Takeda

NAME OF MEDICINAL PRODUCT

FEIBA

Powder and solvent for solution for injection
Factor VIII Inhibitor Bypassing Activity

QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: Factor VIII Inhibitor Bypassing Activity

The presentation FEIBA 500 U*/10 mL (50 U/mL) contains 500 U factor VIII inhibitor bypassing activity in 200 – 600 mg human plasma protein.

The presentation FEIBA 500 U*/20 mL (25 U/mL) contains 500 U factor VIII inhibitor bypassing activity in 200 – 600 mg human plasma protein.

The presentation FEIBA 1000 U*/20 mL (50 U/mL) contains 1000 U factor VIII inhibitor bypassing activity in 400 – 1200 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 coagulant antigen (F VIII C:Ag) is present in a concentration of up to 0.1 U/1 U FEIBA. The factors of the Kallikrein-Kinin system are present only in trace amounts, if at all. For excipients see “List of Excipients”

* A solution containing 1 U of FEIBA shortens the activated partial thrombin (aPTT) of a factor VIII inhibitor plasma to 50% of the buffer value (blank).

Reconstituted FEIBA contains 4 mg of trisodium citrate and 8 mg of sodium chloride per mL.

PHARMACEUTICAL FORM

Powder and solvent for solution for injection

CLINICAL PARTICULARS

Therapeutic Indications

- Treatment and prophylaxis of bleeding in haemophilia A patients with F VIII inhibitor
- Treatment and prophylaxis of bleeding in haemophilia B patients with F IX inhibitor
- Treatment of bleeding in non-haemophiliacs with acquired inhibitors to factors VIII, XI, XII in cases of severe or life-threatening haemorrhages

In one case FEIBA was successfully used in a patient with an inhibitor, suffering from von Willebrand’s disease. FEIBA was also used in combination with Factor VIII concentrate for a long-term therapy to achieve a complete and permanent elimination of the F VIII inhibitor so as to allow for regular treatment with F VIII concentrate as in patients without inhibitor.

For guidelines for treatment of patients with F VIII inhibitors see table 1 in section “Posology and Method of Administration, 3 Prophylactic Treatment”.

Posology and Method of Administration

Treatment should be initiated and supervised by a physician experienced in the management of haemophilia.

Posology

The dosage and duration of the therapy depend on the severity of the disorder of haemostasis, on the location and the extent of bleeding and on the clinical condition of the patient.
Dosage is independent of the patient’s inhibitor titre. Since the response to treatment may differ from patient to patient the dosage recommendations are only guideline.
Dosage and frequency of administration should always be guided by the clinical efficacy in the individual case.

As a general guide a dose of 50 U to 100 U of FEIBA per kg body weight (bw.) is recommended.

A single dose of 100 U/kg bw. and a daily dose of 200 U/kg bw. should not be exceeded.

1. **Spontaneous Haemorrhage**

   Joint, Muscle and Soft Tissue Haemorrhage

   For minor to moderate bleedings a dose of 50 – 75 U/kg bw. is recommended at 12-hour intervals. Treatment should be continued until clear signs of clinical improvement appear, such as relief of pain, reduction of swelling or mobilisation of the joint.
   For major muscle and soft tissue haemorrhage, such as retroperitoneal bleeding, a dose of 100 U/kg bw. at 12-hour intervals is recommended.

   Mucous Membrane Haemorrhage

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

   Other Severe Haemorrhages

   Severe haemorrhages, such as CNS bleedings have been effectively treated with doses of 100 U/kg bw. at 12-hour intervals. In individual cases FEIBA may be given at 6-hour intervals until clear clinical improvement is achieved. (Do not exceed the maximum daily dose of 200 U/kg bw.)

2. **Surgery**

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

3. **Prophylactic Treatment**

   For dosage recommendations for prophylactic treatment, see table 2.

Table 1: Guidelines for Treatment of Patients with F VIII inhibitors

Inhibitor titre (BU*/ml)	Response to F VIII treatment	Minor to moderate bleeding	Severe to life threatening bleeding, surgery
< 5	low responder high responder	F VIII or FEIBA FEIBA	F VIII or FEIBA FEIBA
5 – 10	low responder high responder	F VIII or FEIBA FEIBA	FEIBA FEIBA
> 10	low responder high responder	FEIBA FEIBA	FEIBA FEIBA

*Bethesda Unit is defined as that amount of antibody that will inhibit 50% of the F VIII activity of fresh average human plasma after incubation for 2 hours at 37°C.

Table 2: Prophylactic Treatment

	Factor VIII	FEIBA	Dosage Interval	Duration of treatment
Stage I	75 – 100 U/kg	40 – 60 U/kg	twice a day	until reduction of F VIII inhibitor titre to approx. 1 BU*/ml (= 0.5 Old Oxford Units/ml**)
Stage II	75 – 100 U/kg	-	twice a day	until no inhibitor is detectable
Stage III	75 – 100 U/kg	-	twice a day	until normal F VIII half life and in vivo recovery is obtained

* KASPER C. EWING N. P.: Experience with the Bethesda assay and other methods or inhibitor detection, in MARIANI G., RUSSO M. A., MANBDELLI F. (eds): Activated Prothrombin Complex Concentrates, Praeger, New York 1982, pp. 17 – 30.

** BRACKMANN H. H.: The treatment of inhibitors against factor VIII by continuous treatment of factor VIII and activated prothrombin complex concentrates, in MARIANI G., RUSSO M. A., MANDELLI F. (eds.): Activated Prothrombin Complex Concentrates, Praeger, New York 1982, pp. 194 – 205.

4. 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 functionality 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 whole blood clotting time (WBCT) and the aPTT may not correlate with clinical improvement.

Global haemostatic tests such as thromboelastogram (TEG) or thrombin generation assay (TGA) may be useful tools to monitor and optimize the treatment.

Method of Administration

Reconstitute the product as described under "Instructions for Use and Handling, and Disposal". FEIBA must be administered as an intravenous injection or infusion. The rate of administration should ensure the comfort of the patient and should not exceed a maximum of 2 U/kg bw. per minute.

Contraindications

FEIBA must not be used in the following situations if therapeutic alternatives to FEIBA are available.

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.

Hypersensitivity to the product

Disseminated Intravascular Coagulation (DIC):

- Laboratory and/or clinical symptoms, which are clearly indicative of DIC.
- Laboratory, histological and/or clinical signs of liver damage; due to the delayed clearance of activated coagulation factors such patients are at an increased risk of developing DIC.

Myocardial Infarction, Acute Thrombosis and/or Embolism:

In patients with a tentative or definite diagnosis of coronary heart disease as well as in patients with acute thrombosis and/or embolism the use of FEIBA is only indicated in life-threatening bleeding episodes.

Special Warnings and Special Precautions for Use

Warnings

Risk of Thromboembolic Events

Thromboembolic events, including disseminated intravascular coagulation (DIC), venous thrombosis, pulmonary embolism, myocardial infarction, and stroke, have occurred in the course of treatment with FEIBA.

Some of these events occurred with doses above 200 U/kg/day or in patients with other risk factors (including DIC, advanced atherosclerotic disease, crush injury or septicaemia) for thromboembolic events. Concomitant treatment with recombinant Factor VIIa may increase the risk of developing a thromboembolic event. The possible presence of such risk factors should always be considered in patients with congenital and acquired haemophilia.

FEIBA should be used with particular caution in patients at risk of DIC, arterial or venous thrombosis. See section “Contraindications”.

Thrombotic microangiopathy (TMA) has not been reported in FEIBA clinical studies. Cases of TMAs were reported in an emicizumab clinical trial where subjects received FEIBA as part of a treatment regimen for breakthrough bleeding (see Oldenburg *et al.* Emicizumab Prophylaxis in Hemophilia A with Inhibitors. N Engl J Med 2017:377:809-818). The safety and efficacy of FEIBA for breakthrough bleeding in patients receiving emicizumab has not been established. Consider the benefits and risks if FEIBA must be used in a patient receiving emicizumab prophylaxis. If treatment with FEIBA is considered required for patients receiving emicizumab, patient must be closely monitored by their physicians.

At the first signs or symptoms of thromboembolic events, the infusion should be stopped immediately and appropriate diagnostic and therapeutic measures initiated.

In case of significant clinical changes in blood pressure, pulse rate, respiratory distress, chest pain and cough, the infusion should be stopped promptly and appropriate diagnostic and therapeutic measures are to be initiated.

Laboratory results indicative of DIC are decreased fibrinogen values, decreased platelet count, and/or presence of fibrin/fibrinogen degradation products (FDP).

Other indications of DIC include significantly prolonged thrombin time, prothrombin time, or aPTT.

A single dose of 100 U/kg bw. and a daily dose of 200 U/kg bw. should not be exceeded. Patients given single doses of 100 U/kg bw. should be monitored for the development of DIC, acute coronary ischaemia, and signs and symptoms of other thrombotic or thromboembolic events. High doses of FEIBA should be given only for as long as absolutely necessary to stop the bleeding.

<u>Allergic-Type Hypersensitivity Reactions</u>
FEIBA can precipitate allergic-type hypersensitivity reactions that have included, urticaria, angioedema, gastrointestinal manifestations, bronchospasm, and hypotension; these reactions can be severe and can be systemic (e.g., anaphylaxis with urticaria and angioedema, bronchospasm, and circulatory shock). Other infusion reactions, such as chills, pyrexia, and hypertension have also been reported.

At the first sign or symptom of an infusion/hypersensitivity reaction, FEIBA administration should be stopped and medical care initiated as appropriate.

When considering re-exposure to FEIBA in patients with known or suspected hypersensitivity to the product, the expected benefit and the risk of re-exposure must be carefully weighed, taking into account the known or suspected type of the patient's hypersensitivity (allergic or non-allergic), including potential remedial and/or preventative therapy or alternative therapeutic agents.

See section "Adverse Reactions".

Viral Safety

Because this product is made from human plasma, a risk of transmitting infectious agents, (e.g. viruses, the variant Creutzfeldt – Jakob disease (vCJD) and, theoretically, the Creutzfeldt – Jakob disease (CJD) agent cannot be totally excluded. Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening individual donations and plasma pools for specific markers of infection and the inclusion of effective manufacturing steps for the inactivation/removal of viruses. Despite this, when medicinal products prepared from human blood or plasma are administered, the possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.

The measures taken (including nanofiltration and vapour heating) are considered effective for inactivation/removal of enveloped viruses such as HIV, HBV and HCV and for non-enveloped viruses HAV. 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 (foetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

Appropriate vaccination (against hepatitis A and B) should be considered for patients in regular/repeated receipt of plasma derived products including FEIBA.

It is recommended that every time FEIBA is administered to a patient, the name and batch number of the product are recorded in order to maintain a link between the patient and the batch of the product.

Precautions

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.

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.

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.

FEIBA contains blood group isohemagglutinins (anti-A and anti-B). Passive transmission of antibodies to erythrocyte antigens, e.g. A, B, D, may interfere with some serological tests for red cell antibodies, such as antiglobulin test (Coombs test).

The amount of sodium in the maximum daily dose may exceed the recommended daily allowance of dietary sodium for patients on a low sodium diet. In these patients, the amount of sodium from the product should be calculated and taken into account when determining dietary sodium intake. Feiba 500 U/1000 U contains approximately 80 mg sodium (calculated) per vial.

The recording of the product name and batch number is strongly recommended following each administration.

Non-Haemophilic Patients

Non-haemophilic patients with acquired inhibitor against factors VIII, XI, XII may have both, a bleeding tendency and an increased risk of thrombosis at the same time.

Laboratory Tests and Clinical Efficacy

In vitro tests to control efficacy such as aPTT, whole blood clotting time (WBCT), and thromboelastrogramme (TEG) may not correlate with clinical improvement. For this reason, attempts to normalise these values by increasing the dose of FEIBA may not be successful and are strongly discouraged because of the potential hazard of inducing DIC by overdosage.

Significance of Platelet Count

In case of inadequate response to treatment with FEIBA it is recommended to perform a platelet count, since a sufficient number of functionally intact platelets is considered necessary for the efficacy of FEIBA.

Interaction with Other Medicinal Products and Other Forms of Interaction

No adequate and well-controlled studies of the combined or sequential use of FEIBA and recombinant Factor VIIa, antifibrinolytics, or emicizumab have been conducted.

The possibility of thromboembolic 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, according to available in vitro data and clinical observations, a potential drug interaction may occur (potentially resulting in adverse events such as thromboembolic event).

Clinical experience from an emicizumab clinical trial suggests that a potential drug interaction may exist with emicizumab when FEIBA was used as part of a treatment regimen for breakthrough bleeding (see Oldenburg et al. Emicizumab Prophylaxis in Hemophilia A with Inhibitors. N Engl J Med 2017:377:809-818).

Pregnancy, Lactation, and Fertility

There are no adequate data from the use of FEIBA in pregnant or lactating women. Physicians should balance the potential risks and only prescribe FEIBA if clearly needed, taking into consideration that pregnancy and the postpartum period confer an increased risk of thromboembolic events.

Pregnancy and the postpartum period are characterised by an increased risk of thrombosis, and several complications of pregnancy are associated with an increased risk of DIC.

No animal reproduction studies have been conducted with FEIBA.

The effects of FEIBA on fertility have not been established in controlled clinical trials.

Effects on Ability to Drive and Use Machines

There is no information of the effects of FEIBA on the ability to drive or operate on automobile or other heavy machinery.

Adverse Reactions

Adverse Reactions from Clinical Trials

The adverse reactions presented in this section have been reported from 2 studies with FEIBA for the treatment of bleeding episodes in paediatric and adult patients with haemophilia A or B and inhibitors to Factors VIII or IX. One study also enrolled acquired haemophilia patients with factor VIII inhibitors (2 of 49 patients).

The adverse reactions presented in the table were reported in the original FEIBA studies (Hillgartner 1983, 2003; Sjamsoedin LJ. et al., 1981) for the treatment of bleeding episodes in haemophilia A or B patients with inhibitors to Factors VIII or IX and the randomised, prospective prophylaxis study (090701) comparing prophylaxis with on-demand treatment.

Adverse Reactions From Clinical Trials			
System Organ Class (SOC)	**Preferred MedDRA (version 18.0) Term**	**Frequency Category**	**Frequency Ratio (Percentage)** **n = 36**
BLOOD AND LYMPHATIC SYSTEM DISORDERS	Increase of inhibitor titre (anamnestic response)[*,a]	Unknown	-
IMMUNE SYSTEM DISORDERS	Hypersensitivity[c]	Common	1/36 (2.8)
NERVOUS SYSTEM DISORDERS	Somnolence*	Unknown	-
	Dizziness[b]	Common	1/36 (2.8)
	Dysgeusia*	Unknown	-

	Headache[c]	Common	1/36 (2.8)
VASCULAR DISORDERS	Hypotension[c]	Common	1/36 (2.8)
RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS	Dyspnoea[*]	Unknown	-
GASTROINTESTINAL DISORDERS	Nausea[*]	Unknown	-
SKIN AND SUBCUTANEOUS	Rash[c]	Common	1/36 (2.8)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	Chills[*]	Unknown	-
	Purexia[*]	Unknown	-
	Chest pain[*]	Unknown	-
	Chest discomfort[*]	Unknown	-
INVESTIGATIONS	Hepatitis B surface antibody positive[c]	Common	3/16 (8.3)

Legend: ADR frequency is based upon the following scale: Very Common (≥ 1/10); Common (≥ 1/100 - < 1/10), Uncommon (≥ 1/1,000 - < 1/100), Rare (≥ 1/10,000 - <1/1,000), Very Rare (< 1/10,000)

* A precise estimate of the rate of these adverse reactions is not possible from the available data. ADR reported in the original studies (Hilgartner 1983, 2003; Sjamsoedin LJ. et al., 1981) only.
a Increase of inhibitor titre (anamnestic response) [not a MedDRA PT] is the rise of previously existing inhibitor titres occurring after the administration of FEIBA. See Section "Special Warnings and Precautions for Use"
b ADR reported in the original studies (Hilgartner 1983, 2003; Sjamsoedin LJ. et al., 1981) and prophylaxis study (090701). Frequency shown is from the prophylaxis study.
c ADR reported in the prophylaxis study (090701). Frequency shown is from the prophylaxis study only.

Post-marketing Adverse Reactions

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA (version 18.0) System Organ Class (SOC), then by Preferred Term in order of severity, where feasible.

IMMUNE SYSTEM DISORDERS: Anaphylactic reaction

NERVOUS SYSTEM DISORDERS: Paresthesia, Thrombotic stroke, Embolic stroke

BLOOD LYMPHATIC SYSTEM DISORDERS: Disseminated intravascular coagulation (DIC)

CARDIAC DISORDERS: Myocardial infarction, Tachycardia

VASCULAR DISORDERS: Thrombosis, Venous thrombosis, Arterial thrombosis, Hypertension, Flushing

RESPIRATORY, THORACIC, AND MEDIASTINAL DISORDERS: Pulmonary embolism, Bronchospasm, Wheezing, Cough

GASTROINTESTINAL DISORDERS: Vomiting, Diarrhoea, Abdominal discomfort

SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Angioedema, Urticaria, Pruritus

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Malaise, Feeling hot, Injection site pain

Overdose

Some reported thromboembolic events occurred with doses above 200 U/kg. If signs or symptoms of thromboembolic events are observed, the infusion should be stopped immediately and appropriate diagnostic and therapeutic measures initiated. See “Special Warnings and Precautions for Use”.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: activated prothrombin complex against factor VIII antibodies, ATC Code: B02B D03

Although FEIBA was developed in the early 1970s and its factor VIII inhibitor bypassing activity has been demonstrated both in vitro and in vivo, its active principle is still the subject of scientific debate. However, recent scientific work indicates a role of specific components of the activated prothrombin complex, zymogen prothrombin (FII) and activated Factor X (F Xa), in the FEIBA mode of action.

Pharmacokinetic Properties

Since the active principle is still under discussion, it is not possible to make any definite statement with regard to the pharmacokinetic properties of FEIBA.

Preclinical Safety Data

Based on acute toxicity studies in gene-targeted factor VIII-deficient mice and in normal mice and rats with doses exceeding the maximum daily dose in humans (i.e., greater than 200 U/kg body weight), it can be concluded that adverse events related to FEIBA are primarily the result of hypercoagulation induced by the pharmacological properties of the product.

Repeat-dose toxicity testing in animals is impracticable due to interference with developing antibodies to heterologous protein.

Because human plasma proteins are not seen to cause tumorigenic or mutagenic effects, experimental studies, particularly in heterologous species, are not considered necessary.

PHARMACEUTICAL PARTICULARS

Incompatibilities

No compatibility studies have been performed with the product. Therefore, FEIBA must not be mixed with other medicinal products or solvents.

Coagulation factors derived from human plasma may be adsorbed by the inner surfaces of certain types of injection/infusion devices. If this were to occur, it could result in failure of therapy. Therefore, only approved plastic injection/infusion devices may be used with FEIBA.

Shelf Life

FEIBA must not be use beyond the expiry date indicated on the package.
Two years when stored at 2°C - 8°C (in a refrigerator).
Considering microbiological aspects, FEIBA should be used immediately after reconstitution.
Reconstituted product must not be returned to the refrigerator.

Special Precautions for Storage

Store at 2°C - 8°C (in a refrigerator). Do not freeze.
Store in the original container to protect product from light.
Within the indicated shelf life the product may be stored at room temperature (max 25 °C) for a period of up to 6 months. No data are available on the effect of a subsequent (second) storage period at 2°C - 8°C. The start of room temperature storage should be noted on the package.
Keep out of the reach and sight of children.

Nature and Contents of Container

The powder is supplied in a vial made of surface treated, colourless glass (hydrolytic type I for 500 U/10 mL; hydrolytic type II for 500 U/20 mL and 1000 U/20mL). The solvent is supplied in a vial made of surface treated, colourless type (hydrolytic type I for 10 mL and 20 mL). The product vials and the solvent vials are closed with butyl rubber stoppers.

Each pack also contains: 1 BAXJECT II Hi-Flow for reconstitution, 1 disposable needle, 1 disposable syringe, 1 winged butterfly needle.

Instructions for Use and Handling, and Disposal

FEIBA contains no preservatives. Therefore, it should be reconstituted just prior to administration. Aseptic technique should be used throughout the entire reconstitution process and the solution should then be used immediately.

Swirl gently until all material is dissolved. Ensure that FEIBA is completely dissolved; otherwise, active material will not pass through the device filter.

After reconstitution, the solution should be inspected for particulate matter and discoloration prior to administration.

Do not use solutions that are cloudy or have deposits.

Mixing of FEIBA with other products or substances must be avoided. It is advisable to flush venous access lines with isotonic saline prior to and after infusion of FEIBA. See Section “Incompatibilities”.

Any unused solution must be disposed of appropriately.

If devices other than those supplied with FEIBA are used, ensure use of an adequate filter.

Reconstitution of dried substance:

1. Warm the unopened vial containing the solvent (sterilized water for injections) to room temperature.

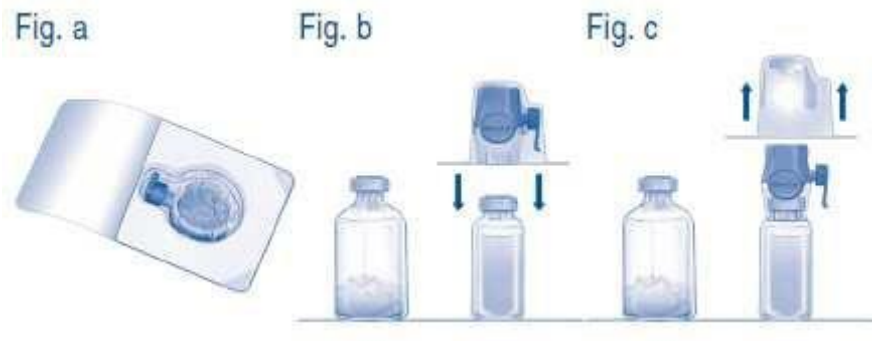
2. Remove protective caps from the concentrate vial and solvent vial and cleanse the rubber stoppers of both. Place the vials on an even surface.

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.



Injection/Infusion:
Use aseptic technique throughout the entire procedure.

1. Remove the protective blue 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 the 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 injection/infusion rate of 2 units FEIBA per kg of body weight per minute.

PRODUCT OWNER
Takeda Manufacturing Austria AG, Vienna, Austria

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