The National Plan for Management of Shortages of Immunoglobulin (Ig) Products

May 30, 2024

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

Canadian Blood Services
BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

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Abbreviations

CBS	Canadian Blood Services
CBS-P/TBLC	Canadian Blood Services Provincial/Territorial Blood Liaison Committee
H/REBMC	Hospital/Regional Emergency Blood Management Committee
Ig	Immunoglobulin
IVIg	Intravenous immunoglobulin
NAC	National Advisory Committee on Blood and Blood Products
NEBMC-Ig	National Emergency Blood Management Committee for Immunoglobulins
P/T	Provincial/Territorial
P/TEBMC	Provincial/Territorial Emergency Blood Management Committee
PBCO/P	Provincial Blood Coordinating Office / Program
RHA	Regional Health Authorities or alternate service providers/structure within a province. Service providers are responsible for the delivery and administrating the operational aspects of the Plan in specified geographic areas authorized by the province
SCIg	Subcutaneous immunoglobulin
WoH	Weeks on hand

Acknowledgements

The National Advisory Committee on Blood and Blood Products (NAC) and the Canadian Blood Services-Provincial and Territorial Blood Liaison Committee (CBS-P/TBLC) wish to acknowledge the contributions of a broad range of relevant parties with interests and experience relevant to the use of immunoglobulin by Canadian patients who provided their input and feedback ensuring *The National Plan for the Management of Shortages of Ig Products* was developed considering all perspectives.

The NAC and CBS-P/TBLC also acknowledges and thanks a subset of NAC members and the NEBMC Secretariat (project management) for their leadership and support in the development of this plan, which was possible through the support of Health Canada and provincial and territorial ministries of health.

Executive summary

Canadian Blood Services manages a pan-Canadian formulary of approximately 50 brands of plasma protein and related products and synthetic alternatives. Globally, the use and demand for these products continue to rise. In particular, Immunoglobulin (Ig) utilization has more than doubled internationally over the past ten years. Ig is used to treat primary and secondary immune deficiency disorders, and autoimmune disorders including autoimmune neurological disorders and other diseases with an immune origin. In some cases, these are lifesaving treatments for which there are no alternative therapies.

The 2018 Expert Panel on Immune Globulin Product Supply and Related Impacts in Canada recommended the development of a national prioritized list of patient groups dependent on Ig and a process to allow appropriate allocation in the setting of a short-term or more prolonged shortage. Limitations in the supply of subcutaneous Ig (SCIg) in the summer of 2019 underscored the need for a dedicated national Ig shortage management plan. Subsequently, the Canadian Blood Services-Provincial and Territorial Blood Liaison Committee (CBS-P/TBLC) identified the development of a national plan for managing Ig shortages as a priority project for the National Advisory Committee on Blood and Blood Products (NAC).

NAC had initiated planning to develop a national Ig shortages plan but had not yet started the work when the COVID-19 pandemic struck in early 2020. The pandemic's potential impact on the global Ig supply chain highlighted the urgent need to have an Ig shortage management plan in place. Given that the development of a comprehensive plan would require significant time and resources, and that COVID-19 impacts to supply may emerge in the short- to medium-term, the NAC and CBS-P/TBLC recognized that proceeding with the development of an interim plan was required and tasked the National Emergency Blood Management Committee Secretariat with having an interim national plan in place within a 3-month time-frame by mid-July 2020.

The National Plan for Management of Shortages of Immunoglobulin (Ig) Products – Interim Guidance, henceforth known as the interim Ig plan, was intended as a response to potential supply impacts on the near horizon and remained in place while this comprehensive plan was developed.

The specific purpose of this national Ig plan is to maximize the effectiveness of a response to any crisis which impacts the adequacy of the overall Ig supply in Canada. This national Ig plan assumes that all efforts to increase the available supply of Ig (IVIg and/or SCIg) have been exhausted and addresses the allocation of the available scarce Ig supply.

The National Plan for the Management of Shortages of Ig Products provides a framework which will enable Provincial/Territorial (P/T) ministries of health and hospitals/regional health authorities (RHA) to develop their own Ig shortage management plans in a manner that is congruent and complementary with the national Ig plan. This approach is aimed at achieving the consistency and collaboration crucial to the effective management of an Ig shortage.

Difficult decisions will need to be made about the allocation of Ig in the event of a shortage. Criteria to guide clinical decisions and triage of Ig products as well as an ethical framework are provided to guide decision making and to assist with doing as little harm as possible – where harm is broadly understood. This naturally includes the physical harm(s) that may be experienced by patients due to limited or no access to Ig products during a shortage. It also includes due consideration of the emotional and relational harms that can occur in the context of anticipated and/or actual shortages of health care resources for patients, health care providers, and decision-makers.

Based on a number of stated assumptions, the national Ig plan addresses five phases of inventory availability – Green, Green Phase Advisory, Amber, Red and Recovery:

- **Green** implies that normal Ig inventory levels exist, and supply generally meets demand. This phase includes a broad range of inventory levels ranging from an ideal inventory to shortages that occur periodically and can be managed with existing Canadian Blood Services and hospital/RHA actions.
- **Green Phase Advisory** implies that Ig inventory levels are low, and that system wide inventory (including resupply estimates) and utilization needs to be understood to inform the likelihood of crossing into Amber or Red Phase. Hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.
- **Amber** implies that Ig inventory is insufficient to continue with routine deliveries and hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.
- **Red** implies that Ig inventory levels are insufficient to ensure that patients identified as having critical need will receive the required product(s).

- **Recovery** implies that Ig inventory levels have begun to increase and are expected to be maintained at a level which would enable the return from Red to Amber to Green Phase Advisory and subsequently to Green Phase (normal inventory levels).

Determination of the need to declare a shortage phase could apply to a single Ig brand or multiple brands in either SCIg or IVIg formulations.

The roles and responsibilities of the key participants, namely Canadian Blood Services, Health Canada, the P/T ministries of health and hospitals/RHA, in each of these phases are described in this document as well as the emergency blood management committees that would be required to successfully manage an Ig shortage.

The optimal management of an Ig shortage will depend upon the commitment of all relevant parties, in the system served by Canadian Blood Services, to work collaboratively to ensure scarce resources are used in a fair and equitable manner. This national Ig plan is intended to provide a framework, which if followed, will ensure that optimization. It is nevertheless recognized that lessons will be learned in each shortage situation.

Revisions and the substantive change history from the interim Ig plan to this comprehensive Ig plan is available for reference in Appendix A.

Steering Committee

Version May 30, 2024 Through the support of Health Canada and provincial and territorial ministries of health work to develop *The National Plan for the Management of Shortages of Ig Products was conducted September 2022 to April 2024*. representatives of the National Advisory Committee on Blood and Blood Products, Health Canada, Canadian Blood Services, and the Provincial / Territorial Blood Liaison Committee provided subject matter expertise, advice on approach, strategic issues, and risks, as well as clinical and governmental perspectives.

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1. Introduction

1.1 The Canadian blood system

Canada has two blood operators - Canadian Blood Services, which manages the blood supply system in all provinces and territories (except Québec); and Héma-Québec, which serves Québec. Canadian Blood Services and Héma-Québec collect blood donations from voluntary donors, prepare blood components and distribute these to hospitals in their respective jurisdictions. Canadian Blood Services and Héma-Québec are funded by the provinces and territories that they serve, but the management of the blood supply is the responsibility of Canadian Blood Services and Héma-Québec within their respective jurisdictions. Both organizations are also responsible for managing the supply of commercially obtained plasma protein and related products (e.g., intravenous immunoglobulin (IVIg), subcutaneous immunoglobulin (SCIg), albumin and coagulation factor concentrates) and recombinant coagulation factors.

Within the ministry of health (ministries) in each province and territory served by Canadian Blood Services there is one identified person, the Provincial / Territorial (P/T) blood representative, who has the primary responsibility for interactions between Canadian Blood Services and their province/territory. The P/T ministries of health select one jurisdiction, on a rotating basis, to act as the lead P/T on behalf of all jurisdictions for a period of two years.

The P/T blood representatives, together with selected representatives from the Canadian Blood Services executive and senior management teams, form a committee known as the Canadian Blood Services Provincial/Territorial Blood Liaison Committee (CBS-P/T BLC). This committee is co-chaired by a Canadian Blood Services representative and the P/T blood representative for the lead province. This committee meets on a regular basis and constitutes the major forum for formal communications between Canadian Blood Services and its funders.

Canadian Blood Services solicits advice from various relevant parties through its advisory committees (as well as other ad hoc forums). One such committee is the National Advisory Committee on Blood and Blood Products (NAC), an advisory committee consisting of health care professionals with expertise in the field of transfusion medicine appointed by their respective P/T ministries, as well as Canadian Blood Services representatives. The NAC reports to the CBS-P/TBLC (NAC membership and its terms of reference are available on www.nacblood.ca).

1.2 Immunoglobulins in Canada

Canadian Blood Services manages a pan-Canadian formulary of approximately 50 brands of plasma protein and related products and synthetic alternatives. The organization also stores, ships, and delivers these medications to hospitals and clinics across the country using a network already approved and funded as part of its national blood supply responsibilities. As per

the memorandum of understanding signed by federal, provincial, and territorial ministers of health (excluding Quebec) which established the national blood authority, Canadian Blood Services' plasma protein and related products formulary leverages the combined buying power of P/T health budgets to offer publicly funded blood products to those who need these at no direct cost to the patient. While Canadian Blood Services offers a substantial range of products, it has a managed formulary – not an open formulary. Selective changes to product listings occur through product selection and tendering processes. While many of these medications are administered in hospital, increasingly these are being manufactured in formulations that permit in-home administration, such as through subcutaneous injection.

Ig products are used to treat primary and secondary immune deficiency disorders, and a wide range of autoimmune disorders across various medical specialties including autoimmune neurological disorders and other diseases with an immune origin. Utilization continues to grow year over year and although there are jurisdictional guidelines available across the country, there is a recognized variation in use between provinces.

1.3 Purpose and scope

While many of the principles within *The National Plan for the Management of Shortages of Labile Blood Components* may also be applicable to a shortage of plasma protein and related products, the CBS-P/TBLC recognized that a national plan to specifically guide the allocation of Ig products in a short or prolonged shortage was needed and identified this as a priority task for NAC in 2019.

NAC had initiated planning to develop a national Ig shortage plan but had not yet started the work when the COVID-19 pandemic struck in early 2020. The pandemic's potential impact on the global Ig supply chain highlighted the urgent need to have an Ig shortage management plan in place. The NAC and CBS-P/TBLC recognized that proceeding with the development of an interim Ig plan was required and tasked the National Emergency Blood Management Committee for Immunoglobulins (NEBMC-Ig) Secretariat with having an interim plan in place within a 3-month timeframe. Intended as a response to potential supply impacts on the near horizon, *The National Plan for Management of Shortages of Immunoglobulin Products (Ig) – Interim Guidance* (interim Ig plan) was approved by the P/T ministries of health in September 2020, and remained in place while this comprehensive national Ig plan was being developed.

Through the support of Health Canada and provincial and territorial ministries of health and building on the interim Ig plan (2020), this national Ig plan delivers the following:

- **Ethical framework:** key principles to guide deliberations and inform decisions about the triage and adjudication of Ig products during times of shortage.
- **Triage and adjudication criteria**: clear criteria informed by, including optimal dosing, for how Ig should be triaged during times of shortage. Ig is used for prophylaxis and treatment of a range of diseases and conditions across various medical specialties. In

this document, the conditions considered for Ig therapy are listed under the following broad categories: dermatology, hematology, immunology, infectious disease, neurology, rheumatology, and transplantation.

- **Alternative therapies**: a list of possible alternate therapies that should be made available and readily accessible during a shortage.
- **Triage and adjudication process / operationalization plan:** suggested triage and adjudication processes, in addition to a number of elements necessary to operationalize the plan, including roles and responsibilities of key relevant parties; plans for communicating during times of shortage; and sample tools for use to document triage and adjudication decisions.

1.4 Key participants and relevant parties

It is intended that the national Ig plan will be used by key blood system participants who, for the purposes of the national Ig plan, are defined to be Canadian Blood Services, the NAC, the P/T ministries of health, Health Canada, regional health authorities, and hospitals. The national Ig plan delineates roles and responsibilities for each of these participants.

Relevant parties for the national Ig plan are these participants, as well as Ig prescribers who are treating patients with conditions that require Ig, administrators assessing and reviewing clinically appropriate access to Ig, and others potentially affected (or representing those potentially affected) by the national Ig plan such as patient/blood recipient societies, health care professional societies, Héma-Québec, product vendors, and others.

1.5 History of Ig shortages in Canada

Since Canadian Blood Services has been providing Ig products to hospital customers, there have been no shortages that would have met criteria to call a national Amber or Red Phase in Canada for the overall Ig supply (including both IVIg and SCIg).

In 2019, Canadian Blood Services did experience a short-term supply constraint for SCIg due to unprecedented SCIg utilization and a NEBMC-Ig was subsequently convened to discuss the situation. In the absence of a national Ig shortages plan, a NEBMC-Ig, working with Canadian Ig prescribers and patient groups, leveraged principles and the framework from *The National Plan for Management of Shortages of Labile Blood Components* to guide decisions and communications. An Amber Phase was declared on May 8, 2019, which facilitated collaboration with relevant parties to implement mitigation measures to reduce risk and understand demand rates. This included ensuring known patients continued to receive SCIg. However, new patients diagnosed with a condition requiring Ig treatment may not have had the option of choosing intravenous versus subcutaneous administration in case demand outpaced available supply. Canadian Blood Services SCIg inventories recovered to levels allowing for discontinuation of the shortage by August 26, 2019.

In March 2020, in response to potential impacts of COVID-19 on the supply chain of Ig products, a Green Phase Advisory was declared and remained active for 7 weeks before a return to Green Phase.

2. Assumptions

The assumptions used in the development of this plan are as follows:

A. The national Ig shortages management plan operates within the existing blood system structure.

The memorandum of understanding signed by federal, provincial, and territorial ministers of health (excluding Québec) which established the national blood authority states Canadian Blood Services has "responsibility for a national blood supply system which assures access to a safe, secure and affordable supply of blood, blood products and their alternatives, and supports their appropriate use."

B. The national Ig shortages management plan assumes that all efforts to increase the available supply of Ig have been exhausted.

As indicated above (Section 1.3) and by the name of this document, the purpose of the national Ig plan is to optimize the allocation of Ig when the supply is severely compromised. It is not the purpose of the national Ig plan to address mechanisms to increase the supply of Ig in the face of threats to that supply. Those aspects of emergency preparedness are important and must be addressed by Canadian Blood Services in their documents and plans regarding management of the blood supply system. For the purposes of this national plan, it is assumed that in the instance of severe Ig shortage Canadian Blood Services has implemented such measures and in spite of this, the supply of Ig is insufficient to meet demand.

C. The national Ig shortages management plan promotes collaboration.

The national Ig plan is intended to promote the most efficient use of a limited supply of Ig in a situation of emergency, through collaboration by participants in the Canadian blood system. The optimal allocation of Ig in a time of shortage will depend upon the ability of all participants to act in a highly professional, collaborative and transparent manner.

D. The national Ig shortages management plan is based upon established ethical principles.

In the event of an Ig shortage, difficult decisions will need to be made about the allocation of Ig products. The overriding goal is to minimize harms caused to some persons because of a shortage and make choices in ways that are as fair as possible all things considered. Given this, a key component of this national plan is the identification, integration, and application of relevant ethical values.

The ethical framework outlined in Appendix C supports the overall Ig plan with respect to developing both ethically justified criteria for Ig allocation and the associated decision-making processes that are to be followed in the event of a shortage. The latter also includes the identification of the appropriate decision-makers at different levels within health organizations and across health systems in relation to these processes.

E. The national Ig shortages management plan recognizes previous and ongoing work in this domain and represents an ongoing process.

The national plan was built upon existing documents including the interim Ig plan, the Government of Québec's *Nonspecific Immunoglobulin* (*Ig) Shortage Management Framework* and *The National Plan for Management of Shortages of Labile Blood Components*.

It will be necessary to refine and amend the national Ig plan over time as more information becomes available, as inventory management and utilization data becomes more robust, and when/if experience is gained in a simulation exercise or actual shortage situation.

F. The national Ig shortages management plan acknowledges potential legal considerations.

The national plan recognizes the potential for legal challenges on behalf of patients denied Ig in a shortage, where a decision not to administer Ig - a decision made pursuant to the agreed-upon protocols in the plan - results in an adverse outcome. It is hoped that the development of this national plan, in and of itself, will assist hospitals and physicians to make the most appropriate medical (and hence legal) decisions.

G. The national Ig shortages management plan assumes that all areas of the country served by Canadian Blood Services would be simultaneously affected in an approximately equal manner; however, P/T and/or regional differences can also be addressed by the plan.

The national Ig plan is written to address an Ig shortage with the assumption that the demand for Ig would be approximately equal across all jurisdictions served by Canadian Blood Services. However, given the large size of the country, it is possible that different scenarios with respect to supply and demand could arise.

H. The national Ig shortages management plan acknowledges Canada's diverse geography and diverse expertise.

The national Ig plan acknowledges Canada's diverse geography, remote locations and the fact that there are many very small hospitals in rural locations that do not carry large Ig inventories. The reality is that there may be limited expertise in these remote and/or rural locations, and this will need to be considered. Any reductions or recommendations will need to take these jurisdictions and their special needs into consideration.

3. Phases of inventory availability

In keeping with other plans to manage shortages, this national Ig shortages plan considers five phases of inventory availability, defined below.

3.1 Phases of inventory availability

The national Ig shortages plan considers five phases of inventory availability – Green, Green Phase Advisory, Amber, Red, and Recovery. Determination of the need to declare a shortage phase could apply to a single Ig brand or multiple brands in either SCIg or IVIg formulations. A number of considerations are critical for the National Emergency Blood Management Committee for Immunoglobulins (NEBMC-Ig) to make informed decisions regarding an Ig shortage, such as: overall availability of product in Canada, utilization rates (national and jurisdictional), future supply outlook, effectiveness of clinical use guidelines, and allocation criteria. Standard data elements and availability of data in real time across the system are also essential and this plan supports the further development of a mechanism and method for monitoring and forecasting utilization. With real time data, Canadian Blood Services and the NEBMC-Ig would be better equipped to determine appropriate actions required to manage a shortage.

3.1.1 Green Phase

Green phase implies that normal Ig inventory levels exist, and supply generally meets demand and future resupplies are expected to be adequate This phase includes a broad range of inventory levels ranging from an ideal inventory to temporary shortages that occur periodically and can be managed within the scope of existing Canadian Blood Services and hospital/RHA actions.

3.1.2 Green Phase Advisory

The Green Phase Advisory is typically when Ig inventory is low or there is a potential supply disruption being forecasted. This phase requires review of all hospital inventories and utilization to determine what the likelihood of entering Amber or Red phase. It would also be an advisory to hospitals and provinces / territories to look at any potential conservation strategies that could help avoid a shortage. Hospitals/RHA will need to share inventory levels and any other utilization data within a specific timeframe to ensure that the NEBMC-Ig can assess what the phase would be. Ideally, inclusion of an estimate of daily demand over the next several days will be useful for decision making.

3.1.3 Amber Phase

Amber Phase implies that Ig inventory levels are insufficient to continue with routine practice and hospitals/RHA will be required to implement specific measures to reduce Ig usage.

3.1.4 Red Phase

Red Phase implies that Ig inventory levels are insufficient to ensure that patients identified as having critical need will receive the required product(s).

3.1.5 Recovery Phase

Recovery Phase implies that Ig inventory have begun to increase and are expected to be maintained at a level that would enable hospitals to move from Red to Amber to Green Advisory Phase and subsequently to Green Phase.

3.2 Canadian Blood Services inventory levels at Green, Green Phase Advisory, Amber, and Red Phases

It is not possible, a priori, to define concisely national inventory levels which would automatically trigger the declaration of an Amber or Red phase, partly because any inventory in patient homes is not considered in the national inventory. Critical levels will vary according to availability of alternate product, shelf-life of all inventories and the anticipated length of a given shortage. Available Ig inventory at Canadian Blood Services is categorized as optimal through critical according to the number of 'weeks on hand' (defined as the number of weeks the inventory would last, based on average historical demand run rates over the previous six months) which, as shown below, correspond approximately to inventory levels that could represent Green, Green Phase Advisory, Amber and Red Phase inventories. The declaration of an Amber or Red Phase would depend on the predicted ability of Canadian Blood Services to increase inventory. It is acknowledged that some patients (at home) also hold inventories of Ig products that would not be reflected in the inventory phase declaration criteria.

Approximate Ig inventory levels that, if sustained, could lead to the declaration of Amber or Red Phase are provided in Table 1.

Table 1. Approximate Ig inventory levels that would be considered in a decision to declare an inventory phase*.

Ig	Green	Green Advisory	Amber	Red
IVIg	> 11 WOH	8-11 WOH	5-8 WOH	< 5 WOH
SCIg	> 11 WOH	8-11 WOH	5-8 WOH	< 5 WOH

*Assumes brand availability is balanced
Weeks on hand (WOH) - Number of weeks the inventory would last (based on average historical demand for the past 6 months).

The NEBMC-Ig is responsible for assessing the level of shortage and the short and long-term impacts the shortage situation may have on the Ig supply. A key element in inventory management during an Ig shortage is knowledge of the available Ig inventory, including in

patient homes, at hospitals, and at Canadian Blood Services, and that which is available from product vendors as well as any estimated resupply time.

3.2.1 Total inventory levels

The inventory levels presented in Table 1 represent a combination of product inventory held by Canadian Blood Services and the vendors in-country supply that is allocated to Canadian Blood Services. Vendors are contractually required to hold a minimum of eight weeks of released inventory in Canada for Canadian Blood Services' needs. However, this represents only a part of the total Ig inventory within the blood system, inventory is also held in hospital/RHA blood banks and some patients also have SCIg inventory at their homes for self-administration.

4. Key participant roles and responsibilities

This section outlines the general roles and responsibilities of the following participants as they relate to Ig products only. Each participant has a responsibility to develop emergency preparedness plans that include Ig shortage management as a key element and are appropriate to each respective agency/institution.

Within all the categories listed below, there is the expectation that each representative to the NEBMC-Ig should ensure that they have identified a designate in the event that they are unavailable. This designate should be clearly communicated to the NEBMC-Ig Secretariat provided by Canadian Blood Services.

There is also relevant, essential work (e.g., consistent guidance for use of Ig, inventory levels etc.) that should be undertaken by each P/T ministry of health during a green phase (normal inventory) to increase preparedness should an Ig shortage occur and, arguably, influence the likelihood of ever needing to activate this national Ig plan.

4.1 Canadian Blood Services

Canadian Blood Services manages the blood supply system in all provinces and territories except Québec. As part of this mandate, Canadian Blood Services currently engages in a number of activities to identify and avert potential shortages. Its main activity in this regard is the ongoing management of the Ig inventory as a single national inventory (as opposed to multiple regional inventories).

Canadian Blood Services has developed and continues to refine business continuity and business recovery plans to minimize the impacts of adverse events on the national Ig inventory. Canadian Blood Services has a *Business Continuity Management Program*, in which it is recognized that events/disasters could negatively affect the availability of Ig, Canadian Blood Services staff, equipment, information-technology systems, transportation systems and/or facilities upon which the maintenance of the national Ig inventory are critically dependent.

Canadian Blood Services plays a key role on the NEBMC-Ig (see Section 5.1) and will have an active role in declaring the inventory phase of an Ig shortage and any recovery from such shortage situations, in addition to providing the secretariat function for the committee. With respect to the distribution of Ig, Canadian Blood Services will issue Ig in accordance with the phase of shortage, and/or triage and adjudication decisions, as applicable. These activities would occur in consultation with the NEBMC-Ig and in consideration of its advice.

Canadian Blood Services will also liaise with relevant parties (e.g., Health Canada, Hema-Québec, Ig product vendors, patient advisory groups, etc.) and coordinate communications as per the established process (see Section 6).

4.2 Health Canada

Health Canada plays a leadership role in addressing medication shortages in the country outside of plasma protein and related products. When an anticipated or actual Ig shortage may have a national impact, coordination with Health Canada will be implemented as and if needed to support work with relevant parties to assess the supply and demand situation; identify options to mitigate the impact of the shortage; promote and facilitate timely and effective communication between all potentially impacted groups; and work together on strategies to prevent shortages and strengthen the supply chain.

In times of Ig shortage, Health Canada will be invited to participate in the NEBMC-Ig. Health Canada will work with Canadian Blood Services to assess the scale and potential impact of a shortage as this will inform the type of shortage and applicable response (if Tier 3 - the most serious level - based on a federal tiered notification and communication framework). If it is determined the situation is an actual or anticipated Tier 3 shortage, it is deemed as such on the Tier 3 shortages website.

If intervention is required at the national level for an Ig shortage situation, Health Canada seeks risk mitigation proposals. Options available to help mitigate the impacts of a severe shortage may include:

- using regulatory powers to allow for medications labelled and approved for other markets to be imported into Canada,
- fast-tracking regulatory reviews,
- extending the shelf life of Ig products if there are suitable supporting data, and
- allowing the temporary usage of Ig products with known impurities.

Finally, in times of Ig shortage, Health Canada may also have a role in coordinating and disseminating information as per an established process (see Section 6).

4.3 National Advisory Committee on Blood and Blood Products

The NAC mandate is to provide medical and technical advice on the utilization management of blood and blood products to the P/T ministries and Canadian Blood Services. Considering this mandate, the CBS-P/TBLC asked NAC to develop an Ig shortages management plan.

The NAC should develop strong communication and knowledge translation activities to support awareness and understanding of this national Ig plan to increase the ability of P/T ministries of health and hospitals/RHAs to develop their own Ig shortages plans to support the implementation the national Ig shortages plan in a shortage situation. This includes and is not limited to:

- Communicating about the plan with relevant parties.
- Executing practice scenarios for applying this Ig plan to build awareness and capacity within different health organizations as well as P/T and national relevant parties noted in this plan.
- Reviewing the implementation and outcomes of the national Ig plan on an ongoing basis and reporting these findings to all members of the NEBMC-Ig.
- Identifying mechanisms to communicate updates and revisions to this plan. This may include how the feedback of relevant parties or new evidence has been considered in revisions to the plan, additional tools or resources that are developed in response to requests, and so on.

The NAC also plays a key role on the NEBMC-Ig; the Chair of the NAC will co-chair the NEBMC-Ig and all NAC members will be members of the NEBMC-Ig (see Section 5.1).

In times of shortage, the NAC will coordinate and disseminate information as per the established process (see Section 6).

4.4 Provincial and Territorial Ministries of Health

Given that the provision of health care and essential services falls under P/T jurisdiction, there are a number of ways in which the ministries of health and their staff will be involved in the execution of the national Ig plan.

Every P/T ministry of health is responsible for the development of detailed P/T plans to manage Ig shortages, including the establishment in each province/territory of a Provincial/Territorial Emergency Blood Management Committee for Immunoglobulins (P/TEBMC-Ig). P/T plans should comply with the requirements outlined in the national Ig plan and should be linked to each P/T's other emergency preparedness plans. It is strongly recommended that a

standardized phasing system of inventory availability (Green, Green Phase Advisory, Amber, Red and Recovery as defined in this national Ig plan) be adopted by all provinces/territories.

P/T ministries of health should play a leadership role in providing support and resources for hospitals/RHAs within their jurisdiction to comply with their P/T plan and this national plan. In collaboration with the P/TEBMC-Ig, the P/T ministry should provide directives to hospitals/RHAs to comply with the minimum standards established for each phase of the shortage (see Section 7) and to monitor the level of compliance in the institutions within their jurisdiction.

Given the potential for legal challenges on behalf of patients denied Ig in a shortage, where a decision not to administer Ig - a decision made pursuant to the agreed-upon protocols in the plan - results in an adverse outcome, jurisdictions should conduct their own legal and ethical reviews of the national plan, and to the extent possible, put protections in place for those who will be applying the national plan and making real-time decisions pursuant to it.

In times of shortage, the P/T ministry is also responsible for coordinating and disseminating information as per the established process (see Section 6).

Some provinces have provincial blood coordinating offices / programs. While not referred to specifically in the national Ig plan, it is assumed that they, under the auspices of the corresponding P/T ministry of health, will also play a key role in the implementation of P/T plans to manage Ig shortages in alignment with the requirements outlined in this national Ig plan.

It is critically important that alternative therapies are available across all P/T jurisdictions in times of shortage. As such, each P/T ministry should conduct a review of the list of alternative therapies outlined in Appendix D to determine which therapies are available in their jurisdiction, and what work might need to be done to ensure timely access to these therapies in an Ig shortage situation.

Recognizing that there is much ongoing work related to the stewardship of Ig products in several parts of the country, there would be value in P/T ministries of health reaching national agreement on – and importantly supporting appropriate utilization management. This includes and is not limited to national clinical guidelines for the use of Ig during Green Phase (normal inventory levels)

Finally, there is a need for more granular data about the use of Ig products to better understand usage patterns, patient population distributions, barriers to access, etc. P/T ministries of health should promote and support improved data collection by ensuring there is a mechanism in place for Ig utilization monitoring to ensure there is appropriate utilization of Ig.

4.4.1 Provincial/Territorial Blood Representatives

The P/T blood representative in each province/territory is responsible to provide advice and support to the respective deputy minister and minister of health on issues affecting the blood

system. In this capacity, P/T blood representatives will play central roles in the establishment of a P/TEBMC-Ig and the development of their respective P/T/hospital/RHA plans to manage shortages of Ig.

All P/T blood representatives will participate on the NEBMC-Ig, providing a link between national and P/T response plans to ensure a consistent and coordinated national response to an Ig shortage. In this capacity, P/T blood representatives will be responsible for ensuring the establishment of both internal and external lines of communications to enable consistency and coordination within and among P/T jurisdictions, hospitals/RHA and Canadian Blood Services.

4.4.2 Lead P/T Blood Representative

The P/T blood representative of the Lead P/T will play a leadership role in facilitating communications between the various participants/relevant parties and their respective P/T ministry.

4.5 Hospitals/Regional Health Authorities

Each hospital/RHA should develop their own detailed hospital/RHA plans to manage Ig shortages in alignment with the P/T and national plans, including the establishment of a Hospital/RHA Emergency Blood Management Committee for Immunoglobulin (H/REBMC-Ig) (see Section 5.3).

The purpose of a hospital/RHA blood shortage management plan is to delineate lines of responsibility, decision-making processes, and effective communication to enable the H/REBMC-Ig to respond appropriately during a shortage. Such hospital/RHA plans should also define which staff members will participate in the H/REBMC-Ig and how a reduction in Ig usage will be achieved. It is strongly recommended that a standardized phasing system of inventory availability (Green, Green Advisory, Amber, Red and Recovery as defined in the interim Ig plan) be adopted by all hospital/RHA Ig shortage management plans.

During a shortage, hospitals/RHAs are responsible for implementing Ig conservation strategies, and triage and adjudication processes (see Section 7), which includes reporting data to the P/T ministries of health and Emergency Blood Management Committees for Ig, as requested.

Careful record-keeping of decisions made pursuant to the national plan will be of paramount importance. Preparations should be undertaken to make the recording of such decisions, in the event of a crisis, as easy and efficient as possible. A sample decision documentation tool is provided in Appendix F.

Finally, hospitals/RHAs will coordinate and disseminate information / messaging per the established process (see Section 6).

5. Emergency Blood Management Committees for Immunoglobulins

This section describes the emergency blood management committees for immunoglobulins at the national, provincial/territorial and hospital/RHA levels that will be necessary to facilitate information flow and decision-making.The activities of these various committees are meant to be collaborative but in the setting of local or regional shortages, there may not be activation of higher level committees such as the NEBMC-Ig. This does not preclude the activities of the Provincial/Territorial or Hospital/RHA committees from occurring to manage a local shortage situation.

5.1 National Emergency Blood Management Committee for Immunoglobulin (NEBMC-Ig)

The NEBMC-Ig is necessary to ensure the implementation and any activation of this national Ig shortage plan. Given this committee will function similarly to the NEBMC for Labile Blood Components. details as to the composition and terms of reference for the NEBMC can be found in *The National Plan of the Management of Labile Blood Components*.

The NEBMC-Ig will convene to discuss an emerging or actual Ig inventory shortage and provide advice regarding determining the appropriateness of declaring a Green Phase Advisory, Amber Phase or Red Phase shortage, and subsequent recovery from these situations. The committee will review available data and consult appropriate subject matter experts, including those with clinical interests and experience relevant to the use of Ig, as needed, to inform their decision making.

Should a Green Phase Advisory, Amber, or Red Phase be declared, the committee will provide conservation actions / recommendations on the distribution of Ig (see Section 7.2), including whether or not to implement rationing procedures.

To promote alignment, consistency and collaboration during a shortage or potential shortage, the NEBMC-Ig will be guided by the established framework outlined in Appendix E in providing actions / recommendations concerning the communication of the shortage to key relevant parties.

Finally, the committee will ensure ongoing refinement and improvements to The National Plan for the Management of Shortages of Ig Products after activation or simulation.

5.2 Provincial/Territorial Emergency Blood Management Committees for Immunoglobulins (P/TEBMC-Ig)

It is the responsibility of the ministries of health of each province or territory to leverage its P/TEBMC-Ig for the purpose of managing an Ig shortage. The responsibilities of the P/TEBMC-

Ig are development of a response plan in accordance with the guidance outlined in this national Ig plan to minimize the P/T impact of Ig shortages; to ensure that the actions / recommendations from the NEBMC-Ig are appropriately communicated and implemented within its jurisdiction; and to establish a process to monitor adherence and manage non-adherence to the P/T Ig plan and other national directives in times of Ig shortages.

Each P/TEBMC-Ig will work collaboratively as required with the NEBMC-Ig and its jurisdiction's H/REBMC-Ig and provide the conduit for communications / feedback between these groups.

Provinces or territories may wish to consider having a core or an executive P/TEBMC-Ig and then an expanded membership depending upon the extent of the shortage including clinical representation reflective of Ig use. Details regarding mandatory and suggested membership are included within *The National Plan for the Management of Shortages of Labile Blood Components*.

5.3 Hospital/RHA Emergency Blood Management Committee for Immunoglobulin (H/REBMC-Ig)

Each hospital or RHA has a responsibility to leverage its H/REBMC-Ig whose mandate is to develop an Ig shortage management plan in accordance with the guidelines outlined in its P/T plan and this national Ig plan. It is the responsibility of the H/REBMC-Ig to ensure that these plans are appropriately communicated and adhered to in times of Ig shortages. Each H/REBMC-Ig should also serve as the communication conduit to the P/TEBMC. In small provinces/territories, it is possible that the P/TEBMC-Ig and H/REBMC-Ig would be one single body.

H/REBMC-Ig membership will vary from facility to facility and should include clinical representation reflective of Ig use. Details regarding suggested membership are detailed in *The National Plan for the Management of Shortages of Labile Blood Components*.

5.4 National Triage and Adjudication Team / Panel

The role of the national triage team / panel is to ensure consistent application of the inclusion and exclusion criteria in Red Phase. This includes addressing physician appeals when an Ig request is denied and screening all requests in the case of a severe shortage in which rationing is required (see Section 7.2).

It is recommended that the national triage team / panel be established in advance of a shortage and provided with detailed information on the triage framework prior to an Ig shortage being declared. The triage team / panel must be a multidisciplinary team with adequate clinical representation from those with interests and experience relevant to the use of Ig, and robust enough to ensure sufficient 24-hour coverage.

Careful record-keeping of decisions made pursuant to the national plan will be of paramount importance. The national triage and adjudication team / panel will document triage decisions, and report to Emergency Blood Management Committees for Ig, as required. Preparations should be undertaken to make the recording of such decisions, in the event of a crisis, as easy and efficient as possible. A sample decision documentation tool is provided in Appendix F.

6. Communication

Effective and timely communication is critical in attempts to mitigate a national Ig shortage, while in a shortage situation and afterwards during recovery efforts. While key relevant parties will have their own communications infrastructure, procedures and complexities, a common course of action is required by these partners, however different they may be, to promote alignment, consistency and collaboration during a crisis or potential crisis.

A framework for the flow of information in times of shortage, allowing all parties to provide timely, accurate and credible information to various internal and external relevant parties for the purposes of operational and informational communication is provided in Appendix E.

A more fulsome communications plan, including overarching and general principles and key messages is available in the *National Plan for Management of Labile Blood Components*. It is imperative that each jurisdiction produces its own communications plan based on its specific needs in alignment with the national plan.

Sample templates for a National Inventory Advisory are provided in Appendix F.

7. Allocation of immunoglobulins in times of shortage

During a shortage, conservation strategies to help preserve the limited supply of Ig should be implemented. This section describes the triage and adjudication criteria and provides recommendations for specific actions during times of shortage.

7.1 Triage and Adjudication Criteria

The issuance of Ig to hospitals/RHA in times of shortages will be determined by Canadian Blood Services in consultation with the NEBMC and / or P/TEBMC-Ig (described in Section 5) and will take into consideration usual requirements, the nature of the shortage, inventory requirements, and the conservation activities described in Section 7.2 below.

Allocation of Ig to patients should be in accordance with the criteria provided in Appendix D. The criteria are not intended to be clinical practice guidelines. Rather, the criteria identify the conditions and circumstances for which the use of Ig products may be considered clinically appropriate given the level of Ig supply available. Indications are divided into the following

categories: dermatology, hematology, immunology, infectious disease, neurology, rheumatology, and transplantation.

7.2 Triage and adjudication process

During a shortage, Ig conservation strategies should be implemented. These may include any or all the actions suggested below, and/or additional measures directed by the NEBMC-Ig in response to the inventory situation.

7.2.1 Green Phase Advisory

Green Phase Advisory implies that Ig inventory levels are low, and that system wide inventory and utilization needs to be understood to inform the likelihood of crossing into Amber or Red Phase. Hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.

- Follow the triage and adjudication criteria outlined in Appendix D. Where use is indicated, confirm that use aligns with the patient's goals of care.
- 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.
- Consider increasing availability of alternative therapies. Prior to starting Ig treatment, consider use of all other safe, effective, and accessible alternative therapies.
- Use a dose calculator based on adjusted body weight, and track Ig levels to adjust dose, as appropriate.
- Review stocking practices and maintain the minimum inventory level required.
- Identify patients that can be switched to SCIg (in the event of an IVIg shortage) or IVIg (in the event of an SCIg shortage), or other alternative therapies to prepare for the potential escalation to Amber Phase and Red Phase.
- Implement local and P/T processes to support the triage and adjudication process:
    - Implement screening of all Ig orders by a physician (or designate) within the hospital transfusion service/blood bank, with support from local / regional stewardship (if applicable) and / or clinical experts, as required.

- Reassess all patients who are already on treatment to confirm they continue to meet the criteria outlined in this phase of the shortage, and if so, reassess to find the minimal clinically effective dose.
- Implement an appeal process for Ig orders that are not approved, in which the ordering physician can follow up with the transfusion medicine physician, in consultation with regional / P/T (clinical) subject matter experts, as needed.
- Document and keep a record of triage and adjudication decisions.
- Restrict approvals to a maximum of three to six (3 – 6) months. This may be shortened further depending on the inventory situation.
- Reduce the refill volume for patients on home infusion products to a maximum of three (3) months. This may be reduced further depending on the inventory situation.
- Ensure there is a mechanism in place to collect and report data, as requested. At a minimum this includes, but is not limited to, data which accurately reflects Ig requests, expected demand, Ig approvals and denials, and Ig inventory levels.

7.2.2 Amber Phase

Amber Phase implies that Ig inventory is insufficient to continue with routine deliveries and hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.

- Follow the triage and adjudication criteria outlined in Appendix D. Where use is indicated, confirm that use aligns with the patient's goals of care.
- 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.
- Increase the availability of alternative therapies. Prior to starting Ig treatment, consider use of all other safe, effective, and accessible alternative therapies.
- Use a dose calculator based on adjusted body weight, and track Ig levels to adjust dose, as appropriate.
- Review stocking practices and maintain the minimum inventory level required.
- Where possible, switch patients to SCIg (in the event of an IVIg shortage) or IVIg (in the event of an SCIg shortage), or other alternative therapies.

- Implement local and P/T processes to support the triage and adjudication process:
    - Implement screening of all Ig orders by a physician (or designate) within the hospital transfusion service/blood bank, with support from the Ig Stewardship Program and / or clinical experts.
    - Reassess all patients who are already on treatment to confirm they continue to meet the criteria outlined in this phase of the shortage, and if so, reassess to find the minimal clinically effective dose.
    - Implement an appeal process for Ig orders that are not approved, in which the ordering physician can follow up with regional / P/T (clinical) subject matter experts.
    - Document and keep a record of triage and adjudication decisions.
    - Restrict approvals to a maximum of one (1) month. This may be shortened further depending on the inventory situation.
    - Reduce the refill volume for patients on home infusion products to a maximum of one (1) month. This may be reduced further depending on the inventory situation.
    - Ensure there is a mechanism in place to collect and report data, as requested. At a minimum this includes, but is not limited to, data that accurately reflect Ig requests, expected demand, Ig approvals and denials, and Ig inventory levels.

7.2.3 Red Phase

Red Phase implies that Ig inventory levels are insufficient to ensure all patients will receive required Ig.

- Follow the triage and adjudication criteria outlined in Appendix D. Where use is indicated, confirm that use aligns with the patient's goals of care.
- 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.
- Increase the availability of alternative therapies. Prior to starting Ig treatment, consider use of all other safe, effective, and accessible alternative therapies.
- Use a dose calculator based on adjusted body weight, and track Ig levels to adjust dose, as appropriate.
- Review stocking practices and maintain the minimum inventory level required.

- Where possible, switch patients to SCIg (in the event of an IVIg shortage) or IVIg (in the event of an SCIg shortage), or other alternative therapies.
- Implement local, P/T and national processes to support the triage and adjudication process:
    - Implement screening of all Ig orders by (clinical) regional / P/T subject matter experts.
    - Reassess all patients who are already on treatment to confirm they continue to meet the criteria outlined in this phase of the shortage, and if so, reassess to find the minimal clinically effective dose.
    - Implement an appeal process for Ig orders that are not approved, in which the ordering physician can follow up with the national triage team / panel.
    - Document and keep a record of triage and adjudication decisions.
    - Restrict approvals to a maximum of one (1) dose at a time.
    - Reduce the refill volume for patients on home infusion products to a maximum of one (1) dose at a time.
    - Ensure there is a mechanism in place to collect and report data, as requested. At a minimum this includes, but is not limited to, data that accurately reflect Ig requests, expected demand, Ig approvals and denials, and Ig inventory levels.
    - In the case of a severe shortage in which rationing is required:
        - Implement screening of all Ig orders by the national triage and adjudication team / panel
        - It is anticipated that there will be no ability to manage an appeals process.

Appendix A. Approval and Revision History

Comprehensive Ig Shortages Plan Version May 30, 2024

a. General changes to the body which include but are not limited to wordsmithing to improve clarity and style, as well as minor editorial changes.

b. Updated 'Key relevant parties' roles and responsibilities' to include Health Canada. Additional details to improve clarity in this section were also added.

c. Updated 'Emergency Blood Management Committees' to include National Triage and Adjudication Team / Panel. Additional details to improve clarity in this section were also added.

d. Addition of the 'Communications' section, and corresponding Appendix E.

e. Addition of 'Allocation of Ig in times of shortage' section to include updates to possible conservation strategies, recommended triage and adjudication processes, and corresponding Appendix D, which includes a more comprehensive list of clinical indications for Ig use, recommended dosing guidelines, and a list of alternative therapies.

f. Changed Appendix B from 'Stakeholder Engagement' to 'Plan Development' and added details on how the national Ig plan was developed.

g. Addition of Appendix C - Ethical Framework

h. July 5, 2024: Two minor formatting edits

Interim Ig Shortages Plan Version July 27, 2020

The CBS-P/TBLC recognized that a national plan to specifically guide the allocation of Ig products in a short or prolonged shortage was needed and identified this as a priority task for NAC in 2019.

NAC had initiated planning to develop a national Ig shortage plan but had not yet started the work when the COVID-19 pandemic struck in early 2020. The pandemic's potential impact on the global Ig supply chain highlighted the urgent need to have an Ig shortage management plan in place. The NAC and CBS-P/TBLC recognized that proceeding with the development of an interim plan was required and tasked the NEBMC Secretariat with having an interim plan in place within a 3-month timeframe by mid-July 2020.

The interim Ig plan was intended as a response to potential short- to medium-term supply impacts and to remain in place while a full plan is developed. To expedite the development of the interim plan, the NEBMC Secretariat leveraged existing documents including the Government of Québec's *Nonspecific Immunoglobulin* (*Ig) Shortage Management Framework* and *The National Plan for Management of Shortages of Labile Blood Components.*

Approximately 400 relevant parties were provided an opportunity to comment on proposed Ig allocation criteria in May 2020 and a final draft interim national plan was prepared and disseminated for relevant parties' review in June 2020.

Version 2020-07-27 was endorsed by the National Advisory Committee on Blood and Blood Products, Canadian Blood Services, and the Provincial/Territorial Ministries of Health in jurisdictions served by Canadian Blood Services.

Appendix B. Plan development

Engagement of relevant parties was essential to the development of this national Ig plan. A fulsome engagement strategy was developed to ensure relevant parties were engaged early and in meaningful ways to help shape the decision-making and facilitate support for implementation of the National Ig Shortages Management Plan

Preliminary engagement

Gathering perspectives to inform approach

Nearly 100 relevant parties, who participated in the development of the interim Ig plan, were invited to share their reflections on what did (or didn't) work well during the development of the interim Ig plan May - July 2020, as well as their thoughts on how to best to approach broad engagement in the development of the comprehensive national Ig Shortages plan. This feedback was gathered through electronic survey as well as 1:1 interviews.

Identification of relevant parties

A list of key relevant parties was developed based on what was created for development the interim Ig plan. This list was verified by the Project Team, with the assistance of Canadian Blood Services' Stakeholder Engagement team.

Relevant parties were then contacted and asked to identify specific representatives from their organization and/or jurisdiction to participate, as well as any relevant party groups who may have been missed.

Ultimately, a broad range of multidisciplinary perspectives were used to develop the Ig Shortages Plan, these include, but are not limited to:

- Project sponsors and Canadian health systems stewards including:
    - Canadian Blood Services
    - Health Canada, Health Product Shortages Directorate
    - National Advisory Committee on Blood and Blood Products
    - Provincial/Territorial Blood Liaison Committee
    - Provincial/Territorial Blood Coordinating Offices / Programs
    - Provincial/Territorial Emergency Blood Management Committees
- Patients and patient organizations including:
    - Guillain-Barré Syndrome/Chronic Inflammatory Demyelinating Polyneuropathy (GBS/CIDP) Foundation of Canada (includes Multifocal Motor neuropathy (MMN))
    - ImmUnity Canada (formerly Canadian Primary Immunodeficiency Organization (CIPO))
    - Myasthenia Gravis (MG) Society of Canada

    - Canadian Hemophilia Society
    - Alpha-1 Antitrypsin Deficiency Canada Inc
    - Network of Rare Blood Disorder Organization
    - Canadian Association for Porphyria
    - Platelet Disorder Support Association
    - Kawasaki Disease Canada
    - Hereditary Angioedema (HAE) Canada
    - Canadian Organization for Rare Disorders
- Immunoglobulin prescribers, clinicians, and clinical societies for: immunology, neurology, rheumatology, hematology, oncology, dermatology, solid organ transplant, stem cell transplantation, and infectious diseases, including:
    - Association of Medical Microbiology and Infectious Disease Canada
    - Canadian Dermatology Association
    - Canadian Hematology Society
    - Canadian Neurological Sciences Federation
    - Canadian Pediatric Society
    - Canadian Society for Immunology
    - Canadian Society of Allergy and Clinical Immunology (CSACI)
    - Canadian Society of Transplantation (CST)
    - Cell Therapy Transplant Canada (CTTC)
    - Clinical Immunology Network Canada
    - Immunodeficiency Canada
    - Primary Immunodeficiency Nurses Network
- Additional relevant parties including:
    - Clinical nurse specialists
    - Ethicists
    - Hospital transfusion medicine supervisors, medical leads, and technologists

Ethical framework

To develop the ethical framework, a group of bioethicists and clinicians from various jurisdictions, met regularly over several months to participate in a series of generative discussions to surface a comprehensive list of values that were important to consider. To complement these discussions, a literature review was conducted to further understand what values are most relevant for the management of medication shortages and the allocation of scarce healthcare resources. Input from a broad group of clinicians, patient advocacy organizations, blood provider representatives, hospitals, government representatives in addition to diversity, equity, and inclusion expert perspectives were sought through small group sessions, and the framework was refined accordingly (see Appendix C).

Ethics Working Group	Province
Dianne Godkin, PhD Director, Regional Ethics Program Trillium Health Partners	ON
Dr. Sheila Harding Professor Pathology and Laboratory Medicine University of Saskatchewan College of Medicine	SK
Bashir Jiwani, PhD Executive Director, Ethics and Diversity Services Fraser Health	BC
Al-Noor Nenshi Nathoo, MA Executive Director, Clinical Ethics Service Alberta Health Services	AB
Dr. Susan Nahirniak Medical Director, Alberta Precision Laboratories Transfusion and Transplantation Medicine Program	AB
Dr. Arjuna Ponnampalam Assistant Professor, University of Manitoba Transfusion Medicine, Shared Health Adult Hematology, CancerCare MB	MB
Christy Simpson, PhD (Working Group Lead) Head and Associate Professor, Department of Bioethics, Faculty of Medicine, Dalhousie University Bioethics Consultant, Canadian Blood Services	NS
Dr. Alan Tinmouth Director, Ottawa Hospital Hemoglobinopathy Program, Department of Hematology Director, Ottawa Hospital Centre for Transfusion Research Ottawa Hospital and Ottawa Hospital Research Institute	ON

Triage and adjudication criteria and alternative therapies

A subset of NAC clinicians was convened to guide and facilitate the development of triage and adjudication criteria.

Provincial Ig guidelines and existing Ig shortages frameworks were reviewed and summarized and this informed a preliminary draft of the criteria for the purposes of guiding discussions with a broad range of clinical experts. The guidelines and frameworks which were reviewed included:

- Atlantic Clinical Indications and Criteria for Intravenous and Subcutaneous Immunoglobulin (IVIg/SCIg) April 2022.
- Ontario Immune Globulin (IG) Utilization Management Guidelines. ORBCoN, Version 4.0; January 31, 2018
- Prairie Collaborative Immune Globulin Utilization Management Framework Project. Criteria for the clinical use of immune globulin. Second edition. Alberta Ministry of Health, Shared Health Manitoba and Saskatchewan Ministry of Health; 2022.
- British Columbia PBCO. Intravenous Immune Globulin (IVIg) Utilization Management Program Recommendations. Version 5.0. Revision Date: 2019-07-25.
- Institut National D'Excellence en Sante et Services Sociaux (INESSS) Quebec. Appendix 3. Nonspecific Immunoglobulin (Ig) Shortage Management Framework. March 2020
- Institut National D'Excellence en Sante et Services Sociaux (INESSS) Quebec. Validation of the management framework for a nonspecific human immunoglobulin shortage. English summary. March 2021.
- The National Plan for Management of Shortages of Immunoglobulin Products (Ig) – Interim Guidance

Criteria Development – Core Working Group

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Ottawa Hospital and Ottawa Hospital Research Institute

Dr. Kathryn Webert
Medical Director and Special Advisor, Plasma
Canadian Blood Services

Several engagement sessions were conducted to review and refine the preliminary draft of the criteria with clinicians across each of the following specialties: hematology, immunology, neurology, dermatology, rheumatology, infectious disease, and transplantation. The ethical framework was also shared with these groups to help inform and guide the discussions.

Clinicians were then invited to review and provide feedback on the revised draft of the criteria. Consultation with additional specialists in ophthalmology, endocrinology, and gastroenterology also took place. Supplementary engagement sessions were held with clinicians to further refine the criteria, prior to another round of broad relevant party review and feedback. The final version of the criteria for inclusion in this national Ig plan (see Appendix D) was agreed upon by the Criteria Development Working Group.

The relevant party engagement sessions described above also informed the development of a list of suitable alternatives to Ig, where applicable, for inclusion in this national plan. This is in addition to the literature reviews that were conducted by Quebec and CADTH for the indications for which Ig is most often utilized – immune thrombocytopenic purpura (ITP), myasthenia gravis (MG), chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy (MMN), Guillain-Barre syndrome (GBS), autoimmune blistering diseases (AIBD), and idiopathic inflammatory myopathies (IIM). The list of suggested alternative therapies available in Appendix D.

More than 400 clinicians were invited to participate in each of phase of the engagement. Contributions, defined as meeting attendance or providing written feedback and/or agreement with the criteria and alternative therapies, were received from more than 130 clinicians. Participating clinicians are listed in the table below.

Table 3: Participating Clinicians

Contributor	Main Affiliation
Dr. Ali Amer	North Bay Regional Health Centre
Dr. Juan P. Appendino	Clinical Associate Professor, Department of Pediatrics, Cumming School of Medicine, University of Calgary
Dr. Donald Arnold	Professor, Department of Medicine, McMaster University
Loris Aro	Registered Nurse, Bayshore HealthCare
Dr. Yuka Asai	Associate Professor, Division of Dermatology, Department of Medicine, School of Medicine, Queen's University
Dr. Mohammed Aslam	Assistant Professor Medical Oncology, Division of Oncology, College of Medicine, University of Saskatchewan
Dr. Yaron Avitzur	Professor, Division of Gastroenterology Hepatology & Nutrition, Department of Pediatrics, University of Toronto
Dr. Marjorie Bagnas	Assistant Professor, Division of Neurology, Department of Medicine, Queen's University
Dr. Jillian Baker	Assistant Professor, Division of Hematology/Oncology, Department of Pediatrics, University of Toronto
Dr. Volodko Bakowsky	Associate Professor, Division of Rheumatology, Department of Medicine, Dalhousie University
Dr. Lisa Barrett	Assistant Professor, Division of Infectious Diseases, Department of Medicine, Dalhousie University
Dr. Katie Beadon	Clinical Assistant Professor, Division of Neurology, Department of Medicine, Faculty of Medicine, University of British Columbia
Dr. Stephen Betschel	Associate Professor, Division of Clinical Immunology and Allergy, Department of Medicine, University of Toronto
Dr. Catherine Biggs	Clinical Assistant Professor, Division of Infectious Diseases, Department of Medicine, Faculty of Medicine, University of British Columbia
Dr. Haley Block	Assistant Professor Neurology, Department of Medicine, College of Medicine, University of Saskatchewan
Dr. Mark Bosch	Associate Professor Hematological Oncology, University of Saskatchewan
Dr. Eric Bow	Professor, Departments of Medical Microbiology and Infectious Diseases, and Internal Medicine, Sections of Infectious Diseases and Haematology/Oncology, Max Rady College of Medicine, The University of Manitoba Department of Medical Oncology and Haematology, CancerCare Manitoba
Dr. Rae Brager	Associate Professor, Division of Rheumatology, Allergy & Immunology, Department of Pediatrics, McMaster University
Dr. Chris Bredeson	Head of Malignant Hematology and Stem Cell Transplantation, The Ottawa Hospital
Dr. Vera Bril	Professor, Division of Neurology, Faculty of Medicine, University of Toronto
Tina Brkin	Manager, Cross Cancer Institute
Dr. Adrian Budhram	Assistant Professor of Neurology, Pathology and Laboratory Medicine, Schulich School of Medicine & Dentistry, Western University
Dr. Jeannie Callum	Professor, Pathology and Molecular Medicine, Department of Medicine, Queen's University
Dr. Bill Cameron	Professor, Faculty of Medicine, University of Ottawa

Dr. Marvin Chum	Associate Professor, Department of Medicine, McMaster University
Dr. Brian Clarke	Clinical Associate Professor, Division of Cardiology, Providence Health Care
Dr. Catherine Corriveau-Bourque	Associate Professor, Faculty of Medicine & Dentistry, Department of Pediatrics, University of Alberta
Dr. Juthaporn Cowan	Assistant Professor, Department of Pathology and Laboratory Medicine, Faculty of Medicine, University of Ottawa
Dr. Megan Crone	Department of Pediatrics, Cumming School of Medicine, University of Calgary
Dr. Christine Cserti-Gazdewich	Assistant Professor, Department of Laboratory Medicine & Pathobiology, University of Toronto
Dr. Jean Jacques De Bruycker	Clinical Assistant Professor, Division of Rheumatology and Immunology, Department of Pediatrics, University of Montreal
Dr. Beata Derfalvi	Professor, Division of Immunology, Department of Pediatrics, Dalhousie University
Dr. Anne Dipchand	Professor, Division of Cardiology, Department of Paediatrics , University of Toronto
Dr. Karen Doucette	Professor, Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
Dr. Mohamed Elemary	Professor Hematological Oncology, University of Saskatchewan
Dr. Anne Ellis	Professor, Department of Medicine, Queen's University
Dr. Sameer Elsayed	Professor, Division of Infectious Diseases, Department of Medicine, Schulich School of Medicine & Dentistry, Western University
Dr. Gerald Evans	Professor, Biomedical & Molecular Sciences and Pathology & Molecular Medicine, Department of Medicine, Queen's University
Dr. Brian Feldman	Professor, Department of Pediatrics, The Hospital for Sick Children, University of Toronto
Dr. Sarah Forgie	Chair, Department of Pediatrics, University of Alberta
Dr. Azim Gangji	Professor, Department of Medicine, McMaster University
Dr. Jenny Garkaby	Assistant Professor, Division of Rheumatology, Allergy & Immunology, Department of Pediatrics, McMaster University
Dr. Winder Gill	
Dr. Susan Gilmour	Professor, Faculty of Medicine & Dentistry, Department of Pediatrics, University of Alberta
Dr. Jennifer Grossman	Clinical Assistant Professor, Department of Medicine, University of Calgary
Dr. Eyal Grunebaum	Professor, Department of Pediatrics, Temerty Faculty of Medicine, University of Toronto
Dr. Christopher Hahn	Associate Clinical Professor of Neurology, Cumming School of Medicine, University of Calgary
Dr. Sheila Rutledge Harding	Professor, Department of Pathology and Laboratory Medicine, University of Saskatchewan
Dr. Abubaker Hassan	Assistant Professor Nephrology, Department of Medicine, College of Medicine, University of Saskatchewan
Dr. Kyla Hildebrand	Clinical Associate Professor, Interim Division Head, Division of Immunology, Department of Pediatrics, Faculty of Medicine, University of British Columbia
Dr. Michael D. Hill	Professor, Department of Clinical Neurosciences, University of Calgary
Dr. Alim Hirji	Associate Professor, Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta
Dr. Carol Hitchon	Associate Professor, Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba

Dr. Julie Ho	Professor, Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba
Dr. Karen Holfeld	Clinical Associate Professor and Division Head Dermatology - Regina, Department of Medicine, College of Medicine, University of Saskatchewan
Dr. Cyrus Hsia	Associate Professor of Medicine, Schulich School of Medicine & Dentistry, Western University
Dr. Adam Huber	Division Head of Pediatric Rheumatology and Professor, Department of Pediatrics, Dalhousie University
Dr. Mark Inman	Assistant Professor, Pediatric Endocrinology & Diabetes, Department of Pediatrics, College of Medicine, University of Saskatchewan
Dr. Mehul Jariwala	Assistant Professor, Section Head, Pediatric Rheumatology, Department of Pediatrics, College of Medicine, University of Saskatchewan
Dr. Andre Jastrzebski	Postgraduate Residency Program Director, Department of Ophthalmology, Max Rady College of Medicine, University of Manitoba
Dr. Chrystyna Kalicinsky	Assistant Professor, Section of Clinical Immunology and Allergy, Department of Internal Medicine, University of Manitoba
Dr. Amin Kanani	Clinical Associate Professor and Division Head, Division of Allergy and Immunology, Department of Medicine, Faculty of Medicine, University of British Columbia
Harminder Kaur-Singh, CPHQ	Director-At-Large, Quality, Cell Therapy Transplant Canada (CTTC)
Dr. Paul Keith	Associate Professor, Division of Clinical Immunology & Allergy, Department of Medicine, McMaster University
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Dr. Meer-Taher Shabani-Rad	Clinical Professor, Department of Pathology & Laboratory Medicine, Cumming School of Medicine, University of Calgary
Dr. Mona Shafey	Clinical Associate Professor, Division of Hematology, Cumming School of Medicine, University of Calgary
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Dr. Ziad Solh	Associate Professor, Department of Pathology and Laboratory Medicine, Schulich School of Medicine & Dentistry, Western University
Dr. David Spaner	Associate Professor, Department of Immunology, Sunnybrook Health Sciences Centre, University of Toronto
Dr. Catherine Streutker	Professor, Department of Laboratory Medicine & Pathobiology, University of Toronto
Dr. David Szwajcer	Assistant Professor, Department of Internal Medicine, Max Rady College of Medicine, University of Manitoba
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Dr. Simon Urschel	Associate Professor, Faculty of Medicine & Dentistry, Department of Pediatrics, University of Alberta
Dr. Donna Wall	Professor, Department of Immunology, University of Toronto
Dr. Scott Walsh	Associate Professor, Division of Dermatology, Department of Medicine, Sunnybrook Health Sciences Centre, University of Toronto
Dr. Theodore Warkentin	Professor Emeritus, Pathology & Molecular Medicine, Department of Medicine, McMaster University
Dr. Susan Waserman	Professor; Director, Division of Clinical Immunology & Allergy, Department of Medicine, McMaster University
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Triage and adjudication processes and operationalization

To inform a proposed approach for triage and adjudication processes in times of shortage, P/T processes currently in place for the distribution of Ig products in green phase (normal inventory) were reviewed. Building on these existing processes, draft processes were then developed for discussion and refinement at two in-person working sessions which included subject matter representatives from the Provincial Blood Coordinating Offices / Programs and Canadian Blood Services. Roles and responsibilities of key relevant parties, a framework for communication, and sample tools and templates for use in times of shortage were also discussed at these sessions.

Provincial Blood Coordinating Office / Program Representatives	Province
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Angela Carpenter Program Manager PEI Department of Health and Wellness	PEI
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Lindy McIntyre Director, Health Policy & Government Relations Canadian Blood Services	Government Relations Advisor
Saba Teklehaimanot Manager, Government Relations Canadian Blood Services	Government Relations Advisor
Dr. Kathryn Webert Medical Director and Special Advisor, Plasma Canadian Blood Services	Medical Advisor

Lindsay Wilson Sr. Project Manager, Enterprise Program and Project Management Office Canadian Blood Services	Project Manager

Information Technology Specialists	Role
Sarfraz Hooda Chief Architect, IT Strategy and Governance Canadian Blood Services	Observer
Trevor Poole Director, IT Strategy and Governance Canadian Blood Services	Observer

Appendix C. Ethical Framework and Analysis

Executive Summary

Difficult decisions will need to be made about the allocation of Ig in the event of a shortage. The overall goal of this ethical framework, as part of the larger national Ig plan, is to assist with doing as little harm as possible – where harm is broadly understood. This naturally includes the physical harm(s) that may be experienced by patients due to limited or no access to Ig products during a shortage. It also includes due consideration of the emotional and relational harms that can occur in the context of anticipated and/or actual shortages of health care resources for patients, health care providers, and decision-makers.

The ethical framework developed for this management plan consists of nine values. Each value, and its relevance, is described in the table below. It is acknowledged that these values can be described in different ways; the goal here was to highlight the key considerations in relation to each value and how it is meant to contribute in the context of an Ig shortage.

There are several key points to keep in mind with respect to applying this ethical framework:

- The overall goal of this framework, as part of the larger management plan, is to do as little harm as possible – where harm is broadly understood. This naturally includes the physical harm(s) that may be experienced by patients due to limited or no access to Ig products during a shortage. And, as the COVID-19 pandemic has dramatically demonstrated, emotional and relational harms can occur in the context of anticipated and/or actual shortages of health care resources. These harms can also be significant and long-lasting, and thus should also be considered as part of an overall shortages management plan.
- The values included in this ethical framework are meant to be applied and used together to guide deliberations and inform decisions about triage and adjudication of Ig products in the event of a shortage.
- There are links between and natural groupings of some of the values listed below. Rather than reducing the number of values listed, each value is included to foster reflection on what it highlights or calls attention to. How the values are presented is intentional to help facilitate ‘telling the story’ or to explain a decision in relation to these values (rather than, e.g., presenting them in alphabetical order).

- During the relevant party sessions, using this ethical framework was likened to that of a sound mixing board,[1] i.e., all of the values are relevant and contribute to highlighting relevant considerations and priorities as part of making decisions about Ig product allocation during a shortage – however, depending on the decision at hand (e.g., whether this is at a national level or at the clinical level), some of the values may play a more significant role in the decision-making process as compared to others. Even while all values are important, the 'mix' of values and the relative importance of any particular value as part of the overall application of the ethical framework may shift between different types of decisions. In line with this, there are no specific weights applied in advance to the values included in this ethical framework.
- This ethical framework puts an emphasis on engagement and responsiveness appreciating that, in general, better decisions tend to be made when there are opportunities for different perspectives to be shared as well as opportunities to update and revise allocation decisions 'in the moment' on the basis of new evidence or information.
- Finally, and in conjunction with the above, this framework also emphasizes preserving relationships and building trust, even while recognizing that the primary focus is on how best to allocate Ig products during a shortage.

[1] Many thanks to Angus Dawson (Centre for Biomedical Ethics, National University of Singapore) as the originator of this comparison.

Ethical Framework

Values	Description	Why is this value relevant in this context?	
Minimize harm	Do as little harm as possible in the context of an Ig shortage, appreciating that harm can be experienced in various ways, including physical, emotional, relational.	Limits the harms that will occur if there is an Ig shortage – expanded definition assists with appreciating range of possible impacts and how these may be experienced by patients, health care providers, decision-makers, and so on.	
Clinical effectiveness	Improvement in a dimension of health status for which treatment is being used (i.e., relative to the specified purpose or intended outcome), demonstrated by positive change in clinical markers or quality of life indicators. Treatment can be Ig products or alternative treatments and can apply at a patient population or individual patient level.	Facilitates identification of 'best use' of Ig or alternative treatment (in terms of benefits). This may be particularly relevant for patients with rare conditions where there is little or no evidence about use of Ig products and who are already using Ig products with positive effect.	Facilitates identification of 'best use' of Ig or alternative treatment (in terms of benefits). This may be particularly relevant for patients with rare conditions where there is little or no evidence about use of Ig products and who are already using Ig products with positive effect.
Evidence-informed	Decisions about Ig allocation (including starting a patient on Ig) are based on accurate, well-justified facts; good quality evidence includes an appropriate range of evidence types, clinical trials to real world, case-based, qualitative data.	Assists with making better decisions about the appropriate use of Ig or alternative treatments.	
Trust-worthiness	People are able to see that the goals that have been established for this framework are well-justified and developed in good faith, and the methods employed in developing, applying, updating, and revising this framework will	Facilitates the use of the management plan during a shortage and will contribute towards achieving the goal of minimizing harm.	

Values	Description	Why is this value relevant in this context?
	help achieve these goals. This includes responsiveness to 'just in time' feedback or needed changes identified during a shortage.	
Transparency	Sharing the rationale and context for decisions, as part of communications about this framework at all levels.	Assists with increasing trust.
Solidarity	Recognizes that in the context of the health system and a shared limited resource, such as Ig, that better outcomes can be achieved by working together at a national level than can be achieved by working alone – this includes working together to understand different perspectives and needs, in order to make and implement decisions in accordance with what has been jointly identified as important/relevant.	Emphasizes how working together collaboratively will help minimize harm and help promote equitable access. Signals that those responsible for making decisions are accountable for doing so in accordance with the criteria and processes outlined in this framework.
Stewardship	The most efficient and fair use of a resource.	Ensures attentiveness to use of Ig in accordance with criteria and processes outlined.
Equity and justice	Access to and distribution of a resource is based on defensible criteria; this requires establishing the relevant criteria and then treating like cases alike to the extent possible in evaluation against these criteria. This will help ensure consistency in	Recognizing that Ig products are used across a wide range of patient populations, the criteria used to determine which will have priority and on what basis needs to be clearly identified.

Values	Description	Why is this value relevant in this context?	
	process and application across different settings. More broadly, this also includes actively identifying and remedying existing implicit biases and institutionalized discrimination. This includes, for example, issues of access and barriers at patient and organizational/system levels to Ig products and alternative treatments. Over time, this may help contribute to bringing into greater harmony the many different systems, structures and processes that make up the larger health system as it relates to Ig usage. This includes efforts to align the principles and policies of these various dimensions with the values outlined here.		
Respect for people and relationships	Due regard for those who are directly affected by an Ig shortage including: support for the relationships between people; respect for patient autonomy and well-being; and meeting obligations to those who can be expected to experience harm during a shortage. This includes patients, health care providers, as well as those in relevant decision-	The uncertainty, concern, distress, and possible/actual harms that may be experienced during an Ig shortage can be anticipated and, as such, it is important to address these aspects as well.	The uncertainty, concern, distress, and possible/actual harms that may be experienced during an Ig shortage can be anticipated and, as such, it is important to address these aspects as well.

Values	Description	Why is this value relevant in this context?	
	making roles within health systems.		

Context and Key Considerations

As noted elsewhere in this document, this more comprehensive development of this Ig Shortages Management Plan builds on earlier related documents that provided initial guidance. These documents include the National Plan for Management of Shortages of Immunoglobulin Products (Ig) – Interim Guidance (2020) developed by the National Advisory Committee on Blood and Blood Products (NAC) and the Nonspecific Immunoglobulin (Ig) Shortage Management Framework (2020) developed by Santé et Services Sociaux Québec. Further, there is the National Plan for Management of Shortages of Labile Blood Components and the Emergency Framework for Rationing of Blood for Massively Bleeding Patients during a Red Phase Blood Shortage developed by NAC. These latter management plans specifically include reference to a number of ethical values, and together all of these documents provided a useful starting foundation for considering whether, and if so how, any of the values they name and discuss may inform this Ig shortages management plan ethical framework.

Beyond these above-named shortages management plans, it is also well-recognized that medication shortages and shortages of other key health care resources, such as ventilators or personal protective equipment, have become part of the fabric of our health care systems in Canada. The commitment to addressing these shortages as well as possible in the moment, and in further developing management strategies and approaches for potential and predictable shortages has correspondingly increased, as has the interest in ethical frameworks to help guide and support decision-makers with the difficult choices they face. This was particularly evident during the COVID-19 pandemic, starting in March 2020, at which time there was a rapid increase in both the development of, and extensive revisions to pre-existing, ethical frameworks and shortages management plans. The pandemic also led to a greater public awareness of the potential magnitude and impacts of the need to allocate resources in the event of different types of shortages. This, along with other aspects of the COVID-19 pandemic (such as the differential health and economic impacts experienced across the country in relation to lockdowns, access to vaccines, etc.), also contributed to heightened awareness and discussion about what matters from an ethical perspective, including what values are and should be central as part of decision-making about allocating scarce resources.

Key considerations

As part of the discussions within the Ethics Working Group, a number of key considerations emerged that further informed the ethical values identified above, the descriptions of these values, and the justification for why each value is relevant for the Ig Shortages Management Plan. Some considerations tied directly to Ig products and their use; other considerations reflect that the descriptions and implementation of some values in ethical frameworks has shifted over time. Key considerations included, but were not limited to, the following:

- The nature and use of Ig products as compared and contrasted with other blood and blood products – for example, this highlights the importance of considering the needs of patients for whom the use of Ig products is ongoing as compared to a one-time use.

- The range of conditions for which Ig products may be used also includes several rare conditions, which can impact the type and availability of evidence with respect to its use for these conditions.
- The existence (or not) of alternative treatments – for some conditions, there are identified alternative treatments. These may come with different degrees of effectiveness and/or side effects for specific patients and patient groups.
    - Closely tied to this are two further considerations:
        - The availability of and access to alternative treatments, such as plasmapheresis, which may differentially impact, e.g., urban-based versus rural-based patients.
        - Whether the costs of an alternative medication, for example, are covered within one's home province/territory or whether the alternative may be an out-of-pocket cost.
- Commitments to the values of equity and justice are increasingly challenging the status quo, including the ways in which things are traditionally done (i.e., historical patterns of how some limited resources have been allocated) and challenging biases or assumptions about what is most relevant in decision-making processes.
- The nature and types of harms that can occur as a result of resource allocation decisions may be broader than typically discussed or addressed. This includes relational and psychological harms in addition to physical harms experienced by patients. This also includes recognizing that health care providers and others in the health system (decision-makers, administrators, support persons) may also experience relational and psychological harms as part of enacting a shortages management plan.

Process and Literature Review

As part of the process of developing the ethical framework for this management plan, an Ethics Working Group was established that consisted of ethicists, clinicians, and members of NAC from across the country. As described in Appendix B, this group met regularly over several months with additional input gathered through the below-described literature review and, importantly, relevant party feedback on the draft ethical framework. The ethical framework was also shared with the Clinical Working Groups to help inform and guide the discussions of these groups.

Literature review

Given the impact of the COVID-19 pandemic and other (primarily medication) shortages on the development of ethical frameworks for resource allocation, a literature review was conducted to ascertain whether there were additional insights or examples that could contribute to the Ethics

Working Group's discussions. In particular, this included the identification and understanding of the role of specific values within ethical frameworks for resource allocation; discussion and analysis of the ethical values relevant for these types of frameworks naturally increased during the COVID-19 pandemic.

Through the literature search, several different resource allocation documents and related ethical frameworks were identified.[2] This included a number of Canadian examples, both with respect to pandemic-specific frameworks (e.g., critical care) and with respect to other medication/therapy shortages.[3] These Canadian examples identified many of the same values that are included in this ethical framework for managing Ig shortages. Given the nature of Canadian health care, and the underlying values articulated in the Canada Health Act, this is not unexpected.

At the same time, there were some insights that emerged from both the Canadian and international resource allocation examples and related papers. First, there is a trend towards being more explicit with the descriptions of the stated values in the ethical framework, i.e., while some frameworks still make use of (what can be characterized as) more general, high level descriptions of values, there is a move towards articulating how a value is meant to be understood in the context of the issue or problem it is meant to be addressing (such as a shortage of a health resource). Second, arguably, there is a marked increase in the number of papers discussing the value of equity in and of itself, and in relation to health care systems. Discussions about this value are ongoing and evolving and have also become a significant aspect of discussions in connection to several pandemic-related resource allocation frameworks, i.e., there is more attention to the need for justification of the ways in which equity is addressed in different resource allocation and ethical frameworks. Third, and closely connected to the previous point, there is also increased attention to what may be most appropriate to measure, demonstrate, and/or design to reflect this value across a range of decision-making frameworks. This includes calls for further reflection on what tools or measures may be selected or developed to help track or demonstrate changes in any identified equity-related issues. Ultimately, these discussions highlight and challenge considerations of who, how, and on what basis some persons gain access to a limited or scarce resource compared to others.

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[2] For example: Emanuel, E; Persad, G; Upshur, R; et al. 2020. Fair Allocation of Scarce Medical Resources in the Time of Covid-19. *New England Journal of Medicine* 382(21): 2049-2055; Fielding, J; Sullivan, SG; Beard, F; et al. 2021. Constructing an Ethical Framework for Priority Allocation of Pandemic Vaccines. *Vaccine* 39: 797-804.

[3] Examples of these articles include: Bell, J; Escaf, M; Schmilovich, Z; et al. 2020. First Ready, First to Go: Ethical Priority-Setting of Allogenic Stem Cell Transplant at a Major Cancer Centre. *Healthcare Policy* 15(3): 102-115; Downar, J; Smith, MJ; Godkin, D; et al. 2022. A Framework for Critical Care Triage during a Major Surge in Critical Illness. *Canadian Journal of Anesthesia* 69: 774-781; Reid, L. 2020. Triage of Critical Care Resources in COVID-19: A Stronger Role for Justice. *Journal of Medical Ethics* 46: 526-530; Steele, D; Duthie, K. 2021. Ethics of Resource Allocation in a Public Health Emergency Context. *Healthcare Management Forum* 343(6): 353-356.

Appendix D: Inventory phase activity and Ig allocation criteria

Table of Contents

Frequently used abbreviations (for Appendix D)

ABW	Adjusted body weight
CIDP	Chronic inflammatory demyelinating polyradiculoneuropathy
CMV	Cytomegalovirus
EBV	Epstein-Barr virus
HIT	Heparin induced thrombocytopenia
HLA	Human leukocyte antigens
HLH	Hemophagocytic lymphohistiocytosis
HSCT	Hematopoietic stem cell transplantation
Ig	Immunoglobulin
IgA	Immunoglobulin A
IgE	Immunoglobulin E
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IVIg	Intravenous immunoglobulin
N/A	Not applicable
PID	Primary Immunodeficiency
PLEX	Plasmapheresis, or plasma exchange
SCIg	Subcutaneous immunoglobulin
SID	Secondary immunodeficiencies
VITT	Vaccine-induced immune thrombotic thrombocytopenia

Background

The criteria in the tables below are solely intended to guide clinical decisions and triage of Ig products in the event of a green phase advisory, amber, or red phase shortage:

- **Green Phase Advisory** implies that Ig inventory levels are low, and that system wide inventory and utilization needs to be understood to inform the likelihood of crossing into Amber or Red Phase. Hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.
- **Amber Phase** implies that Ig inventory is insufficient to continue with routine deliveries and hospitals/RHA will be required to implement specific measures, as outlined in this document, to reduce Ig usage.
- **Red Phase** implies that Ig inventory levels are insufficient to ensure that patients identified as having critical need will receive the required product(s).

The criteria are not intended to be clinical practice guidelines. Rather, the criteria identify the conditions and circumstances for which the use of Ig products may be considered clinically appropriate given the level of Ig supply available.

Indications are divided into the following categories: dermatology, hematology, immunology, infectious disease, neurology, rheumatology, and transplantation. See the Table of Contents for a full list of conditions included in this document.

Refer to provincially endorsed jurisdictional guidelines in times of Green Phase (normal inventory level):

- *Atlantic Clinical Indications and Criteria for Intravenous and Subcutaneous Immunoglobulin (IVIg/SCIg) April 2022.*
- *Ontario Immune Globulin (IG) Utilization Management Guidelines. ORBCoN, Version 4.0; January 31, 2018*
- *Prairie Collaborative Immune Globulin Utilization Management Framework Project. Criteria for the clinical use of immune globulin. Second edition. Alberta Ministry of Health, Shared Health Manitoba and Saskatchewan Ministry of Health; March 2022.*
- *British Columbia PBCO. Intravenous Immune Globulin (IVIg) Utilization Management Program Recommendations. Version 5.0. Revision Date: 2019-07-25.*

Classifications

Each indication in the tables below includes a classification (first row) as well as optimal dosing (second row). The four classifications are as follows:

- **Use is appropriate:** Use of Ig is generally supported in all circumstances.

- **Use may be appropriate if criteria are met:** Use of Ig is generally supported if the criteria outlined are met.
- **Use not appropriate unless there are exceptional circumstances**: Use of Ig is generally not appropriate but may be considered appropriate on a case-by-case basis. Exceptional circumstances generally include instances in which the patient has failed or has contraindications and/or intolerance to available alternate therapies and has severe disease. There should be reasonable evidence that Ig might be effective, and the therapy should be discontinued if there is no evidence of response.
- **Do not use:** Ig should not be used.

Note that these classifications do not replace clinical judgment. If Ig is felt to be necessary for an individual with a life-threatening condition, use will be considered on a case-by-case basis. Furthermore, there may be other clinical circumstances in which Ig will be considered on a case-by-case basis. Decisions will be made per the direction of the National Emergency Blood Management Committee – for Ig and with guidance from clinical experts, in each phase of shortage, as necessary.

Assessment

During times of shortage, for all patients, it is essential that review by an appropriate specialist or physician with experience in the treatment of the condition is done before the start of Ig therapy to ensure diagnosis, all appropriate therapies have been considered, and the dose prescribed is correct.

Patients receiving ongoing use of Ig for chronic conditions should be reassessed regularly by the appropriate specialist to confirm if therapy is effective to determine if the dose and/or dosing frequency can be adjusted. If treatment with Ig does not achieve the desired clinical outcome, it should be discontinued.

Dosing

All dosing refers to intravenous Ig (IVIg) unless otherwise specified.

All dosing is based on adjusted body weight (ABW) unless otherwise specified.

The NAC supports the use of an ABW calculator to calculate IVIg dosing in all adult patients. Slight variation currently exists between available calculators nationally. A recommendation for the use of one single calculator cannot be made until sufficient data are gathered and reviewed. For reference, here are some examples of calculators currently in use:

- Atlantic Provinces - Adjusted Body Weight Calculator with IVIg Dosing in Adults
- Ontario - Ideal Body Weight Calculator with IVIg Dosing
- Alberta - IVIg Dosing based on Adjusted Body Weight Calculation
- British Columbia - IVIg Dosing Calculator

There is limited evidence to support the use of ABW calculators for pediatric patients. However, use may be considered in the context of a pediatric patient's height and weight.

In pregnancy, it is appropriate for IVIg dosing to be based on actual body weight in the first trimester, and then maintained at a consistent dose throughout the pregnancy.

The dosing recommendations vary, depending on the indication and individual patient circumstances. Further adjustments to dosing recommendations may occur depending on the severity of the shortage/directive from the NEBMC.

Consider rounding dose **down** to nearest vial size (within 10-15%) to minimize product wastage. This may occur at the clinical or transfusion medicine level.

Once the condition has stabilized, titrate to the lowest dose and/or interval to maintain clinical effectiveness.

Bleeding

The severity of various types of bleeding included in the criteria are defined in the table below in accordance with the WHO Bleeding Scale[4].

Severity of bleeding	Bleeding grade	Description of bleeding
No bleeding	0	None
Mild bleeding	1	Petechial
Moderate bleeding	2	Mild blood loss
	3	Gross blood loss
Severe bleeding	4	Debilitating blood loss

Disclaimer:

The Ig Shortages plan reflects the best available data at the time of publication. The shortage criteria are based on existing Ig guidelines and extensive clinician and broader engagement. While the number of disorders included within the criteria is extensive, it is recognized that there may be some that are omitted. Further, disease classifications may change with time and new disorders may be recognized. In these instances, clinical judgement using the principles of the plan should be used to determine appropriateness of Ig therapy. The plan will evolve over time and through its use in the event of a shortage.

[4] Miller AB, Hoogstraten B, Staquet M, Winkler A. Reporting Results of Cancer Treatment. Cancer 1981; 47:207-214.

Dermatology

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Atopic dermatitis	Use may be appropriate if the following criteria are met: • Most severe forms of eczema AND • Contraindication or failure to standard immunosuppressive therapies (including topical steroids and calcineurin inhibitors) For patients with primary immunodeficiency (PID), refer to PID criteria in the Immunology section.	Do not use.	Do not use.
	2 g/kg ABW divided over 2-5 days. Administered every 4 weeks initially in the setting of contraindication to conventional immunosuppressive therapy. Once condition has stabilized, interval between infusions should be gradually increased to determine if ongoing treatment is required. IVIg should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles. In rare instances when longer term treatment is required, regular washout periods should be attempted.	Not applicable (n/a)	n/a

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Autoimmune blistering disease Includes pemphigus vulgaris, cicatricial pemphigoid, and pemphigoid gestationis	Use may be appropriate if the following criterion is met: • When no clinically meaningful response or a contraindication to corticosteroids, immunosuppressive agents or biologics (e.g., rituximab)	Use may be appropriate if the following criterion is met: • Disease is rapidly progressing, and other treatments are contraindicated	Do not use.
	2 g/kg ABW divided over 2-5 days. Should be administered every 4 weeks initially, usually in addition to conventional immunosuppressive therapy. Once condition has stabilized, the interval between infusions should be gradually increased to determine whether ongoing treatment is required. IVIg should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles.	1-2 g/kg ABW divided over 2-5 days. Should be administered every 4 weeks initially, usually in addition to conventional immunosuppressive therapy. Once condition has stabilized, the interval between infusions should be gradually increased to determine whether ongoing treatment is required. IVIg should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles.	n/a

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Autoimmune blistering disease Includes pemphigus foliaceus, pemphigoid, linear IgA disease, and epidermolysis bullosa acquisita	Use may be appropriate if the following criterion is met: • When no clinically meaningful response or a contraindication to corticosteroids, immunosuppressive agents or biologics (e.g., rituximab)	Do not use.	Do not use.
	2 g/kg ABW divided over 2-5 days. Should be administered every 4 weeks initially. Once condition has stabilized, the interval between infusions should be gradually increased to determine whether ongoing treatment is required. IVIg should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles.	n/a	n/a
Eosinophilic fasciitis	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Do not use.
	2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur.	1.5 - 2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).	n/a

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Hemophagocytic lymphohistiocystosis (HLH): Primary	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
Hemophagocytic lymphohistiocytosis (HLH): Secondary[5] Includes macrophage activation syndrome (MAS) and virus associated hemophagocytic syndrome (VAHS)	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.

[5] Secondary HLH is a heterogenous group of conditions and includes HLH secondary to conditions including infections (mainly viruses, such as EBV, HIV, and CMV, but also bacteria, parasites, and fungi), malignancies (mainly malignant lymphoma), macrophage activation syndrome in autoinflammatory or autoimmune disorders, other causes (organ or stem cell transplantation; metabolic, traumatic, iatrogenic [immunosuppression, vaccination, surgery, hemodialysis] causes; and pregnancy). Treatment protocols vary and depend on underlying cause. (La Rosee P, Horne A, Hines M et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 2019; 133:2465-77)

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Livedoid vasculopathy	Use may be appropriate if the following criterion is met: • No response to primary standard therapy	Do not use.	Do not use.
	2 g/kg ABW divided over 2-5 days. Should be administered every 4 weeks initially. If clinical response is good, the interval between infusions can be gradually increased. Ig should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles. In rare instances when longer term treatment is required, regular washout periods should be attempted.	n/a	n/a
Mast cell activation syndrome (MCAS) Includes 1º MCAS (caused by clonal mast cell disorder); 2º MCAS (Caused by IgE-mediated allergies or triggers that act directly on mast cells via the MRGPRX2 receptor), and idiopathic MCAS	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.
	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Morphea	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Do not use.
	2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur.	1 - 2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).	n/a
Necrobiotic xanthogranuloma	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.
	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.	Refer to Necrobiotic xanthogranuloma criteria in the Hematology section.
Netherton syndrome	Use may be appropriate if the following criterion is met: • Severe cases when intralesional or oral corticosteroids and steroid-sparing agents are ineffective or contraindicated	Use may be appropriate if the following criterion is met: • Severe cases when intralesional or oral corticosteroids and steroid-sparing agents are ineffective or contraindicated	Do not use.

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	1-2 g/kg ABW divided over 2-5 days, every 4 weeks.	1-1.5 g/kg ABW divided over 2-5 days, every 4 weeks.	n/a
Pre-tibial myxedema	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (e.g., methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Use may be appropriate if the following criterion is met: • Severe cases when corticosteroids and steroid-sparing agents (e.g., methotrexate, azathioprine, cyclosporin, mycophenolate) are ineffective or contraindicated	Do not use.
	2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur.	1 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).	n/a
Psoriasis	Use may be appropriate if the following criterion is met: • All other therapies, including phototherapy, methotrexate, cyclosporine, retinoids, small molecule inhibitors, and biologics are ineffective or contraindicated	Do not use.	Do not use.

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once condition has stabilized, interval between infusions should be gradually increased to determine whether ongoing treatment is required. If clinical effectiveness has not been achieved after 6 treatment cycles, IVIg should be discontinued.	n/a	n/a
Pyoderma gangrenosum	Use may be appropriate if the following criteria are met: • Disease is rapidly progressing, AND • Other treatments are contraindicated	Use may be appropriate if the following criteria are met: • Disease is rapidly progressing AND • Other treatments are contraindicated	Do not use.
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 2 days, every 4 weeks for 4-6 cycles. If there is no clinical response after 3-6 treatment cycles, should be discontinued.	Induction: 1-2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 2 days, every 4 weeks for 4-6 cycles. If there is no clinical response after 3-6 treatment cycles, should be discontinued.	n/a

Dermatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Scleromyxedema	Use recommended if the following criterion is met: • Severe cases when corticosteroids are ineffective or contraindicated	Use recommended if the following criterion is met: • Severe cases when corticosteroids are ineffective or contraindicated	Use recommended if the following criterion is met: • Severe cases when corticosteroids are ineffective or contraindicated
	2 g/kg ABW divided over 2-5 days, every 4 weeks. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur.	2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).	2 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient.
Severe cutaneous adverse reaction (SCAR) (e,g., Drug reaction with eosinophilia and systemic symptoms (DRESS); Toxic epidermal necrolysis (TEN); Stevens-Johnson syndrome; Mycoplasma induced rash and mucositis (MIRM)	Use may be appropriate if the following criterion is met: • Severe cases when other treatments (corticosteroids and steroid-sparing agents) are ineffective or contraindicated	Use may be appropriate if the following criteria are met: • Severe cases when disease is rapidly progressing AND • Other treatments (corticosteroids and steroid-sparing agents) are ineffective or contraindicated	Use may be appropriate if the following criteria are met: • Severe cases when disease is rapidly progressing AND • Other treatments (corticosteroids and steroid-sparing agents) are ineffective or contraindicated AND • When the condition is life-threatening.
	2 g/kg ABW divided over 2-5 days, every 4 weeks. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur.	1 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).	1 g/kg ABW divided over 2-5 days. A single treatment is usually sufficient. One additional dose may be given after an initial response if symptoms recur (exceptional circumstance).

Hematology

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Acquired pure red cell aplasia (PRCA) Associated with parvovirus B19	Use may be appropriate if the following criteria are met: • Immunocompromised patient AND • Other therapies (e.g., steroids, cyclosporin) have failed	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Do not use.
	Up to 2 g/kg ABW divided over 2 to 5 days. Dose may be repeated if clinically indicated.	Up to 2 g/kg ABW divided over 2 to 5 days. Dose may be repeated if clinically indicated.	n/a
Alloimmune thrombocytopenia (HLA)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Aplastic anemia	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Autoimmune hemolytic anemia	Use may be appropriate if the following criterion is met: • Failure, contraindication, or intolerance of other therapeutic options in life-threatening cases Note: IVIg interferes with the direct antiglobulin test and may exacerbate hemolysis in patients who have non-group O blood types.	Do not use.	Do not use.
	1-2 g/kg ABW divided over 1-5 days. A single treatment is usually sufficient.	n/a	n/a
Autoimmune neutropenia	Use may be appropriate if the following criterion is met: • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Failure, contraindication or intolerance to other therapeutic options AND • One of the following: ○ severe, active infections ○ a history of severe infections that responded positively to treatment	Do not use.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	1 g/kg ABW divided over 1-5 days. One additional dose may be given if response to the first dose is suboptimal. Response should be measured by frequency of infections and not simply neutrophil count.	1 g/kg ABW divided over 1-5 days. Do not repeat.	n/a
Coagulation factor inhibitors (allo and autoantibodies, including acquired hemophilia, von Willebrand Disease (vWD), hemophilia B, fibrin stabilizing factor (FXIII))	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a
Fetal/neonatal alloimmune	Use may be appropriate. .	Use may be appropriate. .	Use may be appropriate.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
thrombocytopenia (F/NAIT) Mothers	Maximum dose not to exceed 1g/kg ABW/week. Consider stopping therapy or increasing interval (maximum 1 g/kg every 2 weeks) for low-risk patients (mothers with no history of intracranial hemorrhage in a previous infant and no antibody detected). Consider stopping therapy if mother meets any of the following conditions: • No HPA antibody detected OR • No evidence of HPA incompatibility	Maximum dose not to exceed 1 g/kg ABW/week. Consider stopping therapy or increasing interval (maximum 1 g/kg every 2 weeks) for low-risk patients (mothers with no history of intracranial hemorrhage in a previous infant and no antibody detected). Stop therapy if mother meets any of the following conditions: • No HPA antibody detected OR • No evidence of HPA incompatibility	Maximum dose not to exceed 1 g/kg ABW /week. Consider stopping therapy or increasing interval (maximum 1 g/kg every 2 weeks) for low-risk patients (mothers with no history of intracranial hemorrhage in a previous infant and no antibody detected) Stop therapy if mother meets any of the following conditions: • No HPA antibody detected OR • No evidence of HPA incompatibility
Fetal/neonatal alloimmune thrombocytopenia (F/NAIT) Neonates	Use may be appropriate if the following criteria are met: • Platelet transfusion is unavailable OR • Inadequate response to platelet transfusion OR • There is significant clinical concern such as moderate-severe bleeding	Use may be appropriate if the following criteria are met: • Platelet transfusion is unavailable OR • Inadequate response to platelet transfusion OR • There is significant clinical concern such as moderate-severe bleeding	Use may be appropriate if the following criteria are met: • Platelet transfusion is unavailable OR • Inadequate response to platelet transfusion OR • There is significant clinical concern such as moderate-severe bleeding
	Single dose of 0.8-1 g/kg. Occasionally more than one dose is required if thrombocytopenia persists.	Single dose of 0.8-1 g/kg. Occasionally more than one dose is required if thrombocytopenia persists.	Single dose of 0.8-1 g/kg. Occasionally more than one dose is required if thrombocytopenia persists.
Gestational alloimmune liver disease	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
(GALD)/alloimmune neonatal hemochromatosis Mothers with a previously affected pregnancy	1 g/kg ABW (capped at 60 g/week) for at-risk mothers at 14 weeks, 16 weeks, and then weekly from 18 weeks gestation until delivery between 37 and 38 weeks. The dose is based on mother's ABW at initial presentation and is continued unchanged throughout pregnancy.	1 g/kg ABW (capped at 60 g/week) for at-risk mothers at 14 weeks, 16 weeks, and then weekly from 18 weeks gestation until delivery between 37 and 38 weeks. The dose is based on mother's ABW at initial presentation and is continued unchanged throughout pregnancy.	1 g/kg ABW (capped at 60 g/week) for at-risk mothers at 14 weeks, 16 weeks, and then weekly from 18 weeks gestation until delivery between 37 and 38 weeks. The dose is based on mother's ABW at initial presentation and is continued unchanged throughout pregnancy.
Gestational alloimmune liver disease (GALD)/alloimmune neonatal hemochromatosis Neonates	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	Single dose of 1 g/kg.	Single dose of 1 g/kg.	Single dose of 1 g/kg.
Hematologic malignancy (pediatric)	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.
	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Hemolytic disease of the fetus and newborn (HDFN) Mothers	Use may be appropriate if the following criteria are met: ● Patient had fetal hydrops previously OR ● Severe HDFN early in the previous pregnancy,	Use may be appropriate if the following criteria are met: ● Patient had fetal hydrops previously OR ● Severe HDFN early in the previous pregnancy,	Use may be appropriate if the following criteria are met: ● Patient had fetal hydrops previously OR ● Severe HDFN early in the previous pregnancy,
	1 g/kg ABW (up to a maximum dose of 100 g) weekly from 12 weeks gestation until intrauterine transfusion (IUT) can then be initiated.	1 g/kg ABW (up to a maximum dose of 100 g) weekly from 12 weeks gestation until IUT can then be initiated.	1 g/kg ABW (up to a maximum dose of 100 g) weekly from 12 weeks gestation until IUT can then be initiated.
Hemolytic disease of the fetus and newborn (HDFN) Neonate	Use may be appropriate if the following criteria are met: ● Rising bilirubin despite phototherapy and exchange OR ● Patient predicted to have severe disease based on antenatal investigations/criteria and exchange is not available/feasible OR ● With an elevated risk of exchange based on postnatal bilirubin serum concentration	Use may be appropriate if the following criterion is met: ● Rising bilirubin despite phototherapy and exchange	Use may be appropriate if the following criterion is met: ● Rising bilirubin despite phototherapy and two exchanges

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
	Single dose of 0.5-1 g/kg. Dose may be repeated if clinically indicated.	Single dose of 0.5-1 g/kg. Dose may be repeated if clinically indicated.	Single dose of 0.5-1 g/kg. Dose may be repeated if clinically indicated.
Hemolytic transfusion reaction	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Hemolytic uremic syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Hemophagocytic lymphohistiocystosis (HLH): Primary	Use not appropriate unless there are exceptional circumstances. For secondary immunodeficiency, refer to SID criteria in the Immunology section.	Do not use. For secondary immunodeficiency, refer to SID criteria in the Immunology section.	Do not use. For secondary immunodeficiency, refer to SID criteria in the Immunology section.
	n/a	n/a	n/a

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Hemophagocytic lymphohistiocytosis (HLH): Secondary[6] Includes macrophage activation syndrome (MAS) and virus associated hemophagocytic syndrome (VAHS)	Use may be appropriate if the following criteria are met: ● Severe cases in combination with other therapies OR ● When other therapies are ineffective or contraindicated.	Use may be appropriate if the following criterion is met: ● Severe cases when other therapies are ineffective or contraindicated.	Use may be appropriate if the following criterion is met: ● Severe cases when other therapies are ineffective or contraindicated.
	Adults: Single dose of up to 2 g/kg ABW over 1 – 5 days Pediatrics: Single dose of up to 2 g/kg ABW over 1 – 5 days	Adults: Single dose of up to 2 g/kg ABW over 1 – 5 days Pediatrics: Single dose of up to 2 g/kg ABW over 1 – 5 days	Adults: Single dose of up to 2 g/kg ABW over 1 – 5 days Pediatrics: Single dose of up to 2 g/kg ABW over 1 – 5 days
Heparin-induced thrombocytopenia (HIT) – Classic See also entries for Atypical/Autoimmune HIT and other anti-platelet factor-4 disorders (anti-PF-4) (e.g., spontaneous HIT, vaccine-induced thrombocytopenia/thro	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

[6] Secondary HLH is a heterogenous group of conditions and includes HLH secondary to conditions including infections (mainly viruses, such as Epstein Barr virus (EBV), human immunodeficiency virus (HIV), and cytomegalovirus (CMV), but also bacteria, parasites, and fungi), malignancies (mainly malignant lymphoma), macrophage activation syndrome in autoinflammatory or autoimmune disorders, other causes (organ or stem cell transplantation; metabolic, traumatic, iatrogenic [immunosuppression, vaccination, surgery, hemodialysis] causes; and pregnancy). Treatment protocols vary and depend on underlying cause. (La Rosee P, Horne A, Hines M et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 2019; 133:2465-77)

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
mbosis [VITT], and VITT-like anti-PF4 disorder [without prior vaccination]).			
Heparin-induced thrombocytopenia (HIT) – Aanti-PF4 disorders with HIT-like picture without heparin exposure Includes spontaneous HIT, VITT, and VITT-like anti-PF4 disorders)	Use may be appropriate if the following criteria are met: • Thrombosis and/or D-dimer >8x upper normal limit AND • Thrombocytopenia and/or platelet decrement >50%, unrelated to underlying clinical disorder AND • Positive HIT enzyme-linked immunosorbent assay and/or serotonin release assay OR • Life/limb-threatening thrombosis associated with post-operative course for knee replacement, COVID-19 vaccine (4-30 days post-vaccination), following unspecified viral illness or confirmed adenovirus infection	Use may be appropriate if the following criteria are met: • Thrombosis and/or D-dimer >8x upper normal limit AND • Thrombocytopenia and/or platelet decrement >50%, unrelated to underlying clinical disorder AND • Positive enzyme-linked immunosorbent assay and/or serotonin release assay OR • Life/limb-threatening thrombosis associated with post-operative course for knee replacement, COVID-19 vaccine (4-30 days post-vaccination), following unspecified viral illness or confirmed adenovirus infection	Use may be appropriate if the following criteria are met: • Thrombosis and/or D-dimer >8x upper normal limit AND • Thrombocytopenia and/or platelet decrement >50%, unrelated to underlying clinical disorder AND • Positive HIT enzyme-linked immunosorbent assay and/or serotonin release assay OR • Life/limb-threatening thrombosis associated with post-operative course for knee replacement, COVID-19 vaccine (4-30 days post-vaccination), following unspecified viral illness or confirmed adenovirus infection
	1 g/kg ABW for up to 2 days.	1 g/kg ABW for up to 2 days.	1 g/kg ABW for up to 2 days.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Heparin-induced thrombocytopenia (HIT) – Atypical/Autoimmune HIT (must have heparin exposure). Includes delayed onset, persistent HIT, and heparin flush HIT)	Use may be appropriate if the following criteria are met: • Intermediate to High probability of HIT using 4T-score[7] AND • HIT enzyme-linked immunosorbent assay and/or serotonin release assay positivity OR life/limb-threatening thrombosis and/or strong clinical suspicion before confirmatory testing is resulted AND • Onset/worsening of thrombocytopenia after stopping heparin (delayed onset) OR • Delay in platelet count recovery one week or more after stopping heparin (persistent) OR • Precipitated by heparin flush OR • Multiple venous and/or arterial thromboses	Use may be appropriate if the following criteria are met: • Intermediate to High probability of HIT using 4T-score[6] AND • HIT enzyme-linked immunosorbent assay and/or serotonin release assay positivity OR life/limb-threatening thrombosis and/or strong clinical suspicion before confirmatory testing is resulted AND • Onset/worsening of thrombocytopenia after stopping heparin (delayed onset) OR • Delay in platelet count recovery one week or more after stopping heparin (persistent) OR • Precipitated by heparin flush OR • Multiple venous and/or arterial thromboses	Use may be appropriate if the following criteria are met: • Intermediate to High probability of HIT using 4T-score[6] AND • HIT enzyme-linked immunosorbent assay and/or serotonin release assay positivity OR life/limb-threatening thrombosis and/or strong clinical suspicion before confirmatory testing is resulted AND • Onset/worsening of thrombocytopenia after stopping heparin (delayed onset) OR • Delay in platelet count recovery one week or more after stopping heparin (persistent) OR • Precipitated by heparin flush OR • Multiple venous and/or arterial thromboses
	1 g/kg ABW for up to 2 days.	1 g/kg ABW for up to 2 days.	1 g/kg ABW for up to 2 days.

[7] Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A. Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost 2006; 4:759-65.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Cellular Therapy, Autologous; CAR-T (adult and pediatric)	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.
	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.
Hyperhemolysis syndrome	Use may be appropriate if the following criterion is met: ● Serious, life-threatening reactions	Use may be appropriate if the following criteria are met: ● Severe disease AND ● Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: ● Severe disease AND ● Failure, contraindication or intolerance to other therapeutic options
	2 g/kg ABW divided over 2 to 5 days.	2 g/kg ABW divided over 2 to 5 days.	2 g/kg ABW divided over 2 to 5 days.

Immune thrombocytopenic purpura (ITP) - adult Includes newly diagnosed (0-3 months), persistent ITP (3-12 months), and chronic ITP (more than 1 year)	Use may be appropriate if the following criteria are met: • There is a clinical need to raise the platelet count rapidly AND • Platelets < 50 x 10^9/L, with moderate-severe bleeding OR • Platelets < 10 x 10^9/L with mild bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids OR • Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following: ○ Periprocedural and/or perioperative settings ○ Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation) Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • There is a clinical need to raise the platelet count rapidly AND • Platelets < 30 x 10^9/L, with moderate-severe bleeding OR • Platelets < 10 x 10^9/L with mild bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids OR • Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following: ○ Major periprocedural and/or perioperative settings that are emergent ○ Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation) Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • There is a clinical need to raise the platelet count rapidly AND • Platelets < 20 x 10^9/L, with severe bleeding OR • Platelets < 10 x 10^9/L with moderate bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids OR • Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following: ○ Major periprocedural and/or perioperative settings that are emergent ○ Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation) Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg
	1 g/kg ABW x 1 dose. Some patients may require an additional dose.	1 g/kg ABW x 1 dose. Some patients may require an additional dose.	1 g/kg ABW x 1 dose. Some patients may require an additional dose.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	Maintenance use is not appropriate unless there are no alternatives.	Maintenance use is not appropriate unless there are no alternatives.	Maintenance use is not appropriate unless there are no alternatives.
Immune thrombocytopenic purpura (ITP) – neonates of mothers with ITP Also called: neonatal thrombocytopenia secondary to maternal autoimmune disorders	Use may be appropriate if the following criteria are met: • Platelets < 30 x 10^9/L for a well, term neonate OR • Platelets <50 x 10^9/L in a pre-term or unwell neonate OR • To maintain platelets >50-100 x 10^9/L in the unlikely event of moderate-severe bleeding Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • Platelets <30 x 10^9/L for a well, term neonate OR • Platelets <50 x 10^9/L in a pre-term or unwell neonate OR • To maintain platelets >50-100 x 10^9/L in the unlikely event of moderate-severe bleeding Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • Platelets <30 x 10^9/L for a well, term neonate OR • Platelets <50 x 10^9/L in a pre-term or unwell neonate OR • To maintain platelets >50-100 x 10^9/L in the unlikely event of moderate-severe bleeding Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg
	Single dose of 0.8 - 1 g/kg. Dose may be repeated if clinically indicated.	Single dose of 0.8 - 1 g/kg. Dose may be repeated if clinically indicated.	Single dose of 0.8 - 1 g/kg. Dose may be repeated if clinically indicated.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**

Immune thrombocytopenic purpura (ITP) - pediatric	Use may be appropriate if the following criteria are met:
	• There is a clinical need to raise the platelet count rapidly
	AND
	• Platelets < 50 x 10^9/L, with moderate-severe bleeding
	OR
	• Platelets < 10 x 10^9/L, with mild bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids
	OR
	• Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following:
	  • Periprocedural and/or perioperative settings
	  • Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation)
	  • Neonates
	  • Critically ill children, including disseminated intravascular coagulation
	
	Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg
		Use may be appropriate if the following criteria are met:
		• There is a clinical need to raise the platelet count rapidly
		AND
		• Platelets < 30 x 10^9/L, with moderate-severe bleeding
		OR
		• Platelets < 10 x 10^9/L with mild bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids
		OR
		• Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following:
		  • Major periprocedural and/or perioperative settings are emergent
		  • Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation)
		  • Neonates
		  • Critically ill children, including disseminated intravascular coagulation
		
		Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg
			Use may be appropriate if the following criteria are met:
			• There is a clinical need to raise the platelet count rapidly
			AND
			• Platelets < 20 x 10^9/L, with severe bleeding
			OR
			• Platelets < 10 x 10^9/L with moderate bleeding AND insufficient response to prior steroid therapy or clinical contraindication to steroids
			OR
			• Platelets < 50 x 10^9/L AND insufficient response to prior steroid therapy or clinical contraindication to steroids AND one of the following:
			  • Major periprocedural and/or perioperative settings are emergent
			  • Extenuating circumstances with co-existing inherited/acquired bleeding diatheses (including anticoagulation)
			  • Neonates
			  • Critically ill children, including disseminated intravascular coagulation
			
			Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	0.8 to 1 g/kg ABW with a second dose within 48 hours if the platelet count has not increased to above 20 x 10^9/L. No maximum dose.	0.8 to 1 g/kg ABW, with a second dose within 48 hours if the platelet count has not increased to above 20 x 10^9/L. No maximum dose.	0.8 to 1 g/kg ABW, with a second dose within 48 hours if the platelet count has not increased to above 20 x 10^9/L. No maximum dose.
Immune thrombocytopenic purpura (ITP) – pregnancy associated	Use may be appropriate if the following criteria are met: • Platelets <30 x 10^9/L OR • Platelet count <50 x 10^9/L in the setting of severe bleeding or in preparation for delivery Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • Failure, contraindication or intolerance to steroids AND • At least one of the following: ○ Platelets <10 x 10^9/L OR ○ When the platelet count is 10-30 x 10^9/L and there is moderate to severe bleeding OR ○ Platelet count < 50 x 10^9/L in the setting of severe bleeding or in preparation for delivery Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg	Use may be appropriate if the following criteria are met: • Failure, contraindication or intolerance to steroids AND • At least one of the following: ○ Platelets <10 x 10^9/L OR ○ When the platelet count is 10-30 x 10^9/L and there is moderate to severe bleeding OR ○ Platelet count < 50 x 10^9/L in the setting of severe bleeding or in preparation for delivery Other treatments with more evidence-based and durable responses are to be considered before and/or in addition to IVIg
	Maximum of 1 g/kg ABW x 1 dose. Some patients may require an additional dose.	Maximum of 1 g/kg ABW x 1 dose. Some patients may require an additional dose.	Maximum of 1 g/kg ABW x 1 dose. Some patients may require an additional dose.

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Mast cell activation syndrome (MCAS) Includes 1º MCAS (caused by clonal mast cell disorder); 2º MCAS (Caused by IgE-mediated allergies or triggers that act directly on mast cells via the MRGPRX2 receptor) and idiopathic MCAS)	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.
	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.	Refer to MCAS criteria in the Immunology section.
Necrobiotic xanthogranuloma	Use may be appropriate if the following criterion is met: ● Severe cases when corticosteroids or other therapies are ineffective or contraindicated	Use may be appropriate if the following criteria are met: ● Disease is rapidly progressing, life or limb threatening AND ● Other treatments are contraindicated	Use may be appropriate if the following criteria are met: ● Disease is rapidly progressing, life or limb threatening AND ● Other treatments are contraindicated
	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.	Up to 2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.	Up to 2 g/kg ABW divided over 2-5 days, every 4-6 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.
Post-transfusion purpura (PTP)	Use may be appropriate if the following criteria is met: ● Moderate to severe bleeding AND ● For short term use	Use may be appropriate if the following criterion is met: ● Moderate to severe bleeding if plasma exchange (PLEX) is not feasible	Use may be appropriate if the following criterion is met: ● Life-threatening bleeding if PLEX is not feasible

Hematology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
	Up to 1-2 g/kg ABW divided over 2 to 5 consecutive days, repeat if necessary.	Up to 1 g/kg ABW divided over 2 to 5 consecutive days, repeat if necessary.	Up to 1 g/kg ABW divided over 2 to 5 consecutive days.
Thrombotic thrombocytopenic purpura (TTP)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Vaccine induced immune thrombotic thrombocytopenia (VITT)/vaccine induced prothrombotic immune thrombocytopenia (VIPIT) See also entries for other anti-PF4 disorders (e.g., autoimmune HIT, spontaneous HIT, VITT-like anti-PF4 disorder [without prior vaccination]).	Refer to anti-PF4 disorders criteria in the Hematology section.	Refer to anti-PF4 disorders criteria in the Hematology section.	Refer to Anti-PF4 Disorders criteria in the Hematology section.
	Refer to heparin-induced thrombocytopenia (HIT) - Anti-PF4 Disorders criteria in the Hematology section.	Refer to heparin-induced thrombocytopenia (HIT) - Anti-PF4 Disorders criteria in the Hematology section.	Refer to heparin-induced thrombocytopenia (HIT) - Anti-PF4 Disorders criteria in the Hematology section.

Immunology

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Chronic spontaneous urticaria	Use may be appropriate if the following criteria are met: • Severe disease when the patient has: contraindications or no clinically meaningful response to high dose antihistamines AND • Contraindications or no clinically meaningful response to omalizumab AND • Failure/contraindications to cyclosporine.	Do not use.	Do not use.
	0.4 -0.6 g/kg ABW every 4 weeks Should be administered for 3-6 months to assess efficacy. Some patients do not show a definitive sustained response until they have undergone up to 6 treatment cycles. In rare instances when longer term treatment is required, regular washout periods should be attempted and/or interval between infusions should be increased. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	n/a	n/a

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Hematopoietic stem cell transplant (HSCT) in primary immunodeficiency (PID) / inborn errors of immunity	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	0.4 to 0.6 g/kg ABW every 3-4 weeks. Modify on a case-by-case basis to achieve an IgG trough level of at least the middle of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. SCIg dosing: 100-150 mg/kg ABW/week	0.4 to 0.6 g/kg ABW every 3-4 weeks. Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. More frequent monitoring (3 – 6 months) is required. SCIg dosing: 100-150 mg/kg ABW/week	0.4 to 0.6 g/kg ABW every 3-4 weeks. Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. More frequent monitoring (1 – 3 months) is required. SCIg dosing: 100-150 mg/kg ABW/week
Hemophagocytic lymphohistiocystosis (HLH): Primary	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Hemophagocytic lymphohistiocytosis (HLH): Secondary[8] Includes macrophage activation syndrome (MAS) and virus associated hemophagocytic syndrome (VAHS)	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
Mast cell activation syndrome (MCAS) Includes 1º MCAS (caused by clonal mast cell disorder); 2º MCAS (Caused by IgE-mediated allergies or triggers that act directly on mast cells via the MRGPRX2 receptor) and idiopathic MCAS	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

[8] Secondary HLH is a heterogenous group of conditions and includes HLH secondary to conditions including infections (mainly viruses, such as EBV, HIV, and CMV, but also bacteria, parasites, and fungi), malignancies (mainly malignant lymphoma), macrophage activation syndrome in autoinflammatory or autoimmune disorders, other causes (organ or stem cell transplantation; metabolic, traumatic, iatrogenic [immunosuppression, vaccination, surgery, hemodialysis] causes; and pregnancy). Treatment protocols vary and depend on underlying cause. (La Rosee P, Horne A, Hines M et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 2019; 133:2465-77)

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Primary immunodeficiency (PID) Also called inborn errors of immunity	Use may be appropriate if the following criterion are met: • B cell/antibody deficiencies, combined immunodeficiencies, or other specific inborn errors of immunity and patient-related factors (e.g., frequency and severity of infections, bronchiectasis, and/or presence of immune dysregulation) Should be ordered in consultation with a specialist with experience in treating this condition.	Use may be appropriate if the following criterion are met: • B cell/antibody deficiencies, combined immunodeficiencies, or other specific inborn errors of immunity and patient-related factors (e.g., frequency and severity of infections, bronchiectasis, and/or presence of immune dysregulation) Should be ordered in consultation with a specialist with experience in treating this condition.	Use may be appropriate if the following criterion are met: • B cell/antibody deficiencies, combined immunodeficiencies, or other specific inborn errors of immunity and patient-related factors (e.g., frequency and severity of infections, bronchiectasis, and/or presence of immune dysregulation) Should be ordered in consultation with a specialist with experience in treating this condition.
	0.4 – 0.6 g/kg ABW every 3 – 4 weeks. For maintenance therapy, target IgG levels should be lowered to minimum clinically effective target (per local lab reference ranges). Modify on a case-by-case basis to achieve an IgG trough level of at least the middle limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly)	0.4 – 0.6 g/kg ABW every 3 – 4 weeks. For maintenance therapy, target IgG levels should be lowered to minimum clinically effective target (per local lab reference ranges). Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly)	0.4 – 0.6 g/kg ABW every 3 – 4 weeks. For maintenance therapy, target IgG levels should be lowered to minimum clinically effective target (per local lab reference ranges). Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly)

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Secondary immunodeficiency (SID) (any cause)	Use may be appropriate if the following criteria are met: • Intended for preventing recurrent severe infection due to hypogammaglobulinemia in patients who have a history of infections AND/OR • Documented evidence of impaired responses to vaccines AND/OR • B cell aplasia Treatment dependent on patient-related factors (e.g., frequency and severity of infections, bronchiectasis). .	Use may be appropriate if the following criteria are met: • Intended for preventing recurrent severe infection due to hypogammaglobulinemia in patients who have a history of infections AND/OR • Documented evidence of impaired responses to vaccines AND/OR • B cell aplasia Treatment dependent on patient-related factors (e.g., frequency and severity of infections, bronchiectasis).	Use may be appropriate if the following criteria are met: • Intended for preventing recurrent severe infection due to hypogammaglobulinemia in patients who have a history of infections AND/OR • Documented evidence of impaired responses to vaccines AND/OR • B cell aplasia Treatment dependent on patient-related factors (e.g., frequency and severity of infections, bronchiectasis).

Immunology Indications	National Ig Shortages Pla		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	0.4 to 0.6 g/kg ABW every 3-4 weeks. Aim to use the dose that achieves a significant reduction in the number of infections. Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. Reassess clinical and lab parameters with the aim of finding a minimum clinically effective dose (ideally, at least every 3 – 6 months) SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly)	0.4 to 0.6 g/kg ABW every 3-4 weeks. Aim to use the dose that achieves a significant reduction in the number of infections. Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. Reassess clinical and lab parameters with the aim of finding a minimum clinically effective dose (ideally, at least every 3 months) Consider trial cessation of therapy +/ - trial of antibiotics for patients with more than 6 months without infection and IgG levels greater than 8. SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly).	0.4 to 0.6 g/kg ABW every 3-4 weeks. Aim to use the dose that achieves a significant reduction in the number of infections. Modify on a case-by-case basis to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range, or as needed to achieve clinical effectiveness. Reassess clinical and lab parameters with the aim of finding a minimum clinically effective dose (ideally, at least every 1 – 3 months) Consider trial cessation of therapy +/ - trial of antibiotics for patients with more than 6 months without infection and IgG levels greater than 8. SCIg dosing: 1:1 conversion from IVIg to SCIg (divide monthly to weekly)

Infectious Diseases

Infectious Disease Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Clostridium difficile colitis (severe or recurrent)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Enterovirus meningoencephalitis	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Hepatitis A, post-exposure prophylaxis	Use may be appropriate if the following criteria are met: • Unvaccinated AND/OR • cannot be vaccinated. OR • Coinfection with other chronic hepatitides. Requires consultation with public health or infectious disease experts.	Use may be appropriate if the following criteria are met: • Unvaccinated AND/OR • cannot be vaccinated. OR • Coinfection with other chronic hepatitides. Requires consultation with public health or infectious disease experts.	Use may be appropriate if the following criteria are met: • Unvaccinated AND/OR • cannot be vaccinated. OR • Coinfection with other chronic hepatitides. Requires consultation with public health or infectious disease experts.
	0.1 mL/kg *actual body weight*. Ig should be given as soon as possible after an exposure. Efficacy of Ig is unknown if more than 14 days have elapsed since the last exposure. Do not use after this time period.	0.1 mL/kg *actual body weight* Ig should be given as soon as possible after an exposure. Efficacy of Ig is unknown if more than 14 days have elapsed since the last exposure. Do not use after this time period.	0.1 mL/kg *actual body weight* Ig should be given as soon as possible after an exposure. Efficacy of Ig is unknown if more than 14 days have elapsed since the last exposure. Do not use after this time.
	Use may be appropriate if the following criteria are met:	Use may be appropriate if the following criteria are met:	Use may be appropriate if the following criteria are met:

Infectious Disease Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Measles post-exposure prophylaxis (PEP)	• In pregnant women who are non-immune OR • Infants OR Immune compromised/deficient individuals if intramuscular injection is not an option because of weight >30 kg or inability to receive intramuscular injection AND • Within 6 days of measle exposure	• In pregnant women who are non-immune OR • Infants OR Immune compromised/deficient individuals if intramuscular injection is not an option because of weight >30 kg or inability to receive intramuscular injection AND • Within 6 days of measle exposure	• In pregnant women who are non-immune OR • Infants OR Immune compromised/deficient individuals if intramuscular injection is not an option because of weight >30 kg or inability to receive intramuscular injection AND • Within 6 days of measle exposure
	Single dose of intramuscular Ig 0.5 mL/kg *actual body weight* For patients weighing more than 30 kg or who cannot tolerate the intramuscular volume, IVIg should be provided at a single dose of 0.4 g/kg ABW (use actual body weight in pregnancy)	Single dose of intramuscular Ig 0.5 mL/kg *actual body weight* For patients weighing more than 30 kg or who cannot tolerate the intramuscular volume, IVIg should be provided at a single dose of 0.4 g/kg ABW (use actual body weight in pregnancy)	Single dose of intramuscular Ig 0.5 mL/kg *actual body weight* For patients weighing more than 30 kg or who cannot tolerate the intramuscular volume, IVIg should be provided at a single dose of 0.4 g/kg ABW (use actual body weight in pregnancy)
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)/COVID-19	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Infectious Disease Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Staphylococcus aureus or beta hemolytic streptococcus necrotizing fasciitis or toxic shock syndrome	Use may be appropriate if the following criteria are met: • For severe invasive group A Streptococcal disease associated with hemodynamic compromise OR • Streptococcal OR • Staphylococcal toxic shock syndrome. AND • In addition to surgical intervention, antibiotic therapy, and other supportive measures	Use may be appropriate if the following criteria are met: • For severe invasive group A Streptococcal disease associated with hemodynamic compromise OR • Streptococcal OR • Staphylococcal toxic shock syndrome. AND • In addition to surgical intervention, antibiotic therapy, and other supportive measures	Use may be appropriate if the following criteria are met: • For severe invasive group A Streptococcal disease associated with hemodynamic compromise OR • Streptococcal OR • Staphylococcal toxic shock syndrome. AND • In addition to surgical intervention, antibiotic therapy, and other supportive measures
	1 g/kg ABW on day one and 0.5 g/kg ABW per day on days two and three, OR single dose of 2g/kg ABW	1 g/kg ABW on day one and 0.5 g/kg ABW per day on days two and three, OR single dose of 2g/kg ABW	1 g/kg ABW on day one and 0.5 g/kg ABW per day on days two and three, OR single dose of 2g/kg ABW
Systemic capillary leak syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Varicella-zoster virus (VZV) post exposure prophylaxis	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Acute disseminated encephalomyelitis (ADEM) with or without antibody	Use may be appropriate if the following criterion is met: • First-line therapy with high-dose corticosteroids fails or is contraindicated	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for recurrent or multiphasic ADEM only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for recurrent or multiphasic ADEM only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for recurrent or multiphasic ADEM only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness
Acute flaccid myelitis	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a
Adreno-leukodystrophy	Do not use.	Do not use.	Do not use.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
	n/a	n/a	n/a
Aicardi-Goutieres Syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Alzheimer disease	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Amyotrophic lateral sclerosis (ALS)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Autism	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Autoimmune encephalitis (e.g., NMDA) Specialist input required to confirm diagnosis	Use may be appropriate if the following criteria are met: • Treatment in conjunction with immunosuppressive medications AND • Used as a short-term, temporizing measure For long term use, transitioning to other maintenance immunotherapies should be considered, as appropriate.	Use may be appropriate if the following criteria are met: • Case of failure, contraindication or intolerance to other therapeutic options AND • Used as a short-term temporizing measure For long term use, transitioning to other maintenance immunotherapies should be considered, as appropriate.	Use may be appropriate if the following criteria are met: • Case of failure, contraindication or intolerance to other therapeutic options AND • Used as a short-term temporizing measure For long term use, transitioning to other maintenance immunotherapies should be considered, as appropriate.
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Offered to patients when alternatives are not available or effective. 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Autoimmune retinopathy (AIR)	Use may be appropriate if the following criterion is met: • Immune-mediated, sight-threatening uveitis with persistent activity despite corticosteroid and immunosuppressive therapy	Use may be appropriate if the following criterion is met: • Immune-mediated, sight-threatening uveitis with persistent activity despite corticosteroid and immunosuppressive therapy	Use may be appropriate if the following criterion is met: • Immune-mediated, sight-threatening uveitis with persistent activity despite corticosteroid and immunosuppressive therapy
	Induction: 1.5 g/kg ABW divided over 3 days. Maintenance: 0.4-1.5 g/kg ABW in single or divided dose (maximum 1 g/kg/day) monthly. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. In rare circumstances, longer-term therapy may be required.	Induction: 1.5 g/kg ABW divided over 3 days. Maintenance: 0.4-1.5 g/kg ABW in single or divided dose (maximum 1 g/kg/day) monthly. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. In rare circumstances, longer-term therapy may be required.	Induction: 1.5 g/kg ABW divided over 3 days. Maintenance: 0.4-1.5 g/kg ABW in single or divided dose (maximum 1 g/kg/day) monthly. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. In rare circumstances, longer-term therapy may be required.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Childhood onset epilepsy, medically refractory/intractable	Use may be appropriate if the following criterion is met: • Conventional therapies are ineffective with full assessment by pediatric epileptologist.	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options with full assessment by pediatric epileptologist.	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options with full assessment by pediatric epileptologist.
	0.4 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-4 weeks for 4-6 cycles. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	0.4 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-4 weeks for 4-6 cycles. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-4 weeks for 4 cycles. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.
Chronic fatigue syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Chronic inflammatory demyelinating polyneuropathy (CIDP)	Use may be appropriate if the following criteria are met: • Progression is rapid, walking is compromised or there is significant functional impairment Must be in consultation with a neuromuscular neurologist, where available.	Use may be appropriate if the following criteria are met: • Failure, contraindication or intolerance to other forms of immune-suppressive therapy Must be in consultation with a neuromuscular neurologist, where available.	Use may be appropriate if the following criteria are met: • In cases of failure, contraindication or intolerance to other forms of immune-suppressive therapy Must be in consultation with a neuromuscular neurologist, where available.
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-4 weeks, for at least two treatments. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. Continued use should be based on objective measures of sustained effectiveness. Discontinue if no evidence of response after 3 treatments. SCIg should be considered following stabilization with IVIg.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-4 weeks, for at least two treatments. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. Continued use should be based on objective measures of sustained effectiveness. Discontinue if no evidence of response after 3 treatments. SCIg should be considered following stabilization with IVIg.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks, for at least two treatments. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. Continued use should be based on objective measures of sustained effectiveness. Discontinue if no evidence of response after 3 treatments. SCIg should be considered following stabilization with IVIg.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Critical illness polyneuropathy	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Diabetic amyotrophy	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Guillain-Barre Syndrome (GBS) Includes Miller-Fischer syndrome and other variants	Use may be appropriate if the following criteria are met: • Severe cases OR • Moderate symptoms that are progressing Ideally given within 2 weeks of symptom onset. A second course of IVIg may be considered in disease relapse in absence of alternative diagnoses/etiologies, and only after review with/by a neurologist.	Use may be appropriate if the following criteria are met: • Severe cases OR • Moderate symptoms that are progressing AND • PLEX is not available or feasible Ideally given within 2 weeks of symptom onset. A second course of IVIg may be considered in disease relapse in absence of alternative diagnoses/etiologies, and only after review with/by a neurologist.	Use may be appropriate if the following criteria are met: • Severe cases OR • Moderate symptoms that are progressing AND • PLEX is not available or feasible Ideally given within 2 weeks of symptom onset. A second course of IVIg may be considered in disease relapse in absence of alternative diagnoses/etiologies, and only after review with/by a neurologist.
	Adult: total dose of 2 g/kg ABW divided over 2 to 5 days. Pediatric: total dose of 2 g/kg ABW divided over 2 days. Repeat treatment (adult and peds) with IVIg at 2 g/kg ABW divided over 2 to 5 days. A second course of IVIg should not be given unless the patient has improved or plateaued and then subsequently worsened.	Adult: total dose of 2 g/kg ABW divided over 2 to 5 days. Pediatric: total dose of 2 g/kg ABW divided over 2 days. Repeat treatment (adult and peds) with IVIg at 2 g/kg ABW divided over 2 to 5 days. A second course of IVIg should not be given unless the patient has improved or plateaued and then subsequently worsened.	Adult: total dose of 2 g/kg ABW divided over 2 to 5 days. Pediatric: total dose of 2 g/kg ABW divided over 2 days. Repeat treatment (adult and peds) with IVIg at 2 g/kg divided over 2 to 5 days. A second course of IVIg should not be given unless the patient has improved or plateaued and then subsequently worsened.
Hashimoto encephalopathy	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Refer to autoimmune encephalitis, as necessary	n/a	n/a	n/a
Lambert Eaton Myasthenic Syndrome (LEMS)	Use may be appropriate if the following criterion are met: • For initial treatment for induction and maintenance in combination with other therapies Objective evidence of clinical improvement needed for sustained use in consultation with a neurologist	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options. Objective evidence of clinical improvement needed for sustained use in consultation with a neurologist.	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options. Objective evidence of clinical improvement needed for sustained use in consultation with a neurologist.
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 0.4 to 1 g/kg ABW, every 2-6 weeks. Maximum dose of 2 g/kg ABW in any 4-week period. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. It is preferable to discontinue IVIg in favour of oral immune suppressants, where possible.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 0.4 to 1 g/kg ABW, every 2-6 weeks. Maximum dose of 2 g/kg ABW in any 4-week period. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. It is preferable to discontinue IVIg in favour of oral immune suppressants, where possible.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 0.4 to 1 g/kg ABW, every 2-6 weeks. Maximum dose of 2 g/kg ABW in any 4-week period. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. It is preferable to discontinue IVIg in favour of oral immune suppressants, where possible.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Multifocal motor neuropathy (MMN)	Use may be appropriate.	Use may be appropriate. .	Use may be appropriate. .
	Initial treatment: 2 g/kg ABW over 2-5 days. Maintenance dose: 1 g/kg ABW or less per treatment course (every 2 to 6 weeks). Some patients may require higher doses for efficacy, up to 2 g/kg ABW every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Initial treatment: 2 g/kg ABW over 2-5 days. Maintenance dose: 1 g/kg ABW or less per treatment course (every 2 to 6 weeks). Some patients may require higher doses for efficacy, up to 2 g/kg ABW every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Initial treatment: 2 g/kg ABW over 2-5 days. Maintenance dose: 1 g/kg ABW or less per treatment course (every 2 to 6 weeks). Some patients may require higher doses for efficacy, up to 2 g/kg ABW every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Multiple Sclerosis (MS) (relapsing/remitting or clinically isolated syndrome)	Use may be appropriate if the following criteria are met: • Pregnancy and the immediate post-partum period when other immunomodulation is contraindicated OR • Severe relapse with no clinically meaningful response to high-dose methylprednisolone or other therapies For secondary immunodeficiency as a result of treatment, refer to SID criteria in the Immunology section. Use not appropriate for: long-term therapy; primary progressive MS; progressive phase of MS without relapse.	Use may be appropriate if the following criterion is met: • Pregnancy and the immediate post-partum period when other immunomodulation is contraindicated For secondary immunodeficiency as a result of treatment, refer to SID criteria in the Immunology section. Do not use for: long-term therapy; primary progressive MS; progressive phase of MS without relapse.	Use may be appropriate if the following criterion is met: • Pregnancy and the immediate post-partum period when other immunomodulation is contraindicated For secondary immunodeficiency as a result of treatment, refer to SID criteria in the Immunology section. Do not use for: long-term therapy; primary progressive MS; progressive phase of MS without relapse.
	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day).	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day).	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day).

<table>
<tr><th rowspan="2">Neurology Indications</th><th colspan="3">National Ig Shortages Plan</th></tr>
<tr><th>GREEN PHASE ADVISORY</th><th>AMBER</th><th>RED</th></tr>
<tr><td rowspan="2">Myasthenia gravis (MG)</td><td>Use may be appropriate if the following criteria are met:

• Lack of availability or contraindication to PLEX or other therapeutic options

AND one of the following:
• Acute exacerbation, myasthenic crisis
OR
• Before surgery
OR
• Maintenance therapy for moderate to severe generalized MG with failure, contraindication, intolerance to alternate therapies</td><td>Use may be appropriate if the following criteria are met:

• Lack of availability of, or contraindication to PLEX or other therapeutic options

AND one of the following:
• Severe exacerbation, myasthenic crisis
OR
• Before surgery
OR
• Maintenance therapy for moderate to severe generalized MG with failure, contraindication, intolerance to alternate therapies</td><td>Use may be appropriate if the following criteria are met:

• Lack of availability of, or contraindication to PLEX or other therapeutic options

AND one of the following:
• Severe exacerbation, myasthenic crisis
OR
• Before surgery
OR
• Maintenance therapy for moderate to severe generalized MG with failure, contraindication, intolerance to alternate therapies</td></tr>
<tr><td>Induction (before surgery or during myasthenic crisis): 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg ABW /day).

Maintenance: 0.4-1 g/kg ABW every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td><td>Induction (before surgery or during myasthenic crisis): 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg ABW /day).

Maintenance: 0.4-1 g/kg ABW every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td><td>Induction (before surgery or during myasthenic crisis): 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg ABW /day).

Maintenance: 0.4-1 g/kg ABW every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td></tr>
</table>

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Myelin oligodendrocyte glycoprotein antibody-associated disorders (MOGAD)	Use may be appropriate if the following criterion is met: • First-line therapy with high-dose corticosteroids fails or is contraindicated.	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for relapsing MOGAD only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for relapsing MOGAD only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance (for relapsing MOGAD only): 0.4-2 g/kg ABW every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.
Narcolepsy	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Neuromyelitis optica spectrum disorders (NMOSD)	Use may be appropriate if the following criterion is met: • Patients with active NMOSD despite treatment with corticosteroids (peds, adults) and/or PLEX (adults).	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Do not use. Use alternative maintenance immunotherapies.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Do not use. Use alternative maintenance immunotherapies	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Do not use. Use alternative maintenance immunotherapies
Neuropathic pain	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Neuropathy associated with IgM paraproteinemia in the absence of anti-myelin-associated-glycoprotein (MAG) antibody	Refer to CIDP criteria in the Neurology section.	Refer to CIDP criteria in the Neurology section.	Refer to CIDP criteria in the Neurology section.
	Refer to CIDP criteria in the Neurology section.	Refer to CIDP criteria in the Neurology section.	Refer to CIDP criteria in the Neurology section.
Neuropathy associated with IgM paraproteinemia in the presence of anti-myelin-associated-glycoprotein (MAG) antibody	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
NORSE (New Onset Refractory Status Epilepticus) and FIRES (Febrile Infection-Related Epilepsy Syndrome)	Use may be appropriate if the following criteria are met: • Treatment in conjunction with immunosuppressive medications AND • Used as a short-term, temporizing measure. For long term use, transition to other maintenance immunotherapies should be considered, as appropriate.	Use may be appropriate if the following criteria are met: • Case of failure, contraindication or intolerance to other therapeutic options AND • Used as a short-term temporizing measure For long term use, transition to other maintenance immunotherapies should be considered, as appropriate.	Use may be appropriate if the following criteria are met: • Case of failure, contraindication or intolerance to other therapeutic options AND • Used as a short-term temporizing measure For long term use, transition to other maintenance immunotherapies should be considered, as appropriate.
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Offered to patients when alternatives are not available or effective. 1-2 g/kg ABW monthly, if necessary. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

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<tr><td rowspan="2">Opsoclonus-myoclonus ataxia - adult</td><td>Use may be appropriate if the following criteria are met:
• Treatment in conjunction with immunosuppressive medications
AND
• Use as a short-term, temporizing measure</td><td>Use may be appropriate if the following criteria are met:
• Failure, contraindication or intolerance to other therapeutic options.
AND
• Use as a short-term temporizing measure</td><td>Use may be appropriate if the following criteria are met:
• Moderate or severe failure, contraindication or intolerance to other therapeutic options.
AND
• Use as a short-term temporizing measure</td></tr>
<tr><td>Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day)

Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td><td>Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day)

Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td><td>Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day)

Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks.

Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.</td></tr>
</table>

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Opsoclonus-myoclonus ataxia - pediatric	Use may be appropriate. May be used alone or in conjunction with immunosuppressive medications.	Use may be appropriate if the following criteria are met: • Severe disease AND/OR • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND/OR • Failure, contraindication or intolerance to other therapeutic options
	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) Maintenance: 0.4 to 1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) Includes pediatric autoimmune neuropsychiatric disorders (PANDA)	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. If there is need to continue use of IVIg reassess no later than 3 months. Discontinue as soon as possible.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. If there is need to continue use of IVIg reassess no later than 3 months. Discontinue as soon as possible.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 4-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. If there is need to continue use of IVIg reassess no later than 3 months. Discontinue as soon as possible.
POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal plasma cell disorder, Skin changes) syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Post-polio syndrome	Do not use.	Do not use.	Do not use.
	n/a.	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Postural orthostatic tachycardia syndrome (POTS)	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a
Immune-mediated rapidly progressive cerebellar syndrome/paraneoplastic cerebellar degeneration	Use may be appropriate if the following criteria are met: • Treatment in conjunction with immunosuppressive medications AND • Use as a short-term, temporizing measure	Use may be appropriate if the following criteria are met: • Failure, contraindication or intolerance to other therapeutic options AND • Use as a short-term temporizing measure	Use may be appropriate if the following criteria are met: • Moderate or severe failure, contraindication or intolerance to other therapeutic options AND • Use as a short-term temporizing measure
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1-2 g/kg ABW monthly, if necessary Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: Offered to patients when alternatives are not available or effective. 1-2 g/kg ABW monthly, if necessary Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.
Rasmussen syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Sensory ganglionopathy	Use may be appropriate if the following criterion is met: • In cases of rapid onset and/or severe progression	Use not appropriate unless there are exceptional circumstances.	Do not use.
	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness. Discontinue if there is no clinical benefit.	n/a	n/a
Stiff person syndrome (Moersch-Woltman syndrome)	Use may be appropriate if the following criterion is met: • Failure or contraindications to GABAergic medications	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance too other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance too other therapeutic options
	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	Induction: 2 g/kg ABW divided over 2-5 days. Maintenance: 1 to 2 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 3-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Susac syndrome	Use may be appropriate if the following criterion is met: • Definite or probable diagnosis of Susac syndrome with concurrent steroid therapy, unless contraindicated	Use not appropriate unless there are exceptional circumstances.	Do not use.
	Induction: up to 2 g/kg ABW divided over 2-5 days. Maintenance: 0.5-1 g/kg ABW divided over 1-5 days (maximum 1 g/kg/day) every 2-6 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	n/a	n/a
Sydenham chorea	Use may be appropriate if the following criterion is met: • After failure of other treatments	Use may be appropriate if the following criterion is met: • After failure of other treatments	Do not use.
	Single dose of 2 g/kg ABW divided over 2-5 days	Single dose of 2 g/kg ABW divided over 2-5 days	n/a

Neurology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Vasculitic neuropathy, as part of a systemic disorder (i.e., systemic vasculitis affecting the peripheral nervous system)	Use may be appropriate if the following criterion is met: • Indicated for the systemic disorder	Use may be appropriate if the following criterion is met: • Indicated for the systemic disorder	Use may be appropriate if the following criterion is met: • Indicated for the systemic disorder
	As indicated by the systemic disorder.	As indicated by the systemic disorder.	As indicated by the systemic disorder.
Vasculitic neuropathy, non-systemic (i.e., vasculitis solely affecting the peripheral nervous system; isolated vasculitic neuropathy)	Use may be appropriate if the following criteria are met: • Severe disease AND • When steroids or other therapies are contraindicated or ineffective	Use may be appropriate if the following criteria are met: • Severe disease AND • When steroids or other therapies are contraindicated or ineffective	Use may be appropriate if the following criteria are met: • Severe disease AND • When steroids or other therapies are contraindicated or ineffective
	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.	2 g/kg ABW divided over 2-5 days, every 4 weeks. Once the condition has stabilized, titrate to lowest dose and/or treatment interval to maintain clinical effectiveness.

Rheumatology

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Adult-onset Still's disease	Use may be appropriate if the following criterion is met: • Patients who do not respond to standard therapy	Use not appropriate unless there are exceptional circumstances.	Do not use.
	2 g/kg ABW divided over 2 to 5 days	n/a	n/a
Catastrophic antiphospholipid antibody syndrome (C-APLAS) - adult and pediatric	Use may be appropriate if the following criterion is met: • C-APLAS characterized by widespread small vessel thrombosis leading to multiorgan failure	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	Adults: 2 g/kg ABW divided over 2 to 5 days. Peds: 2 g/kg ABW (max 70 g)	Adults: 2 g/kg ABW divided over 2 to 5 days. Peds: 2 g/kg ABW (max 70 g)	Adults: 2 g/kg ABW divided over 2 to 5 days. Peds: 2 g/kg ABW (max 70 g)
Behcet disease - adult and pediatric	Do not use.	Do not use.	Do not use.
	N/a	n/a	n/a
Congenital heart block, autoimmune (neonatal lupus) Maternal therapy	Use not appropriate unless there are exceptional circumstances.	Use not appropriate unless there are exceptional circumstances.	Do not use.
	n/a	n/a	n/a
Congenital heart block, autoimmune (neonatal lupus) Neonatal therapy	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Dermatomyositis - adult	Use may be appropriate if the following criteria are met: • Severe disease (life-threatening or causing significant muscle weakness with impaired activities of daily living) OR • Urgent need for therapy OR • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease (life-threatening or causing significant muscle weakness with impaired activities of daily living) AND • Urgent need for therapy OR failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease (life-threatening or causing significant muscle weakness with impaired activities of daily living) AND • Urgent need for therapy OR failure, contraindication or intolerance to other therapeutic options
	2 g/kg ABW induction. 1-2 g/kg ABW maintenance, every 4-6 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Transition to other immunomodulatory therapies should take place as soon as possible.	2 g/kg ABW induction. 1 g/kg ABW maintenance, every 4-6 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Transition to other immunomodulatory therapies should take place as soon as possible.	2 g/kg ABW induction. 1 g/kg ABW maintenance, every 6 or more weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Transition to other immunomodulatory therapies should take place as soon as possible.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Dermatomyositis - pediatric	Use may be appropriate if the following criteria are met: • Used in addition to corticosteroid and/or immunosuppressives at the outset of treatment or when response is suboptimal AND • For persistent skin disease when the muscle disease is otherwise well controlled	Use may be appropriate if the following criteria are met: • Severe disease AND/OR • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	2 g/kg ABW to a maximum 70 g every 2 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.	2 g/kg ABW to a maximum 70 g every 2 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.	2 g/kg ABW to a maximum 70 g every 2 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Eosinophilia granulomatosis with polyangiitis (Churg-Strauss disease) - adult and pediatric	Use may be appropriate if the following criterion are met: • Patients hospitalized with comorbidities and severe nervous system or cardiac disorders. OR • Patients who have not responded to primary standard therapy.	Use not appropriate unless there are exceptional circumstances.	Do not use.
	2 g/kg ABW divided over 1-5 days, every 4 weeks. Once the condition has stabilized, titrate to the lowest dose (generally 1 g/kg or lower) and/or longest treatment interval to maintain clinical effectiveness.	n/a	n/a
Hemophagocytic lymphohistiocystosis (HLH): Primary	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Hemophagocytic lymphohistiocytosis (HLH): Secondary[9] Includes macrophage activation syndrome (MAS) and virus associated hemophagocytic syndrome (VAHS)	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.
	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.	Refer to HLH criteria in the Hematology section.

[9] Secondary HLH is a heterogenous group of conditions and includes HLH secondary to conditions including infections (mainly viruses, such as EBV, HIV, and CMV, but also bacteria, parasites, and fungi), malignancies (mainly malignant lymphoma), macrophage activation syndrome in autoinflammatory or autoimmune disorders, other causes (organ or stem cell transplantation; metabolic, traumatic, iatrogenic [immunosuppression, vaccination, surgery, hemodialysis] causes; and pregnancy). Treatment protocols vary and depend on underlying cause. (La Rosee P, Horne A, Hines M et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood 2019; 133:2465-77)

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Immune-mediated necrotizing myositis/myopathy (IMNM), including statin induced -adult and pediatric	Use may be appropriate if the following criteria are met: • Used in addition to corticosteroid and/or immunosuppressives at the outset of treatment or when response is suboptimal AND • For persistent skin disease when the muscle disease is otherwise well controlled	Use may be appropriate if the following criteria are met: • Severe disease AND/OR • Failure, contraindication or intolerance to other therapeutic options	Use may be appropriate if the following criteria are met: • Severe disease AND • Failure, contraindication or intolerance to other therapeutic options
	2 g/kg ABW to a maximum 70 g every 2-4 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to lowest dose (generally 1 g/kg or lower) and/or treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.	2 g/kg ABW to a maximum 70 g every 2-4 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to lowest dose (generally 1 g/kg or lower) and/or treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.	2 g/kg ABW to a maximum 70 g every 4 weeks for 3-5 cycles and then every 4 weeks. Once the condition has stabilized, titrate to lowest dose (generally 1 g/kg or lower) and/or treatment interval to maintain clinical effectiveness. Consider transitioning to SCIg, if available.
Inclusion body myositis	Do not use.	Do not use.	Do not use.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
	n/a	n/a	n/a
Kawasaki syndrome - pediatric	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	2 g/kg ABW given once. Maximum of 70 g per dose. If failure to respond to initial dose, a maximum of one additional dose may be given.	2 g/kg ABW given once. Maximum of 70 g per dose. If failure to respond to initial dose, a maximum of one additional dose may be given.	2 g/kg ABW given once. Maximum of 70 g per dose. If failure to respond to initial dose, a maximum of one additional dose may be given.
Multisystem inflammatory syndrome in children (MIS-C) and adults (MIS-A) associated with SARS-CoV-2/COVID-19 infection	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	2 g/kg ABW (to a maximum of 70 g for pediatrics) given over time that is clinically indicated/tolerated. A single treatment is usually sufficient. One additional treatment may be given in exceptional circumstances in refractory MIS-C and MIS-A with appropriate expert consultation.	2 g/kg ABW (to a maximum of 70 g for pediatrics) given over time that is clinically indicated/tolerated. A single treatment is usually sufficient. One additional treatment may be given in exceptional circumstances in refractory MIS-C and MIS-A with appropriate expert consultation.	2 g/kg ABW (to a maximum of 70 g for pediatrics) given over time that is clinically indicated/tolerated. A single treatment is usually sufficient. One additional treatment may be given in exceptional circumstances in refractory MIS-C and MIS-A with appropriate expert consultation.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Polymyositis or overlap myositis (adult)	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.
	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.	Refer to Dermatomyositis (adult) criteria in the Rheumatology section.
Polymyositis or overlap myositis (pediatric)	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.
	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.	Refer to Dermatomyositis (pediatric) criteria in the Rheumatology section.
Rheumatoid arthritis	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Scleroderma	Use not appropriate unless there are exceptional circumstances. Consider in patients with myositis overlap syndromes, diaphragmatic dysfunction, and calcinosis.	Do not use.	Do not use.
	n/a	n/a	n/a
Scleromyxedema	Refer to Scleromyxedema criteria in the Dermatology section.	Refer to Scleromyxedema criteria in the Dermatology section.	Refer to Scleromyxedema criteria in the Dermatology section.

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	Refer to Scleromyxedema criteria in the Dermatology section.	Refer to Scleromyxedema criteria in the Dermatology section.	Refer to Scleromyxedema criteria in the Dermatology section.
Sjogren's syndrome	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Systemic lupus erythematosus (severe) Also see: Catastrophic antiphospholipid antibody syndrome (C-APLAS) - adult and pediatric	Use may be appropriate if the following criterion is met: • Severe myositis or refractory skin disease when no other treatment options are effective or appropriate. .	Do not use.	Do not use.
	2 g/kg ABW divided over 2-5 days. Long-term therapy may be considered only in exceptional cases. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.	n/a	n/a
Systemic onset juvenile idiopathic arthritis	Use may be appropriate if the following criterion is met: • Resistant to other forms of therapy	Use may be appropriate if the following criterion is met: • Resistant to other forms of therapy	Use may be appropriate if the following criterion is met: • Resistant to other forms of therapy

Rheumatology Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	1 to 2 g/kg ABW (to maximum up to 70 g) every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.	1 to 2 g/kg ABW (to maximum up to 70 g) every 4 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.	1 to 2 g/kg ABW (maximum up to 70 g) every 4 to 8 weeks. Once the condition has stabilized, titrate to the lowest dose and/or longest treatment interval to maintain clinical effectiveness.
Systemic vasculitic syndromes Includes (but not limited to) Antineutrophilic cytoplasmic antibody (ANCA) vasculitis, polyarteritis nodosa, and IgA-associated vasculitis	Use not appropriate unless there are exceptional circumstances.	Do not use.	Do not use.
	n/a	n/a	n/a

Transplantation

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
Adenovirus in solid organ transplantation	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
BK polyomavirus nephropathy in solid organ transplant recipients	Use may be appropriate if the following criterion is met: • Infection resistant to immunosuppression reduction	Use may be appropriate if the following criterion is met: • Infection resistant to immunosuppression reduction	Do not use
	n/a	n/a	n/a
Cellular therapy, allogenic (matched unrelated donor (MUD), sibling matched, cord, haploidentical)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Cellular Therapy, Autologous; CAR-T - adult and pediatric	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Graft-versus-host disease (GVHD) (acute, chronic, prophylaxis)	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.	Refer to SID criteria in the Immunology section.
Cytomegalovirus (CMV) prophylaxis (HSCT and solid organ transplant)	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Community-acquired respiratory virus associated with respiratory syncytial virus (RSV), upper respiratory tract infections	Use may be appropriate if the following criterion is met: • Treatment of proven RSV in high-risk[10] patients.	Do not use.	Do not use.
	Single dose of 1 g/kg ABW with IgG level reassessed weekly. Consider re-treatment if IgG level remains below the lower limit of normal.	n/a	n/a

[10] The term "high-risk patient" signifies: 1) Lung transplant recipients. 2) Recipients of chimeric antigen receptor T-cells (CAR-T) for relapsed or refractory acute leukemia, multiple myeloma, chronic lymphocytic leukemia, or non-Hodgkin lymphoma (or other indication) with ongoing evidence of Bcell lymphopenia who are not receiving regular immunoglobulin replacement. 3) Allogeneic HSCT recipients with at least one of the following: hypogammaglobulinemia, defined as an IgG level less than the lower limit of normal or <4 g/L; absolute lymphocyte count <0.5 x 10^9 /L; CD4 T-cell count <0.2 x 10^9 /L; 6 months post alemtuzumab, anti-thymocyte globulin, rituximab therapy, or other B-cell depleting therapy (e.g., blinatumomab); steroid refractory or steroid dependent acute graft-versus-host disease; moderate to severe chronic graft-versus-host disease; or Prolonged use of systemic corticosteroids at a dose of at least 0.5 mg prednisone equivalents/kg/day for at least 1 week. Reference: von Lilienfeld-Toal, Berger A, et al. European Journal of Cancer 2016;67:200-12

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Community-acquired respiratory virus, lower respiratory tract infections	Use may be appropriate if the following criterion is met: • In addition to antiviral therapy in high-risk[11] patients.	Do not use.	Do not use.
	Single dose of 1 g/kg ABW, with IgG level reassessed weekly. Consider re-treatment if IgG level remains below the lower limit of normal.	n/a	n/a
Epstein-Barr virus (EBV) - associated post-transplant lymphoproliferative disease (HSCT and solid organ transplant)	Do not use. For secondary immunodeficiency, see relevant section.	Do not use.	Do not use.
	n/a	n/a	n/a

[11] The term “high-risk patient” signifies: 1) Lung transplant recipients. 2) Recipients of chimeric antigen receptor T-cells (CAR-T) for relapsed or refractory acute leukemia, multiple myeloma, chronic lymphocytic leukemia, or non-Hodgkin lymphoma (or other indication) with ongoing evidence of Bcell lymphopenia who are not receiving regular immunoglobulin replacement. 3) Allogeneic HSCT recipients with at least one of the following: hypogammaglobulinemia, defined as an IgG level less than the lower limit of normal or <4 g/L; absolute lymphocyte count <0.5 x 10^9 /L; CD4 T-cell count <0.2 x 10^9 /L; 6 months post alemtuzumab, anti-thymocyte globulin, rituximab therapy, or other B-cell depleting therapy (e.g., blinatumomab); steroid refractory or steroid dependent acute graft-versus-host disease; moderate to severe chronic graft-versus-host disease; or Prolonged use of systemic corticosteroids at a dose of at least 0.5 mg prednisone equivalents/kg/day for at least 1 week. Reference: von Lilienfeld-Toal, Berger A, et al. European Journal of Cancer 2016;67:200-12

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Gastrointestinal viruses (proven refractory and persistent enteric viruses (e.g., norovirus or rotavirus) in immunosuppressed patients	Use may be appropriate if the following criterion are met: • Children < 2 years of age. OR • Persistent, proven norovirus or rotavirus in immunosuppressed transplant recipients where reduction of immunosuppression is contraindicated. Consultation with an infectious disease specialist is required.	Do not use.	Do not use.
	25-45 mg/kg 4 times daily for up to 2 days (8 doses)	n/a	n/a
HSCT autologous in Multiple Sclerosis patients	Use may be appropriate if the following criterion is met: • Patients undergoing HSCT for multiple sclerosis.	Use may be appropriate if the following criterion is met: • Patients undergoing HSCT for multiple sclerosis.	Use may be appropriate if the following criterion is met: • Patients undergoing HSCT for multiple sclerosis.
	0.5 g/kg ABW monthly for 12 months	0.5 g/kg ABW monthly for 12 months	0.5 g/kg monthly ABW for 6 months

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
HSCT CMV-induced pneumonitis	Use may be appropriate if the following criterion are met: • If CMV hyperimmune globulin unavailable AND • If antiviral therapy for proven or probably CMV-induced pneumonitis is contraindicated or there is a lack of response	Use not appropriate unless there are exceptional circumstances.	Do not use.
	0.5g/kg ABW every other day for 2 weeks.	n/a	n/a
HSCT with donor-specific HLA antibodies	Use may be appropriate if the following criterion is met: • In combination with PLEX, monoclonal antibody therapy or other agents	Use may be appropriate if the following criterion is met: • In combination with PLEX, monoclonal antibody therapy or other agents	Use may be appropriate if the following criterion is met: • In combination with PLEX, monoclonal antibody therapy or other agents
	1g /kg ABW. May be repeated if clinically indicated.	1g /kg ABW. May be repeated if clinically indicated.	1g /kg ABW. May be repeated if clinically indicated.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Parvovirus B19 in solid organ transplant recipients	Use may be appropriate if the following criterion is met: • Established parvovirus B19 infection Retreatment may be considered for non-response or symptomatic relapse.	Use may be appropriate if the following criterion is met: • Established parvovirus B19 infection Retreatment may be considered for non-response or symptomatic relapse.	Use may be appropriate if the following criterion is met: • Established parvovirus B19 infection Retreatment may be considered for symptomatic relapse.
	1 to 2 g/kg ABW divided over 5 days.	1 to 2 g/kg ABW divided over 5 days.	1 to 2 g/kg ABW divided over 5 days.
Pulmonary graft-versus-host disease	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Solid Organ Transplantation			
	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Heart transplant: Post-transplant, acute antibody-mediated rejection management	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.
Heart transplant: Post-transplant, chronic antibody-mediated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Heart transplant: Post-transplant, T-cell-mediated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Heart transplant: Pre/peri-transplant, desensitization	Use not appropriate unless there are exceptional circumstances.	Use not appropriate unless there are exceptional circumstances.	Use not appropriate unless there are exceptional circumstances.
	n/a	n/a	n/a
Kidney transplant: Post transplant,	Do not use.	Do not use.	Do not use.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
acute/active T-cell mediated rejection management	n/a	n/a	n/a
Kidney transplant: Post-transplant, acute antibody-mediated rejection management	Use may be appropriate. With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3-6 cycles.	Use may be appropriate. With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	Use may be appropriate. With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.
Kidney transplant: Post-transplant, chronic antibody-mediated rejection management	Use may be appropriate. For pathology proven acute antibody mediated rejection. May be given with or without PLEX.	Do not use.	Do not use.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg Without PLEX: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3-6 cycles.	n/a	n/a
Kidney transplant: Pre/peri- transplant, desensitization (e.g., anti-HLA, ABO incompatible)	Use may be appropriate. For secondary immunodeficiency (e.g., after B-cell/plasma cell depletion), see relevant section.	Use may be appropriate if the following criterion are met: • Transplant cannot be delayed. For secondary immunodeficiency (e.g., after B-cell/plasma cell depletion), see relevant section.	Use may be appropriate if the following criteria are met: • Transplant cannot be delayed. For secondary immunodeficiency (e.g., after B-cell/plasma cell depletion), see relevant section.
	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg
Liver transplant: post-transplant, chronic antibody medicated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Liver transplant: pre/peri-transplant, desensitization	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	**AMBER**	**RED**
Lung transplant: Post-transplant, acute/active T-cell mediated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Lung transplant: Post-transplant, acute antibody-mediated rejection management	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW Without PLEX: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW Without PLEX: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW Without PLEX: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.
Lung transplant: Post-transplant, chronic antibody-mediated rejection management	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.
Lung transplant: Pre/peri-transplant, desensitization	Use not appropriate unless there are exceptional circumstances.	Use not appropriate unless there are exceptional circumstances.	Use not appropriate unless there are exceptional circumstances.

Transplantation (solid organ and SCT, including ID in transplant patients) Indications	National Ig Shortages Plan		
	GREEN PHASE ADVISORY	AMBER	RED
	n/a	n/a	n/a
Pancreas transplant: pre/peri-transplant, desensitization	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Pancreas transplant: post-transplant, acute antibody mediated rejection management	Use may be appropriate.	Use may be appropriate.	Use may be appropriate.
	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3-6 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.	With PLEX: 0.1 g/kg ABW after each PLEX to a maximum total dose of 2 g/kg ABW IVIg alone: 2 g/kg ABW divided over 2-5 days. Further doses may be indicated every 4 weeks for a further 3 cycles.
Pancreas transplant: post-transplant, chronic antibody medicated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a
Pancreas transplant: post-transplant, acute/active T-cell medicated rejection management	Do not use.	Do not use.	Do not use.
	n/a	n/a	n/a

Alternative therapies

The following is a non-exhaustive list of alternative therapies that may be suitable for some patients. It is current as of April 24, 2024 and is expected to change as new therapies are developed.

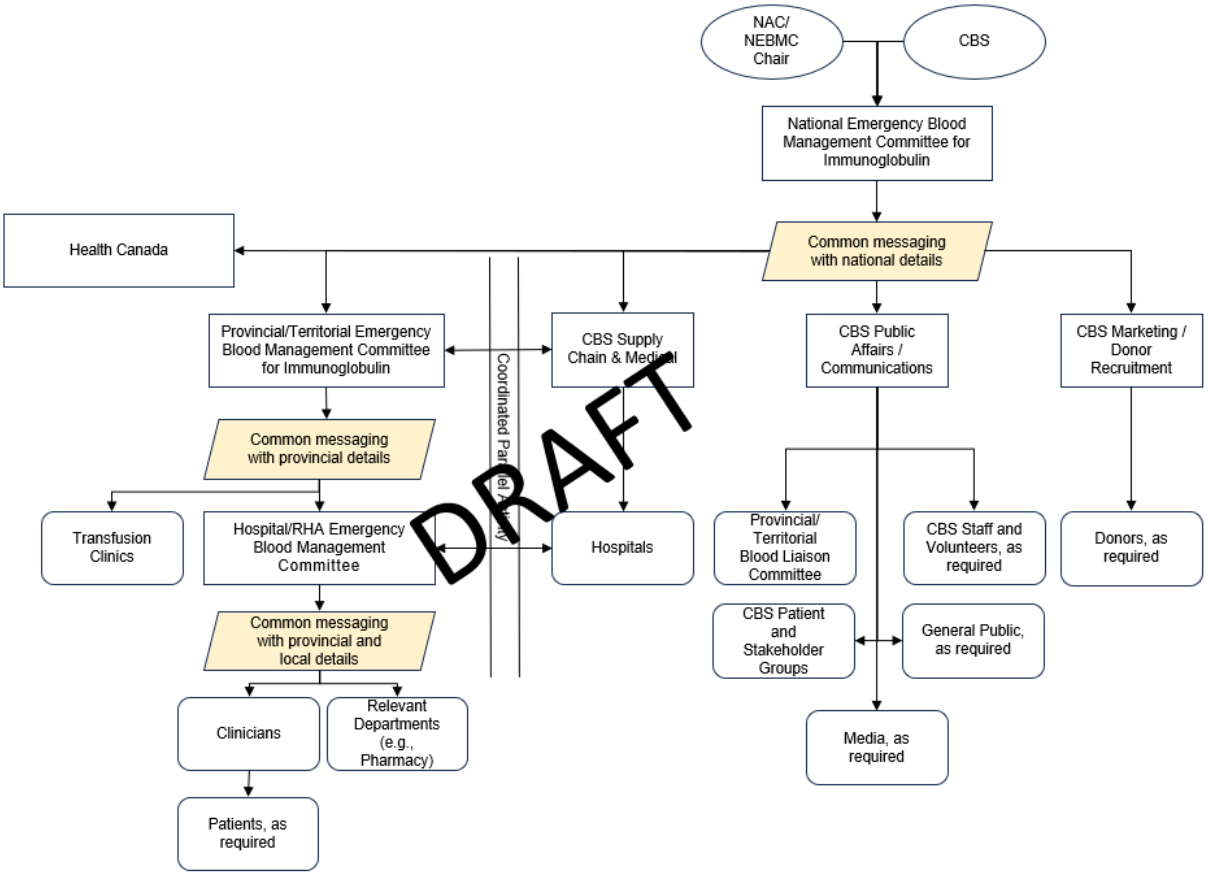
Therapeutic Categories/Classes	Drugs/Interventions
Hyperimmune immunoglobulins (available through Canadian Blood Services Plasma and Protein Related Products Formulary)	Anti-Cytomegalovirus immunoglobulin (anti-CMV Ig)
	Anti-D immunoglobulin (RhIg)
Monoclonal antibodies	Caplacizumab
	Nirsevimab
	Eculizumab
	Omalizumab
	Dupilumab
	Rituximab and anti-CD20 biosimilars
Immunosuppressants	Azathioprine
	Corticosteroids Dexamethasone Hydrocortisone Methylprednisolone Prednisone
	Calcineurin inhibitors Cyclosporin Tacrolimus
	Sirolimus
	Mycophenolate mofetil/mycophenolic acid
	Methotrexate
Cytotoxic chemotherapy	Cyclophosphamide
	Vincristine
Janus kinase (JAK) inhibitors	Baricitinib
	Tofacitinib
	Ruxolitinib
Spleen tyrosine kinase (Syk) inhibitors	Fostamatinib
Tumour necrosis factor-alpha (TNF-alpha) inhibitors	Etanercept
	Infliximab
Selective co-stimulation modulator	Abatacept
Interleukin-6 (IL-6) receptor inhibitor	Tocilizumab
Erythropoietin stimulating agents (ESAs)	Epoetin alfa

	Darbopoetin
Granulocyte colony stimulating factors (G-CSFs)	Filgrastim
	Pegfilgrastim
Thrombopoietin receptor agonists	Romiplostim
	Eltrombopag
Anti-viral therapy	Ganciclovir
	Ribavirin
Anti-infectives	Dapsone
Hormones	Danazol
Potassium channel blockers	Amifampridine (3,4-diaminopyridine)
Anti-inflammatories	Pentoxifylline
Transfusions	Platelets (e.g., irradiated or pathogen reduced platelets)
Procedures	Splenectomy
	Apheresis/immunoadsorption/plasma exchange
	Hyperbaric oxygen treatment

Appendix E: Communication Framework

A framework for the flow of information, decisions and guidance in a shortage situation , allowing all parties to provide timely, accurate and credible information to various internal and external relevant parties for the purposes of operational and informational communication, is provided below.

A more fulsome communications plan, including overarching and general principles and key messages is available in *The National Plan for Management of Labile Blood Components* (National Plan for Management of Shortages of Labile Blood Components)



Appendix F: Sample Tools for Times of Shortage

Sample National Ig Inventory Advisory Template

URGENT: IMMEDIATE ACTION REQUIRED

To: **ALL HOSPITAL SITES**
From: **National Emergency Blood Management Committee for Immunoglobulin (NEBMC-Ig)***
Subject: **<appropriate colour> PHASE**

National Inventory Advisory

Date and time of issue	*<Date and Time> (EST)*
Inventory Availability Phase	***<appropriate colour or recovery> PHASE***
Product(s)	*<product(s)>*
Description	*<Include the following in this section:* • *what has contributed/caused this shortage* • *what corrective actions are being taken* • *how long the shortage is expected to last>*
Impact on hospitals	<In this section provide direction for hospitals> <for advisory activation> Follow directives in the <<*insert phase here*>> section of The National / Provincial / Territorial / RHA or Hospital Ig Shortages Management Plan. **<u>Action required:</u>** Provide inventory levels by <<*indicate time and frequency here*>> until further notice. Inventory is to be reported via <<*indicate process here*>>.
For more information	For additional info, contact: 1. Your Hospital Liaison Specialist, Canadian Blood Services 2. Your representative to the Provincial / Territorial Emergency Blood Management Committee 3. Your representative to your Hospital Emergency Blood Management Committee

*The National Emergency Blood Management Committee for Immunoglobulin (NEBMC-Ig) is comprised of the National Advisory Committee on Blood and Blood Products, Provincial/Territorial Blood Liaison Committee representatives and key Canadian Blood Services personnel as well as Health Canada. This group will develop recommendations and provide advice to the P/T Ministries of Health, hospitals, regional health authorities, and Canadian Blood Services to support a consistent and coordinated response to critical Ig shortages in Canada.

For information about the National Ig Shortages Management Plan, please see: http://www.nacblood.ca/resources/shortages-plan/index.html. If you require this advisory in an accessible format, please contact your local Canadian Blood Services Hospital Liaison.

Sample Only: Decision Documentation Tool

Disposition of Ig During Red Phase

Section A: To be completed by Transfusion Medicine Services Technologist (or designate)		
Patient Initials/Tracking Number:	Hospital Number:	Patient location:
Patient Age:	Patient Height:	Patient Weight:
Product Requested:	Dose Requested:	
Patient Indication for Ig Request:		
Predicted to need Ig in the next 24 hours? □ Yes □ No If no, when is the product needed?		
Does the patient meet the criteria for the current shortage phase as outlined in the National / Provincial / Territorial / RHA or Hospital IgShortages Management Plan? □ Yes □ No If yes, forward to Transfusion Medicine Services Director (or designate)		
Section B: To be completed by Transfusion Medicine Services Director (or designate) / clinical subject matter experts		
Decision to administer products? □ Yes □ No	Rationale:	
Date / Time of Decision:		
Decision documentation completed by:		
Signature:		
Comments from patient/family regarding decision outcome:		
Section C: To be completed by National Triage Team / Panel in the case of an appeal and / or severe shortage (i.e., rationing is in effect).		
Decision to issue products? □ Yes □ No	Rationale:	
Date / Time of Decision:		
Decision documentation completed by:		
Signature:		
Comments from patient/family regarding decision outcome:		