

# Safety and Efficacy of a New High Purity Factor X Concentrate in Subjects with Factor X Deficiency Undergoing Surgery

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## Introduction

Severe factor X deficiency is a rare (1:~1,000,000) and potentially life-threatening bleeding disorder. Replacement therapy for factor X deficiency is currently treated with fresh-frozen plasma (FFP), prothrombin complex concentrates (PCCs) or, in some countries, a factor IX/X concentrate. No specific licensed replacement therapy exists.

**BPL FACTOR X** is the first high-purity plasma-derived factor X concentrate designed specifically for treatment of hereditary factor X deficiency.

Key features:

- small infusion volume high potency FX (100 IU/mL)
- high purity: >100 IU factor X/mg protein
- room temperature storage (< 30°C / 86°F)
- rapid reconstitution
- 3 dedicated virus inactivation steps

## Methods

Safety and efficacy of **BPL FACTOR X** in surgery has been assessed in 2 clinical studies in patients with hereditary factor X deficiency. Interim data are presented.

<b>Patient population</b>	<ul style="list-style-type: none"> <li>• Severe to mild FX deficiency (basal FX:C &lt;20 IU/dL) with a history of bleeding spontaneously or following surgery</li> <li>• Aged ≥ 12 years</li> </ul>
<b>Study objectives</b>	<ul style="list-style-type: none"> <li>• Safety and efficacy in preventing excessive bleeding during major or minor surgery</li> </ul>
<b>Study design</b>	<ul style="list-style-type: none"> <li>• Pre-surgery: doses given to raise FX:C levels to 70-90 IU/dL pre-surgery</li> <li>• Post-surgery: doses to maintain levels at &gt;50 IU/dL post-surgery until no longer at risk of bleeding due to the procedure.</li> </ul>
<b>Efficacy assessments</b>	<ul style="list-style-type: none"> <li>• Investigator's overall assessment of <b>BPL FACTOR X</b>, incorporating: <ul style="list-style-type: none"> <li>– volume of blood loss during surgery</li> <li>– requirement for blood transfusion</li> <li>– number of post-operative bleeding episodes</li> <li>– Hb pre-operatively, within 2 h post-operatively and at discharge (measured centrally)</li> </ul> </li> </ul>
<b>Safety assessments</b>	<ul style="list-style-type: none"> <li>• Checks for <b>excessive bleeding</b></li> <li>• <b>FX inhibitors</b>, using a FX inhibitor screen and Nijmegen-Bethesda assay, at Baseline and at Discharge</li> <li>• <b>Virology assessments</b> for HAV, HBV, HCV, HIV and Parvovirus B19 at Baseline and at Discharge</li> <li>• <b>Physical examination &amp; clinical laboratory measurements</b> performed at Baseline and at Discharge</li> <li>• <b>Vital signs</b> measured pre- and post-infusion</li> <li>• Any adverse changes at physical examination or infusion sites assessments, or spontaneously-reported untoward medical occurrences, were reported as <b>adverse events</b>.</li> </ul>

## Results – Surgical Procedures

Subject #	Severity of subject's FX deficiency	Procedure	Treatment duration (days)	Factor X total exposure (IU/kg)
<b>Major procedures</b>				
1	mild	Left knee replacement	15	151.9
1	mild	Right knee replacement	13	210.1
2	mild	Coronary artery bypass graft	10	209.4
2	mild	6 x tooth extraction	1	44.6
<b>Minor procedures</b>				
3	severe	Tooth extraction	1	51.4
4	moderate	2 x tooth extraction	1	45.0

## Results – Safety

### Excessive Bleeding

There were no cases of excessive bleeding. There were no surgical or bleeding complications.

### Inhibitors

All results were negative.

### Virology

There were no seroconversions in any patients.

### Clinical Laboratory Measurements

There were no clinically significant trends in any parameters, apart from clinically significant low levels of Hb and Hct in 1 patient undergoing 2 x tooth extraction.

### Adverse Events

There were no serious adverse reactions or suspected hypersensitivity reactions.

There were no adverse events considered to be related to study drug.

## Results – Efficacy

There were no blood transfusions required and no post-operative bleeding episodes following any surgical procedure.

Subject #	Procedure	Factor X incremental recovery (IU/dL per IU/kg)	Expected blood loss <sup>§</sup> (mL)	Estimated actual blood loss (mL)	Range in post-dose plasma FX:C (IU/mL)	Hb pre-dose, post-operatively & at discharge (g/dL)	Investigator's assessment of efficacy
<b>Major procedures</b>							
1	Left knee replacement	2.21	150	150	0.34 – 1.32*	16.5, 15.3, 10.2	Excellent
1	Right knee replacement	1.8	50	50	0.43 – 0.97*	15.4, 15.5, 12.3	Excellent
2	Coronary artery bypass graft	2.27	750	402	0.14 – 0.82*	16.2, 12.6, 11.4	Excellent
2	6 x tooth extraction	2.27	40	40	0.29 – 0.77*	15.0, 14.9, 14.8	Excellent
<b>Minor procedures</b>							
3	Tooth extraction	2.34	10	10	1.14 – 1.23	15.2, ND, 15.0	Excellent
4	2 x tooth extraction	1.67	300	100	1.07 – 1.23	12.7, 11.1, 11.5	Excellent

<sup>§</sup> In a patient without a bleeding disorder undergoing a similar procedure.

\* In both subjects plasma factor X levels were maintained lower than 50 IU/dL, due to history of coronary artery disease. ND Not done

## Results – Demography

Six surgical procedures were performed in 4 subjects:

Disease severity:	mild deficiency (5-<20 IU/dL): 2 patients moderate deficiency (1-<5 IU/dL): 1 patient severe deficiency (<1 IU/dL): 1 patient
Gender:	1 female, 3 males.
Age:	median (range): 45 (15 to 59) years

## Conclusions

**BPL FACTOR X** was well tolerated, and effective in preventing bleeding and achieving haemostasis in both major and minor surgeries in patients with factor X deficiency. There was no excessive bleeding, no blood transfusions were required, and no bleeding or clotting complications were observed in any of the surgical procedures.

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