Summary of Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: Factor VIII Inhibitor Bypassing Activity

1 ml contains 50 U* factor VIII inhibitor bypassing activity.
FEIBA 50 U/ml is available in three different presentations:

- The presentation 500 U FEIBA contains 500 U factor VIII inhibitor bypassing activity in 200 – 600 mg human plasma protein,
- The presentation 1000 U FEIBA contains 1000 U factor VIII inhibitor bypassing activity in 400 – 1,200 mg human plasma protein,
- The presentation 2500 U FEIBA contains 2500 U factor VIII inhibitor bypassing activity in 1,000 – 3,000 mg human plasma protein.

FEIBA also contains the factors II, IX and X, mainly in non-activated form, as well as activated factor VII. Factor VIII coagulation antigen (F VIII C:Ag) is present at a concentration of up to 0.1 U./1 U. FEIBA. The factors of the kallikrein-kinin system are present in trace amounts only, if at all.

* 1 unit of FEIBA shortens the activated partial thromboplastin time (aPTT) of a factor VIII inhibitor plasma by 50% of the buffer value (blank value).

Excipients with known effect:
1.8 mmol sodium (40 mg) per vial with 500 U FEIBA.
3.6 mmol sodium (80 mg) per vial with 1000 U FEIBA.
8.9 mmol sodium (200 mg) per vial with 2500 U FEIBA.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for infusion.

White, off-white or pale green powder. The pH value of the ready-to-use solution is between 6.8 and 7.6.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Treatment of bleeding in hemophilia A patients with inhibitors.

- Treatment of bleeding in hemophilia B patients with inhibitors, if no other specific treatment is available (see section 5.1).
- Treatment of bleeding in non-hemophiliacs with acquired inhibitors to factor VIII.
- Prophylaxis of bleeding in hemophilia A patients with inhibitors who have experienced a significant bleed or are at high risk of significant bleeding.

4.2 Posology and method of administration

The treatment is to be initiated and monitored by a physician experienced in the treatment of coagulation disorders.

Posology

Dosing guideline

	Dose (unit/kg)	***Frequency of doses (hours)***	***Duration of Therapy***
Control and Prevention of Bleeding			
Joint Hemorrhage	*50-100*	*12*	*Until pain and acute disabilities are improved.*
Mucous Membrane Bleeding	*50-100*	*6*	*At least 1 day or until bleeding is resolved.*
Soft Tissue Hemorrhage (e.g., retroperitoneal bleeding)	*100*	*12*	*Until resolution of bleed.*
Other Severe Hemorrhage (e.g., CNS bleeds)	*100*	*6-12*	*Until resolution of bleed.*
Perioperative Management			
Preoperative	*50-100*	*One time dose*	*Immediately prior to surgery.*
Postoperative	*50-100*	*6-12*	*Until resolution of bleed and healing is achieved.*
Routine Prophylaxis			
	85	*Every other day*	

- *Dosage and duration of treatment depend on the location and extent of bleeding, and the patient's clinical condition. Careful monitoring of replacement therapy is necessary in cases of major surgery of life-threatening bleeding episodes.*
- ***Do not exceed a single dose of 100 units per kg body weight and a daily dose of 200 units per kg body.***

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.

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. See section 4.4.

Method of administration
Reconstitute the product as described in section 6.6 and slow infusion via the intravenous route. An infusion rate of 2 U/kg body weight per minute must not be exceeded.

4.3 Contraindications

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

- Hypersensitivity to the product or any of the components.
- Disseminated Intravascular Coagulation (DIC).
- Acute thrombosis or embolism (including myocardial infarction).

See section 4.4.

4.4 Special warnings and precautions for use

WARNINGS

Hypersensitivity Reactions

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.
Patients should be informed of the early signs of hypersensitivity reactions, for example erythema, skin rash, generalized urticaria, pruritus, breathing difficulties/dyspnoea, tightness of the chest, general indisposition, dizziness and drop in blood pressure up to allergic shock.
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 suspected hypersensitivity to the product or any of its components, 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.

Thrombotic and Thromboembolic Events

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.

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 septicemia) for

thromboembolic events. Concomitant treatment with recombinant Factor VIIa likely increases the risk of developing a thromboembolic event. The risk of thrombotic and thromboembolic events may be increased with high doses of FEIBA.
The possible presence of such risk factors should always be considered in patients with congenital and acquired hemophilia.

FEIBA should be used with particular caution and only if there are no therapeutic alternatives in patients with an increased risk of thromboembolic complications. These include, but are not limited to, patients with a history of coronary heart disease, liver disease, DIC, arterial or venous thrombosis, post-operative immobilization, elderly patients and neonates.

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 section 2.4 Warning and Precautions of the emicizumab approved Indonesian Summary of Product Characteristics; see also 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.
Therefore, benefit-risk evaluation of FEIBA to be administered to emicizumab exposed patients is required, and patients must be closely monitored by their physicians. (see also section 4.5.)

If signs or symptoms of thrombotic and thromboembolic events are observed, the infusion should be stopped immediately and appropriate diagnostic and therapeutic measures initiated.
A single dose of 100 U/kg body weight and a daily dose of 200 U/kg body weight should not be exceeded unless the severity of bleeding warrants and justifies the use of higher doses.
When used to stop bleeding, the product should be given only for as long as absolutely necessary to achieve the therapeutic goal.

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.

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.

PRECAUTIONS

Thrombotic and Thromboembolic Complications

In the following situations, FEIBA is to be applied only if no reaction to treatment with suitable blood coagulation factor concentrates can be expected – e.g. in case of a high inhibitor titer and a life-threatening hemorrhage or risk of bleeding (e.g. post-traumatically or postoperatively):

- Disseminated intravascular coagulation (DIC): laboratory findings and/or clinical symptoms
- Liver damage: Due to the delayed clearance of activated coagulation factors, patients with impaired liver function are at increased risk of developing DIC.
- Coronary heart disease, acute thrombosis and/or embolism.

Patients who receive FEIBA should be monitored for the development of DIC, acute coronary ischemia, and signs and symptoms of other thrombotic or thromboembolic events. At the first signs or symptoms of thrombotic and thromboembolic events, the infusion should be stopped immediately and appropriate diagnostic and therapeutic measures initiated.

Discordant Response to Bypassing Agents

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.

Anamnestic Responses

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.

Interference with Laboratory Tests 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).

Pediatrics

Case reports and limited clinical trial data suggest that FEIBA can be used in children younger than 6 years of age. The same dose regimen as in adults should be adapted to the child's clinical condition.

Elderly

There are only limited clinical trial data with the use of FEIBA in elderly patients.

Prophylactic use in hemophilia B patients with inhibitors

Due to the rarity of the disease, only limited clinical data is available for the prophylaxis of bleeding in hemophilia B patients (literature case reports, n = 4, and clinical data in prophylaxis study 090701, n = 1).

Transmission of infectious agents

Standard measures to prevent infections resulting from the use of medicinal products prepared from human blood or plasma include selection of donors, screening of 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 are considered effective for enveloped viruses such as HIV, HBV and HCV, and for the non-enveloped virus 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 (fetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia).

It is strongly recommended that every time that FEIBA is administered to the 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.
Appropriate vaccination (hepatitis A and B) should be considered for patients in regular/ repeated receipt of human plasma-derived products including FEIBA.

Excipient related considerations

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 in patients on a low sodium diet.

4.5 Interactions with other medicinal products and other forms of interaction

No adequate and well-controlled studies of the combined or sequential use of FEIBA NF 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 a potential drug interaction cannot be excluded according to available in vitro data and clinical observations (potentially resulting in adverse events such as a 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 which may result in thromboembolic events and thrombotic microangiopathy (see section 4.4).

4.6 Fertility, pregnancy and lactation

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, and several complications of pregnancy that are associated with an increased risk of DIC.
No animal reproduction studies have been conducted with FEIBA, and the effects of FEIBA on fertility have not been established in controlled clinical trials.
See section 4.4 for information on parvovirus B19 infection.

4.7 Effects on the ability to drive and use machines

FEIBA has no, or negligible, influence on the ability to drive or to use machines.

4.8 Undesirable effects

FEIBA can precipitate allergic-type hypersensitivity reactions that have included urticaria, angioedema, gastrointestinal manifestations, bronchospasm, and a drop in blood pressure; these reactions can be severe and can be systemic (e.g., anaphylaxis with urticaria and angioedema, bronchospasm, and circulatory shock). See also section 4.4 Hypersensitivity Reactions.

The adverse reactions presented in this section have been reported from post marketing surveillance as well as from 2 studies with FEIBA for the treatment of bleeding episodes in pediatric and adult patients with hemophilia A or B and inhibitors to factors VIII or IX. One study also enrolled acquired hemophilia patients with factor VIII inhibitors (2 of 49 patients). The adverse reactions from a third study comparing prophylaxis with on-demand treatment have been added.

Frequency categories are defined according to the following convention:

very common	≥ 1/10
common	≥ 1/100 to <1/10
uncommon	≥ 1/1,000 to <1/100
rare	≥ 1/10,000 to <1/1,000
very rare	< 1/10,000
unknown	cannot be estimated from the available data

Adverse Reactions		
System organ class (SOC)	**Preferred current MedDRA Term**	**Frequency* Category**
Blood and lymphatic system disorders	Disseminated intravascular coagulation (DIC) Increase of inhibitor titer (anamnestic response)[a]	Unknown Unknown
Immune system disorders	Hypersensitivity [c] Urticaria Anaphylactic reaction	Common Unknown Unknown
Nervous system disorders	Paresthesia Hypaesthesia Thrombotic stroke Embolic stroke Headache[c] Somnolence Dizziness[b] Dysgeusia	Unknown Unknown Unknown Unknown Commonn Unknown Common Unknown
Cardiac disorders	Cardiac infarction Tachycardia	Unknown Unknown
Vascular disorders	Thrombosis, Venous thrombosis Arterial thrombosis Embolism (thromboembolic complications) Hypotension[c] Hypertension Flushing	Unknown Unknown Unknown Unknown Common Unknown Unknown
Respiratory, Thoracic, and Mediastinal disorders	Pulmonary embolism Bronchospasm Wheezing Cough Dyspnea	Unknown Unknown Unknown Unknown Unknown
Gastrointestinal disorders	Vomiting Diarrhea Abdominal discomfort Nausea	Unknown Unknown Unknown Unknown
Skin and subcutaneous tissue disorders	Sensation of numbness in the face Angioedema Urticaria Pruritus Rash[c]	Unknown Unknown Unknown Unknown Common
General disorders and administration site conditions	Pain at the injection site Malaise Feeling hot Chills Pyrexia Chest pain Chest discomfort	Unknown Unknown Unknown Unknown Unknown Unknown Unknown
Investigations	Drop in blood pressure Hepatitis B surface antibody positive[c]	Unknown Common

* A precise estimate of the rate of these adverse reactions is not possible from the available data.

[a] Increase of inhibitor titer (anamnestic response) [not a MedDRA PT] is the rise of previously existing inhibitor titers occurring after the administration of FEIBA. See section 4.4.
[b] ADR reported in the original and prophylaxis studies. Frequency shown is from the prophylaxis study only.
[c] ADR reported in the prophylaxis study. Frequency shown is from the prophylaxis study

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of FEIBA is important. It allows continued monitoring of the benefit/risk balance of FEIBA. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system (e-meso.pom.go.id)

4.9 Overdose

The risk of thrombotic and thromboembolic events (including DIC, myocardial infarction, venous thrombosis, and pulmonary embolism) may be increased with high doses of FEIBA. 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. See section 4.4.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: blood coagulation factors, **ATC code:** B02BD03.

Although FEIBA was developed in the early seventies and its factor VIII inhibitor bypassing activity has been proven in vitro as well as in vivo, its mode of action is still the subject of scientific discussion. FEIBA, as found with activity assays, is composed of prothrombin complex zymogens which are both procoagulant (prothrombin FVII, FIX, FX) and anticoagulant (protein C) in relatively equal quantities to the arbitrary FEIBA potency unit but its procoagulant enzyme content is relatively low. FEIBA, thus, contains the proenzymes of the prothrombin complex factors, but only very small amounts of their activation products, with the contents of FVIIa being the highest. [Turecek PL and Schwarz HP. Chapter 4: Factor Eight Inhibitor Bypassing Activity, in Production of Plasma Proteins for Therapeutic Use, eds. Joseph Bertolini, Neil Goss, John Curling, Wiley 2013, ISBN: 978-0-470-92431-0].

Current scientific works point to the role of specific components of the activated prothrombin complex, prothrombin (F II) and activated factor X (FXa) in the mode of action of FEIBA. [Turecek PL, Varadi K, Gritsch H, et al. Factor Xa and Prothrombin: Mechanism of Action of FEIBA. Vox Sang. 77: 72-79, 1999]
FEIBA controls bleeding by induction and facilitation of thrombin generation, a process for which the formation of the prothrombinase-complex is crucial. A number of biochemical in vitro and in vivo studies have shown that FXa and prothrombin play a critical role in the activity of FEIBA. The prothrombinase complex has been found to be a major target site for

FEIBA. Apart from prothrombin and FXa, FEIBA contains other proteins of the prothrombin complex, which could also facilitate haemostasis in haemophilia patients with inhibitors.

Treatment of hemophilia A patients with inhibitors
For previously untreated patients receiving FVIII products, the overall incidence of inhibitor development is approximately 3% to 13% in those with mild to moderate disease and 20% to 35% in patients with severe hemophilia A. FEIBA prophylaxis significantly and safely decreased the frequency of joint and other bleeding events in patients with severe hemophilia A and FVIII inhibitors.

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 ± 14 days of prophylactic or on-demand therapy. The 17 patients in the prophylaxis arm received 85 ± 15 U/kg FEIBA administered every other day and the 19 patients in the on-demand arm were treated individually determined by the physician. The majority of treated subjects (33 subjects) had hemophilia A and 3 had hemophilia B. 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 17 patients in the prophylaxis arm (median ABR = 7.9) was lower than that of 19 patients in the on-demand arm (median ABR = 28.7), which amounts to a 72.5% reduction in median ABRs between treatment arms.

In an open, uncontrolled, non-interventional observational Post-Authorization Safety Study of FEIBA (PASS-EU-006), a total of 75 subjects (mean age 34.8 years, 70 males and 5 females), of which 73 had hemophilia A and 2 hemophilia B, were treated with FEIBA. Of the 65 subjects with congenital hemophilia, 63 had congenital hemophilia A and 2 had congenital hemophilia B. At baseline, 43 subjects were prescribed FEIBA for prophylaxis and 32 were prescribed FEIBA for on-demand treatment. The mean dose of FEIBA per infusion per kg of body weight was 68.4 U as regular prophylaxis and 77.0 U as on-demand.

In patients with congenital hemophilia (n=65), the hemostatic effectiveness was rated as ‘excellent’ or ‘good’ in 58 subjects overall, while 6 subjects had a rating of ‘fair’ and one ‘not applicable’. In the prophylaxis subgroup (n=28), 27/28 had a hemostatic effectiveness rating of ‘excellent’ or ‘good’, and 1/28 had a rating of ‘fair’. In the on-demand subgroup (n=18), 15/18 had a rating of ‘excellent’ or ‘good’; and in the mixed regimen group (n=19), 16/19 had a rating of ‘excellent’ or ‘good’ and 3/19 a rating of ‘fair’.

The mean number of bleeds per year was similar in the prophylaxis (mean=9.5, median=5.0, n=51) and in the on-demand subgroups (mean=10.6, median=4.9, n=48).

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 a post-authorization, prospective, uncontrolled, observational, non-interventional, open-label, multicenter cohort study (FEIBA-GO), fifty enrolled patients received FEIBA prophylaxis (n=37) or on-demand treatment (n=13) at screening (hemophilia A: n=49, hemophilia B: n=1; median age at baseline 16.5 years). The mean overall ABR for patients receiving prophylaxis (n=37) or on-demand treatment (n=12) was 6.82 and 10.94 per patient-year, respectively. In patients with more than 2 years of study follow-up, the mean ABR was 6.40 for patients receiving prophylaxis (n=17) and 6.87 for patients receiving the on-demand regimen (n=7). In patients with more than 4 years of study follow-up, the mean ABR was 10.13 for patients receiving prophylaxis (n=5) and 17.16 for patients receiving the on-demand regimen (n=2).
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.

5.2 Pharmacokinetic properties

As the mode of action of FEIBA is still being discussed, it is not possible to make a conclusive statement about the pharmacokinetic properties.

5.3 Preclinical safety data

Based on acute toxicity studies in factor VIII knockout mice and in normal mice, and in rats, with doses higher than the maximum daily dose in humans (> 200 U/kg body weight), it can be concluded that the side effects in connection with FEIBA are mainly the result of hypercoagulation due to the pharmacological properties.

Toxicity studies with repeated administration in animal experiments are practically unfeasible as interference occurs through the development of antibodies to heterologous proteins.

Since human blood coagulation factors are not seen as carcinogenic or mutagenic, experimental animal studies, especially in heterologous species, were not considered necessary.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder: Sodium chloride
Sodium citrate

Solvent: Water for Injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except the solvent mentioned in section 6.6.
As in all blood coagulation preparations, the efficacy and tolerance of the medicinal product may be impaired by being mixed with other medicinal products. It is advisable to rinse a common venous access with a suitable solution, e.g. with isotonic saline solution, before and after the administration of FEIBA.
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 infusion devices may be used with FEIBA.

6.3 Stability after reconstitution

Chemical and physical in-use stability has been demonstrated for 3 hours at room temperature (up to 25°C). From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination (controlled and validated aseptic conditions), the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

Reconstituted product must not be refrigerated.

6.4 Special precautions for storage

Do not store above 25ºC. Do not freeze.

Store in the original package in order to protect from light. For storage conditions of the reconstituted medicinal product – see section 6.3.

6.5 Nature and contents of container

The powder is supplied in a vial made of surface treated, colorless glass (hydrolytic type I for 500 U, and 2500 U; hydrolytic type II for 1000 U). The solvent is supplied in a vial made of surface treated, colorless glass (hydrolytic type I). The vials are closed by a stopper made of butyl rubber.

FEIBA 50 U/ml is available in the following presentations:

1 x 500 U
1 x 1000 U
1 x 2500 U

Presentation 500 U contains

- 1 vial with 500 U FEIBA powder for solution for infusion
- 1 vial with 10 ml Water for Injections
- 1 BAXJECT II Hi-Flow
- 1 disposable syringe

- 1 disposable needle
- 1 butterfly needle

Presentation 1000 U contains

- 1 vial with 1000 U FEIBA powder for solution for infusion
- 1 vial with 20 ml Water for Injections
- 1 BAXJECT II Hi-Flow
- 1 disposable syringe
- 1 disposable needle
- 1 butterfly needle

Presentation 2500 U contains

- 1 vial with 2500 U FEIBA powder for solution for infusion
- 1 vial with 50 ml Water for Injections
- 1 BAXJECT II Hi-Flow
- 1 disposable syringe
- 1 disposable needle
- 1 butterfly needle

6.6 Special precautions for disposal and other handling

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.

After reconstitution, the solution should be inspected for particulate matter and discoloration prior to administration. Do not use solutions which are cloudy or have deposits.

Open containers must not be re-used.

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

Use only the included Water for Injections and the included device set for reconstitution. If devices other than those enclosed are used, ensure the use of an adequate filter with a pore size of at least 149 µm.

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:

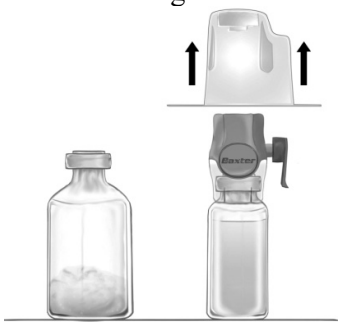
1. Warm the unopened solvent vial (Water for Injections) to room temperature (15°C to 25°C), for example by using a water bath for several minutes (max. 37°C) if necessary.

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.
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

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

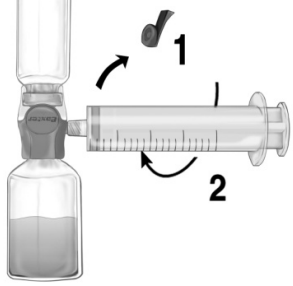
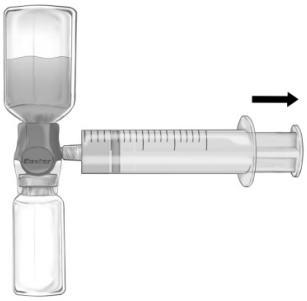


Fig. f



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

7. MARKETING AUTHORISATION HOLDER

PT. Wigo Health Indonesia, Semarang, Indonesia

8. MARKETING AUTHORISATION NUMBERS

Box, 1 vial powder 500 U+1 vial water for injection 10 mL+1 disposable syringe+1 disposable needle+1 butterfly needle + 1 Baxject II Hi-Flow. DKIXXXXXXXXXXXX

Box, 1 vial powder 1000 U+1 vial water for injection 20 mL+1 disposable syringe+1 disposable needle+1 butterfly needle +1 Baxject II Hi-Flow. DKIXXXXXXXXXXXX

Box, 1 vial powder 2500 U+1 vial water for injection 50 mL+1 disposable syringe+1 disposable needle+1 butterfly needle +1 Baxject II Hi-Flow. DKIXXXXXXXXXXXX

Manufactured and released by:

Takeda Manufacturing Austria AG

Vienna, Austria

HARUS DENGAN RESEP DOKTER
ON MEDICAL PRESCRIPTION ONLY

Brosur : Informasi untuk Pasien

FEIBA 50 U/mL
Serbuk dan pelarut untuk larutan infus
Zat aktif: *Factor VIII Inhibitor Bypassing Agent*

Bacalah keseluruhan dari brosur ini dengan seksama sebelum Anda mulai menggunakan obat ini karena brosur ini berisi informasi penting untuk anda.

- Simpan brosur ini, mungkin diperlukan untuk dibaca kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, hubungi Dokter atau Apoteker Anda
- Obat ini diresepkan hanya untuk anda. Jangan berikan pada orang lain karena dapat membahayakan mereka walaupun gejala yang mereka alami sama dengan Anda.
- Jika Anda mengalami gejala efek samping, bicarakanlah dengan Dokter atau Apoteker Anda. Ini termasuk efek samping yang mungkin tidak tercantum dalam brosur ini. Baca bagian 4.

Informasi yang terkandung dalam brosur ini :

1. Apakah FEIBA 50 U/mL dan apa kegunaannya

FEIBA adalah sediaan yang dibuat dari plasma darah manusia yang memungkinkan terjadinya hemostasis, bahkan ketika faktor koagulasi individual berkurang atau tidak ada.

FEIBA digunakan untuk pengobatan perdarahan pada pasien hemofilia A dengan penghambat faktor VIII .
FEIBA digunakan untuk pengobatan perdarahan pada pasien hemofilia B dengan penghambat faktor IX, jika tidak ada pengobatan spesifik lain yang tersedia.
FEIBA juga digunakan untuk profilaksis perdarahan pada pasien hemofilia A dengan penghambat yang pernah mengalami perdarahan signifikan atau berisiko tinggi mengalami perdarahan signifikan.
Selain itu, FEIBA juga dapat digunakan untuk pengobatan perdarahan pada pasien non hemofilia yang mengalami pembentukan penghambat faktor VIII.

2. Apa yang perlu Anda ketahui sebelum menggunakan FEIBA 50 U/mL

Beritahukan dokter Anda jika Anda memiliki alergi.
Beritahukan dokter anda jika Anda sedang menjalani diet rendah natrium.

Jangan gunakan FEIBA
Dalam situasi berikut FEIBA hanya boleh digunakan jika - misalnya karena kadar penghambat yang sangat tinggi - tidak diharapkan akan ada respons terhadap pengobatan dengan konsentrat faktor koagulasi yang sesuai.

- jika Anda alergi (hipersensitif) terhadap salah satu komponen FEIBA.
- jika mengalami koagulasi intravaskular diseminata (DIC). (DIC = koagulopati konsumsi, suatu kondisi yang mengancam jiwa di mana terjadi pembekuan darah yang berlebihan dengan pembentukan gumpalan darah yang nyata di pembuluh darah. Ini kemudian akan menyebabkan konsumsi faktor pembekuan di seluruh tubuh)
- dalam kasus infark miokard, trombosis akut, dan/atau embolisme: FEIBA hendaknya hanya digunakan pada kondisi perdarahan yang mengancam jiwa.

Peringatan dan perhatian

Bicarakan dengan dokter Anda sebelum menggunakan FEIBA, karena reaksi hipersensitivitas dapat terjadi, seperti halnya dengan semua produk plasma yang diberikan secara intravena. Untuk dapat mengenali reaksi alergi sesegera mungkin, Anda harus mewaspadai potensi gejala awal reaksi hipersensitivitas seperti:
- eritema (kemerahan pada kulit)
- ruam kulit
- terjadinya gatal-gatal pada kulit (jelatang/urtikaria)
- gatal di sekujur tubuh
- pembengkakan pada bibir dan lidah
- kesulitan bernafas
- sesak di dada
- rasa tidak enak badan
- pusing
- penurunan tekanan darah

Gejala lain dari reaksi hipersensitivitas terhadap produk plasma termasuk kelesuan dan kegelisahan.

Jika Anda mengalami satu atau lebih dari gejala-gejala ini, segera hentikan infus dan segera hubungi dokter Anda. Gejala yang disebutkan di atas mungkin merupakan indikasi awal syok anafilaksis. Gejala yang parah membutuhkan perawatan darurat segera.

Dokter Anda hanya akan melanjutkan penggunaan FEIBA pada pasien dengan dugaan hipersensitivitas terhadap produk atau salah satu komponennya setelah menimbang dengan cermat manfaat yang diharapkan dan risiko paparan ulang dan/atau bila tidak diharapkan akan ada reaksi terhadap terapi pencegahan lain atau obat terapeutik alternatif.

- Jika Anda mengalami perubahan besar pada tekanan darah atau denyut nadi, kesulitan bernapas, batuk atau nyeri dada, segera hentikan infus dan hubungi dokter Anda. Dokter Anda akan memulai tindakan diagnostik dan terapeutik yang sesuai.
- pada pasien hemofilia dengan penghambat atau mengalami pembentukan penghambat faktor pembekuan. Selama pengobatan dengan FEIBA, pasien ini mungkin memiliki kecenderungan peningkatan perdarahan dan peningkatan risiko trombosis pada saat yang bersamaan.

Kejadian trombotik dan tromboembolisme, termasuk koagulasi intravaskular diseminata (DIC), trombosis vena, emboli paru, infark miokard, dan strok, terjadi dalam pengobatan dengan FEIBA. Penggunaan bersamaan Faktor VIIa rekombinan kemungkinan besar meningkatkan risiko terjadinya peristiwa tromboemboli. Beberapa kejadian tromboemboli tersebut juga terjadi dalam kasus pengobatan dengan FEIBA dosis tinggi.

Dalam penelitian yang dilakukan oleh perusahaan lain terhadap emicizumab (obat untuk mencegah perdarahan pada pasien dengan hemofilia A), beberapa pasien yang menderita *breakthrough bleeding* diobati dengan FEIBA untuk mengontrol perdarahan, dan beberapa dari pasien ini mengalami mikroangiopati trombotik (TMA). TMA adalah kondisi yang serius dan berpotensi mengancam jiwa. Ketika seseorang mengalami kondisi ini, lapisan pembuluh darah bisa rusak dan gumpalan darah dapat terbentuk di pembuluh darah kecil. Dalam beberapa kasus, hal ini dapat menyebabkan kerusakan pada ginjal dan organ lainnya. Jika terjadi *breakthrough bleeding* saat menggunakan emicizumab untuk profilaksis, segera hubungi dokter hemofilia Anda atau Pusat Perawatan Hemofilia.

Terhadap obat-obat yang dibuat dari darah atau plasma manusia, dilakukan tindakan untuk mencegah penularan infeksi ke pasien. Ini termasuk pemilihan donor darah dan plasma yang cermat untuk memastikan mereka yang berisiko membawa penyakit infeksi tidak ikut mendonor, dan pengujian setiap donor dan kumpulan plasma akan adanya tanda-tanda virus/infeksi. Dalam memproses darah dan plasma, produsen produk ini juga melakukan langkah-langkah yang dapat menonaktifkan atau menghilangkan virus. Terlepas dari tindakan ini, ketika obat-obatan yang dibuat dari darah atau plasma manusia diberikan, kemungkinan penularan infeksi tidak dapat sepenuhnya dikesampingkan. Ini juga berlaku untuk virus yang tidak dikenal atau virus baru atau jenis infeksi lain.

Tindakan yang telah diambil dianggap efektif terhadap virus yang berselubung seperti *human immunodeficiency virus* (HIV), virus hepatitis B dan virus hepatitis C, dan untuk virus hepatitis

A yang tidak berselubung. Manfaat dari tindakan tersebut mungkin memiliki efek yang kurang bermakna untuk virus tidak berselubung seperti parvovirus B19. Infeksi Parvovirus B19 mungkin serius untuk wanita hamil (infeksi janin) dan untuk seseorang yang sistem kekebalannya ditekan atau yang memiliki beberapa jenis anemia (misalnya penyakit sel sabit atau anemia hemolitik).

Dokter Anda mungkin menyarankan Anda untuk mempertimbangkan vaksinasi hepatitis A dan B jika Anda secara teratur atau berulang kali menerima produk penghambat Faktor VIII yang bersumber dari plasma.

Setelah pemberian FEIBA dosis tinggi, peningkatan sementara dari antibodi permukaan Hepatitis B yang ditransfer secara pasif dapat mengakibatkan positif palsu dalam pengujian serologis.

FEIBA adalah produk turunan plasma dan dapat mengandung zat yang bereaksi ketika diinfuskan pada pasien, menyebabkan adanya isohemagglutinins (antibodi yang menyebabkan pelekatan sel darah merah dari orang lain). Proses ini dapat menyebabkan hasil tes darah yang keliru.

Sangat disarankan bahwa setiap kali Anda menerima dosis FEIBA, nama dan nomor bets produk dicatat untuk menjaga catatan bets yang digunakan.

Obat-obatan lain dan FEIBA
Beritahukan dokter atau apoteker Anda jika Anda sedang atau baru saja mengonsumsi obat lain, termasuk obat yang diperoleh tanpa resep.

Tidak ada penelitian yang memadai dan terkontrol baik yang pernah dilakukan terhadap penggunaan kombinasi atau berurutan dari FEIBA dan Faktor VIIa rekombinan, antifibrinolitik atau emicizumab. Kemungkinan kejadian trombosis harus dipertimbangkan ketika antifibrinolitik sistemik seperti asam traneksamat dan asam aminokaproat digunakan pada saat sedang menggunakan FEIBA. Oleh karena itu, antifibrinolitik hendaknya tidak digunakan selama kurang lebih 6 sampai 12 jam setelah pemberian FEIBA.

Dalam hal penggunaan bersama rFVIIa, interaksi obat yang potensial tidak dapat dikesampingkan menurut data in vitro dan observasi klinis yang tersedia, yang berpotensi menghasilkan kejadian tromboemboli. Sampaikan kepada dokter Anda jika Anda akan menggunakan FEIBA setelah Anda menerima emicizumab (obat untuk mencegah pendarahan pada pasien dengan hemofilia A) karena ada peringatan dan tindakan pencegahan khusus yang harus dipertimbangkan. Dokter Anda perlu memantau Anda dengan cermat.

Seperti pada semua sediaan pembekuan darah, FEIBA tidak boleh dicampur dengan produk obat lain sebelum pemberian, karena efek dan toleransi sediaan mungkin terganggu.
Dianjurkan untuk membilas selang infus dengan larutan garam fisiologis sebelum dan sesudah pemberian FEIBA.

Kehamilan, menyusui dan kesuburan
Dokter Anda akan memutuskan apakah FEIBA dapat digunakan selama kehamilan dan menyusui. Karena peningkatan risiko trombosis selama kehamilan, FEIBA hendaknya diberikan hanya di bawah pengawasan medis yang cermat dan hanya jika mutlak diperlukan. Informasi tentang infeksi parvovirus B19 diberikan di bagian Peringatan dan Perhatian.

Mengemudi dan menggunakan mesin
Tidak ada tanda-tanda bahwa FEIBA dapat memengaruhi kemampuan mengemudi atau menggunakan mesin.

Informasi penting tentang beberapa bahan FEIBA
FEIBA 50 U/ml mengandung sekitar 4 mg natrium per ml, yaitu sekitar 40 mg natrium dalam 500 U FEIBA, sekitar 80 mg natrium dalam 1000 U FEIBA dan kira-kira 200 mg natrium dalam 2500 U FEIBA. Ini harus dipertimbangkan untuk pasien yang menjalani diet rendah natrium.

3. Bagaimana cara menggunakan FEIBA 50 U/mL

Larutkan serbuk kering-beku FEIBA dengan pelarut yang disediakan dan berikan larutan secara intravena.

Selalu gunakan FEIBA persis seperti yang diberitahukan dokter Anda. Anda hendaknya memastikan ke dokter atau apoteker Anda, jika Anda tidak yakin.

Dengan mempertimbangkan tingkat keparahan gangguan pembekuan darah Anda, lokasi dan luasnya perdarahan, serta kondisi umum Anda dan respons terhadap sediaan, dokter Anda telah menentukan dosis dan interval dosis yang diperlukan untuk Anda secara pribadi. Jangan mengubah dosis yang ditetapkan oleh dokter Anda dan jangan hentikan penggunaan sediaan secara mandiri.

Silakan bicarakan dengan dokter atau apoteker Anda jika Anda mendapat kesan bahwa efek FEIBA terlalu kuat atau terlalu lemah.

Hangatkan produk ke suhu ruangan atau suhu tubuh sebelum pemberian jika perlu.

FEIBA harus dilarutkan segera sebelum pemberian. Larutannya harus segera digunakan (karena sediaan tidak mengandung pengawet).

Aduk memutar perlahan sampai semua bahan larut. Pastikan FEIBA benar-benar larut; jika tidak, lebih sedikit Unit FEIBA yang melewati filter.

Larutan yang keruh atau memiliki endapan, harus dibuang dengan benar.

Jangan gunakan FEIBA yang wadahnya sebelumnya pernah dibuka.

Hanya gunakan Air untuk Injeksi dan alat yang disediakan bersama produk untuk melarutkan obat.

Jika menggunakan perangkat selain yang sediakan, pastikan menggunakan filter yang sesuai dengan ukuran pori setidaknya 149 µm.

Jangan gunakan produk jika penutup sterilnya rusak, kemasannya rusak atau jika menunjukkan tanda-tanda penurunan kualitas.

Semua produk yang tidak terpakai atau limbah produk harus dibuang sesuai dengan persyaratan setempat.

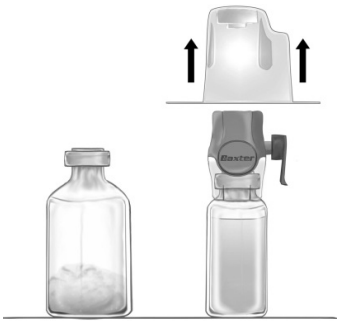
Cara melarutkan serbuk untuk penyiapan larutan infus menggunakan Baxject II Hi-Flow:

1. Hangatkan vial pelarut (Air untuk Injeksi) yang belum dibuka ke suhu kamar atau maksimum +37 ° C jika perlu, contohnya mengunakan penangas air selama beberapa menit.
2. Lepaskan tutup pelindung vial serbuk dan vial pelarut dan desinfeksi sumbat karet pada kedua botol. Letakkan vial pada permukaan yang rata.
3. Buka kemasan Baxject II-Hi-Flow dengan cara menarik lepas foil pembungkus tanpa menyentuh isi kemasan (Gbr. A). Jangan dulu keluarkan alat dari wadahnya.
4. Balikkan kemasan dan tekan pin plastik transparan melalui sumbat karet vial pelarut (Gbr.b). Lalu lepaskan kemasan Baxject II Hi-Flow (Gbr.c). Jangan dulu lepaskan tutup pelindung berwarna biru dari Baxject II Hi-Flow.
5. Lalu putar sistem yang terdiri dari Baxject II Hi-Flow dan vial pelarut, sedemikian sehingga vial pelarut ada di atas. Tekan pin ungu Baxject II Hi-Flow melalui vial FEIBA. Pelarut akan tertarik ke dalam vial FEIBA oleh vakum (Gbr.d)
6. Larutkan serbuk dengan memutar perlahan, jangan dikocok, sampai serbuk larut. Pastikan bahwa FEIBA terlarut sempurna, karena bila tidak zat aktifnya dapat tertahan di filter.

Gbr. a

Gbr. b

Gbr. c



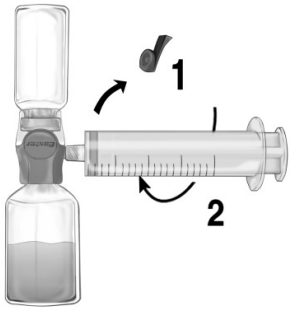
Penyiapan infus

Gunakan teknik aseptik di seluruh prosedur!

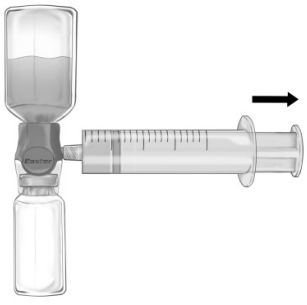
1) Lepaskan tutup pelindung berwarna biru dari Baxject II Hi-Flow. Hubungkan syringe ke Baxject II Hi-Flow dengan erat. JANGAN TARIK UDARA KE DALAM SYRINGE. (Gbr.e). Untuk menjamin hubungan yang erat antara syringe dan Baxject II Hi-Flow, sangat direkomendasikan menggunakan *luer lock syringe* (saat memasang, putar syringe searah jarum jam sampai posisi stop).
2) Balikkan sistem sehingga larutan produk berada di atas. Tarik larutan ke dalam syringe dengan menarik plunger PERLAHAN dan pastikan hubungan yang erat antara syringe dan Baxject II Hi-Flow tetap terjaga selama menarik plunger. (Gbr.f)
3) Lepaskan syringe.
4) Jika dalam syringe terbentuk busa, tunggu sampai semua busa hilang. Secara perlahan berikan larutan secara intravena dengan set infus yang tersedia (atau jarum sekali pakai)

Gbr. d

Gbr. e



Gbr. f



Jangan melebihi kecepatan infus 2 U FEIBA/kg berat badan per menit.

Jika anda menggunakan FEIBA lebih dari yang seharusnya:

Segera sampaikan kepada dokter anda. Overdosis FEIBA dapat meningkatkan risiko efek samping, seperti tromboembolisme (pembentukan gumpalan darah yang terbawa ke dalam pembuluh darah), koagulopati konsumsi (DIC), atau infark miokard. Beberapa kejadian tromboembolik yang dilaporkan terjadi pada dosis di atas 200 U/kg atau pada pasien dengan faktor risiko untuk kejadian tromboembolik. Bila tanda atau gejala kejadian trombotik dan tromboembolik terjadi, infus harus segera dihentikan dan segera lakukan tindakan diagnostik dan terapetik yang sesuai.

4. Efek samping yang mungkin terjadi

Seperti semua obat-obatan, FEIBA dapat menyebabkan efek samping meskipun tidak semua orang mengalaminya.

Efek samping umum (dapat terjadi pada 1 dari 10 orang)
Hipersensitivitas, sakit kepala, pusing, tekanan darah rendah, ruam, antibodi hepatitis B positif.

Efek samping dengan frekuensi yang tidak diketahui (frekuensi tidak bisa diperkirakan berdasarkan data yang ada)

Gangguan sistem limfatik dan darah: koagulopati konsumsi (DIC), peningkatan titer penghambat

Gangguan sistem kekebalan: Reaksi anafilaktik, urtikaria

Gangguan sistem saraf: rasa kebas di kaki atau tangan, sensasi berkurang atau tidak normal, strok, mengantuk, indera perasa terganggu

Gangguan jantung: serangan jantung (infark miokard), detak jantung meningkat

Gangguan pembuluh darah: pembentukan gumpalan darah yang terbawa ke dalam pembuluh darah, peningkatan tekanan darah, kemerahan

Gangguan pernafasan, dada dan mediastinal: obstruksi arteri paru, penyempitan saluran nafas, mengi, batuk, sulit bernafas.

Gangguan saluran pencernaan: muntah, diare, perut tidak nyaman, mual

Gangguan kulit dan jaringan bawah kulit: rasa kebas di wajah, pembengkakan di wajah, lidah dan bibir, urtikaria, gatal-gatal.

Gangguan umum dan kelihan di tempat injeksi: nyeri di tempat injeksi, rasa tidak enak badan, rasa panas, menggigil, demam, nyeri dada dan rasa tidak nyaman di dada.

Investigasi: penurunan tekanan darah,

Infus intravena cepat dapat menyebabkan nyeri ditusuk dan rasa kebas di wajah, lengan dan kaki, serta penurunan tekanan darah.

Infark miokard diamati terjadi setelah pemberian di atas dosis harian maksimum dan atau pemberian yang diperpanjang dan/atau adanya faktor risiko untuk tromboembolisme.

Pelaporan efek samping
Jika Anda mengalami efek samping, sampaikan kepada Dokter Anda. Ini mencakup setiap kemungkinan efek samping yang tidak tercantum dalam brosur ini. Dengan melaporkan efek samping yang Anda alami, Anda dapat membantu memberikan informasi lebih lanjut tentang keamanan obat ini.

5. Bagaimana cara menyimpan FEIBA 50 U/mL

Simpan obat ini di tempat yang aman dan jauhkan dari jangkauan anak-anak.

Jangan disimpan di atas 25^{o}C. Jangan dibekukan.
Simpan di dalam kemasan aslinya untuk melindunginya dari cahaya.
Jangan gunakan FEIBA setelah tanggal kadaluarsa yang ada di dus atau label produk.
Obat tidak boleh dibuang melalui saluran pembuangan rumah tangga. Tanyakan apoteker anda tentang bagaimana membuang obat yang sudah tidak digunakan. Hal ini akan membantu melindungi lingkungan.

6. Isi kemasan FEIBA 50 U/mL dan informasi lainnya

Isi kemasan FEIBA 50 U/mL

Serbuk:
- Zat aktif FEIBA adalah aktivitas pemintas inhibitor faktor VIII.
- Setelah dilarutkan, 1 mL mengandung 50 Unit (U) *factor VIII inhibitor bypassing activity*.
- FEIBA 50 U/mL tersedia dalam 3 sediaan berbeda:
    - Sediaan FEIBA yang mengandung 500 U *factor VIII inhibitor bypassing activity* dalam 200-600 mg protein plasma.
    - Sediaan FEIBA yang mengandung 1000 U *factor VIII inhibitor bypassing activity* dalam 400-1200 mg protein plasma.
    - Sediaan FEIBA yang mengandung 2500 U *factor VIII inhibitor bypassing activity* dalam 1000-3000 mg protein plasma.

  FEIBA juga mengandung faktor II, IX dan X, utamanya dalam bentuk yang tidak teraktivasi, serta faktor VII teraktivasi. Selain itu antigen koagulasi faktor VIII dan faktor-faktor dalam sistem kallikrein-kinin ada dalam jumlah yang sangat kecil, bila ada.

- Kandungan lainnya adalah natrium klorida dan natrium sitrat

Pelarut

- Air untuk injeksi

Tampilan FEIBA 50 U/mL dan isi kemasan

Produk ini disajikan dalam bentuk serbuk beku kering atau padatan rapuh warna putih sampai putih pucat atau hijau pucat. Nilai pH larutan siap pakai adalah antara 6,8 dan 7,6.
Serbuk dan pelarut tersedia dalam vial gelas dengan penutup sumbat karet.

Kemasan yang tersedia:

- Dus, 1 vial serbuk @ 500 U + 1 vial WFI @ 10 mL + 1 *disposable syringe* + 1 *disposable needle* + 1 *butterfly needle* + 1 Baxject II Hi-Flow. DKIXXXXXXXXXX
- Dus, 1 vial serbuk @ 1000 U + 1 vial WFI @ 20 mL + 1 *disposable syringe* + 1 *disposable needle* + 1 *butterfly needle* + 1 Baxject II Hi-Flow. DKIXXXXXXXXXX
- Dus, 1 vial serbuk @ 2500 U + 1 vial WFI 50 mL + 1 *disposable syringe* + 1 *disposable needle* + 1 *butterfly needle* + 1 Baxject II Hi-Flow. DKIXXXXXXXXXX

Kemasan berisi:

- 1 vial dengan FEIBA 500 U/1000 U/2500 U serbuk untuk larutan infus
- 1 vial dengan 10 ml/20 ml/50 ml Air untuk Injeksi
- 1 BAXJECT II Hi-Flow untuk rekonstitusi
- 1 syringe sekali pakai
- 1 jarum sekali pakai
- 1 jarum kupu-kupu

Dibuat oleh: Takeda Manufacturing Austria AG, Vienna, Austria
Pemegang ijin edar: PT. Wigo Health Indonesia, Semarang, Indonesia
HARUS DENGAN RESEP DOKTER