



ספטמבר 2020

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רופא/ה, רוקח/ת נכבד/ה,
ברצוננו להודיעך על עדכון בעלון לרופא של :
BENEFIX 250 IU/VIAL 120-55-30121-00
BENEFIX 500 IU/VIAL 120-56-30122-00
BENEFIX 1000 IU/VIAL 120-57-30123-01
BENEFIX 2000 IU/VIAL 142-66-31926-00

Indications:

Benefix is indicated for the control and prevention of hemorrhagic episodes in patients with hemophilia B (congenital factor IX deficiency or Christmas disease), including control and prevention of bleeding in surgical settings, in previously treated patients (PTP) and previously untreated patients (PUP).

Benefix is not indicated for the treatment of other factor deficiencies (e.g. factors II, VII, and X) nor for the treatment of hemophilia A patients with inhibitors to factor VIII, nor for the reversal of coumarin-induced anticoagulation, nor for the treatment of bleeding due to low levels of liver-dependent coagulation factors.

להלן העדכונים העיקריים בעלון לרופא:

6. Adverse reactions

The most common adverse reactions observed in clinical trials [frequency > 5% of previously treated patients (PTPs) or previously untreated patients (PUPs)] were **fever, cough**, headaches, dizziness, nausea, injections site reaction, injection site pain and skin-related hypersensitivity reactions (e.g., rash, hives).

8.1 pregnancy

Risk Summary

There are no data with BeneFIX use in pregnant women to inform a drug-associated risk. Animal reproduction studies have not been conducted with BeneFIX. It is not known whether BeneFIX can affect reproductive capacity or cause fetal harm when given to pregnant women.

In the U.S. general population, the estimated background risk of major birth defect and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

~~There is no information available on the effect of factor IX replacement therapy on labor and delivery. Use only if needed.~~

There is no information regarding the presence of BeneFIX in human milk, the effect on the breastfed infant, and the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BeneFIX and any potential adverse effects on the breastfed child from BeneFIX or from the underlying maternal condition.

8.4 Pediatric Use

Safety, efficacy, and pharmacokinetics of BeneFIX have been evaluated in previously treated (PTP) and previously untreated pediatric patients (PUP) [see *Clinical Studies (14) and Adverse Reactions (6)*]. On average, lower recovery, **shorter half-life and higher clearance (based on kg body weight)** have been observed in children younger than ~~45~~ **12** years old [see *Clinical Pharmacology (12.3)*]-Dose adjustment may be needed [see *Dosage and Administration (2.1)*].

12.3 Pharmacokinetics

A population pharmacokinetic model was developed using data collected in patients aged 7 months to 60 years who received single doses of BeneFIX ranging from 50 to 75 IU/kg. The parameters estimated using the final 2-compartment model are shown in Table 5. Infants and children had higher clearance, larger volume of distribution, shorter half-life and lower recovery than adolescents and adults.

Table 8: Mean \pm SD Pharmacokinetic Parameters Derived from Population Pharmacokinetic Analysis

Age Group	Infants (<2 years)	Children		Adolescents and Adults (≥ 12 years)
		2 to <6 yr	6 to <12 yr	
Number of subjects	7	16	1	43
Clearance (mL/h/kg)	13.1 \pm 2.1	13.1 \pm 2.8	15.5	8.4 \pm 2.4
Vss (mL/kg)	252 \pm 35	257 \pm 25	303	229 \pm 57
Half-life (h)	15.6 \pm 1.2	16.7 \pm 1.9	16.3	23.1 \pm 4.4
Recovery (IU/dL per IU/kg)	0.61 \pm 0.10	0.60 \pm 0.08	0.47	0.72 \pm 0.19

Abbreviations: SD = standard deviation; Vss = volume of distribution at steady-state

השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה.

העלונים לרופא ולצרכן נשלחו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:
<https://data.health.gov.il/drugs/index.html#!/byDrug>

לחילופין, לקבלת עלון מלא מודפס ניתן לפנות לחברת פייזר פי אף אי פרמצבטיקה ישראל בע"מ, רח' שנקר 9, ת.ד. 12133 הרצליה פיתוח, 46725.

בברכה,
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