patients with inhibitors.

F. Cases of surgery in high-responder haemophilia patients.


Vasc Health Risk Manag

haemostatic cover of rFVIIa in a severe haemophilia patient with a high-titre inhibitor: a case report and literature review of rFVIIa use in major surgeries.

J Cardiothorac Vasc Anaesth

Blood Coagul Fibrinolysis

Haemophilia

with inhibitors, with special emphasis on orthopaedics: Madrid experience.

Haemophilia


38.

37.


Blood Rev

factor VII formulation and a new robust 25°C stable formulation.

Haemophilia

Haemost

for their management on behalf of the UKHCDO.

Blood Transfus

References

BMC Res Notes

2013;60(7):1178-1183.


32. 2010;8:(3)149-154.


38. 2010;16:54-60.


42. 2010;16:902-909.

43. 2009;13(9):1429-1435.

44. 2010;16:84-88.


NAME: EXPERTS IN BBP INictericium


Neufeld EJ, Négrier C, Arkhammar P, et al. MASAC recommendations concerning products licensed for the treatment of hemophilia and other

Orphanet J Rare Dis

Nurden AT. Glanzmann thrombasthenia.

Haemophilia

α

− 0.2% in CHwI, 4% in AH, <0.2% in GT

• Low rate of thrombotic events based on clinical trials and registry data1

Addressing bleeds, whenever they occur

•  Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia

•  Treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with

transfusions, with or without antibodies to platelets

THANKS TO THE DOCTORS, NURSES, NURSE PRACTITIONERS, TECHNICIANS, AND ALL OTHER HEALTHCARE PROVIDERS WHO ARE PROVIDING CARE TO PEOPLE WITH HEMOPHILIA.

Please see additional Important Safety Information throughout.

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IN THE REAL WORLD kids will be kids. Accidents happen to everyone. Life takes unexpected turns. IN THE REAL WORLD our lives are BUILT ON TRUST. Trust in ourselves. Trust in the many decisions we have to make. Trust in those who care for us. IN THE REAL WORLD we are not numbers. We are the sum of our EXPERIENCE. And for patients with bleeding disorders, TRUST COMES FROM EXPERIENCE.
NovoSeven® RT: Experience where it matters

Addressing bleeds, whenever they occur

A well-established safety profile
• Low rate of thrombotic events based on clinical trials and registry data
  – 0.2% in CHwI, 4% in AH, <0.2% in GT

Not made from human serum or human proteins

Proven effective for bleed resolution and surgery across 4 indications
• CHAwI or CHBwI, AH, GT, and CFVIId

Able to quickly treat bleeds when they occur
• Rapid administration and infusion, leading to rapid activity

With NovoSeven® RT, the experience continues
• >30 years of clinical experience

Indications and Usage
NovoSeven® RT (coagulation Factor VIIa, recombinant) is a coagulation factor indicated for:
• Treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with inhibitors, congenital Factor VII (FVII) deficiency, and Glanzmann’s thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets
• Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia

Important Safety Information

WARNING: THROMBOSIS
• Serious arterial and venous thrombotic events following administration of NovoSeven® RT have been reported
• Discuss the risks and explain the signs and symptoms of thrombotic and thromboembolic events to patients who will receive NovoSeven® RT
• Monitor patients for signs or symptoms of activation of the coagulation system and for thrombosis

b请参阅有关出血障碍的额外重要安全信息。

EMILY has GT
CHASE has CHAwI
HENRY has AH
BARBARA has CFVIId

*Suggested for bleed control and surgery in 4 bleeding disorders.*

Please see accompanying Prescribing Information, including Boxed Warning.

CHwI=congenital hemophilia with inhibitors; CHAwI=congenital hemophilia A with inhibitors; CHBwI=congenital hemophilia B with inhibitors; AH=acquired hemophilia; CFVIId=congenital factor VII deficiency; GT=Glanzmann’s thrombasthenia.

Indications and Usage
NovoSeven® RT (coagulation Factor VIIa, recombinant) is a coagulation factor indicated for:
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b Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
I AM GLAD NOVOSEVEN® RT IS ALONGSIDE ME AS I RACE

CHASE, 6 years old, loves anything that has to do with cars and likes to play in the park. Chase lives with congenital hemophilia A with inhibitors.

Important Safety Information
Warnings and Precautions
• Serious arterial and venous thrombotic events have been reported in clinical trials and postmarketing surveillance

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
NovoSeven® RT is there for your patients when bleeds happen

A well-established safety profile, with >30 years of clinical experience

Clinical trials

0.2%

Occurrence of thrombotic events in CHwI

MASAC recommends rFVIIa to treat acute bleeds in patients with congenital hemophilia A with inhibitors taking emicizumab prophylaxis:
- NovoSeven® RT was used to treat bleeds in 34 patients
- No cases of TMA or TE were observed with use of NovoSeven® RT alone
- Two cases of TMA occurred in patients receiving FEIBA and NovoSeven® RT. Simultaneous use of NovoSeven® RT and FEIBA should be avoided.

MASAC=Medical and Scientific Advisory Council; rFVIIa=recombinant activated factor VII; TE=thrombotic event; TMA=thrombotic microangiopathy.

Important Safety Information

Warnings and Precautions (cont’d)
- Patients with congenital hemophilia receiving concomitant treatment with aPCCs (activated prothrombin complex concentrates), older patients particularly with acquired hemophilia and receiving other hemostatic agents, and patients with a history of cardiac and vascular disease may have an increased risk of developing thrombotic events

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
Proven trial results and real-world experience

**Effective bleed control** in congenital hemophilia A or B with inhibitors

- **93%** efficacy seen in adept™<sup>a</sup>,<sup>b</sup> all bleed locations at 12 hours
  - One of the largest clinical trials conducted in patients with CHwI
  - Comparable efficacy seen in joint, mucocutaneous, muscle, and other bleeding episodes
- **98%** effective bleed control in patients ≤18 years, based on real-world experience<sup>c</sup>

**Hemostasis was achieved with a median of 2 doses<sup>9</sup>**

- Median 2 doses
  - A median of 2 doses helped control joint bleeds in as little as 5 hours<sup>9</sup>,<sup>a</sup>
- Maximum activity
  - NovoSeven<sup>®</sup> RT achieved maximum activity within 5–10 minutes of infusion<sup>c</sup>,<sup>d</sup>

**Important Safety Information**

**Warnings and Precautions (cont’d)**

- Hypersensitivity reactions, including anaphylaxis, can occur with NovoSeven<sup>®</sup> RT. Patients with a known hypersensitivity to mouse, hamster, or bovine proteins may be at a higher risk of hypersensitivity reactions. Discontinue infusion and administer appropriate treatment when hypersensitivity reactions occur

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<sup>a</sup>Data from an international, multicenter, randomized, double-blind, active-controlled, confirmatory phase 3 trial of patients with hemophilia A or B with inhibitors (n=69). Primarily carried out in the home setting, all bleeds were treated, and each bleeding episode was randomized (3:2) to infuse either 1 to 3 doses of vaseplasg alfa (240 bleeding episodes, 89 mcg/kg) or 1 to 3 doses of NovoSeven<sup>®</sup> RT (227 bleeding episodes; 90 mcg/kg) when bleed symptoms were recognized, preferably within 2 hours of onset. Primary efficacy endpoint indicated effective bleed control defined as no additional hemostatic reaction (other than the original medication) given within 12 hours after the initial dose.<sup>9</sup>

<sup>b</sup>Data from a randomized, double-blind, parallel-group, multicenter study of patients with hemophilia A and B with and without an inhibitor (n=84). Patients were given NovoSeven<sup>®</sup> 35 or 70 mcg/kg at dosing intervals of 2 to 3 hours. Efficacy reflects the number of patients reporting excellent, effective, or partially effective results. Response was rated as “excellent” if patient demonstrated definitive relief of pain/tenderness and/or if there was a measurable decrease in the size of the bleed (or arrest of bleeding) in 8 hours or less. An “effective” response was measured by any of these 3 events occurring from 8 to 14 hours; a “partially effective” response either occurred after 14 hours or indicated detectable relief of pain/tenderness or decrease in size of the hemorrhage or if the bleeding had closed.<sup>10</sup>

<sup>c</sup>Data from a randomized, double-blind trial of healthy subjects (N=22) who received 1 intravenous bolus injection each of NovoSeven<sup>®</sup> RT and NovoSeven<sup>®</sup>. Both bolus injections were 90 mcg/kg and occurred 2 to 3 weeks apart at consecutive visits. While the comparison is not shown for FVIIa, activity for NovoSeven<sup>®</sup> RT was the bioequivalent range of that for NovoSeven<sup>®</sup> during this period.<sup>2</sup>

<sup>d</sup>FVIIa activity IU/mL.
The speed to control bleeds when they happen

Rapid infusion with less volume

• NovoSeven® RT has 16x less infusion volume than FEIBA\(^1,4\).

<table>
<thead>
<tr>
<th></th>
<th>NovoSeven® RT</th>
<th>FEIBA®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose (mcg/kg)</td>
<td>90</td>
<td>75</td>
</tr>
<tr>
<td>Volume (mL)</td>
<td>8</td>
<td>132</td>
</tr>
</tbody>
</table>

• NovoSeven® RT is up to 18x faster to infuse than FEIBA\(^1,4\).

Take control of acute bleeding episodes\(^a,b\)

• 90 mcg/kg every 2 hours until hemostasis is achieved\(^1\)
• For each patient, both the recommended dose of 90 mcg/kg and dosing interval can be adjusted based on the severity of bleeding until hemostasis is achieved\(^1\)

NovoSeven® RT has no maximum daily dose restrictions\(^1\)

**Important Safety Information**

Warnings and Precautions (cont’d)

• Factor VII deficient patients should be monitored for prothrombin time (PT) and factor VII coagulant activity (FVII:C). If FVII:C fails to reach the expected level, or PT is not corrected, or bleeding is not controlled after treatment with the recommended doses, antibody formation may be suspected and analysis for antibodies should be performed.

• Individual doses for a joint bleed are compared and based on an 88-kg (194 lb) person.

• Patients are cautioned that the maximum injection or infusion rate must not exceed 2 U/kg of body weight.

Please see additional Important Safety Information throughout.

Please see accompanying Prescribing Information, including Boxed Warning.
 USING NOVOSEVEN® RT

WAS THE RIGHT MOVE FOR ME

Important Safety Information
Warnings and Precautions (cont’d)

• Laboratory coagulation parameters (PT/INR, aPTT, FVII:C) have shown no direct correlation to achieving hemostasis

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
Early diagnosis and treatment are crucial in acquired hemophilia

Isolated, prolonged, aPTT in a patient with acute or recent-onset bleeding: a vital clue to acquired hemophilia12,13

Consult
When lab results show an unexplained, isolated, prolonged aPTT, consult a hematologist immediately12,13

Confirm
Delays in diagnosis and treatment put patients with acquired hemophilia at risk12,13.
In fact, AH is fatal in 1 out of 5 patients14.

Control the bleed with NovoSeven® RT

Important Safety Information
Adverse Reactions
• The most common and serious adverse reactions in clinical trials are thrombotic events. Thrombotic adverse reactions following the administration of NovoSeven® RT in clinical trials occurred in 4% of patients with acquired hemophilia and 0.2% of bleeding episodes in patients with congenital hemophilia.

NovoSeven® RT: The first and only bypassing agent FDA approved for AH

Recombinant safety supported by clinical trials

Using NovoSeven® RT first line improves efficacy18

Occurrence of thrombotic events
• Works at the site of vascular injury1,17
• Not made from human serum or human proteins1

Rapid access to treatment
• NovoSeven® RT can be infused in 2-5 minutes1
• Low-volume, flexible dosing for patients with AH1
  – 70-90 mcg/kg every 2-3 hours until hemostasis is achieved
• Room temperature stable up to 77°F1

Clinical trials
4%
95% effective
80% effective

First-line treatment
Salvage therapy

• An international consensus recommends the use of NovoSeven® RT as first-line treatment for acquired hemophilia12

Using NovoSeven® RT first line improves efficacy18

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
19 years old, lives with Glanzmann's thrombasthenia, and is completing her bachelor's degree in biology.

Emily lives with Glanzmann's thrombasthenia with refractoriness to platelets.

Please see accompanying Prescribing Information, including Boxed Warning.

Important Safety Information

Drug Interactions

Thrombosis may occur if NovoSeven® RT is administered concomitantly with Coagulation Factor XIII A2. Please see additional prescribing information, including Boxed Warning.
Recognizing and properly treating Glanzmann’s thrombasthenia

Diagnosing GT isn’t always simple19-23
• Normal PT, aPTT, and platelet count do not indicate the absence of a bleeding disorder
• If a patient has mucocutaneous bleeds, consider screening for platelet defects
  – Automated platelet function tests (eg, PFA-100) screen for platelet dysfunction
  – Definitive diagnosis of GT requires more specific platelet function tests and flow cytometry

Treating with normal platelets has potential complications
Patients who receive platelet transfusions are at risk of developing refractoriness to future transfusions and/or platelet antibodies.20,21

Rapid access to treatment
• NovoSeven® RT can be infused in 2-5 minutes1
• Low-volume, flexible dosing for patients with GT:2
  – 90 mcg/kg every 2-6 hours in severe bleeding episodes requiring systemic hemostatic therapy until hemostasis is achieved
• Room temperature stable up to 77˚F1

Proven effective in GT-related bleeds and surgery

\[
\begin{align*}
\text{All bleeding episodes} &: 94\% \\
\text{All surgical procedures} &: 99\%
\end{align*}
\]

Rapid access to treatment

\[
\begin{align*}
\text{NovoSeven® RT can be infused in 2-5 minutes}^1 \\
\text{Low-volume, flexible dosing for patients with GT:}^2 \\
\quad \text{90 mcg/kg every 2-6 hours in severe bleeding episodes requiring systemic hemostatic therapy until hemostasis is achieved} \\
\text{Room temperature stable up to 77˚F}^1
\end{align*}
\]

Important Safety Information

Warnings and Precautions (cont’d)
• Hypersensitivity reactions, including anaphylaxis, can occur with NovoSeven® RT. Patients with a known hypersensitivity to mouse, hamster, or bovine proteins may be at a higher risk of hypersensitivity reactions. Discontinue infusion and administer appropriate treatment when hypersensitivity reactions occur

Recombinant safety supported by
registry data

Thrombotic events1
• Not made from human serum or human proteins

\[
\begin{align*}
\text{<0.2% rate}
\end{align*}
\]

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Important Safety Information

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• Hypersensitivity reactions, including anaphylaxis, can occur with NovoSeven® RT. Patients with a known hypersensitivity to mouse, hamster, or bovine proteins may be at a higher risk of hypersensitivity reactions. Discontinue infusion and administer appropriate treatment when hypersensitivity reactions occur

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\[
\begin{align*}
\text{<0.2% rate}
\end{align*}
\]
YEARS OF EXPERIENCE HAVE LED ME TO TRUST EARLY TREATMENT

Important Safety Information

WARNING: THROMBOSIS

• Serious arterial and venous thrombotic events following administration of NovoSeven® RT have been reported
• Discuss the risks and explain the signs and symptoms of thrombotic and thromboembolic events to patients who will receive NovoSeven® RT
• Monitor patients for signs or symptoms of activation of the coagulation system and for thrombosis

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
With congenital factor VII deficiency, early treatment is essential

Life-threatening bleeds present early in life\textsuperscript{28,29}

- CNS and GI bleeds occur most frequently during the first 6 months of life
- 70% of patients under the age of 5 years started having joint bleeds

rFVIIa is recommended by MASAC to treat CFVIIId\textsuperscript{20}

Important Safety Information

Warnings and Precautions

- Serious arterial and venous thrombotic events have been reported in clinical trials and postmarketing surveillance

NovoSeven\textsuperscript{®} RT: The only factor product approved for CFVIIId

Effectively control bleeds

- NovoSeven\textsuperscript{®} RT can be infused in 2-5 minutes\textsuperscript{1}
- Low-volume, flexible dosing for patients with CFVIIId
  - 15-30 mcg/kg every 4-6 hours until hemostasis is achieved
- Room temperature stable up to 77\textdegree F\textsuperscript{1}

Rapid access to treatment

- 90% effective at stopping nonsurgical and surgical bleeds in people with CFVIIId\textsuperscript{a}

Data from the published literature and internal sources for patients with FVII deficiency (N=70) treated with NovoSeven\textsuperscript{®} for 124 bleeding episodes, surgeries or prophylaxis regimens. Dosing ranged from 6 mcg/kg administered every 2 to 12 hours (except for prophylaxis [given administered from 2 times per week up to 2 times per day]). Patients were treated with an average of 1 to 10 doses. Treatment was effective if bleeding stopped or the physician rated the treatment as effective.\textsuperscript{1}

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
WITH NOVOSEVEN® RT ON BOARD,
MY TREATMENT TEAM

CAN STAY FOCUSED ON MY SURGERY

Important Safety Information

Warnings and Precautions (cont’d)

• Patients with congenital hemophilia receiving concomitant treatment with aPCCs (activated prothrombin complex concentrates), older patients particularly with acquired hemophilia and receiving other hemostatic agents, and patients with a history of cardiac and vascular disease may have an increased risk of developing thrombotic events.

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
Flexible dosing before, during, and after surgery

- MASAC guidelines recommend administering NovoSeven® RT to CHAwI patients taking emicizumab who will undergo major procedures.
- NovoSeven® RT offers tailored perioperative dosing.

A proven safety profile for perioperative bleed management

- Low rate of thrombotic events in surgery based on clinical trials and registry data.
- Serious arterial and venous thrombotic events following administration of NovoSeven® RT have been reported.

In patients with hemophilia A or B with inhibitors. Actual length of postoperative period may vary. Data from a prospective, randomized trial comparing 35 mcg/kg with 90 mcg/kg rFVIIa, each given every 2 hours intraoperatively and in the first 48 hours, then every 2-6 hours throughout day 5. Beyond day 5, patients were treated with open-label 90 mcg/kg until discharge at the discretion of the investigator. A total of 29 patients underwent 11 major and 18 minor procedures.

Data collected from the GTR and the Hemophilia & Thrombosis Research Society registry showed that 140 patients with GT received NovoSeven® RT for 518 bleeding episodes, surgeries, or traumatic injuries. In the GTR, 1 patient reported a serious adverse reaction (deep vein thrombosis) and 1 patient experienced 3 adverse reactions (nausea, headache, and dyspnea). In addition, 2 patients experienced fever and 1 patient experienced headache.

- 0.2% in patients with CHwI, 4% in patients with AH, <0.2% in patients with GT.

Please see additional Important Safety Information throughout. Please see accompanying Prescribing Information, including Boxed Warning.
Warnings and Precautions
Important Safety Information

2 clinical studies for Prothrombin Complex Factors
1, 4
Able to quickly treat bleeds when they occur

Important Safety Information

Warnings and Precautions (cont’d)

• Factor VIII deficient patients should be monitored for prothrombin time (PT) and factor VII coagulant activity (FVII:C). If FVII:C fails to reach the expected level, or PT is not corrected, or bleeding is not controlled after treatment, additional treatment with antibody formation may be suspected and analysis for antibodies should be performed

>30 years of research and long-term clinical experience

467 patients and 2,785 episodes treated in registrational studies

~400 successful surgeries and procedures

References

2. NovoSeven® RT (recombinant) von Willebrand concentrate (multi-factorial) Indications and Usage in the United States

3. Patients treated with the recommended doses

4. Antibodies formed in patients with inhibitors

5. The action of high-dose factor VIIa in a cell-based model of hemostasis. DOI: 10.1002/mev.240


NovoSeven® RT: Experience you can count on

Addressing bleeds, whenever they occur

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• Low rate of thrombotic events based on clinical trials and registry data1
  – 0.2% in CHwI, 4% in AH, <0.2% in GT

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Proven effective for bleed resolution and surgery across 4 indications1
• CHAwI or CHBwI, AH, GT, and CFVIIId

Able to quickly treat bleeds when they occur
• Rapid administration and infusion, leading to rapid activity1,2

With NovoSeven® RT, the experience continues
• >30 years of clinical experience3,a

*a1988: compassionate use initiated in the United States; 1999: FDA approval received for CHwI.1,4

Indications and Usage
NovoSeven® RT (coagulation Factor VIIa, recombinant) is a coagulation factor indicated for:
• Treatment of bleeding episodes and perioperative management in adults and children with hemophilia A or B with inhibitors, congenital Factor VII (FVII) deficiency, and Glanzmann’s thrombasthenia with refractoriness to platelet transfusions, with or without antibodies to platelets
• Treatment of bleeding episodes and perioperative management in adults with acquired hemophilia

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