FRAMEWORK FOR APPROPRIATE USE AND DISTRIBUTION OF SOLVENT DETERGENT TREATED PLASMA

SOLVENT DETERGENT TREATED PLASMA WORKING GROUP

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LIST OF ABBREVIATIONS

NAC	National Advisory Committee for Blood and Blood Products
PT	Provinces and Territories
CBS	Canadian Blood Services
S/D Plasma	Solvent detergent Plasma
CADTH	Canadian Agency for Drugs and Technologies in Health
PTBLC	Provincial / Territorial Blood Liaison Committee
TTP	Thrombotic Thrombocytopenic Purpura
HUS	Hemolytic Uremic Syndrome
FFPA	Apheresis Fresh Frozen Plasma
FP	Frozen Plasma
TTISS	Transfusion Transmitted Injuries Surveillance System

BACKGROUND

NAC is an interprovincial medical and technical advisory body to the PT health ministries and the blood supplier CBS. NAC provides professional leadership in assisting in identifying, designing and implementing cost-effective blood utilization management initiatives for the optimization of patient care throughout Canada.

S/D Plasma is currently licensed in Canada under the name of Octaplasma™. It is virus inactivated S/D treated human frozen plasma with resulting coagulation activity levels similar to those in single-donor fresh frozen plasma. S/D Plasma treatment is not effective against non-enveloped viruses. For the solvent detergent treatment process, large pools of plasma are treated and then divided into individual units. This pooling and separating lowers the level of proteins in the individual units that cause allergic and immunologic reactions as demonstrated by lower rates of adverse events in hem vigilance studies.

In 2011, the PTs approved the funding and distribution S/D Plasma by CBS for specific patient groups as recommended by the CADTH Panel of Experts in the *"Optimal Therapy Recommendation for the Use of Solvent/Detergent-Treated Human Plasma"*. The original CADTH review was based on systematic review of literature and included an economic (risk-benefit) analysis. Subsequently, the PTBLC requested that NAC develop a further framework to enable the distribution and handling of S/D Plasma, and collaborate with CBS to identify a suitable mechanism by which S/D Plasma would routinely be available for the specific patient groups identified. This NAC Framework for Appropriate Use and Distribution of S/D Plasma provides an update to the 2015 NAC framework document.

At the request of the PTBLC, CADTH completed two evidence-based literature reviews in 2017 related to the use of S/D plasma. These reviews of the literature found no new evidence for the use of S/D plasma in TTP and plasmapheresis, respectively. The original economic (risk-benefit) analysis was not updated. Thus, the PT approved funding for S/D plasma has not been reevaluated and remains based on the original recommendations made by the CADTH Panel of Experts.

In this current revision of the NAC framework document, the specific indications for S/D plasma have been updated by NAC to reflect both current medical practice and the principles outlined by the CADTH expert panel.

The CADTH Panel of Experts recommended S/D plasma for patients receiving high volume plasma transfusions. The specific indications included only patients with TTP, HUS with factor H mutations and patients with clotting factor deficiencies. In the setting of TTP and HUS, patients receive high volume plasma transfusions as part of plasmapheresis treatment. However, plasmapheresis with plasma replacement is indicated in other clinical settings, including (but not limited to) atypical HUS without factor H mutations. **Following the principles outlined by the CADTH expert panel and the bioethical principle of justice, NAC recommends that all patients receiving plasmapheresis with plasma replacement should be eligible to receive S/D plasma as per the revised indications below.**

The 2015 NAC framework also allowed for medical review of individual cases not meeting the CADTH expert criteria. In this update, we have provided further guidance on the specifics for which approval for S/D plasma should be considered. These would include cases where ABO compatible plasma is not available, and rare cases of patients with previous life-threatening adverse reactions to standard plasma. Additional requests would be considered on an individual basis as outlined in Appendix A.

As part of the request process of S/D plasma, all requests from treating physicians should be reviewed by local transfusion medicine experts for completeness and appropriateness.

Ongoing monitoring of S/D Plasma should continue as a means of mitigating the potential for escalating costs associated with the use of this product outside of the current recommendation. Should utilization of S/D Plasma be observed to deviate from the outlined recommendations, the PTs will review the data and follow-up with the respective hospital(s) as appropriate.

The process by which S/D Plasma is available to patients is supported by the PT Ministries of Health.

RECOMMENDATIONS

- CBS should retain the inventory of S/D Plasma for all jurisdictions in Canada (with the exception of Quebec) and distribute it to requesting hospitals for patients with indications in accordance with this framework.
- All requests for S/D Plasma should be reviewed by a local/regional transfusion expert prior to submitting a product request to Canadian Blood Services.
- Requests received by CBS shall be reviewed in accordance with the approved indications by Canadian Blood Services.
  - Requests which align with the approved indications as detailed in this document shall be approved.
  - Requests for S/D plasma outside of the specific indications will be reviewed by a CBS transfusion medical director in consultation with local/regional transfusion expert(s) on individual case basis.
- Distribution and utilization of S/D Plasma should continue to be monitored. Product disposition shall be reported by hospitals to CBS, with data compiled for reporting to the PTBLC
- S/D plasma requests shall be subject to the approval process outlined in (Appendix A) and the use of an associated CBS product request form (Appendix B).

INDICATIONS

The following revised criteria are based on the criteria originally published in the CADTH report dated May 2011. These revised criteria reflect changes in clinical practice, but follow the principles from the initial recommendations by the CADTH Panel of Experts.

S/D Plasma should be considered for:

1. Patients who require a high volume or chronic plasma transfusions (primary qualifier) because they have:
   - **a.** Congenital TTP or,
   - **b.** A need for plasmapheresis with plasma as a replacement fluid for conditions such as (but not limited to) acquired TTP and HUS or,
   - **c.** Clotting factor deficiencies for which specific licensed concentrates may not be readily available (e.g., factor V, factor XI).

   And who have one of the following secondary qualifiers:
   - Have experienced a recurrent clinically significant allergic reaction to plasma

- Have an existing lung disorder that would make them more susceptible to effects of TRALI reaction.

2. Any patient who requires plasma but a blood group compatible product is not available in a timely manner.
3. Patients who have had a previous life-threatening reaction to plasma that could be avoided by the use of S/D plasma, where no alternative therapies are available.

Plasma should be interpreted as any plasma product, e.g.: FFPA, FP, and Cryosupernatant Plasma.

Requests outside the above listed would be subject to review by local transfusion medicine experts and Canadian Blood Services.

An allergic reaction is that which is defined by the TTISS, Public Health Agency of Canada:

a. Minor – a skin reaction characterized by a transient urticarial or other skin rash with pruritus associated with the transfusion. This reaction may be associated with localized angioedema without respiratory distress.
b. Severe/Anaphylactic/ Anaphylactoid – in addition to mucocutaneous signs/symptoms there is airway compromise or severe hypotension requiring vasopressor treatment. The respiratory signs/symptoms may be laryngeal (tightness in the throat, dysphagia, dysphoria, hoarseness, strider) or pulmonary (dyspnea, cough, wheezing /bronchospasm, hypoxemia).
c. Anaphylactic Shock – in addition to the above mentioned, profound hypotension with loss of consciousness, circulatory collapse or death.

DOSING, ADMINISTRATION & MONITORING

S/D Plasma is available in 200 mL bags. Administration, dosing and monitoring should be similar to that of frozen plasma, in adherence with existing local transfusion policies and dependent on the clinical situation.

Adverse reactions observed in patients being treated with S/D Plasma should be reported to Health Canada through the Canada Vigilance Program (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/canada-vigilance-program.html) and the manufacturer, as per local standard process.

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APPENDIX A

S/D PLASMA REQUEST APPROVAL PROCESS