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CSL Behring

8 January 2018

Dear Healthcare Professional,

Notification - update to BIOSTATE® (human coagulation Factor VIII/VWF complex) Label, Carton and Product Information

CSL Behring writes to advise that the BIOSTATE vial Label, Carton and Product Information will shortly be updated to reflect a 1 : 2.4 ratio of factor VIII (FVIII) to von Willebrand Factor (VWF) in the final product.

The first issue of BIOSTATE with the updated labelling will be the 1000 IU FVIII presentation, which is anticipated to be received by Healthcare Providers from late January / February 2018.

The increased VWF content in BIOSTATE has occurred due to a gradual decline in recent years in FVIII levels in the plasma from which Australia's BIOSTATE is manufactured, with minimal change to the VWF levels. As a result the ratio of FVIII to VWF, historically approximately 1 : 2.0, has gradually risen to approximately 1 : 2.4. The updated VWF label content now aligns more closely to levels measured over recent times. No changes to the manufacturing process have occurred.

To align the label with the current product content, CSL Behring has obtained approval from the TGA for a revised FVIII : VWF ratio of 1 : 2.4, and this change will be implemented on the BIOSTATE vial Label, Carton and Product Information[1]. Details of the changes to the label are provided on the following page. The updated BIOSTATE Product Information (Version 25.00) accompanies this letter.

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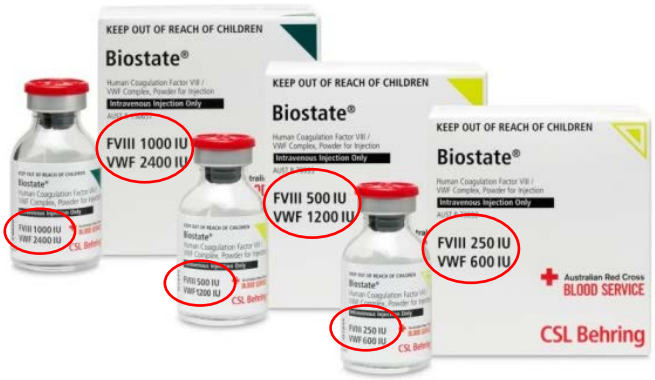
BIOSTATE Labelling changes

Item Number*	Outgoing labelling	Incoming labelling
	(Active ingredients: FVIII : VWF, 1 : 2.0)	(Active ingredients: **FVIII : VWF, 1 : 2.4**)
33000185	BIOSTATE 250 IU FVIII / 500 IU VWF	BIOSTATE 250 IU FVIII / **600 IU VWF**
33000192	BIOSTATE 500 IU FVIII / 1000 IU VWF	BIOSTATE 500 IU FVIII / **1200 IU VWF**
33100194	BIOSTATE 1,000 IU FVIII / 2000 IU VWF	BIOSTATE 1,000 IU FVIII / **2400 IU VWF**

*All item numbers remain the same.

Changes to vial Label and Carton



Updated VWF content on each carton and label

Transition

First supplies of BIOSTATE 1000 IU FVIII with updated labelling are anticipated to reach Health Providers from late January / February 2018. Release of BIOSTATE 500 IU FVIII and BIOSTATE 250 IU FVIII with updated labelling will follow.

Clinical considerations

The change to the VWF content of BIOSTATE has occurred gradually and the updates to the label better align with product content seen in recent times, however healthcare professionals may wish to consider the dosing impact for individual patients. Please refer to the accompanying updated BIOSTATE Product Information[1] for details.

When prescribing and dispensing BIOSTATE, the active entity (FVIII or VWF) being prescribed must be specified. For example: BIOSTATE 1000 IU of FVIII, or BIOSTATE 1000 IU of VWF. This is to avoid dosing errors as a result of the active entity not being specified.

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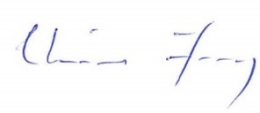
When clinicans prescribe in VWF units, should they wish the dose to be the same number of vials, an adjustment in the number of VWF units prescribed will be required. For example: a person currently being prescribed 2000 IU VWF will require 2400 IU VWF to be prescribed in order to avoid an effective change from their current BIOSTATE dose.

For further information relating to this notification please contact CSL Behring:-
- Dr Sebastian Dinatale, Director, Medical Affairs - Sebastian.Dinatale@cslbehring.com.au,
- Chris Fry, Snr Brand Manager, Coagulation - Christopher.Fry@cslbehring.com.au,
or CSL Behring Medical Information - Medicalinformation@cslbehring.com.au, telephone toll free: 1800 642 865.

Yours sincerely,



Dr Sebastian Dinatale
Director, Medical Affairs
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Chris Fry
Snr Brand Manager, Coagulation
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[1] BIOSTATE® Approved Product Information, Version 25.00. Date of most recent amendment 15 November 2017. Available at www.cslbehring.com.au/au-PI [Attached]