CSL Behring

Package leaflet: Information for the user

Haemocomplettan® P 1 g

Powder for solution for injection/infusion
Human fibrinogen

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Haemocomplettan is and what it is used for

What is Haemocomplettan
Haemocomplettan is a purified concentrate of fibrinogen (coagulation factor I), which is a protein important for blood clotting. It is derived from human plasma (this is the liquid part of the blood).
Haemocomplettan is a powder for solution. The made up solution is to be given by injection or infusion into a vein.

What is Haemocomplettan used for
Haemocomplettan is used for treatment and prophylaxis of bleeding in patients with:
- Congenital hypo-, dys- or afibrinogenaemia
- Acquired hypofibrinogenaemia resulting from
  - disorders of synthesis in cases of severe liver parenchyma damage
  - increased intravascular consumption e.g. as a result of disseminated intravascular coagulation, hyperfibrinolysis
  - increased blood loss

The most important clinical pictures associated with a defibrination syndrome are:
Obstetrical complications, acute leukaemia especially promyelocytic leukaemia, liver cirrhosis, intoxications, extensive injuries, haemolysis after transfusion errors, operative interventions, infections, sepsis, all forms of shock as well as tumours especially in the lung, pancreas, uterus, and prostate.

2. What you need to know before you use Haemocomplettan

The following sections contain information that your doctor should consider before you are given **Haemocomplettan**.

Do not use Haemocomplettan:
- if you are allergic to human fibrinogen or any of the other ingredients of this medicine (listed in section 6.).
- in case of manifest thrombosis and myocardial infarction, except in cases of potentially fatal bleeding.

Warnings and precautions
Talk to your doctor before using Haemocomplettan.
There is an increased risk of blood clots in a blood vessel (thrombosis), particularly:
- in case of a high dose or repeated dosing
- if you have had a heart attack (a history of coronary heart disease or myocardial infarction)
- if you suffer from liver disease
- if you have just had surgery (patients postoperatively)
- if you will be having surgery soon (patients preoperatively)
- in newborn infants (neonates)
- if you are more likely to suffer from blood clots than normal (patients at risk of thromboembolic phenomena or disseminated intravascular coagulation)

Your doctor will consider carefully the benefit of treatment with Haemocomplettan compared with the risk of these complications.
Acquired hypofibrinogenemia is associated with low plasma concentrations of all coagulation factors (not only fibrinogen) and inhibitors and so treatment with blood products containing coagulation factors should be considered (with or without administration of fibrinogen concentrate). Careful monitoring of the coagulation system is necessary.
If allergic or anaphylactic-type reactions occur, the injection/infusion should be stopped immediately. In case of anaphylactic shock, standard medical treatment for shock should be implemented.
In the case of replacement therapy with coagulation factors in other congenital deficiencies, antibody reactions have been observed, but there is currently no data with fibrinogen.

Virus safety
When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:
- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded,
- the testing of each donations and pools of plasma for signs of virus/ infections,
- the inclusion of steps in the processing of the blood that can inactivate or remove viruses.

Despite this, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.
The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV) and for the non-enveloped hepatitis A virus (HAV). These measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.
Parvovirus B19 infection may be serious for pregnant women (fetal infection) and for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).
Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma-derived products.
It is strongly recommended that every time that Haemocomplettan is given, your doctor should record the date of administration, batch number and the injected volume.

Other medicines and Haemocomplettan
- Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.
- This product must not be mixed with other medicinal products, diluents, or solvents except those mentioned in section *"The following information is intended for medical or healthcare professionals only / Reconstitution"*.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
Animal reproduction studies have not been conducted with Haemocomplettan. Since the active substance is of human origin, it is catabolized in the same manner as the patient's own protein. These physiological constituents of the human blood are not expected to induce adverse effects on reproduction or on the fetus.
The safety of human plasma fibrinogen products for use in human pregnancy has not been established in controlled clinical trials.
Clinical experience with fibrinogen products in the treatment of obstetric complications suggests that no harmful effects on the course of the pregnancy or health of the fetus or the neonate are to be expected.
It is unknown whether Haemocomplettan is excreted in human milk. The safety of human plasma fibrinogen products for use during lactation has not been established in controlled clinical trials.
A risk to the suckling child cannot be excluded.
During pregnancy and breast-feeding Haemocomplettan should be given only if it is clearly needed.

Driving and using machines
Haemocomplettan has no influence on the ability to drive and use machines.

Haemocomplettan contains sodium
Haemocomplettan contains up to 164 mg (7.1 mmol) sodium per 1 g fibrinogen. This correlates with 11.5 mg (0.5 mmol) sodium per kg body weight of the patient if the recommended initial dose of 70 mg/kg body weight is applied. Please take this into account if you are on a controlled sodium diet.

3. How to use Haemocomplettan

Treatment should be initiated under the supervision of a physician experienced in the treatment of coagulation disorders.

Dosage
The amount of human fibrinogen you need and the duration of treatment depend on:
- the severity of your disease
- the site and intensity of the bleeding
- your clinical condition.

Overdose
Your doctor should regularly check your blood clot status during the treatment. In case of overdosage, the risk of development of thromboembolic complications is enhanced.

Method of administration
If you have any further questions on the use of this product, ask your doctor or pharmacist (see section *"The following information is intended for medical or healthcare professionals only"*)

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The following side effect has been observed very commonly (affects more than 1 in 10 users):
- Increase in body temperature

The following side effect has been observed uncommonly (affects up to 1 in 100 users):
- A sudden allergic reaction (such as reddening of the skin, skin rash over the whole body, fall in blood pressure, difficulty in breathing).

The following side effect has been observed commonly (affects up to 1 user in 10, however incidence was higher in patients receiving no fibrinogen):
- Risk of increased formation of blood clots (see section 2 *"Warnings and precautions"*).

For safety with respect to transmissible agents, see section "warnings and precautions".

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Haemocomplettan

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the label and carton.
- Store in a refrigerator (2 °C – 8 °C).
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- The reconstituted product should preferably be used immediately.
- If the reconstituted product is not administered immediately, storage shall not exceed 8 hours at room temperature (max. 25 °C).
- The reconstituted product should not be stored in the refrigerator.

6. Contents of the pack and other information

What Haemocomplettan contains

The active substance is:
Human fibrinogen (1 g/vial; after reconstitution with 50 ml of water for injection approx. 20 mg/ml).

The other ingredients are:
Human albumin, sodium chloride, L-arginine hydrochloride, sodium citrate, sodium hydroxide (for pH adjustment).

What Haemocomplettan looks like and contents of the pack
Haemocomplettan is presented as a white powder.
After reconstitution with water for injections the product should be clear or slightly opalescent, i.e. it might sparkle when held up to the light but must not contain any obvious particles.
Haemocomplettan 1g
Pack with 1 g (Figure 1)
1-One vial containing 1 g human fibrinogen
2-Filter: Pall® Syringe Filter
3-Dispensing pin: Mini-Spike® Dispensing Pin

Figure 1

Packed by Benta SAL
Dbayeh- Lebanon
Under license from
CSL Behring GmbH, Marburg, Germany

This leaflet was last revised in September 2019.

The following information is intended for medical or healthcare professionals only:

Posology
The (functional) fibrinogen level should be determined in order to calculate individual dosage and the amount and frequency of administration should be determined on an individual patient basis by regular measurement of plasma fibrinogen level and continuous monitoring of the clinical condition of the patient and other replacement therapies used.
Normal plasma fibrinogen level is in the range of 1.5 – 4.5 g/l. The critical plasma fibrinogen level below which haemorrhages may occur is approximately 0.5 – 1.0 g/l. In case of major surgical intervention, precise monitoring of replacement therapy by coagulation assays is essential.
1. Prophylaxis in patients with congenital hypo-, dys- or afibrinogenaemia and known bleeding tendency.
   To prevent excessive bleeding during surgical procedures, prophylactic treatment is recommended to raise fibrinogen levels to 1 g/l and maintain fibrinogen at this level until haemostasis is secure and above 0.5 g/l until wound healing is complete.
   In case of surgical procedure or treatment of a bleeding episode, the dose should be calculated as follows:

$$\text{Dose of fibrinogen (mg/kg body weight)} = \frac{\text{[Target level (g/l) - measured level (g/l)]}}{\text{0.017 (g/l per mg/kg body weight)}}$$

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Subsequent posology (doses and frequency of injections) should be adapted based on the patient's clinical status and laboratory results. The biological half-life of fibrinogen is 3-4 days. Thus, in the absence of consumption, repeated treatment with human fibrinogen is not usually required. Given the accumulation that occurs in case of repeated administration for a prophylactic use, the dose and the frequency should be determined according to the therapeutic goals of the physician for a given patient.

2. Treatment of bleeding
   Adults
   For perioperative bleeding generally 2 g (or 30 mg/kg body weight) is administered, with subsequent infusions as required. In case of severe haemorrhage i.e. obstetric use / abruption placenta, large amounts (4 – 8 g) of fibrinogen may be required.
   Children
   The dosage should be determined according to the body weight and clinical need but is usually 20 – 30 mg/kg.

General instructions

- Reconstitution and withdrawal should be carried out under aseptic conditions.
- Reconstituted products should be inspected visually for particulate matter and discoloration prior to administration.
- The solution should be almost colourless to yellowish, clear to slightly opalescent and of neutral pH. Do not use solutions that are cloudy or have deposits.

Reconstitution

- Warm both the solvent and the powder in unopened vials to room or body temperature (not above 37 °C).
- Haemocomplettan should be reconstituted with water for injections (50 ml for 1 g not included).
- Wash hands or use gloves before reconstituting the product.
- Remove the cap from the Haemocomplettan vial to expose the central portions of the infusion stoppers.
- Treat the surface of the infusion stopper with antiseptic solution and allow it to dry.
- Transfer the solvent with an appropriate transfer device into the infusion vial. Ensure complete wetting of the powder.
- Gently swirl the vial until the powder is reconstituted and the solution is ready for administration. Avoid strong shaking which causes formation of foam. The powder should be completely reconstituted within max. 15 minutes (generally within 5 to 10 minutes).
- Open the plastic blister containing the dispensing pin (Mini-Spike® Dispensing Pin) provided with Haemocomplettan (Figure 2).

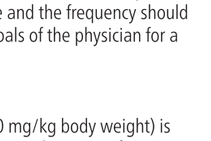

Figure 2

- Take the provided dispensing pin and insert it into the stopper of the vial with the reconstituted product (Figure 3).

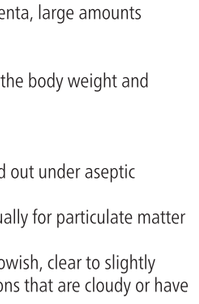

Figure 3

- After the dispensing pin is inserted, remove the cap. After the cap is removed, do not touch the exposed surface.

- Open the blister with the filter (Pall® Syringe Filter) provided with Haemocomplettan (Figure 4).

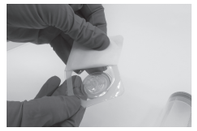

Figure 4

- Screw the syringe onto the filter (Figure 5).

Figure 5

- Screw the syringe with the mounted filter onto the dispensing pin (Figure 6).

Figure 6

- Draw the reconstituted product into the syringe (Figure 7).

Figure 7

- When completed, **remove the filter, dispensing pin and empty vial from the syringe,** dispose of properly, and proceed with administration as usual.
- Reconstituted product should be administered immediately by a separate injection / infusion line (see section 5 "*How to store Haemocomplettan*").
- Take care that no blood enters syringes filled with product.

Any unused product or waste material should be disposed of in accordance with local requirements.

Administration

Intravenous infusion or injection.
Haemocomplettan should be reconstituted according to section "Reconstitution". The reconstituted solution should be warmed to room or body temperature before administration, then injected or infused slowly intravenously at a rate which the patient finds comfortable. The injection or infusion rate should not exceed approx. 5 ml per minute.

This is a medicament

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists