Government of Newfoundland and Labrador

Department of Health and Community Services
Provincial Blood Coordinating Program

REVIEW AND APPROVAL OF REQUESTS FOR IMMUNOGLOBULIN (IG)	NLBCP-007
Office of Administrative Responsibility Medical Advisor to the Provincial Blood Coordinating Program Provincial Blood Coordinating Program	**Issuing Authority** Dr. Christopher Sharpe Daphne Osborne
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Overview

The purpose of this policy is to outline the process to be used for the review and approval of requests for immunoglobulin (Ig) both intravenous immunoglobulin (IVIG) and subcutaneous immunoglobulin (SCIG). In May 2018, the Atlantic Ministries of Health Common Policy for Intravenous and Subcutaneous Immunoglobulin was signed by all Atlantic Deputy Ministers of Health. The Atlantic Blood Utilization Strategy (ABUS), in consultation with Atlantic clinical experts, prepared this document to ensure IVIG and SCIG are used for appropriate indications and in doses recommended by the current literature and expert clinical opinion. The Common Policy will be referenced throughout this policy.

Policy

1. All Newfoundland and Labrador Health Services (NLHS) facilities shall comply with NL Provincial Blood Coordinating Program (NLPBCP) policies, for the review and approval of requests for Ig.

2. All requests for Ig shall be submitted to the Transfusion Medicine Laboratory (TML) for review using the pre-printed Ig request form (PPO). All required information must be provided. In the case of missing information, the PPO must be returned to the ordering physician/patient care area to be completed.

3. Ig patients shall be dosed through the adjusted body weight calculation. The maximum amount of IVIG administered shall reflect adjusted body weight dosing in patients with a minimum height of 152.4 cm (60 inches) and/or a minimum weight of 45 kg.

   Note: SCIG dosing after first PPO may be adjusted according to IgG level for conditions such as Primary Immune Deficiency (PID) and Secondary Immune Deficiency (SID)

4. The TML shall check the dose using the NLPBCP IVIG dose calculator or facility equivalent.

5. Requests for Ig to treat **indicated conditions** in the Atlantic Clinical Indications and Criteria for Intravenous and Subcutaneous Immunoglobulin (IVIG/SCIG) document shall be screened prior to dispensing product to ensure that all specific criteria have been met, and that the dose, duration and frequency of therapy are in accordance with the indications and criteria established by the Atlantic clinical experts.

6. Requests for Ig to treat **possibly indicated conditions** in the Atlantic Clinical Indications and Criteria document shall be screened prior to dispensing product to ensure that all specific criteria have been met, and that the dose, duration and frequency of therapy are in accordance with the indications and criteria established by the Atlantic clinical experts. These requests will be approved for three (3) months only, at which time the

treating physician must re-evaluate the patient's progress and complete an Outcome Questionnaire form. If treatment is deemed ineffective, Ig will be discontinued.

7. The use of Ig for all other conditions shall be reviewed and approved by the NLPBCP in consultation, when necessary, with a designated clinical expert. Approval will be made only on the basis of extenuating circumstances and where there is reasonable evidence indicating that Ig may be of therapeutic value. All other orders will be declined.
8. In order to be considered for conditional approval for a condition that is not indicated or not possibly indicated, the requesting physician must provide:
   8.1. Reasonable evidence for efficacy; and
   8.2. Informed written consent from the patient for the use of Ig as an unlicensed agent for the treatment of an unapproved condition.
9. If requests for conditions that are not indicated or not possibly indicated are approved, the treating physician shall re-evaluate the patient's progress after three (3) months and complete an Outcome Questionnaire form. If treatment is deemed ineffective, Ig will be discontinued.
10. A patient receiving Ig for a possibly indicated condition, or under extenuating circumstances, shall have an Outcome Questionnaire completed by the treating clinician:
    10.1. Three (3) months after the initial prescription;
    10.2. Six (6) months after first outcome evaluation; and
    10.3. Every 12 months thereafter.
11. The TML shall forward the Outcome Questionnaire to the prescribing physician or designate four weeks before the three month trial period will end. If treatment is continued past the three month trial, the Outcome Questionnaire shall be sent again, four weeks before it is required for subsequent prescriptions.
12. The prescribing physician or designate shall complete the Outcome Questionnaire and return to TML no later than one week before treatment is expected to resume.
13. The TML shall forward completed Outcome Questionnaire to NLPBCP for review.
14. NLPBCP shall review, with the Medical Advisor if necessary, to determine if criteria are met to continue IVIG therapy. If necessary, a consult with Nova Scotia clinical expert will occur.
15. Completed Outcome Questionnaires shall be attached to next completed PPO.
16. Physician orders (PPOs) shall be valid for no longer than six (6) months from the start date of Ig therapy. If there is a change in patient information, a new PPO shall be completed.

17. Ig shall **NOT** be issued without a valid PPO, even in emergency situations.
18. If therapeutic value is not realized through Ig therapy, the therapy will be discontinued and alternative treatments must be explored.
19. Serum IgG levels shall be monitored prior to every sixth IVIG dose to ensure optimum dosing for PID conditions.
20. Serum IgG levels, when required, shall be drawn within 24 hours before the next IVIG is given to ensure it is a true trough level.
21. IgG serum levels for SCIG patient with PID and SID are required, initially, at three (3) months and six (6) months after starting SCIG, then, every 12 months to allow for dose adjustment if necessary.
22. Hospitals shall report their use of IVIG and SCIG into the Intravenous Immunoglobulin Network (IVIN) database housed at the Nova Scotia Provincial Blood Coordinating Program (NSPBCP).
23. Transfusion reactions associated with Ig shall be reported to the TML.
24. There shall be no expiry (outdating) of Ig. Inventory management practices shall be in place that prevent the expiry of these products.
25. In the event of an emergency release of IVIG for conditions listed in Appendix B, not indicated or not possibly indicated conditions, the request shall be granted if it meets all the criteria for release and all documentation is complete. For any future doses, the request shall be reviewed through the normal process.

Guidelines

1. Ig should only be used when other equally safe and efficacious alternative therapy has failed.
2. “Adjusted body weight” or “dosing body weight” dosing are common practices used by pharmacists when determining drug doses in obese patients, based on the fact that some drugs, like IVIG, have very little distribution into adipose tissue (fat).
3. Dosing by adjusted body weight improves patient safety by reducing unnecessary exposure to higher doses of Ig which are associated with greater incidence of adverse events including hemolysis and thrombosis.
4. The IVIG dose calculator only accepts heights that equal or exceed 152.4 centimeters (60 inches). Dosing for these patients should use actual body weight.
5. Prescribers should ensure patients on chronic Ig therapy are receiving the minimal effective dose. The suggested titration is following a six month stability period.

6. Dose titration of IVIG may be achieved by:

   6.1. Dosage reduction, maintaining same IVIG interval; or

   6.2. Lengthening IVIG interval, maintaining the same dose.

7. The procedure for dosage reduction, maintaining same IVIG interval is to reduce dose by five grams at three month intervals to the lowest dose of 0.4 g/kg, resuming higher dose if patient condition deteriorates.
8. Lengthening IVIG interval, maintaining the same dose may be attempted by lengthen the interval by no more than one week at three month intervals. If a patient remains in remission with an IVIG interval of eight to ten weeks, it may be possible to attempt withdrawal of IVIG treatment.
9. Regular evaluations are required to ensure that the treatment continues to be effective and appropriate.
10. The recommended target serum IgG level should be maintained between 7-10 g/L for PID and SID conditions.
11. The clinical outcome evaluation is completed to ensure:

    11.1. Ig remains of therapeutic value; and

    11.2. The minimal effective dose of Ig is being prescribed.

Quality Control

1. Transfusion safety officer (TSO) or designated data submitter shall review all requests for Ig.
2. All TML staff shall be trained and familiar with the review and approval of Ig requests. In the absence of TSO or designate, they may issue, if required. The TSO or designate will review when available.
3. The NLPBCP shall review all requests that do not meet the Atlantic Clinical Indications and Criteria for Intravenous and Subcutaneous Immunoglobulin (IVIG/SCIG) to ensure request and approval process is consistent with the Common Policy.

Key Words

Common policy, intravenous immunoglobulin, subcutaneous immunoglobulin IVIG, SCIG, PPO, request, approval

Supplemental Materials

1. Appendix A – IVIG Request Checklist Job Aid
2. Appendix B – IVIG Urgent/Emergency Release Conditions
3. Appendix C – Request/Approval Flowchart
4. NLPBCP Ideal Body Weight Calculator/IVIG Dose Calculator is available at https://www.health.gov.nl.ca/health/bloodservices/resources/dosage_calculator.html
5. Atlantic Ministries of Health Common Policy for Intravenous and Subcutaneous Immunoglobulin
6. Atlantic Clinical Indications and Criteria for Intravenous and Subcutaneous Immunoglobulin (IVIG/SCIG)

References

Canadian Standards Association. (2020). *Blood and blood components*, Z902- 20. Mississauga (ON): Author.

Canadian Society for Transfusion Medicine. (2022). *Standards for Hospital Transfusion Services*. (Version 5.0). Markham, ON: Author.

Krever, H, (1997*). Commission of inquiry on the blood system in Canada: Interim report recommendations*, p.1134. Ottawa, ON: Krever Commission.

Appendix A IVIG Checklist

Patient Name: MCP:

Date:

Complete Section A and C for all patients

Section A

1. Is form the **appropriate** PPO for the condition: Yes_____ No _____

   Is it complete? Yes____ No____ **If No return incorrect/incomplete PPO to patient care area.**

   Is correct dose calculated? Yes____ **If dose calculation is incorrect, discuss with ordering physician.**

2. Is form the **appropriate** PPO for the condition: Yes_____ No _____

   Is it complete? Yes____ No____ **If No return incorrect/incomplete PPO to patient care area.**

   Is correct dose calculated? Yes____ **If dose calculation is incorrect, discuss with ordering physician.**

3. Is the request for an indicated or possibly indicated condition? Yes_____ No_____

   If no, discuss with ordering physician - Complete Section B

4. Was indication a Primary Immune Deficiency? Yes____ No____

   If Yes, IgG level is required before every 6th dose. Contact ordering location if level is due.

   Trough level must be collected < 24 hours before 6th dose. If IgG level was not performed or the result is outside the range, (Between 7-10 g/L) **discuss with ordering physician** (to be performed by TSO, Utilization Management Technologist, or designate)

5. Are the dose, frequency, and duration acceptable? Yes ____Issue IVIG No_____ (number of days of treatment x g/kg must not exceed 2g/kg unless indicated on PPO. If greater than the recommended dose, consult with clinical Expert).

   If No, was the problem with dose____, frequency____, duration ____ **Discuss with ordering physician. Document in comments.**

Section B

1. Result of discussion with ordering physician:

   Request revised____ Request withdrawn____ Request unchanged____ N/A____

   If request was unchanged, consult with Clinical Expert

   (performed by TSO, Utilization Management Technologist, or designate)

2. After Clinical Expert consult, was:

   Request revised to meet guidelines? ____ Request withdrawn? ____ Request unchanged? ____

   Consultation with clinical expert did not occur____ N/A____

   Forward clinical expert consult form to clinical expert (performed by TSO, Utilization Management Technologist, or designate)

Section C

1. Blood Bank History check:

   a) Were there previous reactions to IVIG? Yes____ No____

   If yes, explain: _____

   b) **For possibly indicated/not indicated conditions only:**

   Does history check say Outcome Questionnaire complete, ok to continue treatment? Yes____ No____

If no, do NOT issue. See TSO, Utilization Technologist, or designate, for conditions other than Emergency/Urgent situations.

2. Can IVIG be issued? Yes____ No____ Product Brand _____

Comments:

Appendix B IVIG Urgent/Emergency Release Conditions

Hematology Indications

- Immune thrombocytopenic purpura (ITP)
- Neonatal Alloimmune Thrombocytopenia (NAIT)
- Pregnancy-Associated ITP
- Hemolytic Disease of the Newborn (HDN)
- Post Transfusion Purpura
- Hematological Malignancy
- Acquired Hemophilia with Factor VIII Inhibitor
- Secondary Immune Deficiency
- Factor XIII Inhibitor
- Neonates of Mothers with ITP
- Fetal Alloimmune Thrombocytopenia (FAIT)
- Hemophagocytic Lymphohistiocytosis (HLH)
- Post Car T cell

Neurology Indications

- Guillain-Barré Syndrome
- Autoimmune Encephalitis: Rasmussen's Encephalitis – Adult only
- Autoimmune Encephalitis: N-Methyl-D-Aspartate (NMDA) – Pediatric only
- Myasthenia Gravis (MG) - ventilated patient
- Acute Disseminated Encephalomyelitis (ADEM)

Immunology Indications

- Primary Immunodeficiency - severe/acute infection
- Secondary Immunodeficiency - severe/acute infection

Dermatology Indications

- Kawasaki Syndrome
- Dermatomyositis

Rheumatology Indications

- Immune-Mediated Inflammatory Myositis
- Systemic Onset Juvenile Idiopathic Arthritis
- Juvenile Dermatomyositis
- Catastrophic Antiphospholipid Antibody Syndrome
- Kawasaki Syndrome
- Hematophagocytic Lympohistiocytosis
- Hemophagocytic Lymphohistiocytosis (HLH)

Infectious Disease

- Group A Streptococcus (GAS) Necrotizing Fasciitis or Toxic Shock Syndrome
- Staphylococcus Aureus Toxic Shock Syndrome (TSS)

Appendix C Request/Approval Flowchart