STATEMENT ON CLINICAL EQUIVALENCY OF SELECT FRACTIONATED PLASMA PROTEIN PRODUCTS

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ABBREVIATIONS

A1-PI	Alpha-1-Proteinase Inhibitor
FC	Fibrinogen Concentrate
Ig	Immunoglobulin
IVIg	Intravenous Immunoglobulin
NAC	National Advisory Committee on Blood and Blood Products
PCC	Prothrombin Complex Concentrates
RFP	Request for Proposals
SCIg	Subcutaneous Immunoglobulin

SUMMARY OF REVISIONS

September 2026

General	Formatting and link updates made throughout.
Section 2.0	Clarification added indicating that this document is primarily referring to 10% IVIg formulations. Addition emphasizing that while IVIg products are clinically equivalent, that does not imply there are no administration changes required when switching brands.
Section 3.0	Variable concentrations of SCIg noted, including new higher concentration products, and related administration considerations added.
Section 8.0	New section on alpha-1-proteinase inhibitors added.

1.0 BACKGROUND

In Canada, the blood system is a publicly funded system. Canadian Blood Services is the sole blood provider of blood component and plasma protein products for all provinces and territories with the exception of Québec. In their role as the blood operator, Canadian Blood Services procures plasma protein products by sending Canadian plasma for fractionation to third-party fractionators or purchasing fractionated blood products from biopharmaceutical companies. Plasma protein products include intravenous immunoglobulin (IVIg), subcutaneous immunoglobulin (SCIg), other immunoglobulin (Ig) products, clotting factor concentrates, and other plasma proteins.

As part of the process of obtaining these products, Canadian Blood Services issues requests for proposals (RFPs) or competitive tenders for the purchase of fractionated blood products every 2-5 years. RFPs are requested for specific products and detailed assessments are performed when there are 2 or more licensed products available in Canada. As part of the RFP process, products submitted by biopharmaceutical companies are evaluated for efficacy and safety as well as other factors including convenience and cost. Canadian Blood Services has requested the National Advisory Committee on Blood and Blood Product (NAC) provide a statement regarding the relative clinical efficacy of fractionated plasma protein products where there is more than one supplier. The purpose of this statement is to provide expert clinical recommendations for the use of different fractionated blood products at a population level in the Canadian context, and not to guide the selection process for a specific product. In addition, NAC recommends that there be multiple suppliers for each product category to ensure adequacy of supply.

2.0 INTRAVENOUS IMMUNOGLOBULIN

Currently, Canadian Blood Services distributes multiple brands of IVIg to Canadian hospitals from different suppliers. The Canadian IVIg is primarily comprised of 10% concentration, and this document primarily references these formulations and use. As outlined in NAC's *Statement on Immunoglobulin Utilization and Intravenous Immunoglobulin Brand Switching* (found on the Plasma Protein and Related Products Recommendations page of the NAC website), the use of all Ig products with respect to indications and dosing should follow the applicable provincial/territorial/regional guideline(s). The licensed indications for IVIg are limited to primary immunodeficiency, secondary immunodeficiency, immune thrombocytopenia, chronic inflammatory demyelinating polyneuropathy, Guillain-Barré Syndrome, and multifocal motor neuropathy. However, the appropriate clinical use of IVIg includes other clinical conditions outside of the licensed indications. The Canadian provincial/territorial/regional guidelines for IVIg utilization provide recommendations for use of IVIg for both licensed and non-licensed indications.

With respect to the use of different IVIg products for specific clinical indications, there is no evidence to support that a specific IVIg product has greater efficacy than another IVIg product. Currently, all IVIg products are considered clinically equivalent and, therefore, interchangeable with respect to clinical efficacy for all indications. However, administration changes may be required when switching formulations and the choice of a specific IVIg product for an individual

patient may be guided by other factors, especially previous adverse reactions to specific products. Given the clinical equivalency of IVIg products, brand switches can be safely undertaken if required due to product supply availability (see NAC's *Statement on Immunoglobulin Utilization and Intravenous Immunoglobulin Brand Switching,* found on the Plasma Protein and Related Products Recommendations page of the NAC website) but unique aspects in administration should be noted before doing so. Where possible, transition between IVIg products should be avoided and if necessary should be communicated from the transfusion medicine service to clinical staff as per local policy.

3.0 SUBCUTANEOUS IMMUNOGLOBULIN

SCIg products currently licensed in Canada and distributed through Canadian Blood Services have variable concentrations as outlined in NAC's *Statement on Immunoglobulin Utilization and Intravenous Immunoglobulin Brand Switching* (found on the Plasma Protein and Related Products Recommendations page of the NAC website), the use of all Ig products with respect to indications and dosing should follow applicable provincial/ territorial/regional guideline(s). All SCIg products have licensed indications for primary and secondary immunodeficiencies. In addition, SCIg has a licensed indication for use in Chronic Inflammatory Demyelinating Polyneuropathy. SCIg is also used clinically "off-label" as an alternative to IVIg for other immune related conditions.

There is no evidence to support that any specific SCIg brand has superior efficacy over another as an Ig replacement product or in other clinical indications where SCIg is indicated as a therapeutic strategy. However, a specific SCIg product may be selected or required for an individual patient guided by other clinical factors including administration frequency (notably less frequent dosing observed in formulations with hyaluronidase), previous adverse reactions to specific products, or issues related to product administration. Given the clinical equivalency of SCIg products, brand switches can be safely undertaken if required due to product supply availability, though additional training may need to occur.

4.0 PROTHROMBIN COMPLEX CONCENTRATE

Currently available 4-factor prothrombin complex concentrates (PCCs) are human plasma derived products that have undergone solvent/detergent treatment and/or nanofiltration for viral, bacterial, and parasite inactivation and/or removal. They contain the Vitamin K dependent procoagulant factors (II, VII, IX, and X), Protein C, Protein S, and heparin. The licensed indication for the PCCs is reversal of warfarin and as a coagulation factor treatment for cardiovascular surgery. They are also commonly used for the reversal of direct factor Xa inhibitor anticoagulants in bleeding patients and occasionally as a plasma substitute in other bleeding patients. While there are some differences in the specific concentration of the components, the currently available 4-factor PCCs are considered interchangeable in practice. NAC's *Recommendations for the Use of Prothrombin Complex Concentrates in Canada* (found on the Plasma Protein and Related Products Recommendations page of the NAC website) includes a statement about the interchangeability of the currently available products.

5.0 FIBRINOGEN CONCENTRATES

Fibrinogen concentrate (FC) products currently available from Canadian Blood Services contain fibrinogen and trace amounts of the other substances, such as factor XIII and fibronectin, for which the levels vary within products. Based on in-vitro studies, there are no differences between FCs. Both FCs are licensed for the treatment and prevention of bleeding in patients with congenital afibrinogenemia and hypofibrinogenemia. In addition, one FC is licensed as a complementary therapy during the management of uncontrolled severe bleeding in patients with acquired fibrinogen deficiency during surgical interventions.

Both FCs are considered clinically equivalent as sources of fibrinogen replacement as per NAC's *Statement on Fibrinogen Concentrate Use in Acquired Hypofibrinogenemia* (found on the Plasma Protein and Related Products Recommendations page of the NAC website).

6.0 INTRAVENOUS C1 INHIBITOR

Plasma-derived C1 inhibitor concentrates are available for the treatment of hereditary angioedema in Canada. They are purified from human plasma by filtration and chromatographic procedures. In Canada, there are two products that are administered intravenously. One product is licensed for treatment of moderate to severe acute attacks of hereditary angioedema and the other is licensed as a prophylactic therapy for hereditary angioedema. The latter product is also licensed for treatment of acute attacks in Europe, the USA, and Australia. There are no clinical studies comparing the two products.

Both the intravenous C1 inhibitor concentrates available in Canada are used interchangeably in clinical practice for the treatment of acute hereditary angioedema attacks and for prophylaxis in patients with recurrent events.

7.0 ALBUMIN

Various albumin products in concentrations of both 5% and 25% are distributed by Canadian Blood Services. The different brands of 5% albumin and 25% albumin, respectively, are considered clinically equivalent and are used interchangeably. However, the indications for 5% and 25% albumin are different, and these products should not be used interchangeably.

8.0 ALPHA-1-PROTEINASE INHIBITOR

Various plasma-derived alpha-1-protein inhibitor (A1-PI) formulations exist, indicated for chronic augmentation and maintenance therapy in adults with clinically evident emphysema due to severe hereditary deficiency of A1-PI, also known as alpha-1 antitrypsin deficiency. Currently, an A1-PI product is listed on the Canadian Blood Services Plasma Protein and Related Products formulary as a result of a RFP, approved by provincial and territorial governments.

There is no evidence to support that any specific A1-PI formulation has superior efficacy over another A1-PI replacement formulation, where they are considered clinically equivalent as a class of treatments are used interchangeably.

APPENDIX A: PREVIOUS AUTHORS

Authors of Last Publication: January 2022	
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