NovoSeven® available with solvent in a pre-filled syringe for rapid bleed control[1–6]

Fewer steps, faster reconstitution*[7]

This material is a **DRAFT** for preparatory **internal use in Novo Nordisk® only.** Affiliates are responsible for reviewing the promotional material against local label, more stringent relevant local legislation, and if relevant, local code of conduct (cf. S.O.P. 100965 Approval of Promotional Material in Novo Nordisk) before distribution.

NovoSeven® is indicated for the treatment of bleeding episodes and for the prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups:[1]

- in patients with congenital haemophilia with inhibitors to coagulation factors VIII or IX > 5 Bethesda Units (BU)
- in patients with congenital haemophilia who are expected to have a high anamnestic response to factor VIII or factor IX administration
- in patients with acquired haemophilia
- in patients with congenital FVII deficiency
- in patients with Glanzmann's thrombasthenia with past or present refractoriness to platelet transfusions, or where platelets are not readily available

* Compared with NovoSeven® vial-to-vial reconstitution.[7]

Please see NovoSeven® abbreviated summary of product characteristics on page 7 of this brochure and NovoSeven® package leaflet for complete information

INTENDED FOR USE WITH HEALTHCARE PROFESSIONALS.

novo nordisk®

NovoSeven® Recombinant Factor VIIa

NovoSeven® with pre-filled syringe enables quick and easy reconstitution[1,7]

Pre-filled glass syringe

Contains solvent

Precise label

Displays the medication and the volume for injection

Covered syringe tip

Supports sterility, even when on the go

Vial adapter

Connects the syringe and vial, with 25-µm inline particle filter

Product vial with coloured cap

Enables easy recognition of the prescribed strength by matching the colour of the cap to the units displayed on the vial

1 mg **2 mg** **5 mg** **8 mg**

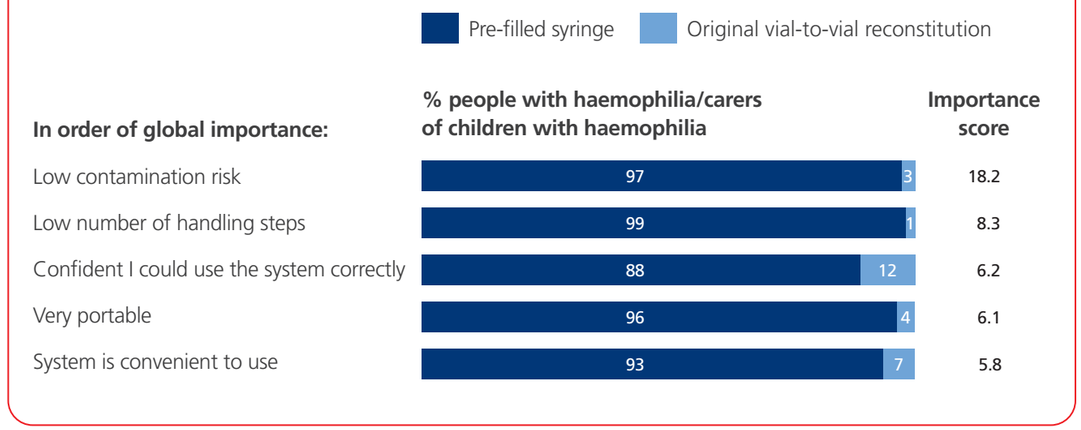
Congenital Haemophilia with Inhibitors **(CHwI)** | Acquired Haemophilia **(AH)** | Glanzmann's Thrombasthenia **(GT)** | Congenital Factor VII Deficiency **(FVIICD)**

Surgery

High preference for the NovoSeven® pre-filled syringe compared to original vial-to-vial reconstitution system:[7]

Over 90% of study participants preferred the pre-filled syringe in 4 out of 5 of the most important parameters[7]

Participant system preference



Source: adapted from Munn et al.[7]

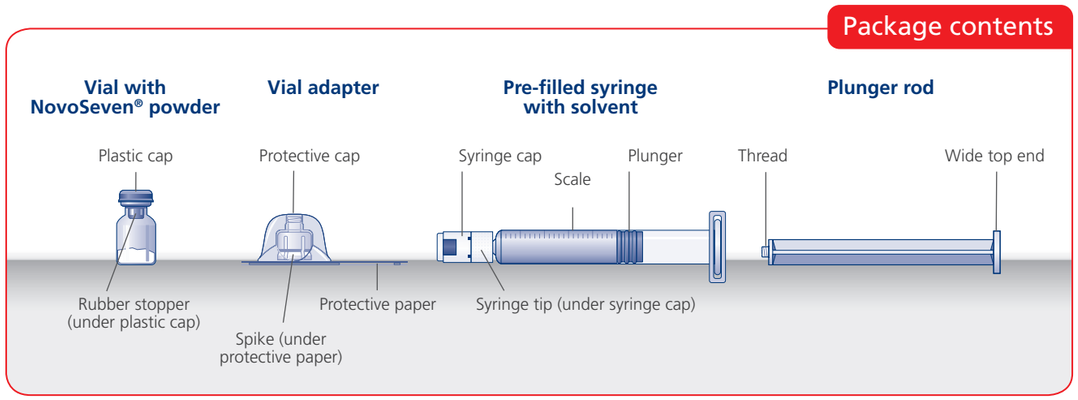
In a study with 67 people with haemophilia and carers of children with haemophilia, participants were asked to rank 18 parameters in order of importance to the design of an infusion system. The participants were also asked to say which reconstitution system performs best on each parameter. The majority of respondents preferred the pre-filled syringe to the original vial-to-vial reconstitution, both overall and when assessed on each individual parameter.[7]

Please see NovoSeven® abbreviated summary of product characteristics on page 7 of this brochure and NovoSeven® package leaflet for complete information.

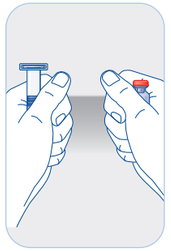
NovoSeven® Recombinant Factor VIIa

4 Simple steps for reconstitution of NovoSeven® with pre-filled syringe[1]

Package contents



Step 1: Prepare the vial and the pre-filled syringe

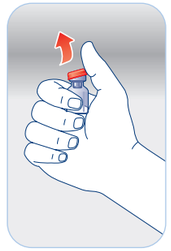


Check the expiry date, name, strength and vial cap colour for each NovoSeven® package.

Wash your hands and dry them properly before opening the carton.

Bring the vial and the pre-filled syringe to room temperature; warm them in your hands.

Leave the plunger rod untouched in the carton.

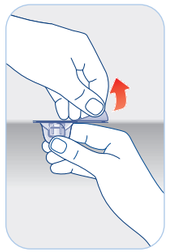


Remove the plastic cap from the vial.

Clean the rubber stopper with a sterile alcohol swab and allow to air dry.

Do not touch the rubber stopper with your fingers as it is sterile.

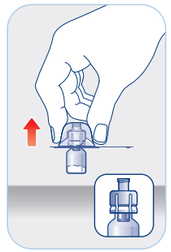
Step 2: Attach the vial adapter



If the protective paper is not fully sealed or if it is broken, do not use the vial adapter.

Remove the protective cap paper to open the vial adapter.

Do not touch the vial adapter, as it is sterile.



Place the vial on a flat and solid surface.

Turn over the protective cap, and snap the vial adapter onto the vial.

Lightly squeeze the protective cap to remove it.

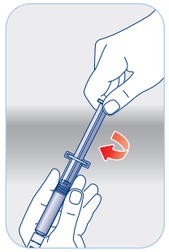
Once attached, do not remove the vial adapter from the vial.

Important information

Congenital Haemophilia with Inhibitors **(CHwI)** | Acquired Haemophilia **(AH)** | Glanzmann's Thrombasthenia **(GT)** | Congenital Factor VII Deficiency **(FVIICD)**

Surgery

Step 3: Attach the plunger rod to the pre-filled syringe

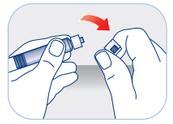


Grasp the plunger rod by the wide top end.

Immediately connect the plunger rod to the pre-filled syringe.

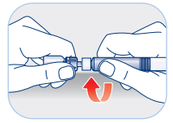
Turn it clockwise until tight.

Avoid touching the sides or the thread of the plunger rod at any time.



If the syringe cap is loose or missing, do not use the pre-filled syringe.

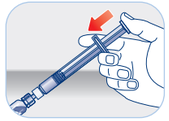
Remove the pre-filled syringe cap from the pre-filled syringe by bending it down until the perforation breaks.



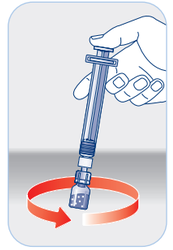
Do not touch the pre-filled syringe tip under the pre-filled syringe cap.

Screw the pre-filled syringe clockwise securely onto the vial adapter.

Step 4: Reconstitute the powder with the solvent



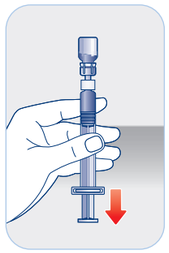
Hold the pre-filled syringe slightly tilted, and push the plunger rod to inject all the solvent into the vial.



Keep the plunger rod pressed down and swirl the vial gently until all the powder is dissolved.

Do not shake the vial as this will cause foaming.

Contents must be colourless. Discard the reconstituted solution if there are visible particles or if it is not colourless.



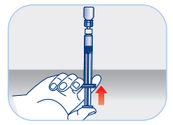
Keep the plunger rod pushed completely in.

Turn the syringe with the vial upside down.

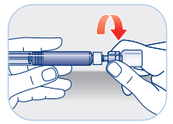
Release the plunger rod to let the reconstituted solution enter the syringe.

Pull the plunger rod slightly downwards to draw the reconstituted solution into the syringe.

While holding the vial upside down, tap the syringe gently to let any air bubbles rise to the top.



Push the plunger rod slowly until all trapped air is gone.



Disconnect the syringe from the vial by unscrewing the vial adapter.

Do not touch the syringe tip.

NovoSeven® is now ready for injection.

Please refer to the NovoSeven® package leaflet for complete information.

Please see NovoSeven® abbreviated summary of product characteristics on page 7 of this brochure and NovoSeven® package leaflet for complete information.

NovoSeven®
Recombinant Factor VIIa

Key information to know about NovoSeven® infusion[1]

- Inject the reconstituted solution intravenously over 2 to 5 minutes.
- Some needleless connectors used with central venous access devices (CVADs) may be incompatible with the pre-filled syringe and prevent administration. Therefore, use of an alternative sterile luer-lock 10 ml plastic syringe may be required for withdrawal and injection of the reconstituted solution. Follow the instructions for proper use of the CVAD and needleless connector.
- Use the reconstituted NovoSeven® at once. If you are unable to use the reconstituted solution right away, see the package insert for more information on storage.
- If the dose requires more than one vial, repeat the four steps with new NovoSeven® vials, vial adapters and pre-filled syringes to achieve the required dose.
- Do not mix NovoSeven® with any other intravenous infusions or medications.
- Discard all waste materials safely (including any unused NovoSeven®) into an appropriate container or as instructed by your doctor or nurse.
- Do not disassemble the equipment before disposal.
- Do not reuse the equipment.
- Please refer to the NovoSeven® package leaflet for complete information.

References

1. NovoSeven® Summary of Product Characteristics. **2.** Lentz SR *et al.*, J Thromb Haemost 2014; 12(8): 1244–1253. **3.** Key NS *et al.*, J Thromb Haemost 1998; 80: 912–918. **4.** Young G *et al.*, Haemophilia 2008; 14(2): 287–294. **5.** Kavakli K *et al.*, J Thromb Haemost 2006; 95: 600–605. **6.** Bysted BV *et al.*, Haemophilia 2007; 13: 527–532. **7.** Munn J *et al.*, J Haem Pract 2016; 3(1): 33–38. **8.** Baudo F *et al.*, Blood 2012;120(1): 39–46. **9.** Di Minno G *et al.*, Haematologica 2015; 100(8): 1031–1037. **10.** Mariani G *et al.*, J Thromb Haemost 2013; 109: 238–247. **11.** Santagostino E *et al.*, J Thromb Haemost 2006; 4(2): 367–371. **12.** Neufeld EJ *et al.*, Blood Rev 2015; 29(S1): S34–S41. **13.** Abshire T, Kenet G. Haemophilia 2008; 14(5): 898–902. **14.** Croom KF, McCormack PL. Biodrugs 2008; 22(2): 121–136.

NovoSeven® Abbreviated Summary of Product Characteristics

Consult Summary of Product Characteristics before prescribing.Presentation: NovoSeven® 1 mg (50 KIU) powder and solvent (vial or pre-filled syringe) for solution for injection. NovoSeven® 2 mg (100 KIU) powder and solvent (vial or prefilled syringe) for solution for injection. NovoSeven® 5 mg (250 KIU) powder and solvent (vial or pre-filled syringe) for solution for injection. NovoSeven® 8 mg (400 KIU) powder and solvent (vial or pre-filled syringe) for solution for injection. **Composition:** eptacog alfa (activated) is recombinant coagulation factor VIIa (rFVIIa) produced in baby hamster kidney cells (BHK Cells) by recombinant DNA technology, 1 mg/vial, 2 mg/vial, 5 mg/vial, 8 mg/vial (corresponds to 50 KIU/vial, 100 KIU/vial, 250 KIU/vial, 400 KIU/vial). 1mg/ml eptacog alfa (activated) after reconstitution. **List of excipients:** *Powder:* Sodium chloride, Calcium chloride dihydrate, Glycylglycine, Polysorbate 80, Mannitol, Sucrose, Methionine, Hydrochloric acid, Sodium hydroxide *Solvent:* Histidine, Hydrochloric acid, Sodium hydroxide, Water for injections. **Indications:** treatment of bleeding episodes and prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups:

- patients with congenital haemophilia with inhibitors to coagulation factors VIII or IX >5 BU;
- patients with congenital haemophilia who are expected to have a high anamnestic response to factor VIII or factor IX administration;
- patients with acquired haemophilia;
- patients with congenital FVII deficiency;
- patients with Glanzmann's thrombasthenia with past or present refractoriness to platelet transfusions, or where platelets are not readily available

Posology: *Haemophilia A or B with inhibitors or expected to have a high anamnestic response:* Mild to moderate bleeding episodes (including home therapy): Early intervention has been shown to be efficacious in the treatment of mild to moderate joint, muscle and mucocutaneous bleeds. Two dosing regimens can be recommended: 1) Two to three injections of 90 µg per kg body weight administered at three-hour intervals. If further treatment is required, one additional dose of 90 µg per kg body weight can be administered 2) One single injection of 270 µg per kg body weight. The duration of the home therapy should not exceed 24 hours. There is no clinical experience with administration of a single dose of 270 µg per kg body weight in elderly patients. Serious bleeding episodes: An initial dose of 90 µg per kg body weight is recommended and could be administered on the way to the hospital where the patient is usually treated. The following dose varies according to the type and severity of the [illegible] initially be every second hour until clinical improveme[illegible] indicated, the dose interval can then be increased to 3 h[illegible] interval can be increased successively to every 4, 6, 8 [illegible] judged as being indicated. A major bleeding episode ma[illegible] extended beyond this if clinically warranted. Invasivepro[illegible] per kg body weight should be given immediately befo[illegible] repeated after 2 hours and then at 2 - 3 hour intervals [illegible] the intervention performed and the clinical status of the patient. In major surgery, the dose should be continued at 2 - 4 hour intervals for 6 - 7 days. The dose interval may then be increased to 6 - 8 hours for another 2 weeks of treatment. Patients undergoing major surgery may be treated for up to 2 - 3 weeks until healing has occurred. *Acquired Haemophilia:* NovoSeven® should be given as early as possible after the start of a bleeding episode. The recommended initial dose, administered by intravenous bolus injection, is 90 µg per kg body weight. Following the initial dose of NovoSeven® further injections may be given if required. The duration of treatment and the interval between injections will vary with the severity of the haemorrhage, the invasive procedures or the surgery being performed. The initial dose interval should be 2 - 3 hours. Once haemostasis has been achieved, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged to be indicated. *Factor VII deficiency:* The recommended dose range is 15 - 30 µg per kg body weight every 4 - 6 hours until haemostasis is achieved. Dose and frequency of injections should be adapted to each individual. Limited clinical experience in long term prophylaxis in paediatric population has been gathered in the paediatric population below 12 years of age, with a severe clinical phenotype. Dose and frequency of injections for prophylaxis should be based on clinical response and adapted to each individual. *Glanzmann's thrombasthenia:* The recommended dose is 90 µg (range 80 - 120 µg) per kg body weight at intervals of two hours (1.5 - 2.5 hours). At least three doses should be administered to secure effective haemostasis. The recommended route of administration is bolus injection as lack of efficacy may appear in connection with continuous infusion. For those patients who are not refractory, platelets are the first line treatment for Glanzmann's thrombasthenia. **Contraindications:** Hypersensitivity to the active substance, or to any of the excipients, or to mouse, hamster or bovine protein. **Interaction with other medicinal products and other forms of interaction:** The risk of a potential interaction between NovoSeven® and coagulation factor concentrates is unknown. Simultaneous use of prothrombin complex concentrates, activated or not, should be avoided. Anti-fibrinolytics have been reported to reduce blood loss in association with surgery in haemophilia patients, especially in orthopaedic surgery and surgery in regions rich in fibrinolytic activity, such as the oral cavity. Experience with concomitant administration of anti-fibrinolytics and rFVIIa treatment is however limited. Based on a non-clinical study it is not recommended to combine rFVIIa and rFXIII. There are no clinical data available on interaction between rFVIIa and rFXIII. **Fertility, pregnancy and breast-feeding** As a precautionary measure, it is preferable to avoid the use of NovoSeven® during pregnancy. Data from non-clinical studies as well as post-marketing data show no indication that NovoSeven® has a harmful effect on male or female fertility. Limited data from exposed pregnancies did not show any adverse effect on pregnancy or on the health of foetus/new-born child. It is unknown whether NovoSeven® is excreted in human breast milk **Undesirable effects:** The most frequent adverse drug reactions (ADR) are pyrexia and rash (uncommon: > 1/1,000 to < 1/100), and the most serious adverse drug reactions are thromboembolic events. The frequency is classified as: Uncommon (≥1/1,000 to <1/100), Rare (≥1/10,000 to <1/1,000) or Not Known. The frequencies of both serious and non-serious adverse drug reactions are listed by system organ class: Blood and lymphatic system disorders: *Rare:* Disseminated intravascular coagulation, related laboratory findings, including elevated levels of D-dimer and decreased levels of Anti Thrombin (AT) and coagulopathy. Gastrointestinal disorders: *Rare:* nausea. General disorders and administration site conditions: *Uncommon:* ADRs are decreased therapeutic response and pyrexia. *Rare:* ADR is injection site reaction including injection site pain. Immune system disorders: Hypersensitivity is *Rare;* anaphylactic reaction frequency is *not known*. Investigations: *Rare:* increased fibrin degradation products, increase of alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase and prothrombin. Nervous system disorders: *Rare:* headache, skin and subcutaneous tissue disorders: *Uncommon:* Rash (including allergic dermatitis and rash erythematous), pruritus and urticaria. Unknown frequency: flushing and angioedema. Vascular disorders: *Uncommon:* venous thromboembolic events (deep vein thrombosis, thrombosis at i.v. site, pulmonary embolism, thromboembolic events of the liver including portal vein thrombosis, renal vein thrombosis, thrombophlebitis, superficial thrombophlebitis and intestinal ischaemia). *Rare:* Arterial thromboembolic events (myocardial infarction, cerebral infarction, cerebral ischaemia, cerebral artery occlusion, cerebrovascular accident, renal artery thrombosis, peripheral ischaemia, peripheral arterial thrombosis and intestinal ischaemia), Angina pectoris. *Unknown:* Intracardiac thrombus. **Inhibitory antibodies:** In post-marketing experience, there have been no reports of inhibitory antibodies against NovoSeven® or FVII in patients with haemophilia A or B. In factor VII deficiency clinical trials: formation of antibodies against NovoSeven® and FVII is the only ADR reported (common). Development of inhibitory antibodies to NovoSeven® has been reported in a post-marketing observational registry of patients with congenital FVII deficiency. **Reporting of suspected adverse reactions** after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. **Overdose:** Four cases of overdose have been reported in patients with haemophilia in 16 years. The only complication reported in connection with an overdose was a [illegible]e in a 16 year-old patient receiving 24 mg rFVIIa instead [illegible]been reported in patients with acquired haemophilia or [illegible]ts with factor VII deficiency, where the recommended [illegible]de of overdose has been associated with a thrombotic [illegible] 80 year) male patient treated with 10 – 20 times the [illegible]elopment of antibodies against NovoSeven® and FVII has [illegible]tient with factor VII deficiency. The dose schedule should [illegible] recommended doses due to the absence of information on the additional risk that may be incurred. **Administration:** NovoSeven® (eptacog alfa activated) is administered intravenously over 2 – 5 minutes. **Caution:** Some needleless connectors with an internal spike used with central venous access devices (CVADs) may be incompatible with the pre-filled glass syringe and prevent administration. Therefore, use of an alternative sterile 10ml luer-lock plastic syringe may be required for withdrawal and injection of the reconstituted solution. Follow the instructions for use for the CVAD and needleless connector. **Storage and shelf life:** The shelf life for the product packed for sale is 3 years when the product is stored below 25°C. In vial: After reconstitution, chemical and physical stability has been demonstrated for 6 hours at 25°C and 24 hours at 5°C. From a microbiological point of view, the product should be used immediately. If not used immediately, storage time and storage conditions prior to use are the responsibility of the user, and should not be longer than 24 hours at 2°C – 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions. The reconstituted solution should be stored in the vial. In syringe (50 ml polypropylene) in hospital settings only: Reconstitution must take place in controlled and validated aseptic conditions by adequately trained staff. Under these conditions, chemical and physical stability has been demonstrated for 24 hours at 25°C when stored in a 50 ml syringe (polypropylene). If not used immediately, the conditions prior to use are the responsibility of the user and the in-use storage time must not be longer than as stated above. **Procedure for pooling of vials for hospital use only:** During in vitro studies, the chemical and physical in-use stability has been demonstrated for 24 hours at 25°C in a 50 ml syringe (polypropylene). Compatibility with the product was demonstrated for the system consisting of a 50 ml syringe (polypropylene), a 2 m infusion tube (polyethylene) and an in-line filter with a 5 micrometer pore size. The syringe with adequately reconstituted product can be used for administration in a CE-marked infusion pump (accepting a 50 ml syringe), for details on pooling the vials (hospital use only) please refer to the SmPC as of Oct 2019. The infusion pump must only be operated by trained hospital personnel. **Legal category:** Prescription-only medicine (POM). MARKETING AUTHORISATION NUMBERS: NovoSeven 1 mg (50 KIU): EU/1/96/006/004, EU/1/96/006/008. NovoSeven 2 mg (100 KIU): EU/1/96/006/005, EU/1/96/006/009. NovoSeven 5 mg (250 KIU): EU/1/96/006/006, EU/1/96/006/010. NovoSeven 8 mg (400 KIU): EU/1/96/006/007, EU/1/96/006/011. **Authorisation holder:** Novo Nordisk A/S, Bagsvaerd, Denmark. **Date of last revision:** October 2019. **For more detailed information please consult the EMEA product information.** Novo Nordisk® is a registered trademark owned by Novo Nordisk A/S. NovoSeven® is a registered trademark owned by Novo Nordisk Health Care AG, Thurgauerstrasse 36-38, 8050 Zürich, Switzerland, Tel +41432224300. HQ20NS00010

Please update this abbreviated summary of product characteristics with local product information.

NovoSeven®
Recombinant Factor VIIa

NovoSeven® with pre-filled syringe provides rapid bleed control[1–6]

Rapid bleed control with consistently high efficacy across 4 indications[1–6,8–10]

Convenience for hospital- and home-based* treatment[1,11]

Favourable safety profile using recombinant technology[1,12–14]

*Home treatment applies to mild-to-moderate bleeds in patients with congenital haemophilia with inhibitors only and should not exceed 24 hours without consultation with the haemophilia treatment centre[1]

INTENDED FOR USE WITH HEALTHCARE PROFESSIONALS.

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HQ20NS00020. Date of preparation: July 2020

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