ORBCoN
Ontario Regional Blood Coordinating Network

Inspiring and facilitating best transfusion practices in Ontario.

Welcome

ORBCoN Ontario Regional Blood Coordinating Network

TRANSFUSIONISTS TALK

bloody easy

TRANSFUSION MADE BLOODY EASY

September 18, 2024

9:30 to 10:10 a.m. (EDT) and 2:30 to 3:10 p.m. (EDT)

[As needed, optional, additional 15 minutes for questions & discussion]

Intravenous Immune Globulin (IVIG): Transfusionists questions answered …

Donna Berta RN, BScN, Clinical Project Coordinator – Nursing, ORBCoN

Land Acknowledgement

As we gather, we begin by acknowledging that this virtual event is hosted from the traditional territories of the Mississauga and Haudenosaunee nations, and within the lands protected by the “Dish with One Spoon” wampum agreement.

Please acknowledge and reflect on the land where you are joining.

Disclosure

"*This video conferenced event will be recorded, archived, and excerpts may be used for educational purposes. By participating, you indicate your consent to recording, archiving and use for educational purposes*."

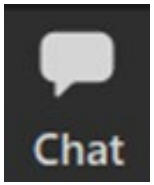
Presentation Information

This presentation is being recorded.
As of September 30, 2024, slides & recording will be posted on www.transfusionontario.org.

Click Resources tab,
Select Presentation Library, and
Scroll to Transfusionists Talk.

Questions for Speaker

During the presentation, enter comments & questions via the Zoom **Chat** function.



Following the presentation, the speaker will be available for an optional, additional 15 minutes to discuss any further questions.

If there are more questions than time permits, answers will be posted with the event recording at www.transfusionontario.org

Practice Polling Question

What is your current role?

a) Front Line Nurse (RN, RPN).
b) Nursing Educator.
c) Transfusion Medicine Lab Technologist.
d) Other.

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Intravenous Immune Globulin (IVIG): Transfusionists questions answered …

Donna Berta RN, BScN
Clinical Project Coordinator – Nursing
Ontario Regional Blood Coordinating Network (ORBCoN)

September 18, 2024

Speaker Disclosure

- No commercial product conflicts of interest to declare.

- Transfusion Transmitted Injuries Surveillance System, member Education Committee.
- Canadian Society of Transfusion Medicine, member Standards Committee.

- Some information is shared for your interest & reference.
- All patient case information is fictitious, fabricated for this learning opportunity.

Transfusion Knowledge Question 1 - Pre

In Ontario (adult, neonatal, pediatric patients), IVIG is indicated when:

a) The patient's drug benefits plan covers IVIG costs.
b) The patient must be immune globulin G (IgG) deficient, serum IgG is less than 6 g/L.
c) The patient's diagnosis is listed in the Ontario Immune Globulin (IG) Utilization Management Guidelines or the IVIG order is approved by the Medical Director of the Transfusion Medicine Laboratory (TML).
d) The patient's ABO/Rh(D) blood group is group O, Rh positive.

Transfusion Knowledge Question 2 - Pre

In Ontario (adult, neonatal, pediatric patients), the IVIG dose is calculated based on:

a) The patient's ABO blood group.
b) The brand of IVIG being administered.
c) The patient's abdominal circumference.
d) The patient's weight and height.

Intravenous Immune Globulin (IVIG): Transfusionists questions answered …

Learning Objectives,
by engaging in this learning, participants will be able to:

1. Apply the responses to transfusionists IVIG questions to their practice.
2. Recognize and understand the clinical indications for IVIG treatment.
3. Define nursing actions to safely administer IVIG.

Outline:

- What is IVIG & Mechanisms of Action
- Supply & Costs; Brands & Suppliers
- Indications & Dose Calculator
- Administration/Infusion & Infusion Rate
- Cautions/Side-Effects/Adverse Reactions
- Specific Patient Populations

Patient Case – Question 1

Barney, a 56-year-old otherwise healthy male, has experienced progressive right-hand weakness, limiting his activities of daily living for the past 18 months. He has been referred to neurology at a tertiary care centre. IVIG treatment might be considered.

Select the correct statement(s) about IVIG (select all applicable).

a) IVIG is a blood product, informed consent is required.
b) Special access for IVIG must be approved by Canadian Blood Services (CBS).
c) If IVIG is given, the antibodies will also protect Barney from developing pneumonia for 1 year.
d) If IVIG is given, the brand required for neurology diagnoses is Privigen.

What is IVIG?

- IV solution containing antibodies (human immunoglobulin proteins) synthesized by B lymphocytes. Antibodies are predominantly IgG, with trace amounts of IgA and IgM.
- Manufactured from plasma (pooled from several thousand donors). It is a blood product; informed consent is required.
- Manufacturing IVIG requires about 9 months of time.
- In all IVIG brands, the amount of IgG is similar to human plasma.
- IVIG brands are **equal in clinical effectiveness** (used interchangeably) but are not pharmaceutically equivalent.
- IVIG brands differ in specific antigen titres, preparation methods, viral inactivation steps (e.g., caprylate, low pH, chromatography, solvent detergent treatment), stabilizing agents, osmolality, & IgA content.

IVIG Mechanisms of Action

- Immunoglobulin (IG) Deficiency: primary (congenital), secondary (acquired)
  - Provides additional antibodies the body is not producing or that are not functioning, to fight infection.
  - Antibodies are capable of both opsonization & neutralization of pathogens & toxins.
- Immunomodulatory & Anti-inflammatory Disorders
  - Unclear; more than 1 mechanism may predominate in different diagnoses.
  - How quickly “IVIG works” is also variable in different diagnoses.
  - Proposed mechanisms include
    - inhibiting certain cellular maturation steps
    - blocking certain receptors (Fc-receptor blockade on macrophages)
    - altering regulatory T cells with effects on remyelination
    - supressing cytokine production
    - affecting the complement system
    - supplying antibodies that neutralize microbial toxins

IVIG Supply & Costs

- Canadian Blood Services (CBS) is the supplier/manager of blood (components & plasma protein products e.g., IVIG) for all provinces & territories (P/T); except Quebec - Héma-Québec.
- One P/T blood representative within each P/T's Ministry of Health; responsible for communications between CBS & their P/T.
- Publicly funded system (our tax dollars).
- CBS sends Canadian source plasma to third-party fractionators (currently accounts for about 17% of IVIG used).
- CBS purchases additional products from biopharmaceutical companies.

- Multiple IVIG suppliers to ensure adequate supply.

- 1 g IVIG costs about $ 60 (depends on the US dollar exchange rate).
- FY 2021-22 Canada used 6,809 kg of IVIG = 450 million dollars (excluding Quebec).

IVIG Brands/Suppliers

- To ensure adequate supply, CBS purchases multiple IVIG brands/suppliers (based on share split/contracts).

Brand	Supplier	Vial Sizes
Gammagard Liquid 10%	Takeda	2.5 g, 5 g, 10 g, 20 g, 30 g
Gammagard S/D (powder) (lowest IgA content, generally for patients with anti-IgA antibodies and IgA deficiency).	Takeda	5 g
Gamunex 10%	Grifols	2.5 g, 5 g, 10 g, 20 g
IGIVnex 10%	Grifols	20 g
Privigen 10%	CSL Behring	2.5 g, 5 g, 10 g, 20 g, 40 g
Octagam 10% and Panzyga 10% (Octapharma) are no longer being purchased by CBS. Residual inventory may still be available at some hospitals.		

- Patients may be required to transition another IVIG brand based on share split targets. TMLs receive monthly share split reports.
- **DO NOT** infuse different IVIG brands in a single infusion/dose.
  Exception: Gamunex & IGIVnex may be infused in a single infusion (undergo same manufacturing processes).

Patient Case – Question 2

Barney, a 56-year-old otherwise healthy male, has experienced progressive right-hand weakness, limiting his activities of daily living for the past 18 months.
Neurology has diagnosed multifocal motor neuropathy (MMN).

This is an appropriate indication for IVIG.

a) True
b) False

IVIG Indications

- For IVIG stewardship, to ensure appropriate utilization of IVIG, the Ontario Ministry of Health endorses an evidence-based framework incorporating specific prerequisites and an authorization process.
- Your hospital TML's approved IVIG indication list is likely based on Ontario IG Utilization Management Guidelines. The guidelines includes Hematology, Neurology, Dermatology, Rheumatology, Infectious Diseases, Immunology, and Solid Organ Transplant specialities.
- Example:

Recommended Neurology Indications

Medical Condition	Recommendations	Dose/Frequency of Administration
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.

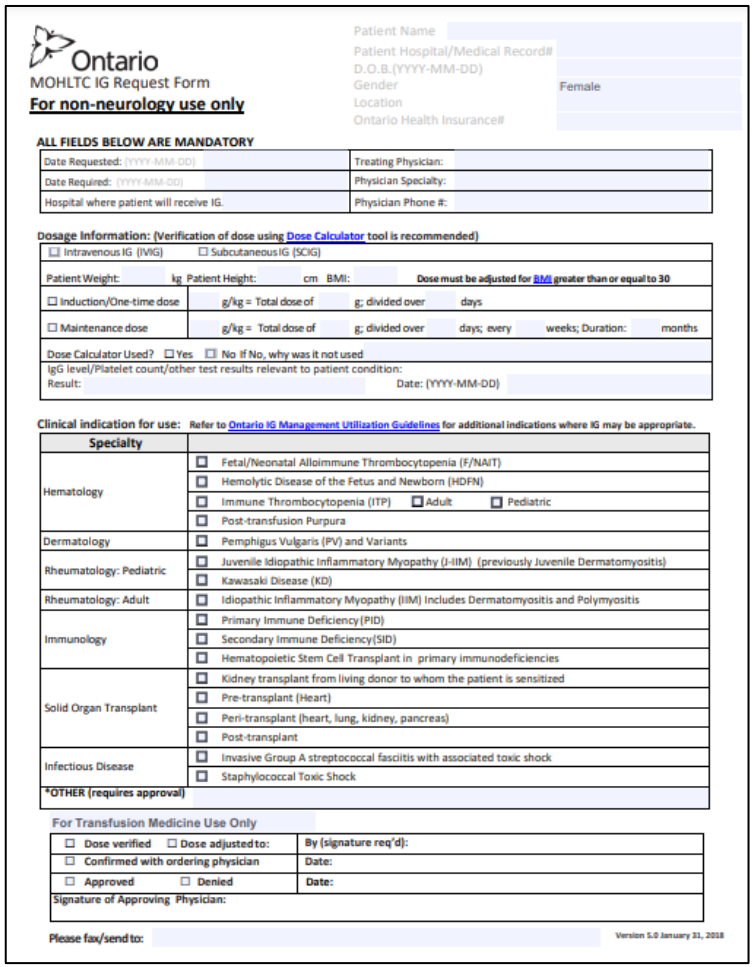
- The Ontario IG guideline (version 4, 2018) is currently being reviewed and updated.

IVIG Indications (2)

In Ontario, IVIG requests must be submitted on an IG Request Form prescribed by the Ministry of Health.

Hospitals may have adapted these forms into their computerized order entry system (CPOE).

Non-Neurology Specialities form



Ontario
MOHLTC IG Request Form
For non-neurology use only

Patient Name
Patient Hospital/Medical Record#
D.O.B.(YYYY-MM-DD)
Gender Female
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: (YYYY-MM-DD)

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

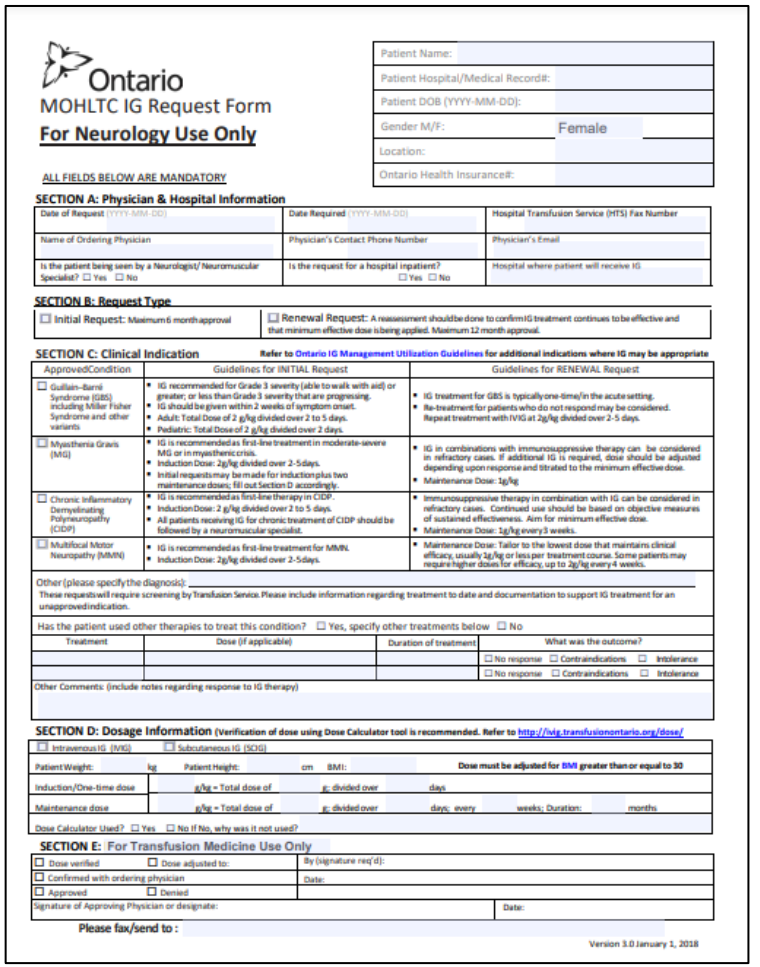
Specialty	
Hematology	☐ Fetal/Neonatal Alloimmune Thrombocytopenia (F/NAIT)
	☐ Hemolytic Disease of the Fetus and Newborn (HDFN)
	☐ Immune Thrombocytopenia (ITP) ☐ Adult ☐ Pediatric
	☐ Post-transfusion Purpura
Dermatology	☐ Pemphigus Vulgaris (PV) and Variants
Rheumatology: Pediatric	☐ Juvenile Idiopathic 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: Version 5.0 January 31, 2018

Neurology Speciality form



Ontario
MOHLTC IG Request Form
For Neurology Use Only

Patient Name:
Patient Hospital/Medical Record#:
Patient DOB (YYYY-MM-DD):
Gender M/F: Female
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 2-5days. • 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 2-5days.	• 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 :

Version 3.0 January 1, 2018

IVIG Indications (3)

- An additional resource is the Prairie Collaborative guidelines (2022). Criteria for the Clinical Use of Immune Globulin
- Example:

✓ Multifocal motor neuropathy (MMN)	
Do Recommendation	IVIG is recommended as first-line treatment. Diagnosis should be made by a neuromuscular specialist with specific electrodiagnostic expertise.
Dose	Induction: 2 g/kg adjusted body weight divided over 2 to 5 days. Maintenance: Maximum 2 g/kg adjusted body weight in a 4-week period. Some patients may require a higher maintenance dose. Once the patient's condition has stabilized, consider titrating the dose and/or the treatment interval to the lowest dose necessary to maintain clinical effectiveness.
Review Criteria	IVIG should be used for no longer than 6 months before determining whether the patient has responded. If there is no benefit after this treatment, IVIG therapy should be abandoned. Review by a neurologist is required no later than 6 months of treatment and annually thereafter. Documentation of clinical efficacy is necessary for continuation of IVIG therapy. For patients in remission on maintenance therapy, a trial of weaning leading to cessation should be considered.

Patient Case – Question 3

Barney, a 56-year-old otherwise healthy male, has experienced progressive right-hand weakness, limiting his activities of daily living for the past 18 months. Neurology has diagnosed multifocal motor neuropathy (MMN).
IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.
Barney's weight is 100 kg, and height is 175 cm.

Select the correct number of grams of IVIG to be administered to Barney on day 1 & again on day 2:

a) 82.5 g, as per dosing using adjusted body weight

b) 100 g

c) 50 g

d) 175 g

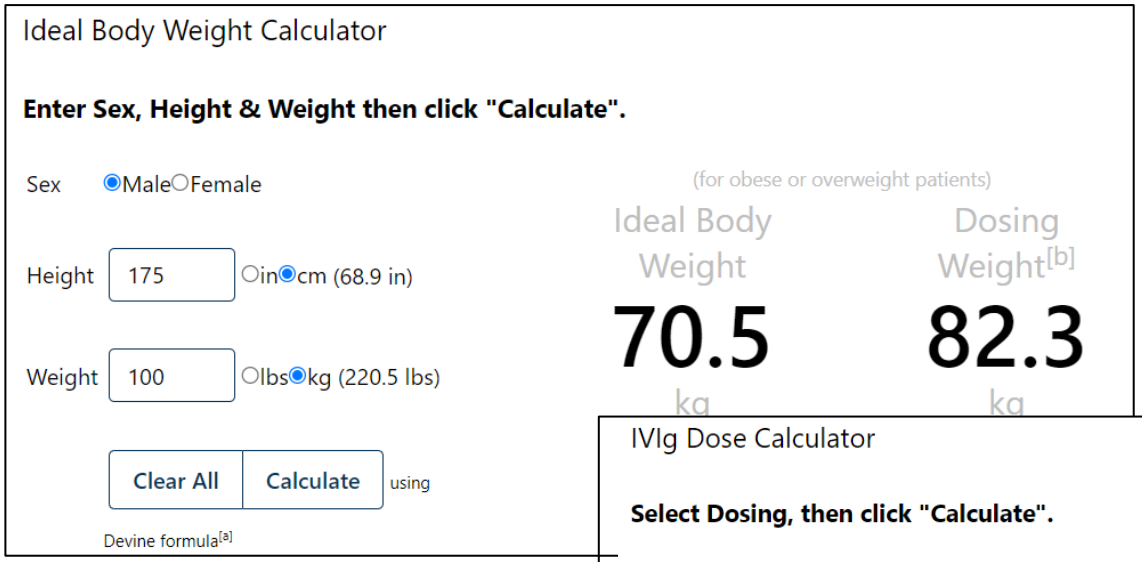
IVIG Dose Calculator

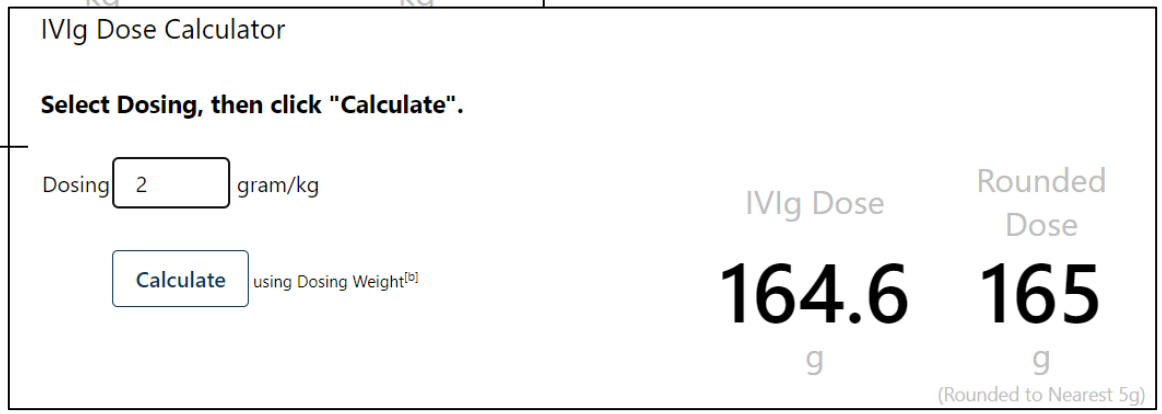
- Indication guidelines includes dose (g/kg) & frequency.
- Adult patients: height 152.4 cm or greater, BMI of 30 kg/m^2 or greater; use ideal body weight calculation & IVIG dose calculator (*to minimize potential adverse effects of high dose IVIG & limit overuse of IVIG*).
- Neonatal & Pediatric (Ontario – under 18 years) patients: IVIG dose calculator not recommended, use actual weight.
- Some hospital TML's policy: for all adult patients & pediatric patients height 152.4 cm or greater, use adjusted body weight computation for IVIG dose calculation (dosing weight is calculated based on the patient's actual weight & ideal body weight; if actual weight is less than ideal body weight, then dosing weight = actual weight).
- Formulae for calculations stem from Pharmacy/Medication practices.

Note: chronic disease IVIG indications when the patient has stabilized, consider titrating dose and/or treatment interval to the lowest dose and/or greatest interval needed to provide clinical effectiveness.

IVIG: Dose Calculator (2)

- IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.
  Barney is male, weight 100 kg, and height 175 cm.
- Ontario IG Dose Calculator





IVIG: Administration/Infusion (1)

Transfusionist must ensure:

- Indication for IVIG (patient diagnosis, signs & symptoms, laboratory test results) & dose align with guidelines.
- Knowledge of product specific administration details.

Order must include:

- Patient's surname, first name & unique hospital identification number.
- Blood product name
- Amount, volume, dosage and/or concentration
- Date to be given
- Rate or duration of infusion, e.g., 150 mL/hour or over 2 hours (or per hospital standard protocol)
- Relevant medication orders, if any (premedication or diuretic)
- Sequence for transfusion of multiple components/products

IVIG: Administration/Infusion (2)

Informed Consent

- Required for IVIG infusion.
- Obtained by health care professional **prescribing** the blood product.
- Valid for current illness/course of treatment or hospital admission; for chronic conditions, some hospitals apply a timeframe for consent to be valid (e.g., 1 year) after which consent is revisited/re-obtained.

  Note: In emergency, life or health threatening situations, the prescriber may declare that infusion proceed without informed consent (extremely rare for IVIG infusion).

- Transfusionist role:
  - Confirm hospital policy/procedure has been fulfilled prior to infusion.
  - If informed consent has not been completed for a non-emergency infusion, do not administer, advise the prescriber.
  - Refer to ORBCoN's IVIG Infusion Guide and Adverse Reaction Chart for risks/cautions/side-effects/adverse reaction information
  - Advocate for patients; Facilitate the informed consent process.

IVIG: Administration/Infusion (3)

Group & Screen Testing

- Not required for IVIG infusion (pooled plasma from donors of diverse ABO blood groups).
- Helpful to have patient's ABO blood group & baseline Hb on record. (IVIG contains anti-A and anti-B antibodies; non-O blood group patients (ABO group A, B, AB) may develop hemolysis post IVIG, especially if high dose IVIG).

Preparing the Patient

- **Patient must be wearing a Patient Identification armband!**
- Education
  - What to expect during infusion (periodic assessments, vital signs).
  - Symptoms indicative of IVIG side-effects/reactions to watch for & report.
- History of previous IVIG infusions.
  - If so, brand received (if known) assess if side-effects/reactions/premedication. If indicated, follow up with prescriber and/or TML.
- Is patient at risk for TACO (Transfusion Associated Circulatory Overload)?

IVIG: Administration/Infusion (4)

TACO (Transfusion Associated Circulatory Overload)

- Leading cause of transfusion related deaths; **Prevention** is imperative!
- Occurs secondary to transfusion at a rapid rate and/or the specific patient's cardiac capacity is unable to tolerate transfusion volume.
- Signs: acute/worsening respiratory distress, decreased oxygen saturation, tachycardia, *increased* blood pressure, acute pulmonary edema.

TACO Risk Factors

- Advanced age
- History of heart failure
- History of myocardial infarction
- Left ventricular dysfunction
- Renal dysfunction
- Positive fluid balance

If risk, review with prescriber for prevention strategies

TACO Prevention Strategies

- Transfuse only 1 unit at a time
- Transfuse slowly over longer time period (maximum 4 hours, *from time each bottle is spiked*)
- **Pre-transfusion diuretic** (PO – 30 minutes prior; IV – just prior)
- TML to divide unit (if equipment available, then transfuse each part over maximum 4 hours)

Patient Case – Question 4

Neurology has diagnosed multifocal motor neuropathy (MMN). Barney's weight is 100 kg, and height is 175 cm.
IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.
Today is day 1 of IVIG treatment. TML issues Gamunex 82.5 g. (Bottle sizes issued: 2.5 g x1, 5 g x2, 10 g x1, 20 g x 3)

Select the appropriate action(s) for Barney's nurse (select all applicable):

a) Confirm Barney is wearing a Patient Identification armband.
b) Start a 16-gauge peripheral IV.
c) Prime blood tubing with a 170 - 260 micron filter with 5% dextrose in water (D5W).
d) Check the lot numbers on all the IVIG bottles with a co-worker.

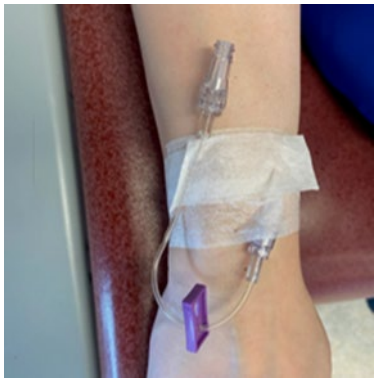
IVIG: Administration/Infusion (5)

Preparing the Equipment

- Dedicated IV line (peripheral or central), any gauge IV is adequate
- IV Fluid: 5% dextrose in water (D5W) or 0.9% sodium chloride (NaCl) (exception: Gammagard S/D – only D5W).
- Do not mix with any other medications. Do not dilute IVIG.
- Use an approved infusion pump to set infusion rate precisely & allows for greater patient mobility
- Set up IV tubing such that if the infusion must be stopped abruptly, then IV access can be maintained:
  - 0.9% sodium chloride flush syringes and an IV line with any IV solution are on hand, ready to infuse TKVO

  OR

  - D5W or 0.9% NaCl IV line is on hand, ready to infuse TKVO



IVIG: Administration/Infusion (6)

Preparing the Equipment

- Standard Vented IV Tubing
  - Allows filtered air to enter the bottle; in-line filter is not required (exception: Gammagard S/D – filter reconstituted product, included in package).
  - One vented tubing set can be used for each IVIG treatment/dose (maximum time 24 hours) or as per tubing manufacturer.
- To prevent/minimize bubbling of IVIG:
  - Allow the IVIG to come to room temperature.
  - Do not shake the IVIG (advise the person transporting the IVIG from TML of this).
  - Prior to spiking each bottle, close the roller clamp and ensure the drip chamber vent of the vented IV tubing set is also closed.
  - Place IVIG bottle on a flat surface, insert the spike of the vented IV tubing set at a 90° angle through the centre circle of the stopper.
  - Invert and hang the bottle on the IV pole, squeeze the drip chamber to ½ full, then open the drip chamber vent and roller clamp.

Patient Case – Question 5

Neurology has diagnosed multifocal motor neuropathy (MMN). Barney's weight is 100 kg, and height is 175 cm.
IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.
Today is day 1 of IVIG treatment. TML issues Gamunex 82.5 g.
(Bottle sizes issued: 2.5 g x1, 5 g x2, 10 g x1, 20 g x 3)
As you, Barney's nurse and a co-worker are checking lot numbers on all the IVIG bottles you notice one of the 5 g bottles has a different lot number & one of the 20 g bottles is not Gamunex but IVIGnex (also has a different lot number).

You should return all these IVIG bottles to TML & request all bottles of Gamunex with the identical lot number be issued.

a) True
b) False

IVIG: Administration/Infusion (7)

Checking IVIG

- Steps must be carried out in the physical presence of the patient.
- Validate IVIG received from TML matches order (bottle sizes = dose ordered).
- Patient must be wearing a patient identification armband.
- Patient identification information must remain attached to IVIG during infusion.

For safety, check following these 3 steps
Follow hospital policy; ideally check each IVIG bottle just prior to infusing it

1. Patient Identification: surname, first name, unique identification number
2. Lot number: Check lot number on TML label attached to the IVIG & manufacturer's label are an identical match. *Lot number check is for traceability in event of product recall. Bottles with differing lot numbers can be given in one IVIG treatment/dose.*

3a. Expiry: Infusion of each bottle must be completed **within 4 hours from time the bottle's seal was punctured**; otherwise discard any remainder.

3b. Visual Inspection: Bottle seal intact, product appears as clear or slightly opalescent solution that is colourless to pale yellow in colour.

Patient Case – Question 6

Neurology has diagnosed multifocal motor neuropathy (MMN). Barney's weight is 100 kg, and height is 175 cm.
IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.

Today, day 1 of IVIG treatment, TML issues Gamunex 82.5 g. (Bottle sizes issued: 2.5 g x1, 5 g x2, 10 g x1, 20 g x 3)

Select the appropriate rate for Barney's IVIG infusion:

a) Initial rate 50 mL/hr., increase to maximum 250 mL/hr.
b) As per the brand specific manufacturer's monograph recommendations.
c) Initial rate 50 mL/hr., increase to maximum 1000 mL/hr.
d) Initial rate 50 mL/hr., increase to maximum 500 mL/hr.

IVIG: Infusion Rate (1)

- All brands are equivalent in terms of clinical effectiveness but are not pharmaceutically equivalent.
- Each brand's monograph defines specific infusion starting rate, gradual rate increases, maximum rate for specific patient clinical factors, & recommended maximum rate. If well tolerated, the rate of infusion may gradually be increased to the recommended maximum.
- Rate calculation formula:

  Rate (mL/kg/hr) x Weight (kg) = Hourly infusion rate (mL/hr).
- Alternative (user friendly):

  ORBCoN's Infusion Guide and Adverse Events
  Refer to Appendix A: IVIG Brands Infusion Rate Tables

NOTE: For some patients tolerating chronic IVIG treatment, their prescriber may order a patient specific treatment plan, excluding some interval infusion rates and increased maximum infusion rate.

IVIG: Infusion Rate (2)

ORBCoN's Infusion Guide and Adverse Events Appendix A

*Gamunex® / *IGIVnex® Infusion Rate Table (mL/hr)																				
Infusion Rate Increments		**Patient weight in kg.**																		
		30	**35**	**40**	**45**	**50**	**55**	**60**	**65**	**70**	**75**	**80**	**85**	**90**	**95**	**100**	**105**	**110**	**115**	**120**	**125**
Starting Rate for first 30 minutes	0.6 mL/kg/hr	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75
Rate next 15 - 30 minutes	1.2 mL/kg/hr	36	42	48	54	60	66	72	78	84	90	96	102	108	114	120	126	132	138	144	150
Rate next 15 - 30 minutes	2.4 mL/kg/hr	72	84	96	108	120	132	144	156	168	180	192	204	216	228	240	252	264	276	288	300
Maximum Rate Remainder of Infusion Receiving IgG for the first time; or Had been receiving another IgG brand; or Have not received IgG in more than 8 weeks	4.8 mL/kg/hr	144	168	192	216	240	264	288	312	336	360	384	408	432	456	480	504	528	552	576	600
Maximum Rate Remainder of Infusion For patients judged to be at increased risk for developing renal dysfunction	4.8 mL/kg/hr	144	168	192	216	240	264	288	312	336	360	384	408	432	456	480	504	528	552	576	600
Maximum Rate Remainder of Infusion Following first infusion of this brand, next 3 consecutive infusions	7.2 mL/kg/hr	216	252	288	324	360	396	432	468	504	540	576	612	648	684	720	756	792	828	864	900
Maximum Rate Remainder of Infusion Per manufacturer's recommended maximum	8.4 mL/kg/hr	252	294	336	378	420	462	504	546	588	630	672	714	756	798	840	882	924	966	1008	1050
Gamunex® monograph IGIVnex® monograph		* Requires dedicated IV line; can be flushed with 5% dextrose in water (D5W) or 0.9 % sodium chloride (NaCl) Contains glycine (an amino acid) as stabilizer (does not contain sucrose)																		

IVIG Administration/Infusion (8)

Guidance

- Subsequent bottles, with the same or different lot numbers do not require returning to the starting infusion rate.
- Begin infusion with smallest bottle size, end with largest bottle size of those issued (to minimize wastage in the event of a reaction).

Patient Assessment & Vital Signs

- 30 minutes prior to starting infusion
- 15 minutes after start
- At each rate increase
- Then hourly until infusion completed
- If a reaction is suspected
- Inpatients: 1-hour post infusion
- Outpatients: 20-30 minutes post infusion, prior to discharge

Patient Case: Question 7

Neurology has diagnosed multifocal motor neuropathy (MMN). Barney's weight is 100 kg, and height is 175 cm.
IVIG ORDER: 2 g/kg, infuse over 2 days, rate per protocol.

To minimize possible IVIG side-effects/reactions (select all that apply):

a) Divide the infusion of high doses (greater than 1g/kg) over more than 1 day.
b) Administer with slow infusion rate, as feasible.
c) Pre-hydration (PO fluids several hours prior to & following or IV fluid).
d) All the above measures minimize possible side effects.

Cautions/Side-Effects/Adverse Reactions (1)

- **Always administer at the slowest infusion rate feasible.**
- IVIG has been associated with:
  - renal dysfunction, osmotic nephrosis, and acute renal failure.
  - thromboembolic events.

  Assess the patient for history, risk factors. If evident, use slow rate of infusion, ensure well hydrated & monitor closely.
- Hemolysis/hemolytic anemia have been reported. Perform baseline lab tests. Monitor patients for signs & symptoms of acute/delayed hemolysis.
  Acute: fever, dyspnea, hypotension, pain (back, IV site), tachycardia, urine - red/brown or tea coloured (during or up to 24 hours post-IVIG)
  Delayed: back pain, decreased hemoglobin, fever, fatigue - extreme/unexplained, jaundice, tachycardia, urine - red/brown or tea coloured (24 hours to 10 days post-IVIG)
- IVIG may affect the efficacy of live attenuated virus vaccines (i.e., measles, mumps, rubella, varicella/chickenpox) for 6 -12 weeks.
- IVIG is manufactured from human plasma. Measures to decrease the risk of transmission of infectious pathogens are followed (donor testing), however potential risk of transmission remains.

Cautions/Side-Effects/Adverse Reactions (2)

- If side effects/adverse reactions are suspected, follow the usual blood steps (stop infusion, maintain IV access, check vital signs, notify prescriber, provide care as ordered, report all to TML, even if minor)

- Minor Side effects/adverse reactions may be more likely
  - if receiving IVIG for the first time
  - when changing to another IVIG brand
  - if prolonged time (more than 8 weeks) since the previous infusion
  - with high doses
  - with rapid infusion rates
  - if the patient is not well hydrated.

- Canadian data – No difference in side effects rates between brands.
- Patients may have side effects/adverse reactions to a certain IVIG lot number or brand but will tolerate a different lot number or brand.

Cautions/Side-Effects/Adverse Reactions (3)

- Not uncommon, some symptoms may occur up to 72 hours post infusion (hemolysis signs/symptoms may occur up to 10 days post).

- Advise patients to report:
  - Chills/rigors
  - Eye pain
  - Facial or tongue swelling, Fatigue, Fever, Flushing
  - Gastrointestinal symptoms: diarrhea, vomiting
  - Headache (often mild, rarely severe), Heart racing/palpitations, Hives: rash, itching
  - Myalgias (muscle aches and pains)
  - Nausea, Neck stiffness
  - Pain – back, chest, abdomen (cramping), Photophobia (light sensitivity)
  - Shortness of breath
  - Urine colour change to red/brown or tea coloured
  - Yellow skin or eye colour

Cautions/Side-Effects/Adverse Reactions (4)

Etiology of side effects/adverse reactions

- Minor
  - Febrile non-hemolytic reaction
  - IVIG headache (most common IVIG reaction)
  - Minor allergic reaction
- Moderate to severe
  - Anaphylaxis/ Anaphylactoid
  - Aseptic meningitis
  - Bacterial contamination (extremely rarely)
  - Hemolysis (acute or delayed)
  - Renal Failure
  - Transfusion Associated Circulatory Overload (TACO)
  - Transfusion Related Acute Lung Injury (TRALI) (extremely rarely)
  - Thrombotic events
- See Appendix B: Suggested treatment & actions, strategies to mitigate

IVIG: Specific Patient Populations

"cautious, given without specific concern"

Neonatal & Pediatric Patients

- Indications outline diagnoses where IVIG is of benefit.
- Dose calculation – actual weight (unless hospital policy is dose calculator for height > 152.4 cm).
- Infusion rate calculation – based on actual weight (unless hospital policy endorses rate table for 30 kg & greater).

Pregnant Patients

- Indications outline diagnoses where IVIG is of benefit.
- Dose calculation – based on pre-pregnancy weight.
- Fetal monitoring is not routine.
- Anecdotally, not well tolerated in pregnancy, infuse very slowly.

Hemodialysis Patients

- Pre-existing renal failure.
- No specific concerns identified; hemodialysis removes molecules similar in size to those that the kidneys filter.

Transfusion Knowledge Question 1 - Post

In Ontario (adult, neonatal, paediatric patients), IVIG is indicated when:

a) The patient's drug benefits plan covers IVIG costs.
b) The patient must be immune globulin G (IgG) deficient, serum IgG is less than 6 g/L.
c) The patient's diagnosis is listed in the Ontario Immune Globulin (IG) Utilization Management Guidelines or the IVIG order is approved by the Medical Director of the Transfusion Medicine Laboratory (TML).
d) The patient's ABO/Rh(D) blood group is group O, Rh positive.

Transfusion Knowledge Question 2 - Post

In Ontario (adult, neonatal, paediatric patients), the IVIG dose is calculated based on:

a) The patient's ABO blood group.
b) The brand of IVIG being administered.
c) The patient's abdominal circumference.
d) The patient's weight and height.

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Many thanks to my ORBCoN and Transfusion Medicine family for their ongoing mentorship and support.

Your participation is appreciated!

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