



Government of Newfoundland and Labrador

Department of Health and Community Services
Provincial Blood Coordinating Program

IMMUNOGLOBULIN SHORTAGE PLAN	NLBSP-069
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Overview

Immunoglobulin (Ig) is a plasma-derived medicinal product used to treat primary and secondary immune deficiency and autoimmune disorders, and other diseases with an immune origin. For some patients, Ig is the only treatment available.

During times of shortage of plasma supply, whether national, provincial or regional, a coordinated response is deployed by Canada's Blood system operator Canadian Blood Services (CBS). Led by the National Emergency Blood Management Committee (NEBMC), which is comprised of CBS, regional health authorities (RHAs), Ig prescribers, provincial and territorial health ministries, and the National Advisory Committee on Blood and Blood products (NAC), response efforts are focused on information sharing and shared decision-making by stakeholders.

There are four phases of Ig inventory availability characterized by the number of weeks of supply on hand – Green, Amber, Red and Recovery. Green implies normal Ig inventory levels exist and supply meets demand. Amber implies that the national Ig inventory levels are low and insufficient for routine utilization. Red implies inventory levels are insufficient to guarantee all patients will receive their required Ig dose. During Recovery Phase, Ig supplies are returning to normal.

This Ig Shortage Plan is focused on the clinical criteria for use and allocation of Ig in the event of a global plasma shortage when all efforts to increase Ig supply have been exhausted, and the available supply is insufficient to meet demand.

Policy

1. In Amber and Red Inventory Phases, Transfusion Medicine Laboratories (TML) shall report all available Ig inventory daily to the NL Provincial Blood Coordinating Program (NLPBCP).
2. The NEBMC, when convened by Canadian Blood Services (CBS), shall initiate communications of Ig Inventory Phases to NEBMC members.
3. The NLPBCP shall convene the NL Emergency Blood Management Committee (NLEBMC) and provide communications and guidance from the NEBMC to the RHAs and prescribers. All NLEBMC members shall identify a designate in the event they are unavailable at any time.
4. The Ig Shortage Plan is guided by principles set out NLPBCP's Emergency Blood Management Plan which can be found [here](#).
5. All RHAs shall develop an Ig Shortage Plan that includes the following:

- 5.1. Lines of responsibility;
 - 5.2. Decision-making processes, including allocation decisions and documentation;
 - 5.3. Inter-regional communication plan; and,
 - 5.4. Regional Ig conservation strategies.
6. During all inventory phases, in all RHAs:
 - 6.1. Ig orders shall be reviewed for appropriateness. Orders that do not meet criteria for use shall not be issued.
 - 6.2. Orders for unlicensed, not indicated conditions require the approval of a clinical expert and informed patient consent to receive a treatment that is not indicated for their condition.
 7. The TMLs shall be responsible for reviewing the issue criteria for Ig for every patient to ensure it follows the guidelines of the Ig Shortages Plan.
 8. RHAs shall record allocation decisions in Amber and Red Phases. The record of allocation shall include:
 - 8.1. Ordering physician;
 - 8.2. Recipient MCP;
 - 8.3. Recipient age;
 - 8.4. IgG level (if required for condition);
 - 8.5. Indication;
 - 8.6. Date of last Ig dose;
 - 8.7. Amount of Ig requested;
 - 8.8. Amount of Ig issued; and,
 - 8.9. Ig brand issued.
 9. Prescribers of Ig shall communicate with patients in the event that their treatment plan changes.
 10. RHAs shall have a system in place to monitor compliance with the Ig Plan.

Guidelines

1. In Green Phase, while normal inventory levels exist, RHAs must monitor Ig usage and utilization rates, with consideration of future supply outlook. This includes ensuring all

utilization complies with the criteria set out in the Atlantic Ministries of Health Common Policy for Utilization of Intravenous and Subcutaneous Immunoglobulins (2018), in particular:

- 1.1. Utilization for approved conditions;
 - 1.2. Dosing by adjusted body weight, and,
 - 1.3. Titration to minimal effective dose.
2. In Green Advisory Phase of Ig shortage, provincial and regional emergency blood management committees convene. Efforts focus on analysis of supply versus predicted demand, and likelihood of progressing to Amber Phase.
 3. In Amber Phase, as Ig inventories are insufficient to continue routine practices, RHAs will be required to implement specific measures to reduce usage. NLEBMC will meet daily, if indicated. Communications from the NEBMC will be distributed to prescribers and stakeholders by the NLEBMC. Prescribers will communicate with their impacted patients.
 4. In Red Phase, Ig inventories are insufficient to ensure all patients will receive their required products. RHAs will be required to implement specific measures to decide which patients will/will not receive product and in what amounts. All committees will meet daily to discuss. Communication to physicians and patients will originate from the NEBMC.
 5. Allocation of available supply is based on a fair, consistent and ethical priority system. See Appendix B for allocation in Amber and Red Phase.

Key Words

Allocation, Ig, immunoglobulin, plasma, shortage

Supplemental Materials

Appendix A Inventory Phase Activity

Inventory Level	Description and Activities
Green	<p>Ig supply/inventory meets demand.</p> <ul style="list-style-type: none"> • Follow jurisdictional best practice recommendations for use of Ig (indications, optimal use guides, modality of administration, and doses). • Use the lowest Ig dose for the shortest duration required to achieve the desired outcome. • For ongoing therapy, ensure the achievement of measurable clinical outcomes; Ig should not be continued in patients with no demonstrable benefit. • Prior to starting Ig treatment, consider use of all other safe, effective, and accessible alternative therapies. • Where use is indicated, confirm that use aligns with the patient's goals of care. • Use a dose calculator based on adjusted body weight, and track Ig levels to adjust dose, as appropriate.
Green Advisory	<p>Ig supply/inventory levels are reduced or there are signs that short-term demand may outstrip capacity. Reduce use by 10 to 20%:</p> <ul style="list-style-type: none"> • Continue to follow all the actions outlined in Green phase. • Round down Ig treatment doses and frequency. Re-assess all patients that are already on treatment to find the minimal effective dose and optimize the treatment for each individual. • Review stocking practices and maintain the minimum inventory level required. • Reduce the refill volume for patients on home infusion products. • Consider the use of alternative therapies. • Consider increasing availability of alternative therapies • Initiate actions to prepare for the potential escalation to Amber and Red phase by: <ul style="list-style-type: none"> ○ Identifying patients that can be switched to SCIg (in the event of an IVIg shortage) or IVIg (in the event of a SCIg shortage), or other alternative therapies. ○ Initiating local and provincial processes to support an adjudication process in the event of a red phase advisory.

Amber	<p>Ig supply/inventory levels are low for a short or prolonged period. Reduce use by 20 to 50%:</p> <ul style="list-style-type: none"> • Continue to follow all the actions outlined in Green phase and Green Advisory phase. • Limit Ig use to clinical circumstances when there are: <ul style="list-style-type: none"> ○ no viable alternatives; and/or ○ the condition is life-threatening or there is a risk for irreversible disability as identified in the table below. • Use the lowest Ig dose for the shortest duration required to achieve the desired outcome. • Implement screening of all Ig orders within the hospital transfusion service/blood bank.
Red	<p>There is a critical and prolonged Ig shortage. Reduce use by over 50%:</p> <ul style="list-style-type: none"> • Limit Ig use to clinical circumstances when there are: <ul style="list-style-type: none"> ○ no viable alternatives; and/or • the condition is life-threatening or there is a risk for irreversible disability as identified in the table below. • Have each case and dose approved by a formally established peer committee as per local jurisdictional guidance. • File a written copy of the decision in the patient's medical record and send another copy to Transfusion Medicine Services (blood bank).

Appendix B

Ig Allocation Criteria

	Condition	Amber Level	Red Level
	Primary or secondary immunodeficiencies known to be associated with hypogammaglobulinemia or dysgammaglobulinemia for which Ig is necessary ¹	<ul style="list-style-type: none"> • Preferential use • Should be based on the expert opinion of the physician, depending on the severity and frequency of infections and presence of additional immune dysregulation (e.g. autoimmunity, hyperinflammation) • For maintenance therapy, target IgG levels should be lowered to minimum clinically effective target (e.g., 5-7 g/L on Day 28 in adult patients with hypogammaglobulinemia on IVIg) • Increase or decrease target IgG on a case by case basis (i.e., based on factors such as clinical conditions or age) 	
	Dermatomyositis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Eosinophilic granulomatosis with polyangiitis (Churg Strauss syndrome)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Juvenile dermatomyositis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Kawasaki disease	<ul style="list-style-type: none"> • First line therapy • Following the initial dose, maximum one additional dose may be given if there is ongoing inflammation 	
	Macrophage activation syndrome (MAS)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Polymyositis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Acquired coagulation factor inhibitors	Should be considered only after adjunctive therapies (such as steroids) in urgent situations, as decided by experts at a hemophilia treatment centre	
	Allogeneic hematopoietic stem cell transplant	In cases of hypogammaglobulinemia, acquired post-hematopoietic stem cell transplant (HSCT) See immunology section	
	Autoimmune hemolytic anemia (AIHA)	In cases of failure to first-line treatment, contraindication or intolerance of other therapeutic options in life-threatening cases.	
	Autoimmune neutropenia	In cases of failure, contraindication or intolerance to other therapeutic options	<ul style="list-style-type: none"> • In cases of failure, contraindication or intolerance to other therapeutic options

			<p>AND one of the following:</p> <ul style="list-style-type: none"> • For severe, active infections • A history of severe infections that responded positively to treatment
	Catastrophic antiphospholipid syndrome	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Fetal and neonatal alloimmune thrombocytopenia (FNAIT)	<ul style="list-style-type: none"> • Treatment for mothers during pregnancy: permitted for use, maximum dose not to exceed 1 g/kg/week • Treatment for newborns: if there is potentially fatal bleeding or a platelet count below 30 x 10⁹/L, when a platelet transfusion (whether selected for human platelet antigen [HPA] or not) is not possible 	
	Hemolytic disease of the fetus and newborn (HDFN)	<p>Should be given only in consultation with neonatology and transfusion medicine:</p> <ul style="list-style-type: none"> • Treatment for pregnant mothers: when there is a high risk AND intrauterine transfusion is contraindicated • Treatment for newborns: in cases of hyperbilirubinemia due to maternal alloimmunization if phototherapy fails 	<p>Should be given only in consultation with neonatology and transfusion medicine:</p> <ul style="list-style-type: none"> • Treatment for pregnant mothers: when there is a high risk AND intrauterine transfusion is contraindicated • Treatment for newborns: in cases of hyperbilirubinemia due to maternal alloimmunization if phototherapy fails and exchange transfusion cannot be done in a reasonable timeframe
	Hyperhemolysis syndrome	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Immune thrombocytopenia, acute	<p>Failure, contraindication or intolerance to steroids and anti-D Ig (if patient is Rh(D)-positive). Also, consider early use of thrombopoietin receptor agonist or rituximab</p> <p>AND one of the following:</p> <ul style="list-style-type: none"> • When platelet count is <10 x 10⁹/L • When <30 x 10⁹/L and there is moderate to severe bleeding • Before urgent surgery and there is a need to rapidly raise the platelet count 	<p>Failure, contraindication or intolerance to steroids and anti-D Ig (if patient is Rh(D)-positive). Also consider early use of thrombopoietin receptor agonist or rituximab</p> <p>AND one of the following:</p> <ul style="list-style-type: none"> • When the platelet count is <30 x 10⁹/L and there is moderate to severe bleeding • Before urgent surgery and there is a need to rapidly raise the platelet count

		<ul style="list-style-type: none"> • There is life-threatening bleeding <p>Dose: Maximum of 1g/kg x 1 dose</p>	<ul style="list-style-type: none"> • There is life-threatening bleeding <p>Dose: Maximum 1g/kg x 1 dose</p>
	Immune thrombocytopenia, chronic	<ul style="list-style-type: none"> • Failure, contraindication or intolerance to steroids and anti-D Ig (if patient is Rh (D)-positive) • Alternative therapies (immunomodulators, thrombopoietin receptor agonist, rituximab) should be considered <p>AND one of the following:</p> <ul style="list-style-type: none"> • When the platelet count is <30 x 10⁹/L and there is moderate to severe bleeding • Before urgent surgery and there is a need to rapidly raise the platelet count • There is life-threatening bleeding <p>Dose: Maximum 1g/kg x 1 dose</p>	
	Immune thrombocytopenia during pregnancy	<p>Failure, contraindication or intolerance to steroids.</p> <p>AND one of the following</p> <ul style="list-style-type: none"> • When the platelet count is <30 x 10⁹/L and / or moderate to severe bleeding • In preparation for delivery to reach a platelet count ≥ 50 x 10⁹/L in cases of failure, contraindication or intolerance to steroids • There is life-threatening bleeding 	
	Post-transfusion purpura	In cases of moderate to severe bleeding if plasma exchange is not feasible	
	Red cell aplasia caused by parvovirus B19	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Acute disseminated encephalomyelitis (ADEM)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Autoimmune Encephalitis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Chronic inflammatory demyelinating polyneuropathy (CIDP)¹	<ul style="list-style-type: none"> • Consider steroids and/or plasma exchange whenever possible • Initial and maintenance treatment in cases of failure, contraindication or intolerance to other forms of immunosuppressive therapy² 	
	Graves' ophthalmopathy	In cases of vision-threatening severe disease with failure, contraindications or intolerance to other therapeutic options	
	Guillain-Barré syndrome (GBS) or variants including Miller Fisher syndrome	<ul style="list-style-type: none"> • Preferential use for initial treatment of GBS if plasma 	In cases of failure, contraindication or intolerance to plasma exchange OR in

		exchange not available or feasible • A second course of IVIG may be considered in patients with clearly demonstrated secondary deterioration, only after assessment by a specialist	cases where plasma exchange is not available
	Lambert-Eaton myasthenic syndrome (LEMS)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Multifocal motor neuropathy (MMN)¹	For front-line therapy ²	
	Myasthenia gravis (MG)	In cases of severe exacerbation, myasthenic crisis or in preparation for urgent or semi-urgent surgery	In cases of severe exacerbation, myasthenic crisis or in preparation for urgent or semi-urgent surgery with failure, contraindication, intolerance or lack of availability of plasma exchange or other therapeutic options
	Opsoclonus-myoclonus syndrome	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Rasmussen's encephalitis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Refractory epilepsy	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Relapsing-remitting multiple sclerosis	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Stiff person syndrome (SPS)	In cases of severe disease and failure, contraindication or intolerance to other therapeutic options ²	
	Enterovirus meningoencephalitis	In severe cases in immunocompromised patients	
	Infectious gastroenterocolitis (such as <i>C. difficile</i> enterocolitis or rotavirus gastroenteritis in immunocompromised patients)	Do not use	

	Invasive group A streptococcal disease or staphylococcal disease	<ul style="list-style-type: none"> For severe invasive group A Streptococcal disease associated with hemodynamic compromise or Streptococcal or Staphylococcal toxic shock syndrome IVIg is recommended in addition to surgical intervention, antibiotic therapy and other supportive measures 	
	Lower respiratory tract infections caused by CMV or RSV in immunocompromised patients	Do not use; preferential use should be made of specific antivirals +/- specific hyperimmune globulin (for CMV)	
	Neonatal sepsis	<ul style="list-style-type: none"> In severe cases in cases of failure, contraindication or intolerance to other therapeutic options Should not be used for prophylaxis 	
	Measles post-exposure prophylaxis	In pregnant women, infants and immune compromised/deficient individuals if IM injection is not an option because of weight 30 kg or greater or inability to receive IM injection	
	Bullous dermatitis (e.g.- pemphigus vulgaris, bullous pemphigoid)	<ul style="list-style-type: none"> Not permitted for use, apart from exceptional cases when disease is rapidly progressing, and other treatments are contraindicated First line therapy: corticosteroids Second line: immunosuppressive agents Third line: IVIG 	Do not use
	Pyoderma gangrenosum	<ul style="list-style-type: none"> Not permitted for use, apart from exceptional cases when disease is rapidly progressing, and other treatments are contraindicated First line therapy: corticosteroids Second line: immunosuppressive agents. Third line: IVIG 	Do not use
	Scleromyxedema	<ul style="list-style-type: none"> Not permitted for use, apart from exceptional cases when disease is rapidly progressing, and other treatments are contraindicated First line therapy: corticosteroids Second line: immunosuppressive agents. Third line: IVIG 	Do not use
	Stevens-Johnson syndrome and toxic epidermal necrolysis	<ul style="list-style-type: none"> Not permitted for use, apart from exceptional cases when disease is rapidly progressing, 	Do not use

		<p>and other treatments are contraindicated</p> <ul style="list-style-type: none"> • First line therapy: corticosteroids <p>Second line: immunosuppressive agents</p> <p>Third line: IVIG</p>	
	<p>Heart, lungs, liver, kidneys, pancreas (humoral rejection or pre-transplant HLA/ABO desensitization)</p>	<p>May be used as part of combination therapy with immunosuppressive therapy and/or plasmapheresis in selected cases</p>	<ul style="list-style-type: none"> • As part of combination therapy with immunosuppressive therapy and/or plasmapheresis, evaluated on a case-by-case basis by a peer committee • For post-transplant treatment only, not new initiation of pre-transplantation desensitization protocol • Consult with transplant team required regarding potential delay in initiation of new transplants

*Derived from The National Plan for Management of Shortages of Immunoglobulin Products (Ig).

Legend:

Immunology
Rheumatology
Hematology
Neurology
Infectious Diseases
Dermatology
Organ Transplant

Notes:

1. Preferential use should be made of SCIg for appropriate indications if available when there is an IVIg shortage.
2. For chronic conditions, when immunoglobulins are administered as maintenance treatment, try to find the minimal effective dose and optimize the treatment for each individual during Amber and Red phases.

References

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