino za infundiranje

Spain

FEIBA 50 U/ml polvo y disolvente para solución para perfusión

Sweden

Feiba 50 enheter/ml pulver och vätska till infusionsvätska, lösning

**This leaflet was last approved in ~~10/2016~~tbc**

**The following information is intended for medical or healthcare professionals only:**

Treatment should be initiated and monitored by a physician experienced in the treatment of coagulation disorders.

***Posology***

Dosage and duration of treatment depend on the severity of the haemostatic disorder, the localization and the extent of the bleeding, as well as the clinical condition of the patient.

Dosage and frequency of administration should always be guided by the clinical efficacy in each individual case.

As a general guideline, a dose of 50 – 100 U FEIBA per kg body weight is recommended; an individual dose of 100 U/kg body weight and a maximum daily dose of 200 U/kg body weight must not be exceeded unless the severity of bleeding warrants and justifies the use of higher doses.

Due to patient-specific factors the response to a bypassing agent can vary, and in a given bleeding situation patients experiencing insufficient response to one agent may respond to another agent. In case of insufficient response to one bypassing agent, use of another agent should be considered.

***Paediatric use (children)***

The experience in children under 6 years of age is limited; the same dose regimen as in adults should be adapted to the child's clinical condition.

**1) Spontaneous bleeding**

**Joint, muscle and soft tissue hemorrhage**

A dose of 50 – 75 U/kg body weight at 12-hour intervals is recommended for minor to moderately severe bleeding. The treatment is to be continued until a clear improvement of the clinical symptoms, e.g. reduction of pain, decrease of swelling or increase of joint mobility, occurs.

For severe muscle and soft tissue bleeding, e.g. retroperitoneal hemorrhages, a dose of 100 U/kg body weight at 12-hour intervals is recommended.

**Mucous membrane hemorrhage**

A dose of 50 U/kg body weight every 6 hours under careful monitoring of the patient (visual control of bleeding, repeated determination of hematocrit) is recommended. If the bleeding does not stop, the dose may be increased to 100 U/kg body weight, however a daily dose of 200 U/kg body weight must not be exceeded.

### **Other severe hemorrhages**

In severe hemorrhage, such as CNS bleeding, a dose of 100 U/kg body weight at 12-hour intervals is recommended. In individual cases, FEIBA may be administered at 6-hour intervals, until clear improvement of the clinical condition is achieved. (The maximum daily dose of 200 U/kg body weight must not be exceeded!)

### **2) Surgery**

In surgical interventions, an initial dose of 100 U/kg body weight may be administered preoperatively, and a further dose of 50 – 100 U/kg body weight may be administered after 6 – 12 hours. As a postoperative maintenance dose, 50 – 100 U/kg body weight may be administered at 6 – 12-hour intervals; dosage, dosage intervals and duration of the peri- and postoperative therapy are guided by the surgical intervention, the patient's general condition and the clinical efficacy in each individual case. (The maximum daily dose of 200 U/kg body weight must not be exceeded!)

### **3) Prophylaxis in hemophilia A patients with inhibitors**

- **Prophylaxis of bleeding in patients with a high inhibitor titer and frequent hemorrhages after failed immune tolerance induction (ITI) or when an ITI is not considered:**

a dose of 70 – 100 U/kg body weight every other day is recommended. If necessary, the dose may be increased to 100 U/kg body weight per day or it may be decreased gradually.

- **Prophylaxis of bleeding in patients with a high inhibitor titer during an immune tolerance induction (ITI):**

FEIBA may be administered concomitantly with factor VIII administration, in a dosage range of 50 – 100 U/kg body weight, twice per day, until the factor VIII inhibitor titer has decreased to < 2 B.U. \*

\* 1 Bethesda Unit is defined as the amount of antibodies which inhibits 50% factor VIII activity in incubated plasma (2 h at 37°C).

### **4) Use of FEIBA in special patient groups**

FEIBA was also used in combination with factor VIII concentrate for a long-term therapy to achieve a complete and permanent elimination of the factor VIII inhibitor.

### ***Monitoring***

In case of inadequate response to treatment with the product, it is recommended that a platelet count be performed because a sufficient number of functionally intact platelets are considered to be necessary for the efficacy of the product.

Due to the complex mechanism of action, no direct monitoring of active ingredients is available. Coagulation tests such as the whole blood coagulation time (WBCT), the thromboelastogram (TEG, r-value) and the aPTT usually show only little reduction and do not necessarily correlate with the clinical efficacy. Therefore these tests have little significance in the monitoring of the therapy with FEIBA.

### ***Method of administration***

FEIBA is to be administered slowly intravenously. An infusion rate of 2 U/kg body weight per minute must not be exceeded.

FEIBA is to be reconstituted immediately prior to administration. The solution should be used immediately (as the preparation does not contain preservatives). Do not use solutions which are cloudy or have deposits. Any unused product or waste material should be disposed of in accordance with local requirements.

### ***Therapy monitoring***

Individual doses of 100 U/kg body weight and daily doses of 200 U/kg body weight must not be exceeded. Patients receiving 100 U/kg body weight or more must be monitored carefully, particularly for the development of DIC and/or acute coronary ischemia and for symptoms of other thrombotic or thromboembolic events. High doses of FEIBA should be administered only as long as strictly necessary – in order to stop a hemorrhage.

If clinically significant changes in blood pressure or pulse rate, respiratory distress, coughing or chest pain occur, the infusion is to be discontinued immediately and appropriate diagnostic and therapeutic measures are to be initiated. Significant laboratory parameters for DIC are a drop in fibrinogen, a drop of the thrombocyte count and/or the presence of fibrin/fibrinogen degradation products (FDP). Other parameters for DIC are a clearly prolonged thrombin time, prothrombin time or aPTT. In patients with inhibitor hemophilia or with acquired inhibitors to factors VIII, IX and/or XI, the aPTT is prolonged by the underlying disease.

Administration of FEIBA to patients with inhibitors may result in an initial anamnestic rise in inhibitor levels. Upon continued administration of FEIBA, inhibitors may decrease over time. Clinical and published data suggest that the efficacy of FEIBA is not reduced.

Patients with inhibitor hemophilia or with acquired inhibitors to coagulation factors, who are treated with FEIBA, may have increased bleeding tendency as well as increased risk of thrombosis at the same time.

**Laboratory tests and clinical efficacy**

In vitro tests, such as aPTT, whole blood coagulation time (WBCT) and thromboelastograms (TEG) as proof of efficacy do not have to correlate with the clinical picture. Therefore, attempts to normalize these values by increasing the dose of FEIBA cannot be successful, and are even to be strongly rejected because of the possible risk of triggering a DIC through overdosing.

**Significance of the thrombocyte count**

If the response to treatment with FEIBA is inadequate, conducting a thrombocyte count is recommended since a sufficient number of functionally intact thrombocytes is necessary for the efficacy of FEIBA.

**Treatment of hemophilia B patients with inhibitors**

The experience in hemophilia B patients with factor IX inhibitors is limited due to the rarity of the disease. Five hemophilia B patients with inhibitors were treated with FEIBA during clinical trials either on-demand, prophylactically or for surgical interventions:

In a prospective open-label, randomized, parallel clinical study in hemophilia A or B patients with persistent high-titer inhibitors (090701, PROOF), 36 patients were randomized to either 12 months  $\pm$  14 days of prophylactic or on-demand therapy. The 17 patients in the prophylaxis arm received  $85 \pm 15$  U/kg FEIBA administered every other day and the 19 patients in the on-demand arm were treated individually determined by the physician. Two hemophilia B patients with inhibitors were treated in the on-demand arm and one hemophilia B patient was treated in the prophylactic arm.

The median ABR (annualized bleeding rate) for all types of bleeding episodes in patients in the prophylaxis arm (median ABR = 7.9) was less than that of patients in the on-demand arm (median ABR = 28.7), which amounts to a 72.5% reduction in median ABRs between treatment arms.

In another completed prospective non-interventional surveillance study of the perioperative use of FEIBA (PASS-INT-003, SURF) a total of 34 surgical procedures were performed in 23 patients. The majority of patients (18) were congenital hemophilia A patients with inhibitors, two were hemophilia B patients with inhibitors and three were patients with acquired hemophilia A with inhibitors. The duration of FEIBA exposure ranged from 1 to 28 days, with a mean of 9 days and a median of 8 days. The mean cumulative dose was 88,347 U and the median dose was 59,000 U. For hemophilia B patients with inhibitors, the longest exposure to FEIBA was 21 days and the maximum dose applied was 7324 U.

In addition 36 case reports are available when FEIBA was used for treatment and prevention of bleeding episodes in hemophilia B patients with factor IX inhibitor (24 hemophilia B patients with inhibitors were treated on-demand, four hemophilia B patients with inhibitors were treated prophylactically and eight hemophilia B patients with inhibitors were treated for surgical procedures).

There are also isolated reports on the use of FEIBA in the treatment of patients with acquired inhibitors to factors X, XI and XIII.