Package Leaflet: Information for the user

Voncento® 250 IU FVIII / 600 IU VWF (5 ml solvent) powder and solvent for solution for injection/infusion
Voncento® 500 IU FVIII / 1200 IU VWF(10 ml solvent) powder and solvent for solution for injection/infusion
Voncento® 500 IU FVIII/ 1200 IU VWF (5 ml solvent) powder and solvent for solution for injection/infusion
Voncento® 1000 IU FVIII / 2400 IU VWF (10 ml solvent) powder and solvent for solution for injection/infusion

human coagulation factor VIII
human von Willebrand factor

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 further questions, ask your doctor, your nurse or your pharmacist.
- This medicine has been prescribed for you. 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Voncento is and what it is used for

The product is made from human plasma (the liquid part of the blood) and contains the active substances called human coagulation factor VIII (FVIII) and human von Willebrand factor (VWF).

Voncento is used for all age groups to prevent or to halt bleeding caused by the lack of VWF in von Willebrand disease (VWD) and the lack of FVIII in haemophilia A. Voncento is only used when treatment with another medicine, desmopressin, is not effective alone or cannot be given.

VWF and FVIII are involved in blood clotting. Lack of either factor means that blood does not clot as quickly as it should so there is an increased tendency to bleed. The replacement of VWF and FVIII by Voncento will temporarily repair the blood clotting mechanisms.

As Voncento contains both FVIII and VWF, it is important to know which factor you most need. If you have haemophilia A your doctor will prescribe you Voncento with the number of units of FVIII specified. If you have VWD your doctor will prescribe you Voncento with the number of units of VWF specified.

2. What you need to know before you use Voncento

Do not use Voncento

- If you are allergic to VWF or FVIII or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Traceability
It is strongly recommended that every time Voncento is given, you record the date of administration, the batch number and the injected volume in your treatment diary.

Talk to your doctor, nurse or pharmacist before taking Voncento.

- Allergic (hypersensitivity) reactions are possible. **If symptoms of hypersensitivity occur, you should stop using the medicine immediately and contact your doctor.** Your doctor should inform you of the **early signs of hypersensitivity reactions**. These include hives, generalised skin rash, tightness of the chest, wheezing, fall in blood pressure and anaphylaxis (a serious allergic reaction that causes severe difficulty in breathing, or dizziness).
- The formation of **inhibitors** (antibodies) is a known complication that can occur during treatment with all factor VIII medicines. These inhibitors, especially at high levels, stop the treatment working properly and you or your child will be monitored carefully for the development of these inhibitors. If your or your child's bleeding is not being controlled with Voncento, tell your doctor immediately.
- If you have been told you have heart disease or are at risk for heart disease, tell your doctor or pharmacist.
- If for the administration of Voncento you will require a central venous access device (CVAD), the risk of CVAD-related complications including local infections, bacteria in the blood (bacteremia) and the formation of a blood clot in the blood vessel (thrombosis) where the catheter is inserted should be considered by your doctor.
- von Willebrand disease
  If you have a known risk of developing blood clots, you must be monitored for early signs of thrombosis (blood clotting). Your doctor should give you treatment to prevent thrombosis.

Virus safety

When medicines are made from human blood or plasma, certain measures are put in place by the manufacturer 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 donation and pools of plasma for signs of virus/infections,

- inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

Despite these measures, 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 so-called “enveloped” viruses such as human immunodeficiency virus (HIV, the AIDS virus), hepatitis B virus and hepatitis C virus (which cause inflammation of the liver), and for the “non-enveloped” hepatitis A virus (which also causes inflammation of the liver).

The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Parvovirus B19 infection may be serious
- for pregnant women (as there is a risk of infection of the unborn child) and
- for individuals with a weakened immune system or with an increased production of red blood cells due to certain types of anaemia (e.g. sickle cell anaemia or haemolytic anaemia).

Your doctor may recommend that you consider being vaccinated against hepatitis A and B if you regularly/repeatedly receive human plasma-derived medicines such as Voncento.

Children and adolescents

The listed warnings and precautions apply to children and adolescents.

Other medicines and Voncento

- Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

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.
- During pregnancy and breast-feeding, Voncento should be given only if it is clearly needed.

Driving and using machines

Voncento does not affect your ability to drive and use machines.

Voncento contains sodium

The presentation 500 IU FVIII /1200 IU VWF (5 ml solvent) contains up to 14.75 mg sodium per vial (main component of cooking/table salt). This is equivalent to 0.74 % of the recommended maximum daily dietary intake of sodium for an adult.

The presentation 1000 IU FVIII /2400 IU VWF (10 ml solvent) contains up to 29.50 mg

sodium per vial (main component of cooking/table salt). This is equivalent to 1.48% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Voncento

Your treatment should be monitored by a doctor who is experienced in the treatment of blood clotting disorders.

If your doctor thinks you could administer Voncento yourself, appropriate instructions will be provided to you by your doctor. Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Dose

The amount of VWF and FVIII you need to take and the duration of treatment depend on:
- the severity of your disease
- the site and intensity of the bleeding
- your clinical condition
- your body weight

(see also section *"The following information is intended for healthcare professionals only"*).
If you have been prescribed Voncento to use at home, your doctor will make sure that you are shown how to inject it and how much to use.

Follow the directions given to you by your doctor.

Use in children and adolescents
Dosing in children and adolescents aged < 18 years is based on body weight and is therefore generally based on the same instructions as for adults. In some cases, especially in younger patients, higher doses may be needed.

If you use more Voncento than you should
Five cases of overdose have been reported from clinical trials. No side effects have been associated with these reports. The risk of developing blood clots (thrombosis) cannot be excluded in case of an extremely high dose, especially in patients with VWD.

If you forget to use Voncento
- Proceed with your next dose immediately and continue at regular intervals as advised by your doctor.
- Do not take a double dose to make up for a forgotten dose.

If you stop using Voncento
Do not stop using Voncento without consulting your doctor.

Reconstitution and application

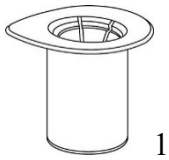
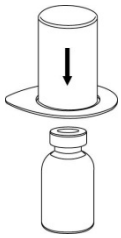
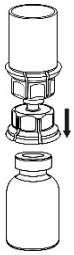
General Instructions
- The powder must be mixed with the solvent (liquid) and withdrawn from the vial under aseptic conditions.

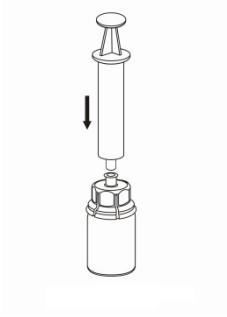
- Voncento must not be mixed with other medicines, diluents or solvents except those mentioned in section 6.
- The solution should be clear or slightly opalescent, i.e. it might be sparkling when held up to the light but must not contain any obvious particles. After filtering or withdrawal (see below) the solution should be checked by eye, before it is used. Do not use the solution if it is visibly cloudy or if it contains flakes or particles.
- Any unused product or waste material should be disposed of in accordance with local requirements and as instructed by your doctor.

Reconstitution

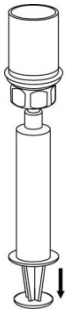
Without opening the vials, warm the Voncento powder and the liquid to room or body temperature. This can be done either by leaving the vials at room temperature for about an hour, or by holding them in your hands for a few minutes.
DO NOT expose the vials to direct heat. The vials must not be heated above body temperature (37 ºC).

Carefully remove the protective caps from the vials, and clean the exposed rubber stoppers with an alcohol swab. Allow the vials to dry before opening the Mix2Vial package (which contains the filter transfer device), then follow the instructions given below.

 1	1. Open the Mix2Vial package by peeling off the lid. Do **not** remove the Mix2Vial from the blister package!
 2	2. Place the **solvent vial** on an even, clean surface and hold the vial tight. Take the Mix2Vial together with the blister package and push the spike of the **blue** adapter end **straight down** through the solvent vial stopper.
 3	3. Carefully remove the blister package from the Mix2Vial set by holding at the rim, and pulling **vertically** upwards. Make sure that you only pull away the blister package and not the Mix2Vial set.
 4	4. Place the **product vial** on an even and firm surface. Turn the solvent vial upside down with the Mix2Vial set attached and push the spike of the **transparent** adapter end **straight down** through the product vial stopper. The solvent will automatically flow into the product vial.

 5	5. With one hand grasp the product-side of the Mix2Vial set. With the other hand grasp the solvent-side and unscrew the set carefully counterclockwise into two pieces to avoid excessive build-up of foam when dissolving the product. Discard the solvent vial with the blue Mix2Vial adapter attached.
 6	6. Gently swirl the product vial with the transparent adapter attached until the substance is fully dissolved. Do not shake.
 7	7. Draw air into an empty, sterile syringe. While the product vial is upright, connect the syringe to the Mix2Vial´s Luer Lock fitting by screwing clockwise. Inject air into the product vial.

Withdrawal and application

 8	8. While keeping the syringe plunger pressed, turn the system upside down and draw the solution into the syringe by pulling the plunger back slowly.
 9	9. Now that the solution has been transferred into the syringe, firmly hold on to the barrel of the syringe (keeping the syringe plunger facing down) and disconnect the transparent Mix2Vial adapter from the syringe by unscrewing counterclockwise.

Use the venipuncture kit supplied with the product, insert the needle into a vein. Let blood flow back to the end of the tube. Attach the syringe to the threaded, locking end of the venipuncture kit. The use of plastic disposable syringes is recommended as the ground glass surfaces of all-glass syringes tend to stick with solutions of this type. **Inject/infuse the reconstituted solution slowly (at a rate not more than 6 ml per minute) into the vein**

following the instructions given to you by your doctor. Take care not to get any blood in the syringe containing the product.

In case large volumes of Voncento are required, it is possible to pool several vials of Voncento together via a commercially available infusion set (e.g. a syringe pump for giving medicines into a vein). However, in these cases the initially reconstituted solution of Voncento should not be diluted any further.

Check yourself for any side effects that might happen straight away. If you have any side effects that might be related to the administration of Voncento, the injection or infusion should be stopped (see also section 2).

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Voncento can cause side effects, although not everybody gets them.

Please contact your doctor immediately if:

- **you notice symptoms of allergic reactions**
  In some cases it may progress to a serious allergic reaction (anaphylaxis) that causes severe difficulty in breathing, dizziness or shock. Allergic reactions may include the following symptoms: Swollen face, tongue, mouth or throat, difficulty in breathing and swallowing, hives, wheezing, burning and stinging where the infusion was given, chills, flushing, skin rash over the whole body, headache, fall in blood pressure, restlessness, faster heart beat, tightness of the chest (including chest pain and chest discomfort), back pain, tiredness (lethargy), nausea, vomiting, tingling.
- **you notice that the medicine stops working properly (bleeding is not stopped).** For children not previously treated with factor VIII medicines, inhibitor antibodies (see section 2) may form very commonly (more than 1 in 10 patients); however patients who have received previous treatment with factor VIII (more than 150 days of treatment) the risk is uncommon (less than 1 in 100 patients). If this happens your or your child's medicines may stop working properly and you or your child may experience persistent bleeding.
  You may develop an inhibitor (neutralising antibody) to VWF, in which case VWF will not work properly any more.
- **you notice any symptoms of an impaired perfusion in your extremities (e.g. cold and pale extremities) or vital organs (e.g. severe chest pain)**
  There is a risk of formation of blood clots (thrombosis), particularly in patients with known risk factors (see also section 2).

The following side effect has been observed *very commonly* (may affect more than 1 in 10 people):

- Headache

The following side effects have been observed *commonly* (may affect up to 1 in 10 people):

- Increase in body temperature

The following side effects have been observed *uncommonly* (may affect up to 1 in 100 people):

- Taste alteration (dysgeusia)
- Abnormal liver function test

Side effects in children and adolescents

Side effects in children and adolescents are expected to be the same as in adults.

Reporting of side effects
If you get any side effects, talk to your doctor or healthcare professional. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the UK Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Voncento

- 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.
- Do not store above 25 °C.
- Do not freeze.
- Voncento does not contain a perservative, so the reconstituted product should be used immediately.
- If the reconstituted product is not administered immediately, storage times and conditions prior to use are the responsibility of the user.
- Keep the vial in the outer carton in order to protect from light.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Voncento contains

The active substance is:
250 IU FVIII and 600 IU VWF per vial; after reconstitution with 5 ml of water for injection approx. 50 IU/ml FVIII and 120 IU/ml VWF.

500 IU FVIII and 1200 IU VWF per vial; after reconstitution with 10 ml of water for injection approx. 50 IU/ml FVIII and 120 IU/ml VWF.

500 IU FVIII and 1200 IU VWF per vial; after reconstitution with 5 ml of water for injections approx. 100 IU/ml FVIII and 240 IU/ml VWF.

1000 IU FVIII and 2400 IU VWF per vial; after reconstitution with 10 ml of water for injections approx. 100 IU/ml FVIII and 240 IU/ml VWF.

See section *"The following information is intended for healthcare professionals only"* for further information.

The other ingredients are:
Calcium chloride, human albumin, sodium chloride, sodium citrate, sucrose, trometamol. See section 2 "Voncento contains sodium".

Solvent: Water for injections

What Voncento looks like and contents of the pack

Voncento is supplied as a white powder and solvent for solutionfor injection/infusion.
The reconstituted solution should be clear to slightly opalescent, i.e. it might sparkle when held up to the light but must not contain any obvious particles.
The immediate container of product and solvent vial consists of glass vial with a rubber stopper, plastic disc, and aluminium cap.

Presentations

One pack with 250 IU/600 IU or 500 IU/1200 IU containing:
- 1 vial with powder
- 1 vial with 5 ml water for injections
- 1 filter transfer device 20/20

One inner box containing:
1 disposable 10 ml syringe
1 venipuncture set
2 alcohol swabs
1 non-sterile plaster

One pack with 500 IU/1200 IU or 1000 IU/2400 IU containing:
- 1 vial with powder
- 1 vial with 10 ml water for injections- 1 filter transfer device 20/20

One inner box containing:
1 disposable 10 ml syringe
1 venipuncture set
2 alcohol swabs
1 non-sterile plaster

Not all pack sizes may be marketed.

Marketing Authorization Holder and Manufacturer

CSL Behring GmbH
Emil-von-Behring-Strasse 76
35041 Marburg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
CSL Behring UK Ltd.
Tel: +44 (0)1444 447405

This leaflet was last revised in 04/2024.

The following information is intended for healthcare professionals only:

Posology

von Willebrand disease
It is important to calculate the dose using the number of IU of VWF:RCo specified. Generally, 1 IU/kg VWF:RCo raises the circulating level of VWF:RCo by 0.02 IU/ml (2 %).

Levels of VWF:RCo of > 0.6 IU/ml (60 %) and of FVIII:C of > 0.4 IU/ml (40 %) should be achieved.

On demand treatment
Usually 40 - 80 IU/kg of VWF (VWF:RCo) corresponding to 20 - 40 IU FVIII:C/kg of body weight (BW) are recommended to achieve haemostasis.

An initial dose of 80 IU/kg VWF:RCo may be required, especially in patients with type 3 VWD where maintenance of adequate levels may require greater doses than in other types of VWD.

Prevention of haemorrhage in case of surgery:
For prevention of excessive bleeding during or after surgery the application should start 1 - 2 hours before the surgical procedure.

An appropriate dose should be re-administered every 12 - 24 hours. The dose and duration of the treatment depend on the clinical status of the patient, the type and severity of the bleeding, and both VWF:RCo and FVIII:C levels.

When using a FVIII-containing VWF product, the treating physician should be aware that continued treatment may cause an excessive rise in FVIII:C. After 24 - 48 hours of treatment, in order to avoid an excessive rise in FVIII:C, reduced doses and/or prolongation of the dose interval or the use of a VWF product containing a low level of FVIII should be considered.

Prophylaxis treatment
For long term prophylaxis in patients with VWD, a dose of 25 - 40 IU VWF:RCo/kg body weight should be considered at a frequency of 1 to 3 times per week. In patients with gastrointestinal bleeds or menorrhagia, shorter dose intervals or higher doses may be necessary. The dose and duration of treatment will depend on the clinical status of the patient, as well as their VWF:RCo and FVIII:C plasma levels.

Paediatric VWD population
Treatment of bleeding
Usually 40 - 80 IU/kg of von Willebrand factor (VWF:RCo) corresponding to 20 - 40 IU FVIII:C/kg of body weight (BW) are recommended in paediatric patients to treat a bleed.

Prophylaxis treatment
Patients aged 12 to 18 years old: Dosing is based on the same guidelines as for adults.
Patients aged <12 years old: Based on results from a clinical trial in which paediatric patients under 12 years of age were shown to have lower exposure of VWF, a prophylactic dose range of 40 – 80 IU VWF:RCo/kg body weight 1 to 3 times a week should be considered.
The dose and duration of treatment will depend on the clinical status of the patient, as well as their VWF:RCo and FVIII:C plasma levels.

Haemophilia A
It is important to calculate the dose using the number of IU of FVIII:C specified.
The dose and duration of the substitution therapy depend on the severity of the FVIII deficiency, on the location and extent of the bleeding and on the patient's clinical condition.

The number of units of FVIII administered is expressed in International Units (IU), which is related to the current WHO concentrate standard for factor VIII products. Factor VIII activity in plasma is expressed either as a percentage (relative to normal human plasma) or preferably in International Units (relative to an International Standard for FVIII in plasma).

1 IU of FVIII activity is equivalent to that quantity of factor VIII in 1 ml of normal human plasma.

On demand treatment
The calculation of the required dose of factor VIII is based on the empirical finding that 1 IU factor VIII per kg body weight raises the plasma factor VIII activity by about 2 % of normal activity (*in vivo* recovery 2 IU/dl). The required dose is determined using the following formula:

Required units = body weight [kg] x desired factor VIII rise [% or IU/dl] x 0.5.

The amount to be administered and the frequency of administration should always be oriented to the clinical effectiveness in the individual case.

In the case of the following haemorrhagic events, the factor VIII activity should not fall below the given plasma activity level (in % of normal or IU/dl) within the corresponding period. The following table can be used to guide dosing in bleeding episodes and surgery:

Degree of haemorrhage / Type of surgical procedure	**Factor VIII level required (% or IU/dl)**	**Frequency of doses (hours) / Duration of therapy (days)**
Haemorrhage		
Early haemarthrosis, muscle bleeding or oral bleeding	20 - 40	Repeat infusion every 12 to 24 hours for at least 1 day, until the bleeding episode as indicated by pain is resolved or healing is achieved.

More extensive haemarthrosis, muscle bleeding or haematoma	30 - 60	Repeat infusion every 12-24 hours for 3 - 4 days or more until pain and acute disability are resolved.
Life-threatening haemorrhages:	60 - 100	Repeat infusion every 8 to 24 hours until threat is resolved.
Surgery		
Minor surgery including tooth extraction	30 - 60	Repeat infusion every 24 hours for at least 1 day, until healing is achieved.
Major surgery	80 - 100 (pre- and postoperative)	Repeat infusion every 8-24 hours until adequate wound healing, then continue therapy for at least another 7 days to maintain a factor VIII activity of 30% - 60% (IU/dl)

Treatment monitoring

During the course of treatment, appropriate determination of factor VIII levels is advised to guide the dose to be administered and the frequency of repeated infusions. Individual patients may vary in their response to factor VIII, demonstrating different half-lives and recoveries. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, a precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor VIII activity) is indispensable.

Prophylaxis treatment

For long term prophylaxis in patients with severe haemophilia A, the usual dose is 20 to 40 IU of FVIII per kg body weight at intervals of 2 to 3 days. In some cases, especially in younger patients, shorter dose intervals or higher doses may be necessary.

Paediatric haemophilia A population

Dosing in in haemophilia A in children and adolescents aged < 18 years is based on body weight and is therefore generally based on the same guidelines as for adults. In some cases shorter dose intervals or higher doses may be necessary. The frequency of administration should always be oriented to the clinical effectiveness in the individual case.

Elderly

No dose adjustment is necessary for the older people.