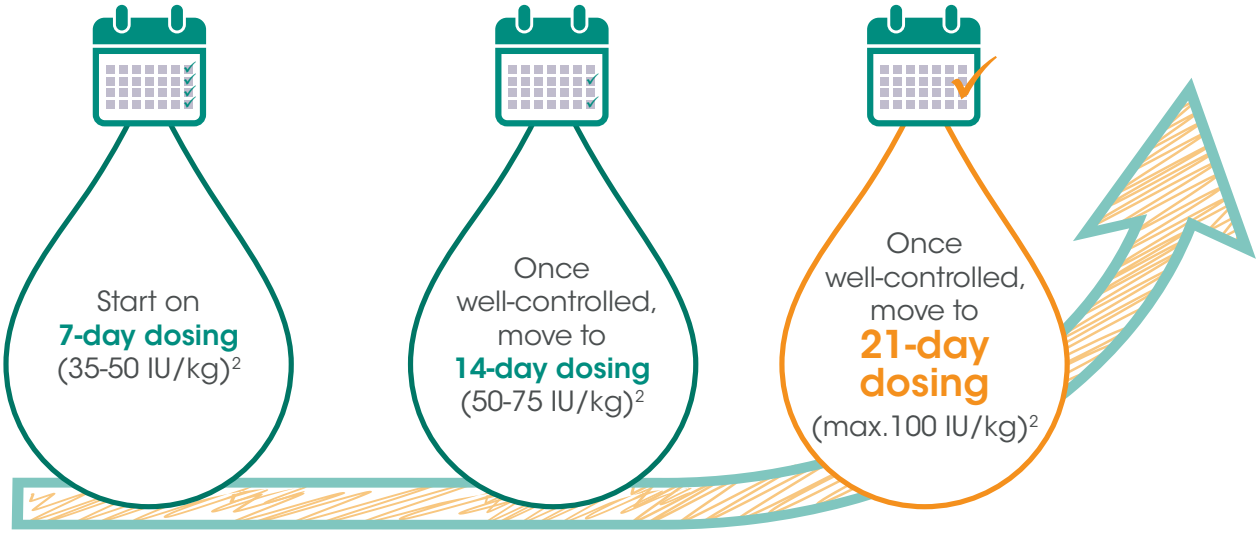
IDELVION®
Coagulation Factor IX (Recombinant), Albumin Fusion Protein

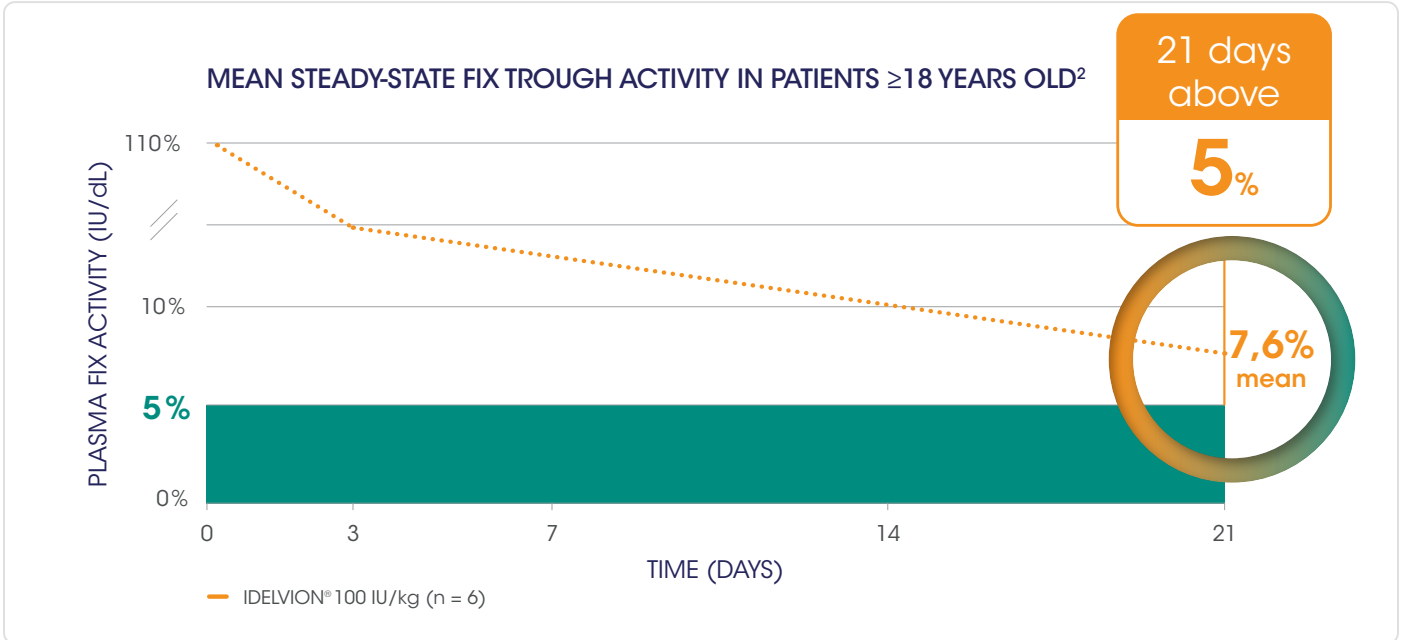
A FACTOR FOR A MORE JOYFUL LIFE

MORE FREEDOM from injections for your ADULT haemophilia B patients with up to 21-day dosing[1,2]



Extended protection with every injection[2]

A single dose keeps FIX levels above 5% for 21 days[2]



Adapted from Mancuso, M.E., et al., Thromb Haemost, 2020.[2]

Biotherapies for Life™ CSL Behring

IDELVION®
Coagulation Factor IX (Recombinant), Albumin Fusion Protein

A FACTOR FOR A MORE JOYFUL LIFE

A protection to count on, also with 21-day dosing[1, 2]

IDELVION® delivered consistent bleed protection on 7-, 14- and 21-day dosing regimens[2]

		7-DAY DOSING	14-DAY DOSING	21-DAY DOSING
Median	AsBR	0.00	0.37	**0.00**
	ABR	1.33	0.92	0.32
	AjBR	0.8	0.13	**0.00**
Mean	AsBR	1.3	1.24	0.60
	ABR	2.50	2.33	1.19
	AjBR	1.79	1.63	0.93

59 patients in total, FIX levels ≤2%, aged 13-63, 21-day dosing only for ≥18

AsBR annual spontaneous bleeding rate, ABR = annual bleeding rate, AjBR= annual joint bleeding rate

1. CSL Behring (02/2021). SPC Idelvion. **2.** Mancuso, M.E., et al., Long-term safety and efficacy of rIX-FP prophylaxis with extended dosing intervals up to 21 days in adults/adolescents with hemophilia B. J Thromb Haemost. 2020 May;18(5):1065-1074.

Name of the medicinal product: Idelvion 250 IU/ 500 IU/ 1000 IU/ 2000 IU/ 3500 IU, powder and solvent for solution for injection. Pale yellow to white powder and clear, colourless solvent for solution for injection.pH: 6,6 – 7,2. Osmolality: Idelvion 250 IU : 175 – 215 mOsm/kg ; Idelvion 500 IU/ 1000 IU/ 2000 IU/ 3500 IU: 260 – 300 mOsm/kg. **Qualitative and quantitative composition :** One vial contains nominally 250 IU/ 500 IU/ 1000 IU/ 2000 IU/ 3500 IU of recombinant fusion protein linking coagulation factor IX with albumin (rIX-FP),(INN=albutrepenonacog alfa). One ml Idelvion 250 IU/ 500 IU/ 1000 IU/ 2000 IU/ 3500 IU contains respectively 100 IU (250 IU/2,5ml) / 200 IU (500 IU/2,5ml) / 400 IU (1000 IU/2,5ml) / 400 IU (2000 IU/5ml) / 700 IU (3500 IU/5ml) albutrepenonacog alfa after reconstitution with 2.5 ml water for injections. The potency (IU) is determined using the European Pharmacopeia one stage clotting test. The specific activity of IDELVION is approximately 54 – 85 IU/mg protein. Albutrepenonacog alfa is a purified protein produced by recombinant DNA technology, generated by the genetic fusion of recombinant albumin to recombinant coagulation factor IX. The genetic fusion of the cDNA of human albumin to the cDNA of human coagulation factor IX enables the protein to be produced as a single recombinant protein and assures product homogeneity by avoiding chemical conjugation. The recombinant factor IX portion is identical to the Thr148 allelic form of plasma-derived factor IX. The cleavable linker between the recombinant factor IX and albumin molecules is derived from the endogenous "activation peptide" in native factor IX. IDELVION contains up to 8,6 mg sodium per vial, equivalent to 0,4% of the WHO recommended maximum daily intake of 2 g sodium for an adult. For the full list of excipients, see summary of product characteristics. **Therapeutic indications:** Treatment and prophylaxis of bleeding in patients with haemophilia B (congenital factor IX deficiency). IDELVION can be used for all age groups. **Posology:** Treatment should be under the supervision of a physician experienced in the treatment of haemophilia B. Previously untreated patients: The safety and efficacy of IDELVION in previously untreated patients have not yet been established. Treatment monitoring: During the course of treatment, appropriate determination of factor IX levels is advised to guide the dose to be administered and the frequency of repeated infusions. Individual patients may vary in their responses to factor IX, demonstrating different half-lives and recoveries. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor IX activity) is indispensable. When using an *in vitro* thromboplastin time (aPTT)-based one stage clotting assay for determining Factor IX activity in patients' blood samples, plasma factor IX activity results can be significantly affected by both the type of aPTT reagent and the reference standard used in the assay. Measurement with a one-stage clotting assay using a kaolin based aPTT reagent or Actin FS aPTT reagent will likely result in an underestimation of activity level. This is of importance particularly when changing the laboratory and/or reagents used in the assay. Posology Dose and duration of the substitution therapy depend on the severity of the factor IX deficiency, on the location and extent of the bleeding and on the patient's clinical condition. The number of units of factor IX administered is expressed in International Units (IU), which are related to the current WHO standard for factor IX products. Factor IX activity in plasma is expressed either as a percentage (relative to normal human plasma) or in International Units (relative to an International Standard for factor IX in plasma). One International Unit (IU) of factor IX activity is equivalent to that quantity of factor IX in one ml of normal human plasma. *On demand treatment:* The calculation of the required dose of factor IX is based on the empirical finding that 1 IU factor IX per kg body weight raises the plasma factor IX activity by an average of 1.3 IU/dl (1.3 % of normal activity) in patients ≥ 12 years of age and by 1.0 IU/dl (1.0 % of normal activity) in patients < 12 years of age. The required dose is determined using the following formulae: Required dose (IU) = body weight (kg) x desired factor IX rise (% of normal or IU/dl) x {reciprocal of observed recovery (IU/kg per IU/dl)} Expected factor IX rise (IU/dl or % of normal) = Dose (IU) x Recovery (IU/dl per IU/kg)/body weight (kg) The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case. Patients < 12 years of age: For an incremental recovery of 1 IU/dl per 1 IU/kg, the dose is calculated as follows: Required dose (IU) = body weight (kg) x desired factor IX rise (IU/dl) x 1 dl/kg. Example: - A peak level of 50 % of normal is required in a 20 kg patient with severe haemophilia B. The appropriate dose would be 20 kg x 50 IU/dl x 1 dl/kg = 1000 IUs. - A dose of 1000 IUs of IDELVION, administered to a 25 kg patient, should be expected to result in a peak post-injection factor IX increase of 1000 IUs/25 kg x 1.0 (IU/dl per IU/kg) = 40 IU/dl (40 % of normal). Patients ≥ 12 years of age: For an incremental recovery of 1.3 IU/dl per 1 IU/kg, the dose is calculated as follows: Required dose (IU) = body weight (kg) x desired factor IX rise (IU/dl) x 0.77 dl/kg. Example: - A peak level of 50 % of normal is required in a 80 kg patient with severe haemophilia B. The appropriate dose would be 80 kg x 50 IU/dl x 0.77 dl/kg = 3080 IUs. - A dose of 2000 IUs of IDELVION, administered to a 80 kg patient, should be expected to result in a peak post-injection factor IX increase of 2000 IUs x 1.3 (IU/dl per IU/kg) /80 kg = 32.5 IU/dl (32.5 % of normal). In the case of the following haemorrhagic events, the factor IX activity should not fall below the given plasma activity level (in % of normal or in IU/dl) in the corresponding period. The following 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);** Haemorrhage: Minor or moderate Haemarthrosis, muscle bleeding (except iliopsoas) or oral bleeding - 30 – 60 - Single dose should be sufficient for majority of bleeds. Maintenance dose after 24 – 72 hours if there is further evidence of bleeding. Major haemorrhage: Life threatening haemorrhages, deep muscle bleeding including iliopsoas - 60 – 100 - Repeat every 24 – 72 hours for the first week, and then maintenance dose weekly until bleeding stops and healing is achieved. Minor surgery: Including uncomplicated tooth extraction -50 – 80 (pre- and postoperative) - Single dose may be sufficient for a majority of minor surgeries. If needed, maintenance dose can be provided after 24 – 72 hours until bleeding stops and healing is achieved. Major surgery: 60 – 100 (pre- and postoperative) Repeat every 24 – 72 hours for the first week, and then maintenance dose 1 – 2 times per week until bleeding stops and healing is achieved. *Prophylaxis* For long-term prophylaxis against bleeding in patients with severe hemophilia B, the usual doses are 35 to 50 IU/kg once weekly. Some patients who are well-controlled on a once-weekly regimen might be treated with up to 75 IU/kg on an interval of 10 or 14 days. For patients >18 years, further extension of the treatment interval may be considered (see summary of product characteristics). In some cases, especially in younger patients, shorter dose intervals or higher doses may be necessary. After a bleeding episode during prophylaxis, patients should maintain their prophylaxis regimen as closely as possible, with 2 doses of IDELVION being administered at least 24 hours apart but longer as deemed suitable for the patient. *Paediatric population* For long term prophylaxis the recommended dose regimen is 35 to 50 IU/kg once weekly (see summary of product characteristics). For adolescents of 12 years of age and above, the dose recommendations are the same as for adults. **Method of administration:**Intravenous use. The reconstituted preparation should be injected slowly intravenously at a rate comfortable for the patient up to a maximum of 5 ml/min. For instructions on reconstitution of the medicinal product before administration, see summary of product characteristics. **Contraindications:** Hypersensitivity to the active substance or to any of the listed excipients. Known allergic reaction to hamster protein. **Undesirable effects:** Summary of the safety profile: 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 rarely and may in some cases progress to severe anaphylaxis (including shock). In some cases, these reactions have progressed to severe anaphylaxis, and they have occurred in close temporal association with development of factor IX inhibitors (see also summary of product characteristics). Nephrotic syndrome has been reported following attempted immune tolerance induction in haemophilia B patients with factor IX inhibitors and a history of allergic reaction. Very rarely development of antibodies to hamster protein with related hypersensitivity reactions has been observed. Patients with haemophilia B may develop neutralising antibodies (inhibitors) to factor IX. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response. In such cases, it is recommended that a specialised haemophilia centre be contacted. Inhibitor development was reported in an ongoing clinical study with previously untreated patients. Inhibitor development has been observed in previously treated patients in the post-marketing experience with IDELVION. 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. The use of high purity factor IX is rarely associated with such adverse reactions. Tabulated list of adverse reactions: The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level). The table lists adverse reactions that were reported in clinical trials and/or were identified in post-marketing use. Frequencies have been evaluated 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), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. *Blood and lymphatic disorders:* not known: FIX inhibition/I-inhibitor development; *Immune system disorders:* uncommon: hypersensitivity; *Nervous system disorders:* common: headache – common: dizziness; *Skin and subcutaneous tissue disorders:* uncommon: rash, eczema; *General disorders and administration site conditions:* common: injection site reactions. Description of selected adverse reactions: One previously untreated patient (PUP) from the ongoing clinical study developed high titre inhibitor against factor IX. There are insufficient data to provide information on inhibitor incidence in PUPs. Paediatric Population: Frequency, type and severity of adverse reactions in children are expected to be similar as in adults. Reporting of suspected adverse reactions Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Federal agency for medicines and health products – Department Vigilance - EUROSTATION II – Mailbox 97 - B-1000 Brussels, Madou - Website: www.fagg.be e-mail: adversedrugreactions@fagg-afmps.be **Marketing authorisation holder**: CSL Behring GmbH, Emil-von-Behring Straße 76, D-35041 Marburg, Duitsland – Idelvion 250 IU EU/1/16/1095/001 – Idelvion 500 IU EU/1/16/1095/002 – Idelvion 1000 IU EU/1/16/1095/003 – Idelvion 2000 IU EU/1/16/1095/004 **On medical prescription**. **Date of revision of the text:** 02/2021

BEL-IDL-0034 march 2022. R.E.: P. Reygaert, Bedrijvenlaan 11 - 2800 Mechelen

Biotherapies for Life™ CSL Behring