NAC Statement on Clinical Equivalency of Select Fractionated Plasma Protein Products

National Advisory Committee on Blood and Blood Products | Comité consultatif national sur le sang et les produits sanguins

NAC STATEMENT ON CLINICAL EQUIVALENCY OF SELECT FRACTIONATED PLASMA PROTEIN PRODUCTS

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LIST OF ABBREVIATIONS

CBS	Canadian Blood Services
CIDP	Chronic Inflammatory Demyelinating Polyneuropathy
FC	Fibrinogen concentrate
IVIg	Intravenous Immunoglobulin
NAC	National Advisory Committee for Blood and Blood Products
PCC	Prothrombin Complex Concentrates
RFP	Requests For Proposals
SCIg	Subcutaneous Immunoglobulin

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BACKGROUND

In Canada, the blood system is a publicly funded system. Canadian Blood Services (CBS) is the sole blood provider of blood component and plasma protein products for all provinces and territories with the exception of Quebec. In their role as the blood operator, CBS 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 products, clotting factor concentrates, and other plasma proteins. As part of the process of obtaining these products, CBS 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. CBS 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, the NAC recommends that there be multiple suppliers for each product category to ensure adequacy of supply.

INTRAVENOUS IMMUNOGLOBULIN (IVIg)

Currently, CBS distributes multiple brands of IVIG to Canadian hospitals from different suppliers. As outlined in the Immunoglobulin Utilization Statement, the use of the all immunoglobulin products with respect to indications and dosing should follow the applicable provincial / regional guideline(s). The licensed indications for IVIg are limited to primary immunodeficiency, secondary immunodeficiency, immune thrombocytopenia purpura, chronic inflammatory demyelinating polyneuropathy, Guillan-Barre Syndrome, and multifocal neuropathy. However, the appropriate clinical use of IVIg includes other clinical conditions outside of the licensed indications. The Canadian provincial / 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. 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 IVIg Brand Switching Guidance).

SUBCUTANEOUS IMMUNOGLOBULIN (SCIg)

SCIg products currently licensed in Canada and distributed through CBS are available in concentrations that vary from 16.5% to 20%. As outlined in the Immunoglobulin Utilization Statement, the use of the all immunoglobulin products with respect to indications and dosing should follow applicable provincial/ regional guideline. 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 (CIDP). SCIg are 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 immunoglobulin 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 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.

PROTHROMBIN COMPLEX CONCENTRATES (PCCs)

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 and Protein S, and heparin. The licensed indication for the PCCs is reversal of coumadin, but these products are also commonly used for the reversal of direct factor Xa inhibitor anticoagulants in bleeding patients and occasionally as a plasma substitute in bleeding patients post-trauma or cardiovascular surgery. While there are some differences in the specific concentration of the components, the currently available 4-factor PCCs are considered interchangeable in practice. The revised NAC Recommendations for the Use of Prothrombin Complex Concentrates in Canada includes a statement about the interchangeability of the currently available products.

FIBRINOGEN CONCENTRATES (FCs)

Fibrinogen concentrate (FC) products currently available from CBS contain fibrinogen and also 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 the 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 the NAC Statement on Fibrinogen Concentrate Use in Acquired Hypofibrinogenemia.

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, USA and Australia. There are no clinical studies comparing the 2 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.

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.