FEIBA NF

Powder and solvent for solution for injection

Factor VIII Inhibitor Bypassing Activity

ABBREVIATED PRESCRIBING INFORMATION

(Before prescribing, please consult the full Prescribing Information)

Active Ingredient: Human Plasma Protein with a Factor Eight Inhibitor Bypassing Activity
500 U (200 – 600 mg), 1000 U (400 – 1200 mg)

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 NF was successfully used in a patient with an inhibitor, suffering from von Willebrand's disease. FEIBA NF 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.

Posology and Method of Administration: The dosage and duration of the therapy depend on the severity of the disorder of haemostasis, on the location and extent the bleeding and on the clinical condition of the patient. Dosage is independent of 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 to 100 U of FEIBA NF 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. FEIBA NF 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: Hypersensitivity to the product, disseminated intravascular coagulation (DIC) and myocardial infarction, acute thrombosis and/or embolism.

Warnings and Precautions: Thromboembolic events, including disseminated intravascular coagulation (DIC), venous thrombosis, pulmonary embolism, myocardial infarction, and stroke, have occurred in the course of treatment with FEIBA NF. Thrombotic microangiopathy (TMA) has not been reported in FEIBA clinical studies. Cases of TMAs were reported in an emicizumab clinical trials where subjects received FEIBA as part of a treatment regimen for breakthrough bleeding.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. FEIBA NF can precipitate allergic-type hypersensitivity reactions; 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 NF administration should be stopped and medical care initiated as appropriate. Appropriate vaccination (against hepatitis A and B) should be considered for patients in regular/ repeated receipt of plasma derived products including FEIBA NF. *In vitro* tests to control efficacy such as aPTT, whole blood clotting time (WBCT), and thromboelastogramme (TEG) may not correlate with the clinical improvement.

Interactions: 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 NF. Therefore, antifibrinolytics should not be used for approximately 6 to 12 hours after the administration of FEIBA NF. 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 possible drug interaction may exist with emicizumab when FEIBA was used as part of a treatment regimen for breakthrough bleeding.

Fertility, Pregnancy and Lactation: Physicians should balance the potential risks and only prescribe FEIBA NF 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.

Effects on Ability to Drive and Use Machines: There is no information of the effects of FEIBA NF on the ability to drive or operate on automobile or other heavy machinery.

Undesirable Effects:

Common (≥ 1/100 - < 1/10)	Hypersensitivity, Dizziness, Headache, Hypotension, Rash, Hepatitis B surface antibody positive
Unknown	Increase of inhibitor titre (anamnestic response), Somnolence, Dysgeusia, Dyspnoea, Nausea, Chills, Pyrexia, Chest pain, Chest discomfort

Overdosage: 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.

Name and Address of Marketing Authorisation (MA) Holder:

Shire Singapore Pte Ltd
8 Marina Boulevard, #15-01
Marina Bay Financial Centre, Tower 1
Singapore 018981

Date of Preparation of the API: 06 August 2019