ORBCoN
Ontario Regional Blood Coordinating Network

Ontario

Immune Globulin Toolkit for Ontario

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Table of Contents

Copies of these documents can be downloaded from http://transfusionontario.org/en/documents/?cat=ivig.

The Ontario Regional Blood Coordinating Network acknowledges with sincere appreciation the funding support of the Ministry of Health and Long-Term Care (MOHLTC).

Introduction

Intravenous immune globulin (IVIG) and subcutaneous immune globulin (SCIG) are products prepared by several commercial manufacturers who use plasma derived from donors to extract immunoglobulin subclass gamma (IgG). Immune Globulin (IG) is commonly used to treat patients for a number of labeled and unlabeled indications through either replacement of IG or immune modulation.

In 2006, the Blood Programs Coordinating Office (now known as the Provincial Agencies Trillium Gift of Life Network/ Blood and Specialized Programs or PATB) in Ontario launched a new blood programs initiative, the Ontario Regional Blood Coordinating Network (ORBCoN). This network was mandated to engage Ontario hospitals with transfusion services by setting up educational and communication opportunities, and to support hospitals with utilization improvement and inventory management tools. One of the many projects undertaken by ORBCoN was an IVIG utilization management initiative.

The first IG toolkit was launched in September 2010 with the purpose to:
- Provide guidelines for appropriate use of Intravenous Immune Globulin
- Provide health care practitioners involved in the infusion of IVIG with best practice information

The second iteration of the toolkit was released in 2012 and this version included a MOHLTC request form, dose calculator, new IG utilization management and infusion guidelines and a subsequent IG audit.

IG use has risen dramatically across Canada over the past 15 years and continues to do so, exceeding a 10% increase in some years. After the introduction of the MOHLTC strategy and new version of the toolkit in 2012, the IG use in Ontario actually decreased by 1.4% in 2012/13. However, since that time, the number of grams issued to hospitals in Ontario increased from approximately 1.78 M in 2012/13 to over 2.28 M in 2016/17. At a cost per gram of between $55 and $65 this translates to over $143 M annually. There are concerns that continued growth in IG utilization may become unsustainable. Seeking ways to ensure use of this product is appropriate the MOHLTC introduced a process to determine the feasibility of implementing an external screening and review mechanism for IG neurology requests. The Immune Globulin Screening Program (IGSP) pilot for neurology was launched on May 30, 2016. Data gathered from this pilot has been analyzed to determine if it is feasible to apply this process in the future to improve monitoring and understanding of IG use in the province of Ontario. See full report here: http://transfusionontario.org/en/documents/?cat=ivig.

This third version of the IG toolkit contains the following changes:
- Ontario IG Utilization Management Guidelines version 4.0 January 31, 2018
- MOHLTC IG Request Forms.
  - Non-Neurology version 5.0 January 2018 and
  - Neurology version 3.0 January 2018
- Implementation of a new Dose Calculator platform with an accompanying tool to calculate the BMI
- New version of the Ontario Intravenous Immune Globulin Infusion Guide and Adverse Reaction Chart version 2.0 October 31, 2015
- IVIG Facts for Outpatients version 2 0 October 31, 2015
- Travelling with IVIG; documents to support patients travelling with IG version1.0 January 31, 2018.

For more information relating to specific brands of IVIG available please refer to the following Canadian Blood Services document "Immune Globulin Comparison table". The current version can be found on the CBS website at www.blood.ca.

Abbreviations and Definitions

Abbreviations

ADEM	Acute Disseminated Encephalomyelitis
AIHA	Auto Immune Hemolytic Anemia
AvWD	Acquired von Willebrand disease
BMI	Body Mass Index
CBC	Complete blood count
CIDP	Chronic Inflammatory Demyelinating Polyneuropathy
F/NAIT	Fetal Neonatal Alloimmune Thrombocytopenia
GBS	Guillain–Barré Syndrome
GVHD	Graft vs Host disease
HDFN	Hemolytic Disease of the Fetus and Newborn
HIT	Heparin Induced Thrombocytopenia
HIV	Human Immunodeficiency Virus
HSCT	Hematopoietic Stem Cell Transplant
HTR	Hemolytic Transfusion Reaction
HTRSC	Hemolytic Transfusion Reaction in Sickle Cell disease
IBM	Inclusion Body Myositis
IgG	Immunoglobulin G
IGSP	Immune Globulin Screening Pilot
IIM	Idiopathic Inflammatory Myopathy
ITP	Immune Thrombocytopenia
IVIG	Intravenous Immune Globulin
J-IM	Juvenile Idiopathic Myopathy
LEMS	Lambert Eaton Myasthenic Syndrome
MG	Myasthenia Gravis
MMN	Multifocal Motor Neuropathy
NMDA	N-methyl-D aspartate encephalitis
MOHLTC	Ministry of Health and Long-Term Care
ORBCoN	Ontario Regional Blood Coordinating Network
PANDAS	Pediatric Autoimmune Neuropsychiatric Disorders with Streptococcal Infections
PID	Primary Immune Deficiency
PTP	Post Transfusion Purpura
PV	Pemphigus Vulgaris
SCD	Sickle Cell Disease
SCIG	Subcutaneous Immune Globulin
SID	Secondary Immune Deficiency
SJS	Stevens-Johnson Syndrome
TACO	Transfusion Associated Circulatory Overload
TEN	Toxic Epidermal Necrolysis
TML	Transfusion Medicine Laboratory
TTISS	Transfusion Transmitted Injuries Surveillance System
VAHS	Virus Associated Hemophagocytic Syndrome

Abbreviations and Definitions

Definitions

Adverse events	An undesirable and unintended occurrence during or after the administration of whole blood, blood components, or blood products, whether or not considered to be related to the administration of the blood, blood component, or blood product
Dyspnea	Difficult or labored respiration
Pharyngitis	Sore throat caused by inflammation of the back of the throat
Photophobia	An abnormal sensitivity to, and discomfort from, light
Urticaria	Hives; skin that erupts into red welts, often with severe itching

IVIG Utilization Management Guidelines and IVIG Strategy

On November 11, 2009, physicians in charge of Blood Transfusion Services and contact personnel in Transfusion Medicine Laboratories (TML) received Version 1.0 of the Ontario Intravenous Immune Globulin Utilization Management Guidelines. The Ministry of Health and Long-term Care acknowledged that work and on April 1, 2012 launched an IVIG strategy. Part of the strategy was to formally endorse the Ontario IVIG Utilization Management Guidelines. Version 4.0 of these guidelines accompany this document.

A document titled "Ontario Intravenous Immune Globulin Strategy Update" is also included to describe the update to the overall strategy and the place the guidelines hold within that strategy. This summary of guidelines and information on IVIG utilization has been prepared specifically for use in Ontario. The guidelines document provides clinicians with updated information about the common and clinically appropriate uses of Immune Globulin. In 2015 working groups from each medical specialty updated the guidelines which were subsequently endorsed by their associations before approval by the Ontario IG Advisory Panel. It is critically important that physicians in each hospital are aware of this information.

Recommendations on Maximum Dose of IVIG

Recommendations on Maximum Dose of IVIG
For the following clinical indications that appear on the Ontario IVIG Utilization Management Guidelines under 'IVIG is recommended', ***the maximum dose is 2 g/kg per treatment course***, as quoted in the Feasby et al article listed below:

- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
- Idiopathic Inflammatory Myopathy (IIM)

For the following clinical indications that appear on the Ontario IVIG Utilization Management Guidelines under "IVIG is recommended as an Option for treatment", ***the maximum dose is 2 g/kg per treatment course****, as quoted in the Feasby et al article listed below:

- Lambert-Eaton Myasthenic Syndrome
- Stiff Person Syndrome

*except in rare circumstances like some cases of TENS (Dermatology)

Source of Maximum Dose Recommendations:
Feasby T et al. Guidelines on the use of intravenous immune globulin for neurologic conditions Transfusion Medicine Reviews 2007(April); 21(1, Suppl 1):S57-S107.

Communication of the guidelines documents:

Electronic copies can be downloaded from:
http://transfusionontario.org/en/download/ontario-ig-utilization-management-guidelines/

Ministry of Health and Long-Term Care

Ontario IG Utilization Management Strategy Update

Provincial Agencies Trillium Gift of Life Network, Blood and Specialized Programs
Ministry of Health and Long -Term Care

January 31, 2018

Ontario

IG Utilization Management Strategy Update

Background

The Ontario Ministry of Health and Long-Term Care (MOHLTC) developed its first Ontario IG Utilization Management Strategy in 2012 and it was updated in 2015. The following items reflect the core requirements from these strategies that are still valid in mitigating unsustainable increases in IG utilization.

Scope

The IG Utilization Management Strategy applies to all hospitals where IG is dispensed by either a transfusion service or pharmacy. Physicians and practitioners who order IG must be made aware of and adhere to these directives.

Strategy

1. Adherence to Ontario IG Utilization Management Guidelines. The clinical indication, dose, frequency and duration of therapy must be in accordance with the Ontario IG Utilization Management Guidelines. The Guidelines are located in the IG Toolkit available at http://transfusionontario.org/en/download/immune-globulin-toolkit-for-ontario/
2. Implementation of the MOHLTC IG Request Form. All new requests for IG must be submitted using the MOHLTC Form. A record of the completed forms must be retained for five (5) years to permit spot audits. The record can be either paper, microfilm or electronic.
3. Review/Approval for Indications NOT Listed on Request Form. IG ordered for clinical indications not approved in the guidelines will be subject to screening at the hospital level. A physician appointed to serve as the approving physician, or their designate, must sign the form. NOTE: in the case of a life-threatening situation, the request for IG will be filled immediately.
4. Dosing Through “Adjusted Body Weight” Calculation. Ideal dosing reduces both the demand for IG and adverse events like hemolysis. Hospitals may elect to use the dose calculator for all patients to confirm the accuracy of the requested dose, but it must be used for all obese patients. The dose calculator and BMI tool can be found on : http://transfusionontario.org/en/download/bmi-dose-calculator/
5. Evaluating Clinical Outcomes and Need for Reassessment. For patients being treated regularly over a period of time, a mechanism to evaluate clinical impact must be established. A patient must be evaluated 6 months after the initial

prescription and every 12 months after that. A new MOHLTC request form must be completed initially and for each reassessment, especially for patients on long term therapy. The target shall be to prescribe the minimum effective dose.

6. No Outdating of Product. There must be no expiry of IG. Canadian Blood Services does not accept returns, but the Ontario Regional Blood Coordinating Network (ORBCoN) will assist you in the redistribution of this expensive product to another hospital that will use it before it expires.
7. Use for both IVIG and SCIG. The MOHLTC request form is to be used for both IVIG and SCIG requests.

In the Future

The MOHLTC is currently exploring alternate funding models with an expert working group. A letter was sent to patient groups and LHIN CEOs on September 29, 2017 informing them of this initiative. Depending on the solutions developed by this group, there may be upcoming changes to the IG ordering process at Ontario hospitals. The MOHLTC in conjunction with ORBCoN will keep hospitals apprised of any changes.


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Ontario Immune Globulin (IG) Utilization Management Guidelines

Version 4.0

January 31, 2018

Table of Contents

Page

Disclaimer:

The Ontario IG Utilization Management Guidelines are not intended to replace sound clinical judgment concerning a patient's unique situation.

Furthermore, although the advice and information contained in these guidelines is believed to be true and accurate at the time of going to press, neither the authors nor the publishers can accept any legal responsibility for any errors or omissions that may have been made.

Introduction

The information in this document is version 4.0 of the Ontario Immune Globulin Management Guidelines Version 1.0 was first circulated November 5, 2009 with subsequent versions in March, 2012 and May 2016. The guidelines were also included in the Intravenous Immune Globulin Toolkit, published by the Ontario Regional Blood Coordinating Network in September 2010 and October 2015.

The information in this document is intended as a guideline document for clinicians seeking clarification on the common and clinically appropriate uses of Immune Globulin.

This summary of guidelines and information on IG Utilization has been prepared specifically for use in Ontario, based on the input from the Ontario IG Advisory Panel. In 2015, the Ontario IVIG guidelines were reviewed by physicians within each of the specialties with indications for IVIG following a literature review of current evidence. The guidelines for Rheumatology, Neurology, Hematology, and Solid Organ Transplantation were published in May 2016. No revisions were deemed necessary at that time for Infectious Disease conditions and review of Dermatology and Immunology were completed in July 2017.

Recommended Hematology Indications

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Hematology	Fetal/ Neonatal alloimmune thrombocytopenia (F/NAIT) [1,2,38]	**Antenatal treatment**: IVIG (with or without corticosteroids) is recommended as first line treatment for women with a previously affected infant.	**Maternal dose** based on the following risk stratification: • Previous fetus with intracranial hemorrhage: Up to a total of 2 g/kg weekly starting as early as 12-16 weeks gestation. • No previous fetus with intracranial hemorrhage: Up to 1g/kg weekly, starting as early as 20-26 weeks current gestation.
		Newborn with F/NAIT: IVIG is recommended as adjunct to provision of platelets for infants with F/NAIT who have severe thrombocytopenia. Treatment should be administered in consultation with obstetrical medicine and transfusion medicine with expertise in F/NAIT.	**Infant dose:** initial dose of 1 g/kg, reassess following initial dose.
	Hemolytic Disease of the Fetus and Newborn (HDFN) [1,2,3]	IVIG is recommended in infants with HDFN and severe hyperbilirubinemia if total serum bilirubin (TSB) is rising despite intensive phototherapy/hydration, in consultation with experts in fetomaternal medicine and transfusion medicine.	0.5 g/kg over 4 hours.
	Immune thrombocytopenia (ITP) Adult [1,2,3,4]	**Acute ITP with or at risk for severe bleeding:** IVIG is recommended as part of multimodality therapy for patients with ITP, severe thrombocytopenia (platelets less than 30 x 10^9/L) and severe bleeding. **IVIG may be considered in the following situations:** • ITP in pregnancy: when platelets are less than 30 x 10^9/L, or in preparation for delivery. • Planned surgery: safe platelet threshold will vary with the nature of the surgery. • Treatment of ITP in patients with other concurrent risk factors for bleeding (e.g. concurrent anticoagulant therapy). **Chronic ITP:** IVIG may be considered as a possible adjunctive therapy as a steroid-sparing measure.	**Acute:** 1 g/kg as a single dose. Repeat if platelet count does not respond. I.e. still less than 30 x 10^9/L. **Chronic:** In consultation with a hematologist, as adjunctive therapy or where other therapies have failed or are not appropriate. Consider 1-2 g/kg. The use of regular IVIG as a treatment for chronic ITP should be considered as exceptional and alternative approaches (e.g. splenectomy, rituximab, thrombopoietin receptor agonists) should be considered.
	Immune Thrombocytopenia (ITP) Pediatric [1,2,3,4]	Acute: Children with no bleeding or mild bleeding only (mild bruising or petechiae) should be managed with observation alone regardless of platelet count. For children with moderate to severe mucosal and/or cutaneous bleeding and platelet count less than 30 x 10^9/L, IVIG can be used. Chronic: IVIG can be used in chronic ITP for previous responders.	For patients who require treatment, a single dose of IVIG may be considered a front-line treatment (0.8 to 1 g/kg). A second dose can be repeated if there is no clinical response. IVIG will result in a faster increment in platelet count compared with steroids. In emergent management, IVIG is recommended as part of multimodal therapy.
	Post-transfusion purpura (PTP) [1]	IVIG is recommended as standard first-line therapy for PTP.	Up to 2 g/kg divided over 2 to 5 consecutive days, repeat if necessary; for short term use.

For the following conditions, IVIG treatment is not recommended for routine use.
When screening requests for approval the following information may be taken into account as there is some evidence for IVIG to be considered as an option.

Specialty: Hematology	Medical Condition	Recommendations	Dose/Frequency of Administration
	Acquired hemophilia [1]	IVIG may be considered one option among adjunctive therapies, such as steroids, in urgent situations. Not recommended for routine use. Prescribed only in consultation with specialized hemophilia care centre.	Up to a total of 2 g/kg divided over 2 to 5 consecutive days, for short term use.
	Acquired red cell aplasia[1,3]	IVIG is an option for patients with immunologic pure red cell aplasia (PRCA) who have failed other therapies (e.g. prednisone or cyclosporin). IVIG should be considered first-line therapy for viral PRCA associated with parvovirus B19 in immunocompromised patients.	Up to 2 g/kg divided over 2 to 5 consecutive days; for short term use. Repeated on relapse.
	Acquired von Willebrand's disease (AvWD) [1,3]	IVIG should be considered part of multimodal therapy in emergent situations (together with desmopressin and FVIII/VWF concentrates) in patients who have not responded to other treatments. Prescribed only in consultation with specialized hemophilia care centre.	Initial therapy: Up to 2 g/kg divided over 2 to 5 consecutive days.
	Allogeneic bone marrow or stem cell transplantation[2,3,38]	IVIG is not recommended for routine use after HSCT. IVIG may be considered in exceptional cases: 1) Active CMV-induced pneumonitis following transplantation. 2) High risk allogeneic stem cell transplantation (e.g. If hypogammaglobulinemia) for prevention of GVHD.	1) No recommended dose or duration listed; use in conjunction with appropriate antiviral medication. 2) 0.4 g/kg weekly, starting one day before transplantation and continuing to day 100 post-transplant.
	Autoimmune hemolytic anemia[1,3] (AIHA)	May be considered one option among adjunctive therapies in urgent situations. Not recommended as routine.	No recommended dose or duration listed; however, expert panel recommends up to 2 g/kg divided over 2 to 5 consecutive days.
	Autoimmune neutropenia[1,3]	May be considered one option among adjunctive therapies in urgent situations.Not recommended as routine.	
	Hemolytic transfusion reaction in sickle cell disease[1] (HTRSCD)	IVIG may be considered among the options for treatment of serious, life-threatening, delayed hemolytic transfusion reactions in SCD patients.	
	Virus associated hemophagocytic syndrome[1] (VAHS)	IVIG is not recommended for routine use in the treatment of VAHS. IVIG may be considered among the options for treatment of severe life threatening VAHS.	
	Hemolytic transfusion reaction [1](HTR)	IVIG may be considered as an option among supportive therapies for urgent situations in this disorder.	Up to 2 g/kg divided over 2 to 5 consecutive days, short term up to 3 months.

Recommended Neurology Indications

Specialty: Neurology	Medical Condition	Recommendations	Dose/Frequency of Administration
	Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)[2,5,6,7]	IVIG is recommended as first-line therapy in CIDP. Immunosuppressive therapy in combination with IVIG can be considered in refractory cases. All patients receiving IVIG for chronic treatment of CIDP should be followed by a neuromuscular specialist.	Initial dose: 2 g/kg divided over 2 to 5 days Maintenance dose: 1g/kg every 3 weeks. Continued use should be based on objective measures of sustained effectiveness. Aim for minimum dose to maintain optimal functional status.
	Guillain-Barré Syndrome (GBS) including Miller-Fisher syndrome and other variants[2,5,8]	IVIG is recommended for symptoms of grade 3 severity (able to walk with aid) or greater; or symptoms less than grade 3 severity that are progressing. Treatment should be given within 2 weeks of symptom onset. Re-treatment for patients who do not respond may be considered.	Adult: Total dose of 2 g/kg divided over 2 to 5 days. Pediatric: Total dose of 2 g/kg divided over 2 days. Repeat treatment with IVIG at 2 g/kg divided over 2 to 5 days.
	Multifocal motor neuropathy (MMN)[2,5,9]	IVIG is recommended as first-line treatment for MMN.	Initial dose: 2 g/kg divided over 2 to 5 days. Maintenance dose: tailor to the lowest dose that maintains clinical efficacy, usually 1g/kg or less per treatment course. Some patients may require higher doses for efficacy, up to 2 g/kg every 4 weeks.
	Myasthenia gravis (MG)[2,5,10,11,12,13]	IVIG is recommended as first-line treatment in moderate-severe MG or in myasthenic crisis. IVIG in combinations with immunosuppressive therapy can be considered in refractory cases.	Initial dose: 2 g/kg divided over 2 to 5 days. If additional therapy is required, the dose should be adjusted depending upon response and titrated to the minimum effective dose.

For the following conditions, IVIG treatment is not recommended for routine use.
When screening requests for approval the following information may be taken into account as there is some evidence for IVIG to be considered as an option.

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Neurology	Acute disseminated encephalomyelitis[3,5] (ADEM)	IVIG is an option for monophasic ADEM when first-line therapy with high-dose corticosteroids fails or when there are contraindications to steroid use, and for treatment of relapsing ADEM to eliminate steroid dependency or for those patients who fail to respond, or have contraindications, to steroids.	Adults: Total dose of 2 g/kg divided over 2 to 5 days. Pediatric: Total dose of 2 g/kg divided over 2 days.
	Lambert-Eaton Myasthenic Syndrome[3,5] (LEMS)	IVIG is an option for treatment of LEMS. Objective evidence of clinical improvement is needed for sustained use of IVIG.	Initial dose: Total dose of 2 g/kg divided over 2 to 5 days. Maintenance dose: a systematic approach should be taken to determine the minimum effective dose, and continued use of IVIG should be based on objective measures of its sustained effectiveness. The maximum dose of IVIG per treatment course should be 2 g/kg.
	Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections[3,5] (PANDAS)	IVIG is an option for treatment of patients with PANDAS. Diagnosis of PANDAS requires expert consultation.	Total dose of 2 g/kg divided over 2 days is recommended as a reasonable option.
	Rasmussen's encephalitis[3,5]	IVIG is an option as a short-term, temporizing measure for patients with Rasmussen's encephalitis. Not recommended for long-term therapy.	Adults: Total dose of 2 g/kg divided over 2 to 5 days. Pediatric: Total dose of 2 g/kg divided over 2 days.
	Stiff Person's syndrome[3,5]	IVIG is an option for treatment of Stiff Person syndrome if GABAergic medications fail or for patients who have contraindications to GABAergic medications.	Initial dose: Adults: Total dose of 2 g/kg divided over 2 to 5 days. Pediatric: Total dose of 2 g/kg divided over 2 days. Maintenance dose: A systematic approach should be taken to determine the minimum effective dose, and continued use of IVIG should be based on objective measures of its sustained effectiveness. Maximum dose of IVIG per treatment course should be 2 g/kg.
	N-methyl-D-aspartate (NMDA) encephalitis[14]	IVIG is an option for treatment of patients with NMDA. Diagnosis of NMDA requires expert consultation. IVIG is used in conjunction with immunosuppressive medications and/or plasmapheresis.	Initial dose: Total dose of 2 g/kg divided over 2 to 5 days in adults and children. Maintenance dose may be considered depending on response to treatment.

Recommended Dermatology Indications

Specialty: Dermatology	Medical Condition	Recommendations	Dose/Frequency of Administration
	Pemphigus Vulgaris (PV) and Variants [2,3,39,40]	Consider IVIG when there is no response or a contraindication to corticosteroids, immunosuppressive agents or biologics (e.g. rituximab) in conjunction with one of the above. First line therapy: corticosteroids Second line: immunosuppressive agents Third line: IVIG	Total dose 2 g/kg divided over 2 to 5 days every 4 weeks. Dose every 6 weeks after 6 months of therapy.

For the following conditions, IVIG treatment is not recommended for routine use.
When screening requests for approval the following information may be taken into account as there is some evidence for IVIG to be considered as an option.

Specialty: Dermatology	Medical Condition	Recommendations	Dose/Frequency of Administration
	Toxic epidermal necrolysis (TEN)/ Stevens-Johnson Syndrome (SJS)[3,38,40]	IVIG is an option when other treatments are contraindicated, or when the condition is life-threatening. Early intervention is strongly recommended.	3 g/kg divided over 3-5 days.

Recommended Rheumatology Indications

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Pediatric Rheumatolog	Juvenile Idiopathic Inflammatory Myopathy (J-IIM)[2,5,15,16,17] (Previously Juvenile Dermatomyositis)	IVIG is recommended when there is a lack of response or contraindication to corticosteroids, Methotrexate and/or Azathioprine therapy. 1st line: Corticosteroids and Methotrexate 2nd line: IVIG 3rd line: Cyclosporine	Initial dose: Total dose of 2 g/kg divided over 2 days. Maintenance dose: A systematic approach should be taken to determine minimum effective dose. Continued use should be based on objective measures of sustained effectiveness. Maximum dose should not exceed 2 g/kg.
	Kawasaki Disease [2,18,19,20,21,22]	IVIG is recommended when Kawasaki diagnosis confirmed.	2 g/kg for 1 day (second dose can be given for patients who fail to respond to initial dose).
Specialty: Adult Rheumatology	Idiopathic Inflammatory myopathy (IIM) [2,5,15,23,24,26,25] Includes Dermatomyositis and Polymyositis *does not include Inclusion Body Myositis (IBM)	IVIG is indicated in patients with IIM as adjunctive therapy to corticosteroids and/or a steroid sparing agent in patients with IIM who have failed 1st line therapy or as clinically indicated in the management of severe disease. *IVIG benefit has not been established in IBM. 1st line: Corticosteroids and Methotrexate and/or Azathioprine 2nd line: IVIG 3rd line: Cyclosporine or cellcept	Maximum dose is 2 g/kg to be given over 2 days initially monthly for 3-6 months and if effective to be continued at decreasing frequency (determine minimum effective dose) over approximately 2 years. Survival of patients with IIM has been shown to be substantially improved in patients given IVIG.

Recommended Infectious Disease Indications

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Infectious Diseases	Staphylococcal toxic shock[2,3,15]	IVIG is recommended when evidence of systemic inflammation and end organ hypoperfusion with fever, tachycardia, tachypnea and hypotension.	1 g/kg on day one and 0.5 g/kg per day on days 2 and 3 **OR** 0.15 g/kg per day for 5 days.
	Invasive Group A streptococcal fasciitis with associated toxic shock[2,3,15,29,30]		

Recommended Immunology Indications

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Immunology	Primary Immune Deficiency (PID)[2,31] Secondary Immune Deficiency (SID)[2,31]	IVIG is recommended in hypogammaglobulinemia (total IgG reduced or inadequate antibody production) with recurrent bacterial infections. Children and adults with a suspected immunodeficiency should be referred to an immunologist with expertise in the field of primary immunodeficiency ('expert' in PID). Ideally, this should be carried out in an academic centre with the capability of performing specialized diagnostic tests for immunodeficiency. Management should be performed by a specialized team including physicians, nurses and allied health care providers.	Adult: 0.4-0 .6 g/kg every 3-4 weeks Pediatric: 0.3-0 .6 g/kg every 3-4 weeks Doses or frequency to be adjusted by experts according to desired trough level (more than 500 mg/dL and ideally 700 mg/dL) and according to individual patient clinical needs.
	Hematopoietic Stem Cell Transplant in primary immunodeficiencies[3]	IVIG is recommended in PID patients undergoing stem cell transplant.	0.4 to 0.6 g/kg every 3-4 weeks; requirements may increase and should be based on clinical outcome.

Recommended Solid Organ Transplant Indications

	Medical Condition	Recommendations	Dose/Frequency of Administration
Specialty: Solid Organ Transplantation	Kidney transplant from living donor to whom the patient is sensitized[15,32]	IVIG is recommended to decrease donor-specific sensitization.	2 g/kg/month for 4 months.
	Pre-Transplant (heart)[32,33,34,35,36]	For desensitization in selected heart transplant recipients who are highly sensitized, medically urgent and unlikely to receive a transplant otherwise – this should be preceded by discussion at the transplant program level.	Suggested dose is up to 1 g/kg/month until transplant.
	Peri- Transplant (heart, lung, kidney, pancreas[31,33,34,35,36]	Solid-organ transplant recipient with donor-specific antibodies identified at time of transplant surgery (heart, lung, kidney, pancreas) on virtual crossmatch – first-line agent.	Suggested dose 1 g/kg, can give as divided doses if in association with a course of plasmapheresis.
	Post-Transplant [32,33,34,35,36,37]	Acute antibody-mediated rejection in a solid-organ transplant recipient – first-line agent. Chronic antibody-mediated rejection in a solid-organ transplant recipient.	1 g/kg/dose, can give as divided doses if in association with a course of plasmapheresis. 1 g/kg/month.

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Use of the MOHLTC IG Request Form

ALL requests for IG must be submitted using the appropriate MOHLTC IG Request Form:
Use the Neurology form for IG requests for neurology requests only.
Use the Non–neurology form for all non-neurology requests for IG.
*This includes initial or renewal requests for all patients whether for induction or maintenance therapy with either IVIG or SCIG.

Duration of Approval. When a request for an Approved medical condition includes multiple infusions of IG (e.g. a course of treatment rather than a single infusion), completing the form once is sufficient until:
a. Dose is modified, or
b. Six months have elapsed since the initial treatment, or
c. Twelve months have elapsed for renewal requests.

Duration of Approval for Unapproved Medical Conditions. If a request for an Unapproved medical condition is approved, IG will be provided for up to a maximum trial period of three months. A reassessment should be done to confirm IG treatment continues to be effective and that minimum effective dose is being applied.

URGENT Requests. IG will always be provided in life-threatening situations, the appropriate request form to be completed when time allows.

Completing the Form (Complete all requested information and print clearly to avoid delays in access to IG)

Ordering Physician (or Designate) is responsible for completing the MOHLTC IG Request Form and submitting it to their TML.
1. Complete all requested physician, patient and hospital information.
2. Complete to indicate if request is for SCIG or IVIG.
3. Complete to indicate the medical condition for which IG is being requested. Check 'Other' if the medical condition does not appear on the list of approved conditions. **Please refer to the Ontario IG Guidelines for additional conditions for which IG may be appropriate.** If applicable, include information to confirm diagnosis and describe treatment to date to explain/ support the need for IG.
4. Complete to indicate dose and duration of IG treatment. Dose must be adjusted for obese patients (i.e., BMI ≥ 30). Hospitals that do not adopt the Dose Calculator tool are required to use an alternative strategy for adjusting dose for obese patients. Consider adjusting dose for overweight patients to ensure minimum effective dose is being applied. For other patients, the Dose Calculator maybe used to verify dose calculations. Use actual body weight to calculate dose for both adult and pediatric patients less than 5 feet in height. Requests for dose/duration greater than what is recommended in the Ontario Guidelines will be sent for review by the approving physician (or designate).

HealthCare Professional receiving the request (e.g. Laboratory technologist, pharmacy personnel)
1. Verify that the clinical indication coincides with one of the clinical indications listed. If not refer to 4 below.
2. Verify the dose requested using the dose calculator if appropriate.
3. Doses that require adjustment must be confirmed with the treating physician and documented on the bottom of the form.
4. Requests listing 'Other' as the clinical indication or requesting a dose that is greater than what is recommended in the Ontario Guidelines should be referred to an approving physician for screening.

Approving Physician or Designate
1. Screening of all IG requests for clinical indications listed under 'Other' or those with a dose greater than recommended in the Ontario Guidelines is required.
2. Document whether the request is approved or denied using the shaded area at the bottom of the request form including a signature, date and checking the appropriate box.

Hemolytic reactions due to anti-A and/or anti-B in IVIG have been noted.
Patients should be monitored for signs of hemolysis. CBC, blood group and antibody screen should be ordered prior to initial infusion. In Group A, B or AB patients, within 1 week of initial infusion the following tests are recommended: CBC, direct antiglobulin test (DAT), total and direct bilirubin, reticulocyte count, LDH, and haptoglobin.
Refer to the Adverse Reaction Chart for IVIG Infusion for more information.

MOHLTC IVIG Request Form

The forms on the following pages of this toolkit are intended to be used by hospitals where IVIG/SCIG is infused.

MOHLTC IG Request form for Non-neurology indications:
This form is to be used for all IG requests for indications other than neurology.

This type of ordering form can be built into a Laboratory Ordering System or Intranet, or used in paper format. The form is available at http://transfusionontario.org/en/download/ontario-mohltc-ig-request-form-non-neurology/.
All new non-neurology requests for IVIG must be ordered using the MOHLTC IG Request Form, whether the product is handled through the Transfusion Service or through the Pharmacy. This will ensure that the request is in accordance with provincial guidelines and that any specific prerequisites have been addressed. Hospitals that have already implemented an IG Request Form will need to adopt the MOHLTC January 31, 2018 version. Modification of the Request Form is not permitted. This will prevent the addition of indications not on the Guidelines and allow for standardized data collection. A record of completed Request Forms must be kept for five (5) years to allow for spot audits to measure compliance with the IG Strategy. The record can be paper based, electronic, or microfilm.

MOHLTC IG Request form for Neurology indications:

In May 2016, the MOHLTC implemented a pilot to provide an external screening process for immune globulin (IG) requests for neurological indications. Named the immune globulin screening program (IGSP) pilot*, a request form was developed for all requests for IVIG or SCIG for any neurology requests. Following the pilot, a revised IG request form for neurology indications is to be used. http://transfusionontario.org/en/download/ontario-mohltc-ig-request-form-neurology/.

*IGSP report is under review by the MOHLTC, final version will be posted here http://transfusionontario.org/en/download/.

Ontario

MOHLTC IVIG Request Form

For non-neurology use only

Patient Name
Patient Hospital/Medical Record#
D.O.B.
Gender
Location
Ontario Health Insurance#

ALL FIELDS BELOW ARE MANDATORY

Date Requested: (YYYY/MM/DD)	Treating Physician:
Date Required: (YYYY/MM/DD)	Physician Specialty:
Hospital where patient will receive IG.	Physician Phone #:

Dosage Information: (Verification of dose using Dose Calculator tool is recommended)

☐ Intravenous IG (IVIG) ☐ Subcutaneous IG (SCIG)						
Patient Weight: kg	Patient Height: cm	BMI:	**Dose must be adjusted for BMI greater than or equal to 30**			
☐ Induction/One-time dose	g/kg = Total dose of	g; divided over	days			
☐ Maintenance dose	g/kg = Total dose of	g; divided over	days; every	weeks; Duration:	months	
Dose Calculator Used? ☐ Yes ☐ No If No, why was it not used						
IgG level/Platelet count/other test results relevant to patient condition: Result: Date:						

Clinical indication for use: **Refer to Ontario IG Management Utilization Guidelines for additional indications where IG may be appropriate.**

Specialty	
Hematology	☐ Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)
	☐ Hemolytic Disease of the Fetus and Newborn (HDFN)
	☐ Immune Thrombocytopenia (ITP) ☐ Adult ☐ Pediatric
	☐ Post-transfusion Purpura
Dermatology	☐ Pemphigus Vulgaris (PV) and Variants
Rheumatology: Pediatric	☐ Juvenile Idiopathic Inflammatory Myopathy (J-IIM) (previously Juvenile Dermatomyositis)
	☐ Kawasaki Disease (KD)
Rheumatology: Adult	☐ Idiopathic Inflammatory Myopathy (IIM) Includes Dermatomyositis and Polymyositis
Immunology	☐ Primary Immune Deficiency (PID)
	☐ Secondary Immune Deficiency (SID)
	☐ Hematopoietic Stem Cell Transplant in primary immunodeficiencies
Solid Organ Transplant	☐ Kidney transplant from living donor to whom the patient is sensitized
	☐ Pre-transplant (Heart)
	☐ Peri-transplant (heart, lung, kidney, pancreas)
	☐ Post-transplant
Infectious Disease	☐ Invasive Group A streptococcal fasciitis with associated toxic shock
	☐ Staphylococcal Toxic Shock
***OTHER (requires approval)**	

For Transfusion Medicine Use Only

☐ **Dose verified** ☐ **Dose adjusted to:**	**By (signature req'd):**
☐ **Confirmed with ordering physician**	**Date:**
☐ **Approved** ☐ **Denied**	**Date:**
Signature of Approving Physician:	

Please fax/send to:

Medical Condition	Suggested initial dose and duration
Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)	*Maternal*: Previous fetus with intracranial hemorrhage: Up to 2 g/kg/week starting as early as 12-16 weeks gestation. No previous fetus with intracranial hemorrhage: Up to 1 g/kg/week. Starting as early as 20 -26 weeks current gestation. *Infant*: Initial dose of 1 g/kg reassess following initial dose.
Hemolytic Disease of the Fetus and Newborn (HDFN)	0.5 g/kg over 4 hours
Immune Thrombocytopenia (ITP) Adult	*Acute*: 1 g/kg as a single dose. Repeat if PLT count does not respond I.e. still less than 30 x 10^9 /L. *Chronic*: In consultation with a hematologist, as adjunctive therapy or where other therapies have failed or are not appropriate. Consider 1-2 g/kg. The use of regular IVIG as a treatment for chronic ITP should be considered as exceptional and alternative approaches (e .g. splenectomy, rituximab, thrombopoietin receptor agonists) should be considered.
Immune Thrombocytopenia (ITP) Pediatric	For patients who require treatment, a single dose of IVIG may be considered a front-line treatment (0 .8 to 1 g/kg). A second dose can be repeated if there is no clinical response. IVIG will result in a faster increment in platelet count compared with steroids. In emergent management, IVIG is recommended as part of multimodal therapy
Post-transfusion Purpura	Up to 2 g/kg divided over 2 to 5 consecutive days. Repeat if necessary; for short term use.
Pemphigus Vulgaris (PV) and variants	Total dose of 2 g/kg divided over 2 to 5 days every 4 weeks. Dose every 6 weeks after 6 months of therapy.
Juvenile Idiopathic Inflammatory Myopathy (J-IIM) (previously Juvenile Dermatomyositis)	*Initial dose*: Total dose of 2 g/kg divided over 2 days. *Maintenance dose*: A systematic approach should be taken to determine minimum effective dose.Continued use should be based on objective measures of sustained effectiveness. Maximum dose should not exceed 2 g/kg.
Kawasaki Disease (KD)	2 g/kg for 1 day (second dose can be given for patients that fail to respond to initial dose).
Idiopathic Inflammatory Myopathy (IIM) Includes Dermatomyositis and Polymyositis * does not include Inclusion Body Myositis	Maximum dose is 2 g/kg to be given over 2 days initially monthly for 3-6 months and if effective to be continued at decreasing frequency (determine minimum effective dose) over approximately 2 years.Survival of patients with IIM has been shown to be substantially improved in patients given IVIG.
Primary Immune Deficiency (PID) Secondary Immune Deficiency (SID)	*Adult*: 0.4-0.6 g/kg every 3-4 weeks *Pediatric*: 0.3-0.6 g/kg every 3-4 weeks Doses or frequency to be adjusted by experts according to desired trough level (more than 500 mg/dL and ideally 700 mg/dL) and according to individual patient clinical needs.
Hematopoietic Stem Cell Transplant in primary immunodeficiency	0.4-0.6 g/kg every 3-4 weeks; requirements may increase and should be based on clinical outcome.
Kidney transplant from living donor to whom the patient is sensitized	2 g/kg/month for 4 months.
Pre-transplant (Heart)	Suggested dose up to 1 g/kg/month until transplant.
Peri-transplant (heart, lung, kidney, pancreas)	Suggested dose 1 g/kg can give as divided doses if in association with a course of plasmapheresis.
Post-transplant	*Acute*: 1 g/kg/dose. Can be given as divided doses if in association with a course of plasmapheresis. *Chronic:* 1 g/kg/month.
Invasive Group A streptococcal fasciitis with associated toxic shock	1 g/kg on day one and 0 .5 g/kg per day on days 2 and 3 OR 0.15 g/kg per day for 5 days .
Staphylococcal Toxic Shock	

*** Refer to Ontario IVIG Management Utilization Guidelines for additional indications where IG may be appropriate.**
If you are unsure of the process for IG requests please refer to Ordering IG in Ontario

Ontario

MOHLTC IG Request Form

For Neurology Use Only

Patient Name:
Patient Hospital/Medical Record#:
Patient DOB (YYYY/MM/DD):
Gender M/F:
Location:
Ontario Health Insurance#:

ALL FIELDS BELOW ARE MANDATORY

SECTION A: Physician & Hospital Information

Date of Request (YYYY/MM/DD)	Date Required (YYYY/MM/DD)	Hospital Transfusion Service (HTS) Fax Number
Name of Ordering Physician	Physician's Contact Phone Number	Physician's Email
Is the patient being seen by a Neurologist/ Neuromuscular Specialist? ☐ Yes ☐ No	Is the request for a hospital inpatient? ☐ Yes ☐ No	Hospital where patient will receive IG

SECTION B: Request Type

☐ Initial Request: Maximum 6 month approval	☐ Renewal Request: A reassessment should be done to confirm IG treatment continues to be effective and that minimum effective dose is being applied. Maximum 12 month approval.

SECTION C: Clinical Indication

Refer to Ontario IG Management Utilization Guidelines for additional indications where IG may be appropriate

Approved Condition	Guidelines for INITIAL Request	Guidelines for RENEWAL Request
☐ Guillain–Barré Syndrome (GBS) including Miller Fisher Syndrome and other variants	▪ IG recommended for Grade 3 severity (able to walk with aid) or greater; or less than Grade 3 severity that are progressing. ▪ IG should be given within 2 weeks of symptom onset. ▪ Adult: Total Dose of 2 g/kg divided over 2 to 5 days. ▪ Pediatric: Total Dose of 2 g/kg divided over 2 days.	▪ IG treatment for GBS is typically one-time/in the acute setting. ▪ Re-treatment for patients who do not respond may be considered. Repeat treatment with IVIG at 2g/kg divided over 2-5 days.
☐ Myasthenia Gravis (MG)	▪ IG is recommended as first-line treatment in moderate-severe MG or in myasthenic crisis. ▪ Induction Dose: 2g/kg divided over 2-5 days. ▪ Initial requests may be made for induction plus two maintenance doses; fill out Section D accordingly.	▪ IG in combinations with immunosuppressive therapy can be considered in refractory cases. If additional IG is required, dose should be adjusted depending upon response and titrated to the minimum effective dose. ▪ Maintenance Dose: 1g/kg
☐ Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)	▪ IG is recommended as first-line therapy in CIDP. ▪ Induction Dose: 2 g/kg divided over 2 to 5 days. ▪ All patients receiving IG for chronic treatment of CIDP should be followed by a neuromuscular specialist.	▪ Immunosuppressive therapy in combination with IG can be considered in refractory cases. Continued use should be based on objective measures of sustained effectiveness. Aim for minimum effective dose. ▪ Maintenance Dose: 1g/kg every 3 weeks.
☐ Multifocal Motor Neuropathy (MMN)	▪ IG is recommended as first-line treatment for MMN. ▪ Induction Dose: 2g/kg divided over 2-5 days.	▪ Maintenance Dose: Tailor to the lowest dose that maintains clinical efficacy, usually 1g/kg or less per treatment course. Some patients may require higher doses for efficacy, up to 2g/kg every 4 weeks.

Other (please specify the diagnosis): _____

These requests will require screening by Transfusion Service. Please include information regarding treatment to date and documentation to support IG treatment for an unapproved indication.

Has the patient used other therapies to treat this condition? ☐ Yes, specify other treatments below ☐ No

Treatment	Dose (if applicable)	Duration of treatment	What was the outcome?
			☐ No response ☐ Contraindications ☐ Intolerance
			☐ No response ☐ Contraindications ☐ Intolerance

Other Comments: (include notes regarding response to IG therapy)

SECTION D: Dosage Information (Verification of dose using Dose Calculator tool is recommended. Refer to http://ivig.transfusionontario.org/dose/)

☐ Intravenous IG (IVIG) ☐ Subcutaneous IG (SCIG)

Patient Weight: kg Patient Height: cm BMI: **Dose must be adjusted for BMI greater than or equal to 30**

Induction/One-time dose	g/kg = Total dose of	g; divided over	days			
Maintenance dose	g/kg = Total dose of	g; divided over	days; every	weeks; Duration:	months	

Dose Calculator Used? ☐ Yes ☐ No If No, why was it not used?

SECTION E: For Transfusion Medicine Use Only

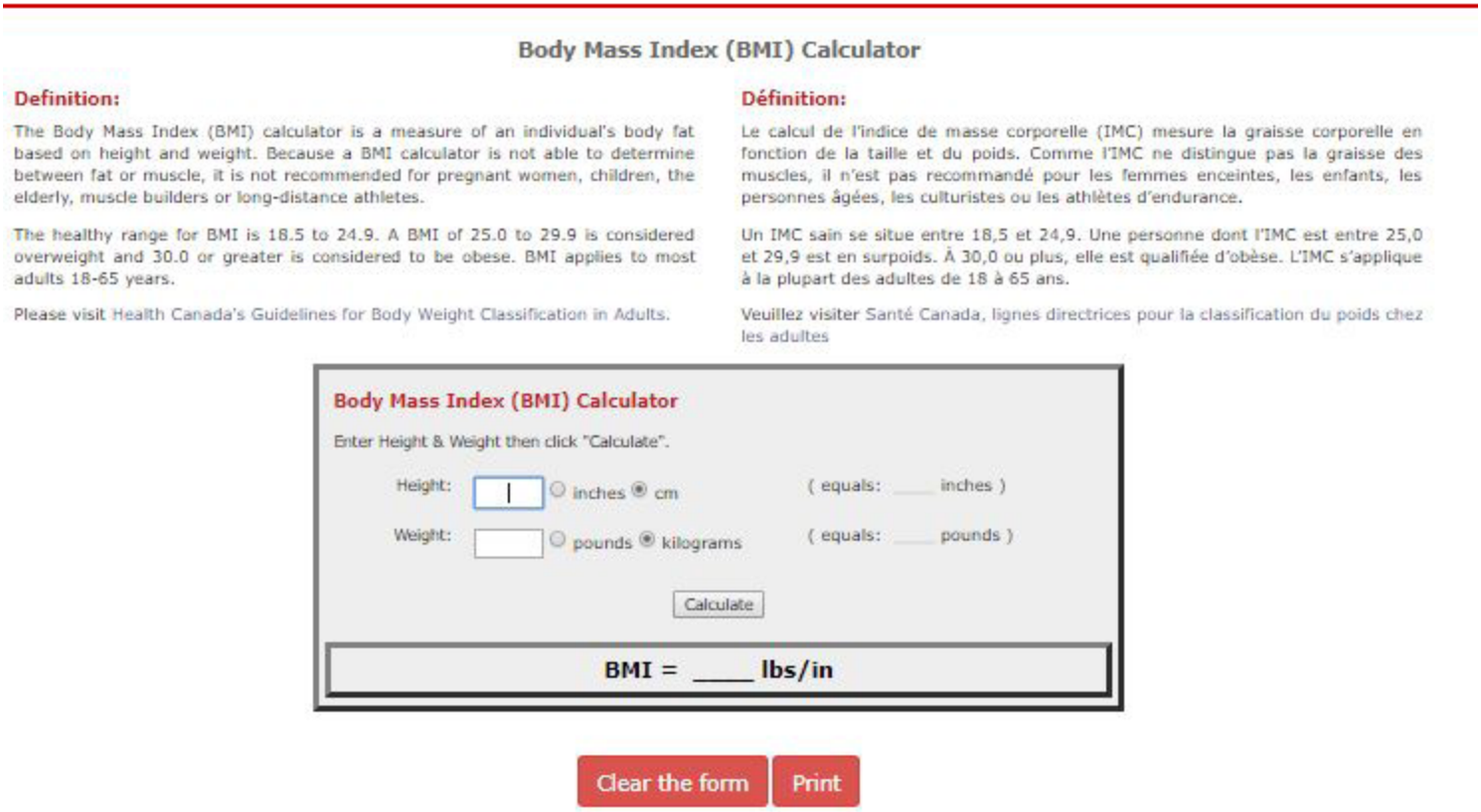
☐ Dose verified ☐ Dose adjusted to:	By (signature req'd):
☐ Confirmed with ordering physician	Date:
☐ Approved ☐ Denied	
Signature of Approving Physician or designate:	Date:

Please fax/send to :

Dosing Using Adjusted Body Weight

IG therapy has been used for many years to treat both primary immune deficiency patients and patients with several autoimmune disorders. While its usefulness in treatment cannot be denied, caregivers need to remember IG must be used with caution. One issue of particular concern is the proper dosage of product, especially in the obese patient.

According to Statistics Canada's published data for 2005, the rate of Canadians in the obese category (body mass index BMI higher than 30 kg/m^2) has almost doubled between 1978 and 2005, rising from 13.8% to 24.3% of the adult population, almost 1 in 4 individuals. In 2005, the number of obese Canadians 18 or older was 5.5 million; 36% of the adult population was considered overweight. We have provided a BMI calculator http://transfusionontario.org/en/download/bmi-dose-calculator/ to help determine your patients BMI.



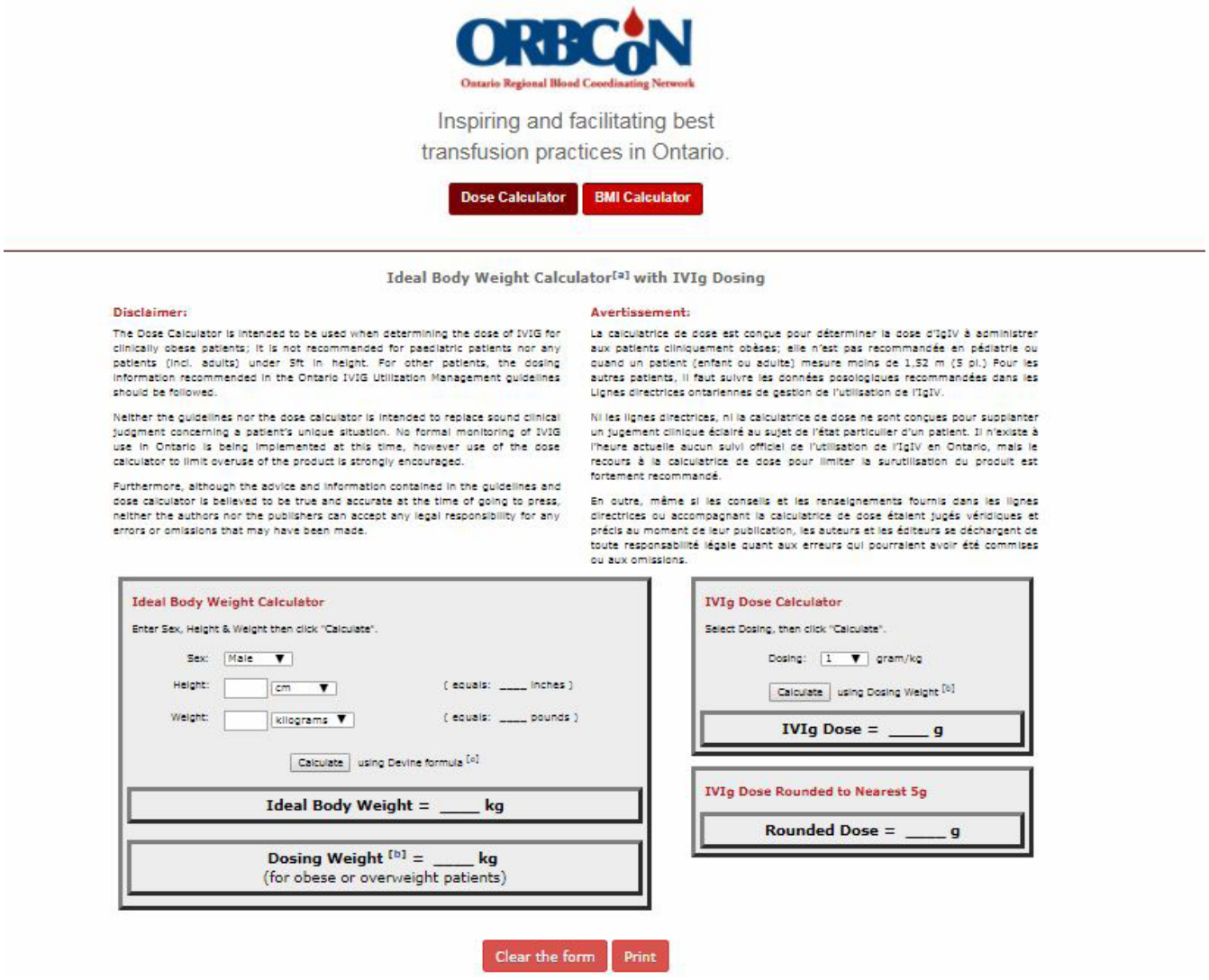
Dosing Using Adjusted Body Weight

The dose of IVIG administered varies depending on the clinical indication In the case of obese patients. The appropriate dosing regimen is unclear. There is some agreement in the literature that IVIG should be dosed using actual body weight in patients weighing up to 100 kg, with a BMI less than 30 kg/m 2. In contrast, obese patients should have IVIG dosing calculated using an adjusted body weight to account for the increase in volume of distribution (Vd) without accounting for the increase in fat.

Adverse reactions due to IVIG are substantially more likely to happen when a high dose of the product is infused Adverse reactions are summarized in the Adverse Reactions Chart for IVIG Infusion. http://transfusionontario.org/en/download/ontario-ivig-infusion-guide-adverse-reaction-chart/.

There are jurisdictions in Canada, the United States and abroad where the use of a dose calculator is either in place and recommended, or is in the works for future implementation.

See "Ontario IVIG Strategy Update Nov 2015" for the policy statement on use of a mechanism to adjust doses for obese patients. A link to a Dose Calculator tool is available on the Transfusion Ontario website: http://transfusionontario.org/en/download/bmi-dose-calculator/.



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Relevant Sources of Information

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IVIG (Intravenous Immune Globulin) Infusion Guide for Ontario

Purpose

To provide health care practitioners involved in the infusion of IVIG with best practice information. This document can be incorporated into institution specific policies and procedures.

This guide does not apply to Subcutaneous Infusion of Immune Globulin.

General Principles

- **Refer** to institution specific policies
- **Use** the Adjusted Body Weight Dosing Calculator where appropriate for calculating dosage for adult patients. http://www.transfusionontario.org/dose
    - At least every 6 months
    - If significant weight change reported by patient
- **Round** dose to the nearest vial size (e.g. 2.5 or 5g to ensure adequate therapy and efficient use of product).
- **Avoid** infusing different brands at a single visit/infusion course. Maintain chronically infused patients on the same IVIG brand when possible.
- **Use aseptic technique** when handling IVIG.
- **Pooling** of product is generally not recommended due to risk of contamination and potential wastage. If required, pooling of the product should be performed in a laminar flow hood in the Transfusion Medicine Laboratory (TML) or Pharmacy.
    - Pooling is not required to prevent bubbling. Bubbling can be eliminated by bringing product to room temperature prior to infusion

Pre-Infusion

- **Verify** that there is an order and the clinical indication is documented.
- **Verify** that informed consent for transfusion has been obtained.
- **Identify** patients at increased risk for:
    - TACO (Transfusion Associated Circulatory Overload) – neonates, elderly, hypertension, cardiac or renal dysfunction
    - Hemolysis - blood group A, B or AB; more common with high dose treatment
    - Thromboembolic events – obesity, elderly, hypertension, history of vascular disease or thrombotic episodes or disorders, hyperviscosity syndrome, decreased mobility, severe dehydration, diabetes, presence of indwelling lines (central venous access devices)
    - Aseptic Meningitis - history of migraines
    - Anaphylaxis – patients known to have anti-IgA antibodies
- **Review** history of previous reactions to IVIG or other blood components.
- **Assess** patient's clinical status on day of infusion and document relevant changes since previous infusion.
- **Record** known allergies, medications, and weight if indicated.
- **Document** baseline vital signs.
- **Determine** whether any pre-infusion blood work is required
    - blood group before first infusion
    - CBC at prescribed intervals
    - liver and renal function tests if indicated
    - platelet count for ITP patients
    - plasma IgG levels for immunodeficient patients at prescribed intervals

Infusion

Preparing Infusion

Prime line with normal saline or 5% dextrose (refer to package insert/monograph). Use standard vented IV tubing – no filter is required. Minimize bubbling by allowing product to come to room temperature and avoid shaking.

To ensure proper venting of IVIG bottle:

- Close roller clamp on IV set
- Place bottle on a flat surface and spike at a 90° angle through the center circle of the stopper
- Invert and hang bottle on IV pole
- Squeeze drip chamber to ½ full
- Open vent on drip chamber – this allows air to enter the bottle. IVIG will not flow if not properly vented
- **Important:** Close vent prior to spiking the next bottle, then hang bottle and open vent.

Starting Infusion

- **Set** initial infusion rate. An infusion pump is recommended to set precise infusion rates and detect air in the line when the IVIG bottle is empty thereby providing added safety.

Initial rate: A slow infusion rate (e .g. 0.5 mL/kg/hr) is recommended for the first 30 minutes

↓

Check vital signs

↓

Rate increases: as per institutional policy and patient tolerance

↓

Repeat vital signs at required intervals.
(e.g. when increasing rate)

↓

Maximum rate: as per institutional policy (e.g. 4mL/kg/hr)
CAUTION: Manufacturer's monographs may allow for faster rates.
These high infusion rates only apply to patients who previously tolerated this IVIG brand and have no preexisting risk factors (see list in pre-infusion section) or history of adverse reactions.

- **Monitor** patient for signs of adverse reactions. If an adverse reaction is suspected STOP infusion, maintain IV access, record vital signs, notify patient's physician, and report to TML or Pharmacy (refer to Adverse Reaction Chart).

Post Infusion

- **Complete** documentation including dose, lot numbers, and brand if known.
- **Report** and return to TML or Pharmacy any unused or defective vials including any vials associated with serious adverse reactions.
- **Educate** patients by providing them with a fact sheet including post- infusion adverse reactions instructions (refer to IVIG Facts for Outpatients).

Adverse Reaction Chart for IVIG Infusion

STOP infusion and notify patient's physician if:

- Change in systolic or diastolic blood pressure of 20 percent or more.
- Temperature 38°C or more and increased by at least 1°C from baseline
- Appearance of flushing, rigors (shivering), urticaria, itching, wheezing, tightness in chest, abdominal cramps, headache, nausea/vomiting or red urine.

Report all suspected reactions to TML or Pharmacy.

Signs and Symptoms	Severity	Frequency	Reaction Type	Actions
Headache (during or 1-3 days post- infusion)	Mild	Common	IVIG headache	**Stop IVIG. Consult Physician.** The infusion may be restarted at a reduced rate. Recurrent reactions may require appropriate premedication and/or a change in IVIG product. **Report to TML/Pharmacy.**
Low grade fever, flushing, rigors, chills	Mild	Occasional	Febrile Non Hemolytic Reaction	**Stop IVIG. Consult Physician.** Give medications as ordered. If symptoms are mild, infusion may be restarted at a reduced rate as per physician's order. Recurrent reactions require appropriate premedication and/ or a change in IVIG product. **Report to TML/Pharmacy.**
Urticaria, rash, itchiness, flushing, abdominal pain, nausea, and vomiting	Mild	Occasional	Minor Allergic	**Stop IVIG. Consult Physician.** Give medications as ordered. If symptoms are mild, infusion may be restarted as per physician's order. Recurrent reactions require appropriate premedication and/ or a change in IVIG product. **Report to TML/Pharmacy.**
Dyspnea, itchiness, urticaria, facial and/or tongue swelling, chest tightness, airway edema, hypotension, tachycardia, nausea/ vomiting, and anxiety	Moderate to Severe	Rare	Anaphylaxis/ Anaphylactoid	**Stop IVIG. Consult Physician.** May require epinephrine promptly. Reaction can be caused by an allergen to which the patient has a significant allergy. Testing for anti-IgA antibodies should be done following an anaphylactic reaction. **Report to TML/Pharmacy.**
Dyspnea, hypertension, orthopnea, cyanosis, cough tachycardia, increased jugular venous pressure	Mild to Severe	Occasional	Transfusion Associated Circulatory Overload (TACO)	**Stop IVIG. Consult Physician.** Give medications as ordered (e.g. diuretic). Slow infusion rate for subsequent infusions. **Report to TML/Pharmacy.**
Fever, back pain, dyspnea changes in urine colour (red/brown urine), jaundice, extreme fatigue, feeling faint	Mild to Severe	Occasional	Acute (less than 24hr) or Delayed (greater than 24hr) Hemolysis*	**Stop IVIG. Consult Physician.** Do not restart. Usually due to anti-A or anti- B antibodies in IVIG directed against a patient whose blood group is A, B, or AB. **Report to TML/Pharmacy.**

*Hemolysis is defined as:

A drop in hemoglobin of at least 10g/L
a positive direct antiglobulin test (DAT)
AND
at least two of the following:
increased reticulocyte count
increased lactate dehydrogenase
low haptoglobin
hyperbilirubinemia
hemoglobinemia
hemoglobinuria

Adverse Reaction Chart for IVIG Infusion

Severe and incapacitating headache with nuchal rigidity, drowsiness, fever, lethargy, photophobia, painful eye movements, nausea, vomiting, diarrhea, pharyngitis, deterioration of mental status	Severe	Rare	Aseptic Meningitis	**Stop IVIG. Consult Physician.** Do not restart. Usually resolves spontaneously in 1-2 days. **Report to TML/Pharmacy.**
Peripheral edema, periorbital edema, urination changes, increased serum creatinine, hypertension, back pain, flank pain, blood in urine	Severe	Rare Usually seen with products containing sucrose (none currently licensed)	Acute Renal Failure	**Stop IVIG. Consult Physician.** Predisposing factors: age>65, diabetes mellitus, preexisting renal insufficiency. **Report to TML/Pharmacy.**
Symptoms related to myocardial infarction, transient ischemic attack, stroke, deep vein thrombosis	Severe	Rare	Thromboembolic events	**Stop IVIG. Consult Physician.** Possibly related to increased viscosity and patient comorbidities. **Report to TML/Pharmacy.**
Symptoms of new viral or prion infection (variable) and presenting weeks following infusion	Severe	No reported cases of HIV or HBV. No reported HCV since 1995 Prion (vCJD) transmission theoretical risk	Transfusion Transmitted Infections	**Report any new infections suspected to be due to the blood product to TML/ Pharmacy.**

References-Sources of Information for the IVIG (Intravenous Immune Globulin) Infusion Guide for Ontario

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Acknowledgements

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IVIG *Facts* FOR OUTPATIENTS

What is IVIG?

Intravenous Immune Globulin (IVIG) is a blood product that contains antibodies in a concentrated form. It is made from plasma collected from human blood donors. There are several different brands of IVIG in Canada and they are all similar.

Why am I getting it? What does it do?

IVIG is used to replace antibodies in patients that have lower than normal levels (e.g. Primary Immunodeficiency). These antibodies help to fight infections.

It can also be used to treat other conditions, some in which the body attacks its own tissues or organs (e.g. autoimmune disease).

Ask your doctor to explain your individual treatment with IVIG.

You will be asked to sign a consent for blood transfusion as IVIG is made from blood plasma.

Risks

IVIG is considered to be a safe blood product with a low risk of transmitting disease.

Blood donors are carefully tested before they donate, and during manufacturing IVIG is treated to destroy the viruses that cause HIV, Hepatitis B and Hepatitis C.

How is it given?

Your nurse will start an intravenous (IV) line.

IVIG is given through a vein in your arm or hand. It is a clear liquid that usually comes in glass bottles and is given slowly over several hours.

Your nurse will check your vital signs (blood pressure, temperature and pulse) before and during the infusion.

Side effects

Side effects from IVIG usually occur during or up to 24 hours following infusion and tend to be mild and short lived.

Patients who are well hydrated before infusion seem to have fewer side effects.

5-10% of patients experience minor side effects related to the rate of transfusion, these can often be reduced by slowing the rate of infusion and giving medications such as acetaminophen (e.g. Tylenol®) or an antihistamine (e.g. Benadryl®).

Seek immediate, emergency medical attention if you experience:

- Severe headache, eye pain, extreme drowsiness
- Facial and/or tongue swelling
- Difficulty breathing, chest tightness
- Changes in urine colour (red urine, dark coloured urine)
- Intense back pain that is new
- Feeling faint or severe fatigue

It is important to report any of these symptoms to your doctor or nurse.

If symptoms happen after you have returned home your records need to be updated, therefore at your earliest convenience please notify the clinic of any side effects you might experience at home.

Please contact:

Out of Ontario Administration of IVIG

In rare circumstances, it may be necessary for patients to take IVIG dispensed in Ontario to be infused outside of the province, and in many cases outside of Canada. Patients working outside of Ontario for periods of time, attending school or vacationing may all require this service.

If Ontario patients are eligible for provincial health insurance benefits during their travel period, then Ontario hospitals may provide IVIG for this time period when requested by the treating physician or health care provider.

Instructions and examples of helpful documents are provided in this section of the IG Toolkit for patients and physicians involved with the administration of IVIG outside of Ontario.

Instructions for Requests for Intravenous Immune Globulin (IVIG) for Infusion out of Province or out of Country

Occasionally, requests are received from patients currently receiving IVIG therapy to obtain sufficient product to take with them if they are traveling out of province or out of the country for extended periods of time. These requests are rare according to an ORBCoN survey done in 2016 (5 of 53 hospitals responded they had received a request in the past 5 years). In order to provide a consistent approach to these requests across Ontario, information is provided within this toolkit.

In general, the following should be suggested/considered:

1. Encourage the patient's physician to consider transitioning the patient to SCIG if feasible.
2. If the patient is traveling outside of the province but within Canada, request that the patient's physician to arrange for a treating physician in the other province so that the patient can receive their infusion treatment at a hospital. There are agreements in place between the Ministries of Health in each province to cover such requests to ensure patient care is not interrupted.
3. If the patient is traveling outside of the country and their medical insurance will not cover this treatment during this time, it is possible to issue IVIG for up to six months as long as the patient is still eligible to be covered by Ontario Health Insurance.
4. It is important that the processes for travel and infusion of this product follow the same elements of a home infusion program for safe issue/storage/transport of the product, documentation of the disposition of the product, reporting of any adverse reaction to the product. Instructions for home infusion can be found on ORBCoN's website at: http://transfusionontario.org/en/documents/?cat=home-infusion-toolkit.

Policy and Procedure Considerations for Patients Traveling with IVIG Outside of Ontario

The Ontario Regional Blood Coordinating Network (ORBCoN) conducted a survey to determine the frequency of these types of requests in Canada and they are rare. Therefore, a hospital may want to seek the authority of the transfusion medical director or manager for each request, but this should be defined in each individual hospital's policies and procedures.

When developing these documents, some points to consider are:

1. Preparation of an IG inventory list: itemize the IG products eligible for transportation outside of Ontario and the maximum amount permitted per out of Ontario infusion occurrence. While constructing this list, hospital transfusion services may also want to consider what other blood and blood products may need to be included. For example: RhIG, SCIG and C1 esterase inhibitor (see Home Infusion Toolkit also).
2. Patients: How will the patient be trained on transporting and storing the product? What record keeping needs to be done by the patient? What records, if any, are submitted to the provider hospital in Ontario? How will the patient handle broken, outdated or inappropriately stored product? What are the disposal requirements should this occur? Does the patient know what to do if an adverse event occurs during or after infusion? Which health care provider(s) will receive the adverse event information?
3. Issuing and disposition: How does the Ontario hospital issue the product? Are there any special comments to be included? Is the default entry "presumed transfused"? How are the infusion records the patient returns reconciled? Are these infusion records returned to the Ontario physician caring for this patient?
4. Physician communication: Arrangements between the treating and external physicians are the responsibility of the physicians, although some tools are provided in this toolkit to facilitate this communication.
5. Additional costs: Patients are responsible for extra costs incurred including ancillary supplies and any costs for infusion procedures not covered by Ontario or private health insurance.

Patient Participation Agreement Form

Physician Information

Patient Information

PARTICIPATION AGREEMENT - I will -

- ☐ Obtain, transport and store IVIG according to instructions
- ☐ Arrange to carry out the infusions as instructed
- ☐ Keep accurate infusion notes to provide to my Ontario physician
- ☐ Report to the appropriate health care provider any possible adverse reactions to IVIG and seek treatment if necessary
- ☐ Be responsible for any expenses incurred by out of Ontario infusion of IVIG
- ☐ Ensure these parameters are met, or I will not receive any further IVIG

I acknowledge that IVIG for out of Ontario infusion can be withdrawn at any time if I fail to adhere to the above or to any other requirements, or if unmanageable complications of IVIG infusion therapy occur.

X _____
Signature of patient

_____
Date & time of signature

If applicable:

_____
Signature of Caregiver

_____
Date

_____
Print Caregiver's Name

Caregiver: Retain a copy for your records and give one to the patient

Letter from treating (home) physician to travel (remote) physician/health care provider for IVIG administration outside of Ontario

[insert address or letterhead if desired]

Date:

Dear Health Care Provider:

Re: Patient's name, DOB, etc.

This patient has a medical condition requiring regular IV infusions of immunoglobulins (IG) which are manufactured from human blood. He/she will be outside of Ontario for an extended period of time and requires medical assistance in accessing this necessary medical treatment.

To maintain sufficient levels of immunoglobulins, this patient requires ___g of IVIG to be infused every ___ weeks. The patient will be given a sufficient supply of this product for ___ weeks and he/she will maintain it at a controlled temperature. Coordination and assistance will be required in infusing this product either in his/her home environment or in a medical facility or clinic. Ancillary supplies will be needed for each infusion.

This patient will need to be monitored for any adverse events from these infusions and will require an emergency contact (e.g. the local emergency department of a hospital) in the event of any severe reactions.

Please feel free to contact me at _____ with any questions. Thank you for your assistance in caring for this patient.

Sincerely,

IVIG Travel Letter

Re: Required medical supplies for _____

Date of birth: _____

To whom it may concern:

_____ has a chronic medical condition which is treated by injections of replacement immunoglobulins in the form of a medication called intravenous immune globulin (IVIG) which is manufactured from human blood.

To maintain sufficient levels of immunoglobulins and avoid significant impacts to their health, patients need to take this medication and the equipment required to administer it with them when traveling. This product must be kept at a controlled temperature and the following items will need to be carried onto the airplane (or other mode of travel) by the above named individual:

- IVIG vials
- Possibly administrative supplies like needles, administration sets, alcohol swabs, gauze and tape
- Medication to manage side-effects (non-drowsy antihistamine and over the counter pain medication)
- A container and possible gel packs (required to keep IVIG and other medications at the correct temperature during travel)

Yours sincerely,

Treating physician

If additional information is required, please contact Dr. _____ at (_____) _ _ _ - _ _ _ _.

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