En cas de choc, le traitement symptomatique de l'état de choc devra être instauré.
Des réactions comparables à la maladie sérique (due à une réaction allergique) décrite après administration de protéines animales peuvent apparaître environ six jours après le début du traitement. Fièvre, prurit (démangeaisons), érythème (rougeurs) ou urticaire, adénopathie (augmentation de la taille des ganglions lymphatiques) et arthralgies (douleurs des articulations) en sont les symptômes cliniques. Ces réactions sont observées chez environ 1 % des sujets après administration de fragments $F(ab')_2$ d'immunoglobulines de cheval.
Si vous remarquez des effets indésirables non mentionnés dans cette notice, veuillez en informer votre médecin ou pharmacien.

5. COMMENT CONSERVER VIPERFAV ?

Tenir hors de la portée et de la vue des enfants.
À conserver entre + 2°C et + 8°C. Ne pas congeler.
Ne pas utiliser après la date de péremption figurant sur la boîte.
N'utilisez pas VIPERFAV si vous constatez que la solution est trouble ou qu'elle contient un dépôt.
La dernière date à laquelle cette notice a été approuvée est le : 11/2001

VIPERFAV

EQUINE EUROPEAN VIPER ANTI-VENOM IMMUNOGLOBULIN $F(ab')_2$ FRAGMENTS (*Vipera aspis, Vipera berus, Vipera ammodytes*)

Solution for dilution for intravenous infusion

Please read this leaflet carefully, as it contains important information.
- Keep this leaflet, you may need to refer to it again.
- If you have any questions or doubts, ask your doctor or pharmacist for further information.
- This medicine has been prescribed for you personally in a given situation. Do not give it to anyone else. Even if this person presents the same symptoms as you, this medicine may not be suitable for his or her treatment.

- The active ingredients are equine anti-venom immunoglobulin $F(ab')_2$ fragments which neutralize:

Vipera aspis venom ..... ≥ 1000 LD_{50} in mice
Vipera berus venom ..... ≥ 500 LD_{50} in mice
Vipera ammodytes venom ..... ≥ 1000 LD_{50} in mice
for 4 ml

- The other ingredients are sodium chloride, polysorbate 80 and water for injections.

Holder/Manufacturer:
SANOFI PASTEUR SA, 2, avenue Pont Pasteur, 69007 Lyon - France

1. WHAT IS VIPERFAV AND WHEN IS IT USED?

VIPERFAV is presented in the form of a solution for dilution for intravenous infusion (4 ml vial).
This medicinal product is a preparation of specific equine (horse) European viper venom immunoglobulins.
This medicinal product is indicated for the treatment of envenomation (grade II or III) by European vipers (*Vipera aspis, Vipera berus, Vipera ammodytes*), in patients showing rapidly extensible oedema and/or the occurrence of systemic (general) signs: vomiting, diarrhoea, abdominal pains, arterial hypotension.

Prognostic clinical criteria for severity:
Grade II: extensive regional oedema extending on the bitten limb with or without systemic signs (vomiting, diarrhoea, arterial hypotension).
Grade III: oedema extending beyond the bitten limb, reaching the trunk, associated with severe systemic signs (prolonged collapse, state of shock (faintness with drop in blood pressure), vomiting, diarrhoea, bleeding).

Prognostic biological criteria for severity (criteria INDICATING severe progression):
Hyperleukocytosis (increase in white blood cell level in blood) greater than 15 000/mm^3, thrombopaenia (decrease in blood platelet level) less than 150 000/mm^3, fibrinaemia (fibrinogen level in blood) less than 2 g/l, prothrombin level (clotting test) less than 60 % indicate severity.
Regional, systemic and biological prognostic signs of severity may appear in a dissociated manner in the first hours following envenomation and should be assessed repeatedly every 5 to 6 hours on the first day.

2. INFORMATION REQUIRED BEFORE USING VIPERFAV

Do not use VIPERFAV:
- If you are allergic to horse proteins or to any of the excipients (ingredients) contained in VIPERFAV (see next section).
- The fatal risk associated with envenomation outweighs any potential contra-indication.

Take special precautions with VIPERFAV:
The treatment must be administered in a hospital to be able to control any immediate hypersensitivity reaction as early as possible.
Given the heterologous (non-human) nature of VIPERFAV, the risk of generalized allergy type effects should always be assessed:
- In order to detect if they are pre-sensitized to heterologous proteins, patients must be questioned in detail on their history of allergies, paying particular attention to previous injections of heterologous (non-human) proteins and possible reactions.
- Subjects should also be questioned on animal contact allergies (particularly to horses) and food allergy.

In the event of signs of intolerance, slow down or stop the infusion if required.
If allergic or generalized allergic reactions occur, the injection must be stopped immediately.

In the event of shock (sudden faintness with drop in arterial pressure), a symptomatic treatment of the state of shock must be set up.
The infusion should always be started under strict medical supervision at a slow rate of 15 drops/minute or 50 ml/hour.

Pregnancy and lactation:

The safety of the product during pregnancy has not been established by clinical trials in humans with VIPERFAV. In view of the fatal risk associated with envenomation, pregnancy does not constitute a contraindication to the set-up of post-exposure anti-venom treatment.
Always ask for your doctor's or pharmacist's advice before using a medicinal product.

Drivers and machine users:

There is no evidence that VIPERFAV impairs the ability to drive or operate machines.

List of excipients with a known effect:

Sodium (chloride) (less than one millimole (or 23 mg) of sodium per dosage unit).

Administration or use of other medicinal products:

No interaction with other medicinal products has been reported with VIPERFAV.
Please inform your doctor or pharmacist if you are taking or have recently taken another medicinal product, even without a prescription.

3. HOW TO USE VIPERFAV?

VIPERFAV must be administered as soon as possible after signs of severity appear, within the first 6 hours, if possible. The expected therapeutic benefit may be less marked if the treatment is set up at a later stage.
It is important to associate the VIPERFAV treatment with a symptomatic treatment.
VIPERFAV is particularly recommended in children (the venom/body weight ratio is an essential factor of severity), adults suffering from a chronic disease (diabetes, haemophilia, history of cardiovascular disease) and pregnant women.
Thorough local disinfection must be carried out.
The total initial dose is a 4 ml intravenous infusion of VIPERFAV.
– Children:
In children, the same dose as for adults is used, irrespective of age or weight.
This infusion may be readministered twice every 5 hours, depending on the clinical progression.
The 4 ml of solution must be diluted in 100 ml of 0.9% NaCl and administered by slow intravenous infusion under medical supervision. The infusion should be started at a slow rate of 15 drops/minute or 50 ml/hour.
The total infusion time is one hour.

4. WHAT ARE THE POSSIBLE UNDESIRABLE EFFECTS?

Like all medicinal products, VIPERFAV is liable to have undesirable effects.
After the administration of VIPERFAV, the following immediate signs have been observed: sweating, nausea, skin eruption, moderate drop in blood pressure, anaphylactoid (allergic type) reaction associating coughing and facial erythema (rash); the following delayed signs have been observed: isolated fever, isolated arthralgia (joint pain), urticaria.
Like with other equine (horse) immunoglobulin fragment preparations immediate or delayed allergic type reactions are liable to occur.
Anaphylactoid (allergic type) reactions with hypotension (decrease in blood pressure), dyspnea (breathing problems), urticaria, Quincke's oedema (sudden swelling of the face and the neck of allergic origin) or severe allergic shock may take place. However, true generalized allergic shock (sudden faintness with drop in blood pressure) remains exceptional.
In the event of shock, a symptomatic treatment of the state of shock must be set up.
Serum sickness like reactions (caused by an allergic reaction) reported after the administration of proteins of animal origin may occur about six days after the beginning of treatment. Clinical symptoms are fever, pruritus (itching), erythema (rash) or urticaria, adenopathy (increase in lymph gland size) and arthralgia (joint pain). These reactions are observed in approximately 1 % of subjects after administering horse immunoglobulin $F(ab')_2$ fragments.
Report to your doctor or to your pharmacist any undesirable effects which might not be mentioned in this leaflet.

5. HOW TO STORE VIPERFAV?

Keep out of the reach and sight of children.
Store between + 2°C and + 8°C. Do not freeze.
Do not use after the expiry date marked on the box.
Do not use VIPERFAV if you notice that the solution is cloudy or contains deposit.

The last date on which this package insert was approved is: 11/2001

VIPERFAV

FRAGMENTOS $F(ab')_2$ DE INMUNOGLOBULINAS EQUINAS NEUTRALIZANTES DEL VENENO DE VIBORAS EUROPEAS (*Vipera aspis, Vipera berus, Vipera ammodytes*)

Solución diluible para perfusión

Lea atentamente la totalidad del prospecto antes de utilizar este medicamento, contiene información importante.
– Conserve este prospecto para posteriores consultas.
– Si tiene algunas preguntas o dudas, consulte con su médico o farmacéutico.
– Este medicamento le ha sido prescrito personalmente. No lo administre nunca a otras personas, aunque muestren signos idénticos, ya que podría resultar nocivo.

– Las sustancias activas son los fragmentos $F(ab')_2$ de inmunoglobulinas equinas antiveneno, que tienen la facultad de neutralizar el:
Veneno de *Vipera aspis* ..... ≥ 1000 DL_{50} en el ratón