100 mm

280 mm

For the use of a Registered Medical Practitioner or a Hospital only.
Human Coagulation Factor IX I.P. 600 I.U.

FACTOCEL™ IX
600 IU

Manufactured from human plasma.

फेक्टोसेल™ IX
600 IU

For Intravenous Use Only

PRODUCT DESCRIPTION
FACTOCEL IX is a sterile, lyophilized concentrate of coagulation Factor IX. It is prepared from large pools of the human plasma obtained from healthy donors. The reconstituted solution of 5 mL containing 600 IU of Factor IX is intended for intravenous use only.

The Factor IX potency is expressed in International Units (IU) as determined using an *in vitro* one stage clotting assay that is calibrated against the international standard for Factor IX concentrate from World Health Organization (WHO).

PRODUCT SAFETY
Collected blood plasma used for the manufacturing of FACTOCEL IX, is screened for multiple infectious diseases. In addition to serology based screening of individual plasma units and plasma pools for HBsAg, HCV antibodies, HIV I & II antibodies, the individual donor units and pooled plasma are also tested for viral markers like HBV, HIV & HCV by NAT procedure as recommended by regulatory authorities.

The manufacturing procedure incorporates two dedicated orthogonal virus clearance steps ensuring viral safety of the product. This includes solvent detergent treatment and virus retentive filtration. The use of 20 nm virus retentive filter provides additional safety against small non-enveloped adventitious virus.

The drug product is also tested for viral markers like HBV, HIV & HCV. Multiple chromatography steps have been incorporated for assurance of product safety. The process parameters, characterizations and final product quality are designed such, that they meet the regulatory requirements. FACTOCEL IX contains no preservative and is free from blood group antibodies.

Abbreviation: HIV: Human Immunodeficiency Virus; HCV: Hepatitis C Virus; HBsAg: Hepatitis B surface antigen; HBV: Hepatitis B Virus; RNA: Ribose Nucleic Acid; NAT: Nucleic Acid Test.

COMPOSITION
Each vial contains:

Factor IX	600 IU
Sodium Citrate	20.0 mg
Sodium Chloride	40.0 mg
Total Protein	NMT 15 mg

Formulation does not contain preservatives

CLINICAL PHARMACOLOGY
Human Coagulation Factor IX is used to treat Hemophilia B (Christmas disease) which is an X linked recessively inherited disorder for Factor IX synthesis. The insufficient and abnormal synthesis of the clotting Factor IX causes defects in blood coagulation.

Factor IX is a vitamin K-dependant coagulation factor which is synthesized in the liver. The zymogen form of Factor IX is activated by Factor VIII/ tissue factor complex in extrinsic coagulation pathway and by Factor XIa in the intrinsic coagulation pathway. Factor IX in combination with Factor VIII activates Factor X. This process leads to conversion of prothrombin to thrombin. Thrombin then converts fibrinogen to fibrin resulting in clot formation.
The infusion of exogenous Factor IX to replace the deficiency present in Hemophilia B temporarily restores haemostatis and corrects the coagulation defect in patients.

INDICATIONS AND USAGE
Human coagulation Factor IX is indicated for treatment and prophylaxis of bleeding episodes in patients with Hemophilia B (Congenital Factor IX deficiency or Christmas disease).

DOSAGE AND ADMINISTRATION
FACTOCEL IX should always be administered intravenously only. It should be reconstituted with 5 mL of Sterile Water for Injection and administered within four hours of reconstitution. Do not refrigerate after reconstitution. After administration, any unused solution and the administration equipment should be discarded.

One International Unit (IU) of Factor IX activity is equivalent to the quantity of Factor IX in 1 mL of normal human plasma.

The calculation of the required dosage of Factor IX is based on the empirical formula where one international Unit (IU) of Factor IX per kg body weight raises the plasma Factor IX activity by 1 % of the normal activity.

The required dosage is determined using the following formula:
Required units = body weight (kg) x desired Factor IX rise (%) (IU/dL) x 0.8

The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case.
In case of the following haemorrhagic events, Factor IX activity should not go below the given plasma activity level (in % of normal) in the corresponding period.
The below mentioned table can be used to guide dosing in bleeding episodes and surgery:

Degree of haemorrhage / Type of surgical procedure	**Factor IX level required (%) (IU/dL)**	**Frequency of doses (hours) / Duration of therapy (days)**
Hemorrhage		
Early haemarthrosis, muscle bleeding or oral bleeding	20 - 40	Repeat every 24 hours. At least 1 day, until the bleeding episode as indicated by pain is resolved or healing is achieved.
More extensive haemarthrosis, muscle bleeding or haematoma	30 - 60	Repeat infusion every 24 hours for 3 - 4 days or more until pain and acute disability are resolved.
Life-threatening haemorrhages	60 - 100	Repeat infusion every 8 to 24 hours until threat is resolved.
Surgery		
Minor Surgery including tooth extraction	30 - 60	Every 24 hours, at least 1 day, until healing is achieved.
Major Surgery	80 – 100 (pre-and/ post-operative)	Repeat infusion every 8-24 hours until adequate wound healing, then therapy for at least another 7 days to maintain a Factor IX activity of 30% to 60% (IU/dL).

Prophylaxis
For long term prophylaxis against bleeding in patients with severe haemophilia B, the usual doses are 20 to 40 IU of Factor IX per kilogram of body weight at intervals of 3 to 4 days. In some cases, especially in younger patients, shorter dosage intervals or higher doses may be necessary.

Paediatric Population
In the study conducted in 25 children under 6 years of age, the median dose administered per exposure day was similar for prophylaxis and treatment of bleeding, i.e. 35 to 40 IU/kg Body Weight.

POSSIBLE SIDE EFFECTS:
Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the infusion site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) have been observed infrequently in patients treated with Factor IX-containing products. In some cases, these reactions have progressed to severe anaphylaxis, and they have occurred in close temporal association with development of Factor IX inhibitors.
Nephrotic syndrome has been reported following attempted immune tolerance induction in hemophilia B patients with Factor IX inhibitors and a history of allergic reaction. On rare occasions, fever has been observed.
Patients with haemophilia B may develop neutralising antibodies (inhibitors) to Factor IX. If such inhibitors occur, the condition will manifest as an insufficient clinical response. In such cases, it is recommended that a specialised haemophilia centre be contacted.

There is a potential risk of thromboembolic episodes following the administration of Factor IX products, with a higher risk for low purity preparations. The use of low purity Factor IX products has been associated with instances of myocardial infarction, disseminated intravascular coagulation, venous thrombosis and pulmonary embolism.

USE IN SPECIAL POPULATIONS
Pregnancy
Animal reproduction studies have not been conducted with FACTOCEL IX. It is also not known whether FACTOCEL IX can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. FACTOCEL IX should be given to a pregnant woman only if clearly needed.

CONTRAINDICATIONS
FACTOCEL IX is contraindicated in patients with hypersensitivity to the active substance or to any of the excipients.
It is also contraindicated in high risk of Disseminated intravascular coagulation (DIC) and/or hyperfibrinolysis or thrombosis.
Once these conditions have been checked through adequate diagnostic tests, human coagulation Factor IX should only be administered to treat life-threatening bleeding episodes.

WARNINGS & PRECAUTIONS
Allergic type of hypersensitivity reaction is possible as with any intravenous protein product. Patients should be informed of the early signs of hypersensitivity reactions including hives, generalized urticaria, tightness of the chest, wheezing, hypertension, and anaphylaxis. If these symptoms occur, they should be advised to discontinue use of the product immediately and contact their physician.
Because of the risk of allergic reactions with Factor IX products, the initial administration of Factor IX should be according to the treating physician's judgement and should be performed under medical observation where proper medical care for allergic reactions could be provided.

In case of shock, the current medical standards for shock treatment should be observed.

After repeated treatment with human coagulation Factor IX products, patients should be monitored for the development of neutralising antibodies (inhibitors) and should be quantified in Bethesda Units (BU) using appropriate biological testing.

In patients with a risk of thrombosis, (e.g. patients with a history of liver disease, thrombophilia, hypercoagulability states, angina pectoris, coronary disease or acute myocardial infarction or in premature newborns) Factor IX level should not be raised beyond 60% of normal.

During the course of treatment, determination of daily Factor IX level is advised to guide the dose to be administered and the frequency of repeated infusions. Individual patient may vary in their response to human coagulation Factor IX, achieving different level of *in vivo* recovery and demonstrating different half lives.

The listed warnings and precautions apply both to adults and children.

DRUG INTERACTIONS
No interaction of human coagulation Factor IX products with other medicinal products is known.

STORAGE
Store between +2ºC and +8ºC. Do not freeze.
After reconstitution, the product should be used within four hours. Store in an air tight container. Protect from light. Keep out of reach and sight of children.

EXPIRY
Three years from the date of manufacture. Do not use after expiry date.
Report suspected adverse reaction at: Hemofluidsafety@intaspharma.com
Date of preparation: 12-Oct-2021

Manufactured and Marketed by:
INTAS
INTAS PHARMACEUTICALS LTD.
Plot No. 496/1/A&B, Sarkhej-Bavla Highway,
Village: Matoda, Taluka: Sanand,
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AW-024-02

Front **Back**

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Department	QA	Production	Regulatory	Marketing	Medical	QA	QA
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Designation							

Product Name : Factocel IX Leaflet
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12.10.21

Colour Shade No. : Black
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Fold size : ~100 mm X ~35 mm

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GSM of Paper : 50 ± 10% gsm