

INFORMATION ABOUT

BIOSTATE[®]

Human Coagulation Factor VIII



New Zealand
Blood Service
The gift of life

CSL
Bioplasma[®]

Your doctor has prescribed BIOSTATE® for you. This guide has been produced as a source of information about BIOSTATE.

While this guide aims to answer some commonly asked questions, it should not take the place of speaking to your doctor.

If you have any concerns after reading this guide, feel free to talk to your doctor or to the staff at your Haemophilia Treatment Centre. Remember to always follow your doctor's advice, even if it differs from the advice in this guide.

BIOSTATE is a high purity factor VIII concentrate.^{1,2}

Factor VIII is a protein that is essential for normal blood clotting. BIOSTATE is a highly purified factor VIII concentrate, made from human plasma. BIOSTATE also contains von Willebrand factor, which is a protein that carries factor VIII in the blood. The presence of von Willebrand factor helps to stabilise the factor VIII in BIOSTATE and prolong its duration in the blood.

What is BIOSTATE used for?¹

BIOSTATE replaces the missing factor VIII in people with haemophilia A. BIOSTATE helps to prevent bleeding and is also used to treat bleeding into muscles, joints and internal organs as well as preventing and controlling bleeding associated with surgery.

Can BIOSTATE be used to treat von Willebrand's Disease?

Although BIOSTATE does contain von Willebrand factor, it has not been fully assessed for use in von Willebrand's Disease. Studies are underway to determine the suitability of BIOSTATE for treating von Willebrand's Disease.



How is BIOSTATE made?^{1,2}

BIOSTATE is made from human plasma (the straw coloured liquid part of blood) collected from healthy blood donors. The factor VIII in the plasma is purified and concentrated using a technique called chromatography. Chromatography uses a special gel to separate proteins such as factor VIII and von Willebrand factor from other components of plasma.

Chromatography is a gentle way of purifying and concentrating the proteins and does not alter their structure.

BIOSTATE incorporates two steps to remove and kill viruses. The first step is known as solvent detergent treatment and the second step is a heat treatment step, where the product is heated at 80°C for 72 hours.

These steps are effective against enveloped viruses such as human immunodeficiency virus (HIV) and hepatitis B and C, and also the non-enveloped virus, hepatitis A.

After manufacture, BIOSTATE is tested to ensure that it meets national and international standards before it is finally released for use.

BIOSTATE is made by CSL Bioplasma, a division of CSL Limited.

BIOSTATE is made in Melbourne, Australia at CSL Bioplasma's state-of-the-art manufacturing facility, which was commissioned in 1994.

New Zealand's blood collection system.^{3,4}

BIOSTATE is manufactured from plasma collected by the New Zealand Blood Service. The plasma used to manufacture BIOSTATE is collected from volunteer donors who are carefully assessed to ensure their blood and plasma are suitable for transfusion to other people. Only those donors who meet strict guidelines are accepted as blood or plasma donors.

The New Zealand Blood Service tests all blood and plasma donations for the following:

- human immunodeficiency virus (HIV)
- hepatitis B and C viruses
- syphilis.

The New Zealand Blood Service also initially tests all blood donors for human T-cell lymphotropic virus (HTLV). This is an uncommon virus which rarely causes blood or nervous system problems.

Thorough testing ensures international viral safety standards are met.²⁻⁵

The New Zealand Blood Service currently performs two types of tests for hepatitis C and HIV on all blood and plasma that is donated.

The first test, called antibody testing, detects antibodies that a person's immune system produces in response to a virus being present. The second test, known as NAT (nucleic acid amplification technology), detects the actual HIV and hepatitis C viruses. NAT can detect infection at an earlier stage than the antibody tests, providing an additional level of safety for the New Zealand blood supply. Only plasma that tests negative is sent to CSL Bioplasma by the New Zealand Blood Service.

When the plasma arrives at CSL Bioplasma, it is tested again for HIV and hepatitis C using the above tests. The plasma is also tested again for hepatitis B surface antigen. Only donations that CSL Bioplasma test negative for these viruses are used to manufacture BIOSTATE.

In addition to the testing of the plasma by both the New Zealand Blood Service and CSL Bioplasma, two steps are incorporated into the manufacture of BIOSTATE that are designed to further reduce viral risk. These steps are effective against enveloped viruses (such as HIV and hepatitis B and C) and also the non-enveloped virus, hepatitis A.

Why have we changed from AHF (HP) to BIOSTATE?²

AHF (HP) was used for many years as the main treatment for haemophilia A. BIOSTATE was developed as part of CSL Bioplasma's commitment to continuous product improvement.

BIOSTATE has several enhancements, compared to AHF (HP).

First, BIOSTATE is 'more pure'. That is, it contains fewer proteins that are not needed in the treatment of haemophilia A. Put simply, the fewer proteins in the product which aren't necessary for its effectiveness, the better.

Second, BIOSTATE has enhanced viral safety due to an additional viral-inactivation step.

Third, treatment with BIOSTATE is more convenient, as BIOSTATE is reconstituted with a smaller volume of Water for Injections so it has a smaller infusion volume, reducing the time needed for your dosage.

Other features of BIOSTATE:

- BIOSTATE has a self-adhesive peel-off label to help you keep an accurate record of your treatment with BIOSTATE
- BIOSTATE has an easy to remove flip-top lid
- BIOSTATE is packaged with a Preparation Device that makes reconstitution and filtering simple and reduces the risk of needle-stick injuries.

Is the infusion volume for BIOSTATE the same as AHF (HP)?¹

The infusion volume for BIOSTATE is half that of AHF (HP). This is because AHF (HP) was available in a 250 IU bottle size and was reconstituted in 10 mL Water for Injections, while BIOSTATE is available in a 250 IU bottle size and is reconstituted in only 5 mL Water for Injections.

This means that, for example, if you needed 4 bottles of AHF (HP) (or 40 mL of reconstituted AHF (HP)) to treat a bleed in the past, you will still need 4 bottles of 250 IU BIOSTATE, but this is now only 20 mL of reconstituted BIOSTATE.

- 250 IU of BIOSTATE is reconstituted in only 5 mL of Water for Injections.

Are there more chemicals in BIOSTATE than AHF (HP)?²

BIOSTATE has increased purity compared to AHF (HP) and also has an extra viral inactivation step. While there are more steps in the manufacture of BIOSTATE, any additional chemicals are removed before BIOSTATE is put into bottles and freeze-dried.

Any trace amounts of chemicals that may remain in BIOSTATE at the end of the manufacturing process must be below stringent limits that have been set by Australian control authorities and have been proven not to be harmful.

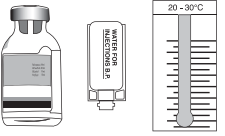
Are there any side effects from using BIOSTATE?¹

Research has found that the side effects of BIOSTATE are very similar to those of AHF (HP) and other plasma-derived factor VIII concentrates. Side effects are usually mild and don't last very long. Possible side effects include bone pain, dizziness, headache, anxiety, chest pain, fever, back pain, joint pain and reddening of the face or neck.

How do I make up BIOSTATE?¹

The following diagrams and brief instructions will help you to prepare BIOSTATE. The complete instructions for making up BIOSTATE are printed in the Product Information that is in each pack of BIOSTATE.

1




Ensure product and Water for Injections are at room temperature before use.

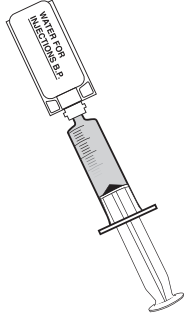
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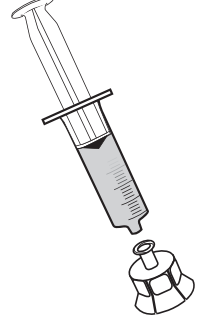
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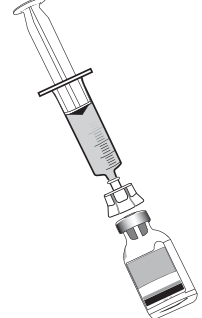
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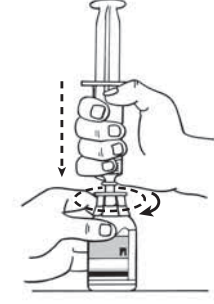
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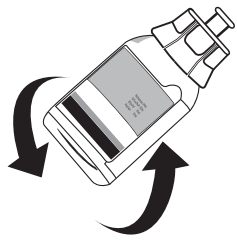


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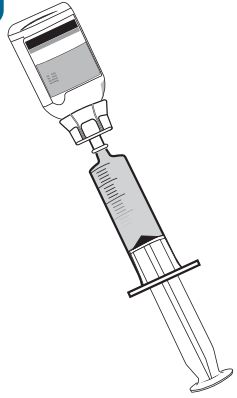
1. Place the bottle on a hard surface.
2. Hold the syringe as shown.
3. Push downward and rotate bottle at the same time.
After several turns, the Preparation Device will pierce the stopper, and should stay firmly in place.

8



Gently swirl to dissolve. Do not shake.

9



The Preparation Device.

The Preparation Device has replaced the filter needle that was supplied with AHF (HP). The Preparation Device features a shield around the needle to prevent injuries. Being made entirely of plastic, the Preparation Device does not have to be disposed of in a sharps container.



Should you have any difficulty using the Preparation Device after reading the instructions in this booklet, and the instructions in the Product Information (which accompanies each pack of BIOSTATE), please contact the staff at your Haemophilia Treatment Centre.

How to store BIOSTATE.¹

BIOSTATE should be stored in the refrigerator at 2°C to 8°C (do not freeze). After BIOSTATE is made up, it should be administered as soon as possible.

Further information:

The following information is available to help you use BIOSTATE:

- A video presentation explaining how to prepare BIOSTATE using the Preparation Device
- A leaflet showing how to use the Preparation Device
- A Treatment Diary for recording details about your treatments, including pages on which you can stick the peel-off labels.

Improvements to BIOSTATE

When you first receive BIOSTATE, it will be packed with the Preparation Device and Water for Injections (in a plastic ampoule) as explained in this booklet. Your BIOSTATE, when packed with these items, will need to be stored in the fridge at 2-8°C

As part of CSL Bioplasma's Product Improvement Strategy, BIOSTATE that will be made available later in 2005 will be packed with an improved version of the Preparation Device, called a Mix2Vial filter transfer set, and Water for Injections (in glass vials). These components are easier to use, hence CSL Bioplasma's decision to change the components supplied with BIOSTATE. BIOSTATE packed with the new Mix2Vial and Water for Injections (in glass vials) can be stored at room temperature (below 25°C).

The staff at your Haemophilia Treatment Centre will let you know when you will be receiving BIOSTATE with these improvements – the Mix2Vial, Water for Injections (in glass vials) and the ability to store BIOSTATE below 25°C. Educational materials will be available to help you to use the new components.

Until notified by your Haemophilia Treatment Centre, please use the instructions in this booklet to reconstitute and store your BIOSTATE.

Who should I contact for more information?

To access more information about BIOSTATE, or to report any concerns about BIOSTATE, please contact either your doctor or the staff at your Haemophilia Treatment Centre. To obtain copies of the video, leaflets and Treatment Diary described on the previous page, please contact either the staff at your Haemophilia Treatment Centre, or CSL Bioplasma by e-mail at customer.service.bmw@csl.com.au.

For further information of a general nature on BIOSTATE, please contact either the New Zealand Blood Service on 09 523 5744, or CSL Bioplasma using the contact details listed on the back cover of this guide.

References:

1. Approved Product Information for BIOSTATE, July 2003, Ver 3.00
2. National Haemophilia No. 141, Nov 2002 p 4-5.
3. NZBS Collection Standards and NZBS Manufacturing Standards
4. New Zealand Code of Good Manufacturing Practice for Manufacture and Distribution of Therapeutic Goods.
5. Australian Code of Good Manufacturing Practice – Human Blood and Tissues (2002). Therapeutic Goods Administration, Woden, ACT, Australia.

Please review approved Product Information before administering BIOSTATE

Product Information accompanies each pack of BIOSTATE

Refer to Boxed Warning in Product Information

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