Comparison of Prothrombinex®-VF and Beriplex® P/N

Blood Matters

OFFICIAL

Comparison of Prothrombinex®-VF, Beriplex® P/N

Both products are sterile freeze-dried powders - prothrombin complex concentrates (PCC) of purified human coagulation factors.

This is not complete information on these products.

Please use the product information contained with the product, or on CSL Behring website <https://www.cslbehring.com.au/products/products-list>, or in MIMS.

NOTE: Further information on Beriplex® AU will be available closer to its implementation date, anticipated to be late 2024 or early 2025. Please refer to the National Blood Authority website <https://www.blood.gov.au>.

Product	**Prothrombinex®-VF**	**Beriplex® P/N**
Composition	Prothrombinex®-VF is a three-factor PCC. • contains human coagulation factors II, IX and X and low levels of factors V and VII. • Manufactured from human plasma collected by Australian Red Cross Lifeblood.	Beriplex® P/N is a four-factor PCC. • contains human coagulation factors II, VII, IX, and X, protein S and protein C. • Manufactured from overseas sourced human plasma. • Beriplex® P/N contains up to 343 mg sodium (approximately 15 mmol) per 100 mL.
Active ingredient	Factors II, IX and X	Factors II, VII, IX, and X.
Indications	• Treatment and perioperative prophylaxis of bleeding in acquired deficiency of prothrombin complex factors, such as: – deficiency caused by treatment with vitamin K antagonists, or in case of overdose of vitamin K antagonists, where rapid correction of the deficiency is required. • Treatment and prophylaxis of bleeding in patients with single or multiple congenital deficiency of factor IX, II or X when purified specific coagulation factor product is not available.	• Treatment and perioperative prophylaxis of bleeding in acquired deficiency of prothrombin complex coagulation factors, such as: – deficiency caused by treatment with vitamin K antagonists, or in case of overdose of vitamin K antagonists, where rapid correction of the deficiency is required. Use is generally restricted to circumstances where rapid correction of the prothrombin complex levels is necessary, such as in major bleeding or urgent surgical care.

Product	**Prothrombinex®-VF**	**Beriplex® P/N**
Dosage	• It is recommended that specialist guidelines are referred to when administering Prothrombinex®-VF. Warfarin reversal guidelines.	• General dosage guidelines are provided below. It is recommended that specialist guidelines are referred to when administering Beriplex® P/N. • Treatment should be initiated under the supervision of a physician experienced in the treatment of coagulation disorders. – The dosage and duration of the substitution therapy depend on the severity of the disorder, on the location and extent of bleeding and on the patient's clinical condition. – Dosing depends on pretreatment INR (which should be taken as close as possible to administration). Precise monitoring of the substitution therapy by means of coagulation assays is essential. – Dose is based on body weight up to but not exceeding 100 kg. For patients weighing more than 100 kg see PI for maximum dose dependant on initial INR. • Consider simultaneous administration of Vitamin K in patients receiving Beriplex® P/N for urgent reversal of vitamin K antagonists. • Repeat dosing for reversal of Vitamin K antagonists is not recommended. The correction of the vitamin K antagonist-induced impairment of haemostasis is commonly reached approximately 30 minutes after the injection.
Administration	• Give the dose slowly (approximately 3 mL per minute or as tolerated by the patient) intravenously. – When the contents of more than one vial are to be given, it may be convenient to pool the total amount prior to administration in a large syringe or sterile bag. This must be done aseptically. • To reduce microbiological hazard, use as soon as practicable after reconstitution/preparation. • The solution must not be stored, and infusion should be completed	• Beriplex® P/N should be reconstituted according to the instructions provided. • The reconstituted solution should be administered by a separate injection/infusion line by slow intravenous injection, at a rate not exceeding 3 IU/kg body weight/minute, max. 210 IU/minute, approximately 8 mL/minute. • Whilst the stability of the reconstituted solution has been demonstrated for 24 hours at room temperature (max. 25°C), Beriplex® P/N contains no antimicrobial preservative, therefore it is recommended that the product is used immediately after reconstitution.

Product	**Prothrombinex®-VF**	**Beriplex® P/N**
	within three hours of reconstitution.	• Use in one patient only. Any unused solution should be discarded appropriately. If a clot or gel forms, do not use the product.
Contraindications	• Hypersensitivity to the active substances or to any of the excipients including known allergy to heparin or history of heparin-induced thrombocytopenia (HIT). • Prothrombinex®-VF is also contraindicated in patients who have evidence of active thrombosis or disseminated intravascular coagulation (DIC).	• Hypersensitivity to the active substance or to any of the excipients. • In the case of disseminated intravascular coagulation, prothrombin complex-preparations may only be applied after termination of the consumptive state. • Known history of Heparin-Induced Thrombocytopenia (HIT). Beriplex® P/N contains heparin.
Interactions with other medications	The interaction of Prothrombinex®-VF with other medicines has not been established in specific studies. The use of Prothrombinex®-VF with tranexamic acid is not recommended as only limited data are available on the concomitant administration of prothrombin complex products and antifibrinolytic agents. The reconstituted solution must not be added to or mixed with any other fluids to be given, including whole blood.	Human prothrombin complex products neutralise the effect of vitamin K antagonist treatment, but no interactions with other medicinal products are known. Do not mix Beriplex® P/N with other medicinal products; administer through a separate injection/infusion line.
Storage	Store at 2°C to 8°C.Do not freeze. Prothrombinex®-VF can be stored below 25°C for a single period of 6 months. The product must not be returned to refrigeration after storage below 25°C. Protect from light. Do not use after the expiry date. The product does not contain an antimicrobial preservative. It must, therefore, be used immediately after reconstitution.	Store below 25°C. Do not freeze. Keep the vial in the outer carton, to protect from light. Do not use after the expiry date. Beriplex® P/N contains no antimicrobial preservative. Therefore, it is recommended that the product should be used immediately after reconstitution.
Packaging and vial size	Prothrombinex®-VF comes in one concentration. Each package contains: • One glass vial containing 500 IU of factor IX, approximately 500 IU of factor II and approximately 500 IU of factor X, with a rubber	Beriplex® P/N is available in one concentration. Each package contains: • One glass vial containing 500IU of factor concentrate in powder form, with a rubber stopper closed with an

Product	**Prothrombinex®-VF**	**Beriplex® P/N**
	stopper closed with an aluminium seal and plastic flip-top cap. • One glass vial of 20 mL Water for Injections with a rubber stopper closed with an aluminium seal and plastic flip-top cap. • One Mix2Vial™ filter transfer set.	aluminium seal and plastic flip-top cap. • One glass 20mL vial Water for Injections with a rubber stopper, closed with an aluminium seal and plastic flip-top cap. • One Mix2Vial™ filter transfer set.
References	CSL Behring Product information Prothrombinex®-VF, < https://labeling.cslbehring.com/PI/AU/PROTHROMBINEX-VF/EN/PROTHROMBINEX-VF-Product-Information.pdf> revised March 2020, accessed August 2024.	CSL Behring Product information Beriplex® P/N, < https://www.cslbehring.com.au/-/media/cslb-australia/documents/aus-pis-and-cmis/beriplex-pn-pi-600.pdf> January 2022, accessed August 2024.

Example of Beriplex® P/N dosing:

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

e.g. a 70kg person with pre-treatment INR of 4.9 would receive a dose of 98mL (round up to 100mL) or 2500 IU.

NOTE: There is a product with a similar name available from CSL, Berinert® IV or SC (Human C1 esterase inhibitor).

The following is modified from CSL Behring Australia's Prothrombin Complex Concentrate is transitioning Brochure:

Differences	**Prothrombinex®-VF**	**Beriplex® P/N and Beriplex® AU**
Presentation	500 IU	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)

Rate of administration	Approx. 3mL per minute or as tolerated by the patient	Not exceeding 3 IU/kg body weight/minute. Max. 210 IU/minute, approx.. 8mL per minute
Storage conditions	Store 2-8ºC (do not freeze) Can be stored below 25ºC for a single continuous period of 6 months	Store below 25ºC (do not freeze)
Shelf life	3 years	3 Years
Plasma source	Australia	Beriplex® P/N – International Beriplex® AU - Australia
Estimated available date	Until mid 2024	Beriplex® P/N – From mid-2024 Beriplex® AU – From late 2024 to early 2025*

* Variation to manufacturing using Australian plasma pending regulatory approval.

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Authorised and published by the Victorian Government, 1 Treasury Place, Melbourne.

ISBN 978-1-76131-582-4 **(online/PDF/Word)**

Available at Blood Matters <www.health.vic.gov.au/patient-care/blood-matters-program>

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.