HAEMATE P® POWDER AND SOLVENT FOR SOLUTION FOR INJECTION OR INFUSION

Human Coagulation Factor VIII/ Human Von Willebrand Factor (250IU FVIII / 600IU VWF, 500IU FVIII / 1200IU VWF, 1000IU FVIII / 2400IU VWF)

What is in this leaflet

What Haemate P® is used for

Haemate P® is supplied as powder and solvent. The made up solution is to be given by injection or infusion into a vein.

Haemate P® is made from human plasma (this is the liquid part of the blood) and it contains human von Willebrand factor and human coagulation factor VIII.

As Haemate P® 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 Haemate P® with the number of units of FVIII specified. If you have VWD your doctor will prescribe you Haemate P® with the number of units of VWF specified.

How Haemate P® works

Von Willebrand disease (VWD)

Haemate P® is used for the prevention and treatment of bleedings or surgical bleeding caused by the lack of von Willebrand factor, when desmopressin (DDAVP) treatment alone is ineffective or contra-indicated.

Haemophilia A (congenital factor VIII deficiency)

Haemate P® is used to prevent or to stop bleedings caused by the lack of factor VIII in the blood.

It may also be used in the management of acquired factor VIII deficiency and for treatment of patients with antibodies against factor VIII.

Before you use Haemate P®

- When you must not use it

Tell your doctor if you:

- are hypersensitive (allergic) to human von Willebrand Factor or human coagulation factor VIII or any of the other ingredients of Haemate P®
- are allergic to any medicine or food.

- Before you start to use it

Talk to your doctor or pharmacist:

- in case of allergic or anaphylactic-type reactions (a serious allergic reaction that causes severe difficulty in breathing or dizziness). Allergic hypersensitivity reactions are possible. Your doctor should inform you of the early signs of hypersensitivity reactions, such as 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). If these symptoms occur, you should stop the use of the product immediately and contact your doctor.
- if the formation of inhibitors (neutralising antibodies) has been observed. This means that the applied coagulation factor is going to be ineffective and success of treatment will be inadequate.

Von Willebrand disease

- In case you have a known risk of developing blood clots (thrombotic events including blood clots in the lung), particularly in case you have known clinical or laboratory risk factors (e.g. in the perioperative period without conduct of thromboprophylaxis, no early mobilization, obesity, overdose, cancer). In this case, you must be monitored for early signs of thrombosis. Prophylaxis against venous thrombosis should be instituted, according to the current recommendations.
- if you are pregnant or breast-feeding.
- if you are on a controlled sodium diet. Haemate P® contains up to 35 mg sodium per 500 IU.

Your doctor will consider carefully the benefit of treatment with Haemate P® compared with the risk of these complications.

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, and
- the testing of each donation and pools of plasma for signs of virus/infections.
- the 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 enveloped viruses such as human immunodeficiency virus (HIV, the AIDS virus), hepatitis B virus and hepatitis C virus (inflammation of the liver) and for the non-enveloped hepatitis A virus (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 (infection of the unborn child) and
- for individuals with a depressed 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 vaccination against hepatitis A

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and B if you regularly/repeatedly receive human plasma-derived von Willebrand factor and coagulation factor VIII products.

It is strongly recommended that every time you receive a dose of Haemate P® the name and batch number of the medicine are recorded in order to maintain a record of the batches used.

- Taking other medicines
Tell your doctor or pharmacist if you:
- are taking, have recently taken or might take any medicines, including medicines obtained without a prescription.
- Haemate P® must not be mixed with other medicinal products, diluents or solvents.

How to use Haemate P®
- How much to use
The amount of von Willebrand factor and factor VIII you need and the duration of treatment will depend on several factors, such as your body weight, the severity of your disease, the site and intensity of the bleeding or the need to prevent bleeding during an operation or investigation.

If you have been prescribed Haemate P® 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 or haemophilia center nurse.

- When to use it
Treatment should be started and supervised by a physician who is experienced in this type of disorder.

- How long to use it
Use as directed by your doctor.

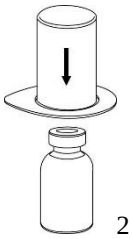
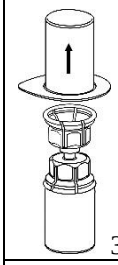
- If you forget to use it
If you think you have missed a dose, speak to your doctor as soon as possible.

- If you use too much (overdose)
If you think you have had too much Haemate P®, speak to your doctor as soon as possible. No symptoms of overdose with VWF and FVIII have been reported. However, the risk of developing blood clots (thrombosis) cannot be excluded in case of an extremely high dose, especially in the case of VWF products with a high FVIII content.

While you are using it
- Things you must do
General Instructions
- The powder must be mixed (reconstituted) with the diluent (liquid) and withdrawn from the vial under aseptic conditions.
- The solution should be clear or slightly opalescent. After filtering/withdrawal (see below) the reconstituted product should be inspected visually for particulate matter and discoloration prior to administration. Even if the directions for use for the reconstitution procedure are precisely followed, it is not uncommon for a few flakes or particles to remain. The filter included in the Mix2Vial device removes those particles completely. Filtration does not influence dosage calculations.
- After administration any unused product or waste material should be disposed of in accordance with national requirements and as instructed by your doctor.

Reconstitution
Without opening either vial, warm the Haemate P® powder and the solvent to room 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.

Carefully remove the protective caps from the diluent vial and the product vial. Clean the exposed rubber stoppers of both vials with one alcohol swab each and allow them to dry. The diluent can now be transferred to the powder with the administration set (Mix2Vial) attached. Please 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. Invert the solvent vial 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 and with the other hand grasp the solvent-side and unscrew the set carefully into two pieces to avoid excessive build up of foam when dissolving the product. Discard the solvent vial with the

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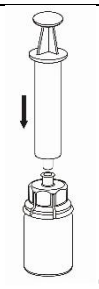
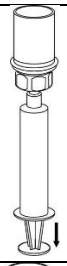
	blue Mix2Vial adapter attached.
 6	6. Gently swirl the product vial with the transparent adapter attached until the substance is fully dissolved. Do not shake.
 7	7. Draw air into an empty, sterile syringe. While the product vial is upright, connect the syringe to the Mix2Vial´s Luer Lock fitting. Inject 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.

- Things you must not do

- Do not use visibly cloudy solutions or solutions still containing flakes or particles after filtration.
- Do not expose the vials to direct heat. The vials must not be heated above body temperature (37°C).

- Things to be careful of

Application

For injection of Haemate P® 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.

The reconstituted solution should be administered slowly intravenously at a rate not more than 4 ml per minute. Take care that no blood enters the syringe filled with product. Once the product is transferred into the syringe it should be used immediately.

In case larger amounts of the factor have to be administered, this can also be done by infusion. For this purpose transfer the reconstituted product into an approved infusion system. Infusion should be carried out as instructed by your doctor.

Observe yourself for any immediate reaction. If any reaction takes place that might be related to the administration of Haemate P®, the injection/infusion should be stopped.

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

Side effects

Like all medicines, Haemate P® can cause side effects, although not everybody gets them.

The following side effects have been observed very rarely (less than 1 of 10,000 patients):

- A sudden allergic reaction (such as angioedema, burning and stinging at the infusion site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) have been observed very rarely, and may in some cases progress to severe anaphylaxis (including shock).
- Increase in body temperature (fever).

Von Willebrand disease

- Very rarely, there is a risk of thrombotic/thromboembolic events including blood clots in the lung (risk of formation and migration of blood clots into the arterial/venous vessel system with a potential impact on organ systems).
- In patients receiving VWF products sustained excessive FVIII:C plasma levels may increase the risk of formation of blood clots.
- Patients with VWD may very rarely develop inhibitors (neutralising antibodies) to VWF. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response leading to continuous bleeding. This happens especially in patients with a specific form of von Willebrand disease, the so-called type 3. Such antibodies are precipitating and may occur concomitantly to anaphylactic reactions. Therefore, patients experiencing anaphylactic reaction should be evaluated for the presence of an inhibitor. In such cases, it is recommended that a specialised haemophilia centre be contacted.

Haemophilia A

- You may very rarely develop inhibitors (neutralising antibodies) to factor VIII. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response leading to continuous bleeding. In such cases, it is recommended that a specialised haemophilia centre be contacted.

Side effects in children and adolescents

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of side effects

If you get any side effects, talk to your doctor, nurse or pharmacist. 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.

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You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers→ Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

Pregnancy, breast-feeding and fertility

- Based on the rare occurrence of haemophilia A in women, experience regarding the use of factor VIII during pregnancy and breastfeeding is not available.
- In case of von Willebrand disease women are even more affected than men, because of additional bleeding risks like menstruation, pregnancy, labour, child birth and gynecological complications. Based on post-marketing experience substitution of VWF in the prevention and treatment of acute bleedings can be recommended. There are no clinical studies available on substitution therapy with VWF in pregnant or lactating women.
- During pregnancy and breast-feeding Haemate P® should be given only if it is clearly indicated.

Driving and using machines
Haemate P® has no influence on the ability to drive and use machines.

Storage and Disposal of Haemate P®
- Storage

- 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.
- Keep the vial in the outer carton, in order to protect from light.
- Haemate P® does not contain a preservative so the made-up solution should preferably be used immediately.
- If the made-up solution is not administered immediately it must be used within 3 hours.
- Once the product is transferred into the syringe it should be used immediately.

- Disposal
Do not throw away any medicines via waste water or household waste.

Ask your doctor or healthcare professional how to throw away medicines you no longer use. These measures will help protect the environment.

Product Description
- What it looks like
Haemate P® is presented as a white or pale yellow powder or friable solid and is supplied with water for injections as solvent. The made-up solution should be clear or slightly opalescent, i.e. it might sparkle when held up to the light but must not contain any obvious particles.

Presentations
Pack with 250 IU FVIII/ 600IU VWF containing:
1 vial with powder
1 vial with 5ml water for injection
1 filter transfer device 20/20

Pack with 500 IU FVIII /1200 IU VWF containing:
1 vial with powder
1 vial with 10ml water for injection
1 filter transfer device 20/20

Pack with 1000 IU FVIII /2400 IU VWF containing:
1 vial with powder
1 vial with 15ml water for injection
1 filter transfer device 20/20

Not all pack sizes may be marketed.

- Ingredients
- Active ingredient(s)
human coagulation factor VIII and human von Willebrand factor

- Inactive ingredients
Human albumin, aminoacetic acid, sodium chloride, sodium citrate, sodium hydroxide or hydrochloric acid (in small amounts for pH adjustment)
Solvent: Water for injections

- MAL number:
MAL20051437ARZ
MAL22046010ARZ

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Product Registration Holder
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