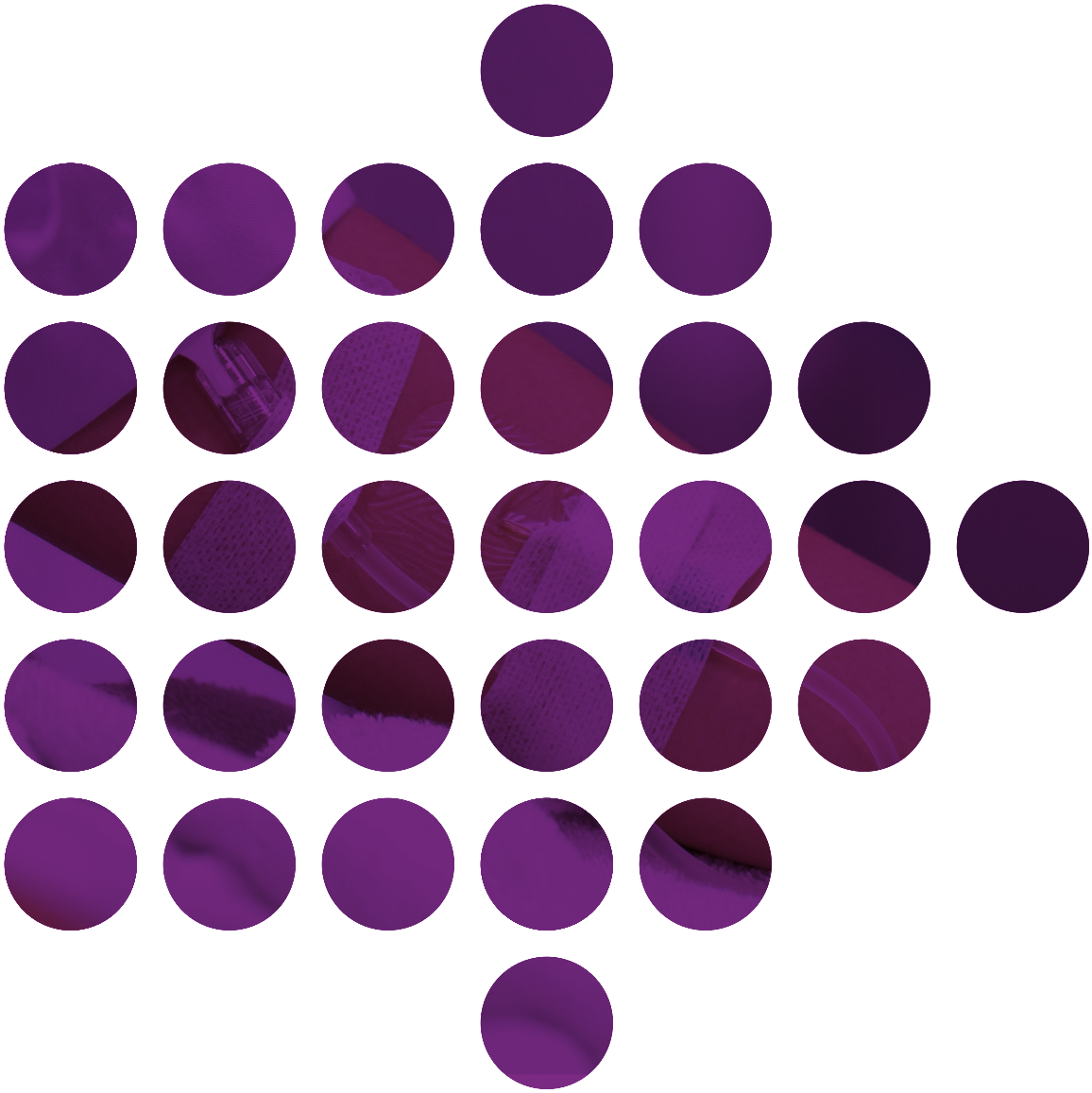
CSL Behring

Australia's Prothrombin Complex Concentrate is transitioning[1]



In mid 2024, PROTHROMBINEX®-VF will be discontinued and replaced with BERIPLEX®.[1] Please read this leaflet containing important information about the BERIPLEX® products.

FOR HEALTHCARE PROFESSIONALS

Australia's Plasma, Global Process

Under the National Fractionation Agreement for Australia in place between the National Blood Authority and CSL Behring, CSL Behring has been investing in new facilities at its manufacturing site in Broadmeadows, Victoria to provide expanded capacity for processing Australia's growing annual domestic plasma collections.

CSL Behring, Australia's chosen national plasma fractionator and manufacturer, is transitioning five domestic plasma products to new, purpose-built manufacturing facilities. These plasma products will continue to be manufactured from plasma collected on-shore by the Australian Red Cross Lifeblood but will be manufactured using CSL Behring's global manufacturing processes. As per the current products, the new products will comply with the safety and efficacy requirements set by the Therapeutic Goods Administration.

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Prothrombin complex, manufactured by CSL Behring

This document discusses the transition of PROTHROMBINEX®-VF to BERIPLEX®.

From mid 2024 **PROTHROMBINEX®-VF** will be replaced by **BERIPLEX®**. For a period of approximately 6 months **BERIPLEX® P/N** will be supplied using international plasma. This will then be replaced by **BERIPLEX® AU**, subject to regulatory approval, made using Australian Plasma.

Differences	PROTHROMBINEX®-VF[2]	BERIPLEX® P/N 500 IU[3]	BERIPLEX® AU 500 IU[4]
Presentations	500 IU		
Active ingredients	Factor IX (500 IU) Factor II (approx. 500 IU) Factor X (approx. 500 IU)	**Factor II (400–960 IU)** **Factor VII (200–500 IU)** **Factor IX (400–620 IU)** **Factor X (440–1200 IU)** **Protein C (300–900 IU)** **Protein S (240–760 IU)**	
Dosing	Dosing differences between PROTHROMBINEX®-VF and BERIPLEX® include the dosing algorithm (initial International Normalised Ratio (INR) ranges, target INR and related dose), maximum single dose by INR range and inclusion of dosing in mL/kg body weight.		
Rate of administration	Approximately 3 mL per minute or as tolerated by patient	**Not exceeding 3 IU/kg body weight/minute, max. 210 IU/minute, approximately 8 mL per minute**	
Storage conditions	Store 2–8°C *(do not freeze)* Can be stored below 25°C for a single period of 6 months	**Store below 25°C *(do not freeze)***	
Shelf life	3 years		
Plasma source	Australia	International	Australia
Estimated available date	Until mid 2024	From mid 2024	From late 2024/ early 2025*

* Variation to manufacture using Australian plasma pending regulatory approval.

BERIPLEX® P/N and BERIPLEX® AU indication

Treatment and perioperative prophylaxis of bleedings in acquired deficiency of the prothrombin complex coagulation factors, such as deficiency caused by treatment with vitamin K antagonists, or in case of overdose of vitamin K antagonists, when rapid correction of the deficiency is required.[3,4]

Always read and refer to the BERIPLEX® P/N and BERIPLEX® AU Product Information prior to administration.

PROTHROMBINEX®-VF Human Prothrombin Complex

Beriplex® P/N Prothrombin Complex Concentrate

Beriplex® AU Prothrombin Complex Concentrate

What are the differences between PROTHROMBINEX®-VF and BERIPLEX® P/N and BERIPLEX® AU?

Vial volume changes

- BERIPLEX® P/N and BERIPLEX® AU will be available in a 20 mL vial size, approved for storage at room temperature (below 25°C; do not freeze).[3,4]

Change to a four-factor prothrombin complex concentrate

- BERIPLEX® P/N and BERIPLEX® AU are a four-factor prothrombin complex concentrates containing human coagulation factors II, VII, IX, and X. BERIPLEX® P/N and BERIPLEX® AU also contain Protein C and Protein S.[3,4] PROTHROMBINEX-VF® only contains factors II, IX, and X.[2]

Changes to warnings, precautions, and elderly use

- BERIPLEX® P/N and BERIPLEX® AU may be unsuitable in patients who have had thromboembolic events in the last 3 months.[3,4]
- Safety and efficacy of BERIPLEX® P/N in elderly people (>65 years) has been demonstrated in clinical studies.[3,4]
- Please review the BERIPLEX® P/N and BERIPLEX® AU Product Information for the full list of precautions and warnings.[3,4]
- In disseminated intravascular coagulation requiring substitution of prothrombin complex factors, this may only be carried out after termination of the consumptive state.[3,4]

Dosage calculation[3,4]

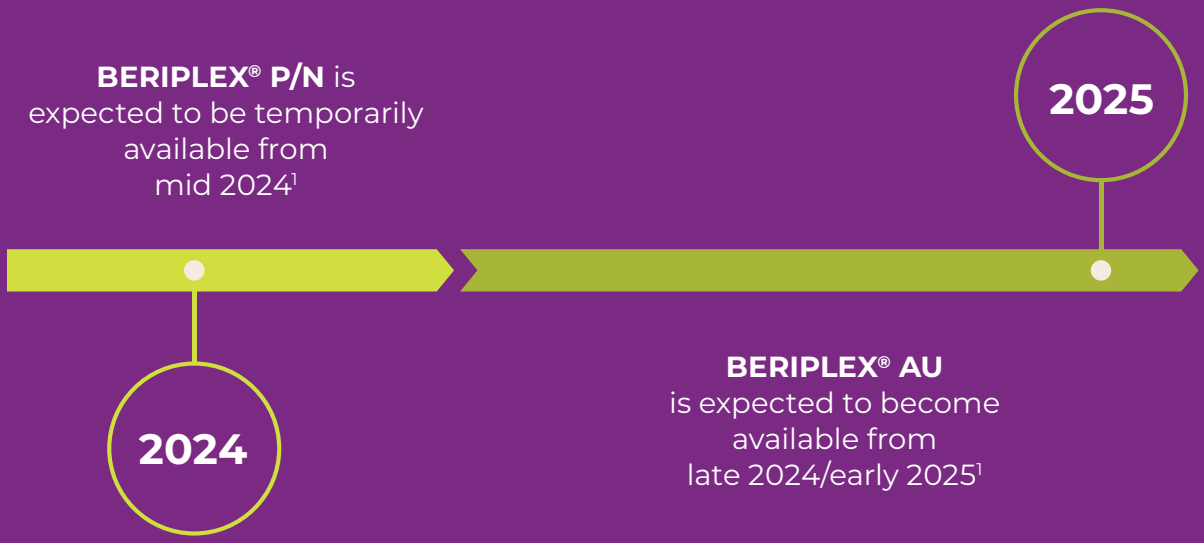
The dose will depend on the international normalised ratio (INR) before treatment and the target INR. Pre-treatment INR should be measured as close as possible to time of dosing in order to calculate the appropriate dose. The table below displays approximate doses required for normalisation of INR at different initial INR levels.

Pre-treatment INR	2.0–3.9	4.0–6.0	>6.0
Approximate dose mL/kg body weight	1	1.4	2
Approximate dose IU (factor IX)/kg body weight	25	35	50

- Dose is based on body weight up to but not exceeding 100 kg.
- Dosing intervals must be adapted to the different circulating half-lives of the respective coagulation factors in BERIPLEX® P/N and BERIPLEX® AU.
- Monitoring of INR during treatment is mandatory.
- These are only general dosing guidelines. Dosing should be adjusted to the individual patient and initiated under the supervision of a physician experienced in the treatment of coagulation disorders.

Timing of changes[1]

BERIPLEX® P/N is expected to be temporarily available from mid 2024[1]



BERIPLEX® AU is expected to become available from late 2024/early 2025[1]

Composition comparison between PROTHROMBINEX®-VF, BERIPLEX® P/N and BERIPLEX® AU

Item / Product	PROTHROMBINEX®-VF[2]	BERIPLEX® P/N AND BERIPLEX® AU[3,4]
Excipients	• Plasma proteins (human) • Antithrombin III (human) • Heparin sodium (porcine) • Sodium* • Phosphate* • Citrate* • Chloride* **Present as sodium citrate, sodium phosphate and sodium chloride*	• Heparin sodium (porcine) • Albumin • Antithrombin III • Sodium chloride • Sodium citrate • HCl or NaOH (in small amounts for pH adjustment)

Product name	GTIN	CARTON DIMENSION
BERIPLEX ® P/N	09347408001781	124 mm x 79 mm x 63 mm
BERIPLEX ® AU	09347408002429	124 mm x 79 mm x 63 mm

For more information on BERIPLEX® P/N and BERIPLEX® AU barcoding and to obtain sample barcodes, please visit the NBA website www.blood.gov.au/barcoding

What is staying the same?

BERIPLEX® AU will be made from Australia's plasma.

Safety first

Our research and vigilance to develop safe, high-quality products for patients continues to be of paramount importance. CSL Behring products continue to comply with the safety and efficacy requirements set by the Therapeutic Goods Administration.

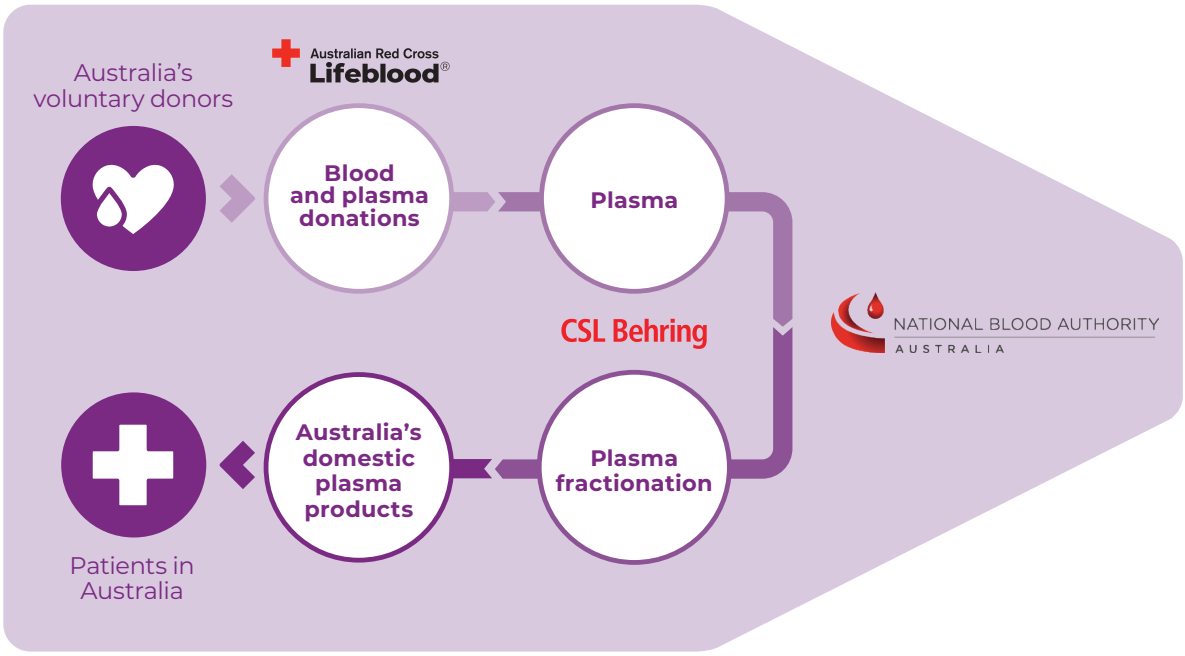
Investing for generations of Australians

CSL has invested in Australia's health for over 100 years. Alignment with global manufacturing processes and the ongoing dedication to continuous improvement demonstrate that CSL is committed to the health and wellbeing of Australians.

Australia's plasma

Trusted since 1916, CSL is Australia's only national plasma fractionator. CSL Behring manufactures a near-complete range of high-quality plasma products using plasma collected on-shore by the Australian Red Cross Lifeblood.

CSL Behring



Benefits in aligning with the global CSL Behring manufacturing processes

Robust new facilities. Reliable supply

CSL Behring's new manufacturing facilities ensure the continued reliable and high-quality production of plasma products for Australia.

Access to Innovation

With this alignment to our global processes, CSL Behring unlocks access to plasma products which cannot currently be manufactured at CSL Behring in Australia.

Australian Red Cross Lifeblood®

This product is made possible through the generosity of Australia's voluntary blood and plasma donors.

CSL Behring

PROTHROMBINEX®-VF

Beriplex® P/N
Prothrombin Complex Concentrate

Scan QR codes to access the Product Information of each product

These products are funded under arrangements implemented by the National Blood Authority.

Please refer to the National Blood Authority for details www.blood.gov.au.

For more information about these products, please contact your CSL Behring Key Account Executive or customer service.

For Medical/Technical Inquiries
Phone: 1800 642 865. Email: medicalinformation@cslbehring.com.au

For Customer Service Inquiries
Phone: 1800 063 892. Email: customerservice@cslbehring.com.au

For healthcare professional resources: hcp.cslbehring.com.au

References: 1. National Blood Authority. Update on the transition of PROTHROMBINEX-VF (prothrombin complex concentrate). Available at: https://blood.gov.au/update-transition-prothrombinex-vf-prothrombin-complex-concentrate-0. Accessed: 6 March 2024. **2.** PROTHROMBINEX®-VF Approved Product Information. **3.** BERIPLEX® P/N Approved Product Information. **4.** BERIPLEX® AU Approved Product Information.