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What Beriate is used for

Beriate 250/500/1000 is made from human plasma (this is the liquid part of the blood) and it contains human coagulation Factor VIII. It is used to prevent or to stop bleedings caused by the lack of Factor VIII (haemophilia A) in the blood. It may also be used in the management of acquired Factor VIII deficiency.

How Beriate works

Factor VIII is involved in blood clotting (coagulation). Lack of Factor VIII means that blood does not clot as quickly as it should and so there is an increased tendency to bleed. The replacement of Factor VIII with Beriate 250/500/1000 will temporarily repair the coagulation mechanisms.

Before you use Beriate

It is strongly recommended that every time that Beriate 250/500/1000 is given, you should record the date of administration, the batch number and the injected volume in your treatment diary.

- When you must not use it

If you are allergic (hypersensitive) to the human coagulation factor VIII or to any of the ingredients of this medicine (listed in section Product Description).

Pregnancy and lactation

If you are pregnant or breast-feeding, ask your doctor or pharmacist for advice before taking this medicine. During pregnancy and breast-feeding, Beriate 250/500/1000 should be given only if it is clearly indicated. No fertility data are available.

- Before you start use it

Talk to your doctor or pharmacist before using Beriate 250/500/1000.

Allergic type hypersensitivity reactions are possible. 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). **If these symptoms occur, you should stop the use of the product immediately and contact your doctor.**

- The formation of **inhibitors** (neutralising antibodies) to Factor VIII 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. You will be monitored carefully for the development of inhibitors. If your bleeding is not being controlled with Beriate 250/500/1000, tell your doctor immediately.

Your doctor will consider carefully the benefit of treatment with Beriate 250/500/1000 compared with the risk of these complications.

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. Manufacturers of these products also include steps in the production process that can inactivate or remove viruses or other pathogens. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be completely 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 viruses hepatitis A virus and parvovirus B19.

Your doctor may recommend that you consider vaccination against hepatitis A

and B if you regularly/repeatedly receive human plasma-derived products (e.g. Factor VIII).

- Taking other medicines

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Beriate 250/500/1000 must not be mixed with other medicinal products, diluents and solvents except for those that are recommended by the manufacturer (see section Product Description).

How to use Beriate

- How much to use

The amount of 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 bleeding or the need to prevent bleeding during an operation or investigation. If you have been prescribed Beriate 250/500/1000 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

Use as directed by your doctor or pharmacist.

- How long to use it

Continue taking Beriate for as long as your doctor recommends.

- If you forget to use it

Consult your doctor or pharmacist on what you should do if you forget to use it.

- If you use too much (overdose)

No symptoms of overdose with FVIII have been reported.

Reconstitution and application

General instructions:

- The powder must be mixed (reconstituted) with the solvent (liquid) and withdrawn from the vial under aseptic conditions.
- The reconstituted solution should be clear or slightly opalescent, i.e. it might be sparkling when held up to the light. Occasionally, a few flakes or particles may appear in the vial. The filter included in the Mix2Vial removes these particles. After filtering and withdrawal

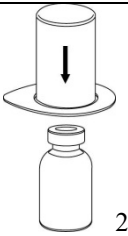
(see below) of the product into the syringe, the solution should be checked by eye for small particles and discoloration, before it is administered. Do not use the solution if it is visibly cloudy or if it contains flakes or particles while in the syringe.

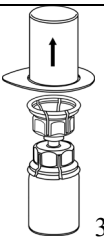
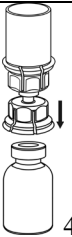
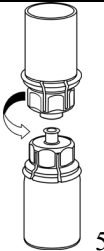
- Once the product is transferred into the syringe, it should be used immediately. Do not store the product in the syringe.
- Any unused product or waste material should be disposed of in accordance with local requirements and as instructed by your doctor.

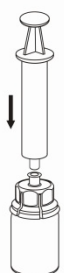
Reconstitution:

Without opening either vial, warm the Beriate powder and the solvent 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°C).

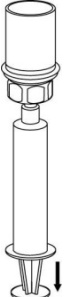
Carefully remove the protective caps from the vials containing powder and the solvent, and clean the exposed rubber stoppers with an alcohol swab. Allow the vials to dry before opening the Mix2Vial package, then follow the instructions given below.

	1. Open the Mix2Vial package by peeling off the lid. Do not remove the Mix2Vial from the blister package!
	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. 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. Place the Beriate 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 Beriate vial stopper. The solvent will automatically flow into the Beriate vial.
	5. With one hand grasp the Beriate - side of the Mix2Vial set and with the other hand grasp the solvent-side and unscrew counter clockwise the set carefully into two pieces. Discard the solvent vial with the blue Mix2Vial adapter attached.

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

Withdrawal and application:

	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. 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 counter clockwise.

Inject the reconstituted solution slowly 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.

Where a large volume is required, infusion is an alternative option. The reconstituted preparation should be transferred to an approved infusion system. Infusion should be carried out as instructed by your doctor.

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 Beriate 250/500/1000, the injection or infusion should be stopped (see also section Before you use Beriate).

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

While you are using it

- Things you must do

Take your medicine exactly as your doctor has told you.

Tell all the doctors, dentists and pharmacists treating you that you are taking Beriate.

Tell your doctor immediately if you become pregnant while taking this medication.

- Things you must not do

Do not stop taking the medicine unless advised by your doctor.

Do not take any new medicines without consulting your doctor.

Do not give Beriate to anyone else, even if they have the same symptoms or condition as you.

- Things to be careful of

Beriate 250/500/1000 contains sodium
Beriate 250 contains up to 7 mg sodium per 250 IU.

Beriate 500 contains up to 14 mg sodium per 500 IU.

Beriate 1000 contains up to 28 mg sodium per 1000 IU.

Please take this into account if you are on a controlled sodium diet

Beriate 250/500/1000 has no influence on the ability to drive and use machines

Side effects

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

If any of the following happen, contact your doctor immediately or go to the Emergency Department or

Haemophilia Centre at your nearest hospital:

- Symptoms of angioedema such as ~ swollen face, tongue or pharynx ~ difficulty to swallow ~ hives and difficulties to breathe

These side effects have been observed very rarely, and may in some cases progress to severe allergic reactions (anaphylaxis) including shock.

- Loss of effect (continuous bleeding).

For patients not previously treated with Factor VIII medicines, inhibitor antibodies formation (see section 3) is very common (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 you develop inhibitor antibodies your medicines may stop working properly and you may experience persistent bleeding. If this happens, it is recommended that a specialised haemophilia centre be contacted.

Other side effects are:

- Allergic (hypersensitivity) reactions, which may include: ~ burning and stinging where the injection or infusion was given ~ chills, flushing, skin rash over the whole body, wheals ~ headache ~ fall in blood pressure, restlessness, faster heart beat, tightness of the chest, wheezing ~ tiredness (lethargy) ~ nausea, vomiting ~ tingling

These side effects have been observed very rarely, and may in some cases progress to severe allergic reactions (anaphylaxis) including shock.

- Very rarely, fever has been reported.

Side effects in children and adolescents

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

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-78835490, or visiting the website nptra.gov.my [Consumers→ Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)]

Storage and Disposal of Beriate

Do not use this medicine after the expiry date, which is stated on the label and carton.

- Storage

- Store in a refrigerator at 2 to 8 °C.
- Within the shelf-life, Beriate 250/500/1000 may be stored at up to 25 °C, not to exceed a cumulative storage period of 1 month. The single room temperature periods should be documented in your treatment diary, to comply with the overall 1 month period.
- Beriate 250/500/1000 does not contain a preservative so the reconstituted product should be used immediately.
- Do not freeze.
- Keep the container in the outer carton in order to protect from light.

Keep out of the reach and sight of children

- Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Product Description

- What it looks like

Beriate 250/500/1000 is presented as a white powder and is supplied with water for injection.

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.

Presentations

Box containing:

Box containing 250, 500, 1000IU:

1 Vial with powder containing 250,500, 1000 IU coagulation factor VIII

1 vial with 2.5,5,10ml water for injections.

1 filter transfer device

Not all pack sizes may be marketed.

- Ingredients

-Active ingredient(s)

Beriate 250 is presented as a powder (containing nominally 250 IU human coagulation Factor VIII per vial) plus a liquid (diluent). The reconstituted solution is for injection or infusion. The product reconstituted with 2.5 ml of water for injections contains approximately 100 IU/ml human coagulation Factor VIII.

Beriate 500 is presented as a powder (containing nominally 500 IU human coagulation Factor VIII per vial) plus a liquid (diluent). The reconstituted solution is for injection or infusion. The product reconstituted with 5 ml of water for injections contains approximately 100 IU/ml human coagulation Factor VIII.

Beriate 1000 is presented as a powder (containing nominally 1000 IU human coagulation Factor VIII per vial) plus a liquid (diluent). The reconstituted solution is for injection or infusion. The product reconstituted with 10 ml of water for injections contains approximately 100 IU/ml human coagulation Factor VIII.

-Inactive ingredients

Glycine, calcium chloride, sodium hydroxide (in small amounts) for pH adjustment, saccharose, sodium chloride. *Solvent:* Water for injection 10 ml.

- MAL number(s):

- Beriate 250 IU Powder and solvent for solution for injection or infusion MAL21086005AZ
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- Beriate 500 IU Powder and solvent for solution for injection or infusion MAL21086006AZ
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- Beriate 1000 IU Powder and solvent for solution for injection or infusion MAL21086007AZ

Manufacturer

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

Product Registration Holder

DKSH Malaysia Sdn Bhd
B-11-01, The Ascent, Paradigm, No.1,
Jalan SS7/26A, Kelana Jaya, 47301
Petaling Jaya, Selangor, Malaysia.

Date of revision

9/12/2022

Serial Number

NPRA (R3/01)15112022/0225