



NAC Recommendations for the Use of Solvent-Detergent Plasma in Canada



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Date of Original Release:	March 10 2023
Date of Last Revision	March 10 2023
Publication Date:	March 13 2023



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LIST OF ABBREVIATIONS

S/D	Solvent Detergent Plasma
CADTH	Canadian Agency for Drugs and Technologies in Health
FP	Frozen Plasma
TTP	Thrombotic Thrombocytopenic Purpura



BACKGROUND

On March 27, 2023, the restrictions on the use of Octaplasma Solvent-Detergent Human Plasma (S/D Plasma) in Canada (outside the province of Quebec) will be removed. Prior to this date, S/D Plasma was restricted to specific patient groups as recommended by the Canadian Agency for Drugs and Technologies in Health¹. The restrictions on the use of S/D Plasma were based on clinical evidence showing no difference in effectiveness as compared to regular frozen plasma (FP), and a substantial increase in cost associated with S/D Plasma as compared to FP². In July 2022, the Canadian Blood Services announced a transition to pathogen-reduced to platelet and plasma components as an additional layer of safety to the blood supply system in Canada. The first phase in the implementation of pathogen-reduced plasma is the transition from FP and S/D Plasma with a target of 80% of all transfused plasma to be S/D Plasma by September 2023. The second phase (planned for 2024-25) is to replace the remaining 20% of FP with pathogen-reduced frozen plasma using the same technology (Intercept Blood System) currently in use to produce pathogen-reduced platelets.

S/D Plasma has been used in Canada since 2011 on a restricted basis, and in many European countries (Netherlands, Finland, Sweden, Norway, United Kingdom) as the primary plasma product with no concerns for either clinical efficacy or safety. S/D Plasma is made from large pools of plasma that undergo pathogen inactivation using a solvent-detergent process and is then divided into 200 mL units. As a result of the manufacturing process, S/D Plasma units have relatively standard or uniform levels of coagulation factors. The levels for all clotting factors are similar to those in FP with the exception of lower protein S and anti-plasmin levels. The pooling of units for S/D Plasma results in decreased allergic reactions³⁻⁶ and possibly a reduction in TRALI reactions⁷.

The transition to S/D Plasma represents a significant change in hospital transfusion practice in Canada. While S/D Plasma and FP have the same clinical indications, there are some differences in the products themselves and the packaging of the product, which are important for health care practitioners and hospital transfusion medicine services. Further information from Canadian Blood Services on S/D Plasma and the transition to this product can be found at <https://profedu.blood.ca/en/transfusion/publications/faq-solvent-detergent-sd-treated-plasma-octaplasma>⁸.

This document from the National Advisory Committee on Blood and Blood Products provides additional clinical recommendations regarding the indications, dosing, and the use in special populations.



INDICATIONS

The main indication for plasma transfusion is the replacement of deficient coagulation factor(s) in patients with active bleeding, or prior to a surgery or invasive procedures. Specific guidelines and recommendations for the use of plasma transfusion have been previously published^{9,10}.

In general, most patients who would be treated with FP can receive S/D Plasma, these would include the following indications:

- Bleeding patients or patients undergoing invasive procedures who require replacement of multiple plasma coagulation factors,
- Patients with massive transfusion with clinically significant coagulation abnormalities,
- Patients on warfarin who are bleeding or need to undergo an invasive procedure before vitamin K could reverse the warfarin effect, and where prothrombin complex concentrate is not available or is contraindicated,
- Patients with selected coagulation factor or with rare specific plasma protein deficiencies for which a more appropriate alternative therapy is not available,
- Preparation of reconstituted whole blood,
- Patients with thrombotic thrombocytopenic purpura (TTP).

There are a limited number of specific contraindications to S/D Plasma:

- Patients with IgA deficiency and documented anti-IgA antibodies. These patients will also potentially have allergic reactions to regular FP and should only receive FP from IgA deficient donors. IgA deficiency alone (no anti-IgA antibodies) is not a contraindication as most patients with this relatively common deficiency do not form antibodies and will not have an adverse reaction to blood components¹¹.
- Patients with severe deficiency of protein S. S/D Plasma has significantly lower levels of protein S as compared to FP, which may result in an increased risk of blood clots. If these patients with severe deficiencies of protein S require a plasma transfusion, they should receive FP.

SPECIAL POPULATIONS:

- (a) Pediatrics. Based on limited data, S/D Plasma and FP should be considered equally effective in pediatric patients and can be used interchangeably. Two studies which included 91 pediatric patients receiving S/D Plasma did not identify any safety concerns¹²⁻¹³. A secondary analysis of a large multinational study identified 62 pediatric critical care patients who received S/D plasma; there was no difference in the reduction in the INR compared to patients receiving FP and S/D plasma was associated with reduced mortality¹⁴. Adoption of S/D plasma for routine use in other jurisdictions has also not identified any concerns with pediatric patients⁵.
- (b) Neonatology. Based on limited data, there is no reason to expect differences in clinical efficacy with S/D Plasma as compared to FP. A retrospective study included 41 neonate patients reported no clinical or safety concerns with S/D Plasma¹⁵. One non-published study reported no adverse



events in 55 neonates receiving S/D plasma¹⁶. The reduction in adverse transfusion reactions associated with S/D Plasma may be advantageous.

- (c) Pregnancy. Based on limited clinical data, SD Plasma and FP can be considered equally effective in pregnant patients and can be used interchangeably. A retrospective study including 37 obstetrical patients reported no clinical or safety concerns¹⁶. Adoption of S/D plasma for routine use including obstetric and gynecology patients also did not identify any clinical concerns in gynecology or obstetrical patients⁵.
- (d) Geriatrics. S/D plasma and FP Plasma should be considered equally effective in geriatric patients and can be used interchangeably with FP. While there are no studies of evaluating S/D plasma specifically in geriatric patients, there are no physiologic reasons that S/D plasma would be less effective or have increased adverse effects in geriatric patients. The reduction in adverse events associated with S/D Plasma may be considered advantageous in this patient group who would be at greater risk on adverse outcomes associated with a transfusion reaction.
- (e) Liver transplantation / Liver disease. S/D Plasma and FP can be considered equally effective in patients undergoing liver transplantation or coagulopathy associated with liver disease and can be used interchangeably. Three randomized controlled trial studies (n=115) evaluated S/D Plasma in patients with coagulopathy associated with liver disease or liver transplant patients¹⁷⁻¹⁹. There were no differences in clinical efficacy or adverse events.
- (f) TTP. Clinical studies have shown that S/D plasma is effective and safe when used as part of plasmapheresis treatments in patients with TTP²⁰⁻²². No clinical studies have compared the effectiveness of S/D plasma to FP or cryosupernatant. In the 2 clinical trials evaluating cryosupernatant in TTP patients, there was no evidence of improved outcomes as compared to FP²³⁻²⁵. The reduction in adverse events and lower risk of transfusion transmitted infections with S/D plasma may be considered advantageous in patients receiving large volume plasma transfusions as part of plasmapheresis treatment.

DOSING CONSIDERATIONS:

An important factor in the dosing of S/D Plasma is the smaller unit volumes. FP units, which are made from individual blood donations, vary in size with an average volume of 289 mL (\pm 16 mL)²⁵ and have more variability in coagulation factor levels as each unit is from an individual donor. Overall, the mean concentration of coagulation factors in S/D plasma and FP are similar²⁵, but as a pooled blood product, the concentrations are more uniform in S/D Plasma.

The correct dose of plasma is determined by either weight-based dosing (hemodynamically stable patients) or ratio-based dosing (massively bleeding patients):

- (1) For the correction of coagulation factor levels in patients with acute bleeding, or prior to surgery or invasive procedures, the recommended dose for FP is 10-15 mL/kg^{9,27}, which is the volume required to increase coagulation factors levels above the minimum hemostatic threshold of 30%²⁸. Given the similarity in coagulation factor levels, this dose is also appropriate for S/D Plasma. In pediatric patients weighing less than 40 kg, the plasma is usually ordered in mL/kg. For larger pediatric patients and adult patients, plasma is usually ordered in units. As S/D Plasma is supplied in a smaller standard 200 mL bag compared to an average 289 mL per unit of FP, a



larger number of units of S/D Plasma may be required to deliver a therapeutic dose of plasma. Most adult patients (60-90 kg) will require 4-6 units of S/D Plasma or 3-4 units of FP to achieve hemostatic levels of coagulation factors. The prescribed dose of plasma should be guided by the clinical situation and coagulation results.

- (2) The NAC recommends that the number of plasma units prescribed in Massive Hemorrhage Protocols (MHPs) be the same whether S/D Plasma or FP is used. For patients with massive hemorrhage requiring transfusion support, resuscitation with fixed ratio of FP to Red Blood Cells (RBCs) is commonly used in MHPs²⁹. This practice is based on observational studies that report improved outcomes in military patients with massive hemorrhage secondary to trauma. While a high transfusion ratio of FP:RBC has been recommended in trauma patients requiring massive transfusion, the ideal ratio is unknown³⁰. In clinical practice, there is variability in the volumes of the FP and RBC units transfused, and often the desired ratio of FP:RBC units is not achieved. As a result, there is significant inherent variability in the actual volumes of plasma and red cells transfused. FP:RBC ratios of 1:1 to 1:3 have been recommended as sufficient to provide hemostatic levels of coagulation factors in trauma patients³¹. Additionally, no benefit has been demonstrated for higher FP:RBC ratios in the resuscitation of patients with non-traumatic massive hemorrhage, who represent the majority of MHP activations in the civilian setting. Therefore, based on the limited evidence available, the NAC does not recommend increasing the initial ratio of plasma to RBC units in MHPs when using S/D plasma despite the lower volume of S/D plasma units. However, as per recent recommendations, patients requiring massive transfusion require frequent monitoring of coagulation tests and should be transitioned to laboratory guided administration of blood components as soon as possible²⁹.



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