

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

Purpose

- This document provides health care practitioners involved in the infusion of IVIG with evidence informed, best practice guidance.
- The information can be incorporated into hospital specific policies and procedures.
- The material is limited to IVIG infusion and *is not applicable to infusion of subcutaneous immune globulin*.

Possible IVIG Shortage

- The growing demand for IG leaves the global supply limited. Canadian Blood Services communicated with all manufacturers to obtain additional IVIG. The global situation is ever changing; an IVIG shortage may occur.
- In Canada at least until spring 2022, some vial sizes and some IVIG brands will be in short supply.
- Patient Care Implications:
 - To administer the ordered dose, vial sizes may be substituted (e.g., for a 40 g dose, two 20 g or four 10 g vials may be issued).
 - Some patients will need to change to another IVIG brand.
 - The first infusion of each brand of IVIG must be given at a slower rate.
For patients receiving chronic IVIG treatment, if changed to a different brand, infusion time and thus their clinic appointment will be longer.

General Principles

- Refer to hospital specific policies/procedures.
- Documented IVIG clinical indication and dose (g/kg) must align with [Ontario IG Utilization Management Guidelines](#) or be approved by your hospital's Transfusion Medicine Medical Director.
- As appropriate, the [Dose Calculator](#) is used to calculate the patient's dosing weight and IVIG dose.

Dose Calculator:

- Is referenced from the Pharmacy perspective, for prescribing when actual body weight should be adjusted in the dose calculation
- Is NOT recommended for pediatric patients
- Is NOT recommended for patients less than 5 feet (152.4 cm) in height
- Is recommended for clinically obese or overweight adult patients
- Requires the patient's height and weight to be entered
- Calculates the patient's *ideal body weight (IBW)* based on the Devine formula
males = 50.0 kg + 2.3 kg (each inch > 5 feet)
females = 45.5 kg + 2.3 kg (each inch > 5 feet)
- Calculates the dosing weight based on the patient's actual weight and *IBW*
$$\text{dosing weight} = \text{IBW} + [0.4 \times (\text{actual weight} - \text{IBW})]$$

Exception - if patient's actual weight is less than *IBW*,
then dosing weight = actual weight

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- Uses dosing weight to calculate IVIG dose
- Rounds the calculated IVIG dose to the nearest 5 g dose
- Is used in some hospitals for calculating IVIG dose for all adult patients with height of 5 feet (152.4 cm) or greater (high dose IVIG is associated with adverse effects)
- If patient reports significant weight change, re-assess IVIG dose.
- For chronic disease IVIG indications, objective measures of the effectiveness of IVIG should be determined at the onset of treatment. Assess these measures 6 months after initiation of treatment. Subsequently, re-assessment should be annually at minimum. IVIG should be discontinued if clinical effectiveness is not demonstrated.
- For chronic disease IVIG indications when the patient has stabilized, titrating dose and/or treatment interval to the lowest dose and/or greatest interval needed to provide clinical effectiveness should be considered.
- Caution (also refer to Appendix B IVIG Adverse Reaction Chart):
 - IVIG has been associated with renal dysfunction, osmotic nephrosis, and acute renal failure. For patients with renal insufficiency or at risk of developing renal dysfunction (i.e., pre-existing renal insufficiency, diabetes mellitus, hypertension, age greater than 64 years, volume depletion, sepsis, paraproteinemia, or receiving known nephrotoxic drugs), administer IVIG at a slow rate of infusion, the patient should be well hydrated (additional PO fluids several hours prior to and following IVIG or IV pre-hydration) and monitored closely.
 - IVIG has been associated with thromboembolic events (i.e., deep vein thrombosis, myocardial infarction, pulmonary embolism, stroke, transient ischemic attack). Assess patients for risk factors for thrombotic events. IVIG should be administered at a slow rate of infusion, the patient should be well hydrated (additional PO fluids several hours prior to and following IVIG or IV pre-hydration) and monitored closely.
 - Administer IVIG at the slowest infusion rate feasible.
 - Hemolysis/hemolytic anemia have been reported post IVIG administration. Monitor patients for clinical signs and symptoms of hemolysis.
 - Patients with severe immunoglobulin A (IgA) deficiency (serum IgA less than 0.05 g/L), with known anti-IgA antibodies [assess if IVIG benefits outweigh risks; Gammagard S/D - lowest IgA (2.2 micrograms/mL) content].
 - For diabetic patients, some IVIG brands contain sugars that may interfere with test results of some glucose monitoring devices (refer to product monograph and manufacturer of the glucose monitoring device).
 - IVIG administration may temporarily impact the efficacy of live attenuated virus vaccines (i.e., measles, mumps, rubella, and varicella/chickenpox) for 6 weeks to 3 months. Notify prescriber if vaccination is planned within this timeframe post IVIG administration.
 - IVIG is manufactured from human plasma (plasma is pooled from thousands of healthy donors). The manufacturing procedures and donor screening steps reduce the risk of transmission of infectious pathogens, however potential risk of transmission cannot be entirely excluded.
- All IVIG brands are equivalent in terms of clinical effectiveness (even though there are slight differences in licensed indications/medical conditions).
- Adverse reactions occur with all IVIG brands. Canadian data has not found a difference in rates of adverse reactions between brands.
- An adverse reaction may be more likely when receiving IVIG for the first time, when changing to another IVIG brand, when there is a prolonged time (more than 8 weeks) since the previous infusion, with high doses of IVIG, with rapid infusion rates and if the patient is not well hydrated.
- Suggestions to mitigate recurrent adverse reactions (refer to Appendix B: IVIG Adverse Reaction Chart):
 - Divide the infusion of high doses (greater than 1g/kg) over more than 1 day

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- Slow infusion rate
- Pre-hydration
- Premedication
- Some patients may have an adverse reaction to a certain IVIG lot number or brand but will tolerate a different IVIG lot number or IVIG brand.

Pre-Infusion

- Validate IVIG clinical indication and dose (confirm details of prescriber's order).
- Verify informed consent for transfusion has been obtained and is valid based on hospital specific policy.
- Prior to first IVIG infusion
 - Record allergies, medications, and baseline height and weight.
 - Review history for previous IVIG treatment; if previously received IVIG, any history of adverse reactions to IVIG or to other blood components (history of anaphylaxis, anti-IgA antibodies).
 - As per prescriber, baseline blood work:
 - ABO blood group
 - Hemoglobin (IVIG contains anti-A and anti-B antibodies; non-O blood group patients treated with IVIG may develop hemolysis, especially if given high dose IVIG)
 - Kidney function tests.
 - Additionally, as patient's clinical status and IG indication infer (e.g., liver function tests, platelet count, serum IgG level).
- Assess patient for TACO (Transfusion Associated Circulatory Overload) risk factors (advanced age, history of heart failure or myocardial infarction, left ventricular dysfunction, renal dysfunction, positive fluid balance).
If risk identified, review with prescriber for prevention strategies (slow infusion rate, pre-infusion diuretic, divide infusion of high doses/high volumes over more than 1 day).
- As per prescriber, interval bloodwork to monitor IG treatment (e.g., hemoglobin, kidney and liver function tests, platelet count, serum IgG level).
- All patients should be well hydrated before and after IVIG treatments, especially patients with or at risk for renal dysfunction (pre-hydration reduces possible nephrotoxic effects of IVIG protein molecules and stabilizers).
- Anaphylaxis precautions, ensure readily available:
 - Rescue IV line [5% dextrose in water (D5W) or 0.9 % sodium chloride (NaCl)].
 - Epinephrine (as well as IV steroid and antihistamine).
- As per the manufacturers' direction, IVIG should be allowed to reach room temperature prior to infusion.

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Infusion

- Prescriber or their delegate must be readily available (on pager or as per hospital policy) during IVIG treatment.
- Follow hospital specific policy for checking blood products [patient identification (must be wearing armband; check surname, first name and unique identification number), lot number, visual inspection, and expiry time].
- Visual inspection: bottle seal intact, product appears as clear or slightly opalescent solution that is colourless to pale yellow in colour. If seal is broken or if solution appears turbid, cloudy, or having deposits, do not infuse and follow up with Transfusion Medicine Laboratory (TML).
- Expiry time: Manufacturer's expiry date is noted on packaging. Infusion of each bottle must be completed within 4 hours from time the bottle's seal was punctured; otherwise discard any remainder.
- DO NOT infuse different IVIG brands during a single infusion (Exception: Gamunex and IGIVnex).
- Begin infusion with smallest bottle size and end with largest bottle size of the bottles issued for the dose ordered (to minimize wastage in the event of a reaction).
- Requires dedicated IV line (IV site or lumen of a multi-lumen catheter).
- Can be flushed with 5% dextrose in water (D5W) or 0.9 % sodium chloride (NaCl) for injection (exception: Gammagard S/D – only D5W).
- Do not mix with any other medications.
- Do not dilute IVIG.
- Use aseptic technique when handling IVIG.
- Administer with standard vented IV tubing (to allow filtered air to enter the bottle). An in-line filter is not required (exception: Gammagard S/D – filter for the reconstituted product included in packaging).
- One standard vented IV tubing set can be used for each IVIG treatment (maximum time 24 hours) or as specified by the tubing manufacturer.
- To minimize bubbling of IVIG:
 - Allow the IVIG to come to room temperature.
 - Do not shake the IVIG.
 - 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.
 - Prior to spiking each bottle, close the roller clamp and ensure the drip chamber vent of the vented IV tubing set is also closed.
- For added patient safety, administration using a Health Canada approved infusion pump is suggested to set the infusion rate precisely and allow for greater patient mobility.
- Infusion Rate: Refer to Appendix A: IVIG Brands Infusion Rate Tables
 - Confirm per prescriber's order and hospital specific policies.
 - Review General Guidance information.
 - Select the Infusion Rate Table specific to the IVIG brand being infused and then select the patient's weight column (round down).
 - Select the corresponding suggested infusion rates and the maximum rate remainder of infusion appropriate for the incidence of this IVIG infusion and the patient's clinical status as detailed.

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- For patient safety, comply with each brand's suggested guidance for infusion rate.
- Subsequent bottles, with same or different lot numbers do not require returning to the starting infusion rate.
- Patient assessment and vital signs, at minimum:
 - Within 30 minutes prior to the start of the infusion
 - 15 minutes after of start of the infusion
 - After each rate increase, then hourly until the infusion is completed
 - On completion of the infusion
 - For inpatients, 1 hour following completion of the infusion
 - For outpatients, prior to discharge
 - If clinically indicated, or when a reaction is suspected
- Patient Education (side-effects are not uncommon, some symptoms may occur up to 72 hours post infusion; hemolysis signs/symptoms may occur up to ten days after infusion)
Advise patient to report:
 - Chills/rigors
 - Diarrhea
 - Eye pain
 - Facial or tongue swelling
 - Fatigue
 - Fever
 - Flushing
 - 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
 - Vomiting
 - Yellow skin or eye colour
- If an infusion reaction is suspected, refer to Appendix B: IVIG Adverse Reaction Chart

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Post-Infusion

- Document as per TML/hospital policy:
 - Complete infusion chart label/tag (includes IVIG brand, dose, and lot numbers; add date and infusion start time and stop time)
 - Record volume infused
 - Patient assessments and vital signs
- Return any IVIG (intact bottles) not infused to TML. Discard empty IVIG bottles and tubing in biohazardous waste.
- For IVIG infused in an outpatient setting
 - Monitor patient for 30 minutes post infusion for potential side effects.
 - At discharge, provide instructions (e.g., [IVIG Facts for Outpatients](#)).
 - Specify contact information for follow up if any patient concerns or symptoms arise post discharge.

Appendix A: IVIG Brands Infusion Rate Tables

General Guidance IVIG Brands Infusion Rate Tables (Patients weighing 30 to 125 kg)

- Refer to hospital specific policies/procedures.
- For each IVIG brand, based on patient's weight, the table includes suggested starting rate, suggested subsequent rate increase intervals, and considerations for maximum rate remainder of infusion.

NOTE:

All IVIG brand monographs designate infusion starting rate, maximum rate for specific patient clinical factors, and a recommended maximum rate. As well, all IVIG brand monographs specify that if well tolerated, the rate of infusion may gradually be increased to the recommended maximum. The following tables reflect suggested gradual increases for the rate of infusion (specific hospital policies/procedures may include alternative gradual increases for the rate of infusion).

- If patient's weight is between 2 increments, round down and administer at the hourly rates for the rounded down category.
- For patients weighing less than 30 kg (pediatric and neonates), suggest calculating hourly infusion rates with patient specific weight. Formula: Rate (mL/kg/hr) x Weight (kg) = Hourly infusion rate (mL/hr). Perform double check of all calculations as per hospital specific policy.
- For each IVIG infusion, select maximum rate remainder of infusion as appropriate for the incidence of this IVIG infusion and the patient's clinical status.
- Patients at risk of renal dysfunction or thrombotic events: for maximum rate remainder of infusion, administer at the minimum infusion rate feasible.
- Infusion rate can be ordered at a decreased rate at the discretion of the prescriber.
- Some hospitals may specify a maximum mL/hr infusion rate regardless of patient weight (e.g., maximum infusion rate of 250 mL/hr).
- For patients tolerating chronic IVIG treatment, prescriber may order a patient specific treatment plan, excluding some interval infusion rates and increased infusion rates (absolute maximum infusion rate as per manufacturer's recommendations).
- Assess the patient (document vital signs) at each rate change.
- Slower infusion rates will ease rate related adverse reactions (symptoms: headache, flushing, chills).
- As per hospital specific policy, it may be appropriate for nursing staff to notify the prescriber and resume the infusion at a previously tolerated rate if the patient's rate related symptoms resolve with stopping the IVIG infusion.
- All IVIG adverse reactions must be documented and reported to TML.
- Refer to Appendix B IVIG Adverse Reactions Chart for additional strategies to mitigate rate related symptoms.

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

*Gammagard Liquid® 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	0.5 mL/kg/hr	15	18	20	23	25	28	30	33	35	38	40	43	45	48	50	53	55	58	60	63
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	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
Receiving IgG for the first time; or Had been receiving another IgG brand; or Have not received IgG in more than 8 weeks																					
Maximum Rate Remainder of Infusion	2.0 mL/kg/hr	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
For patients judged to be at increased risk for developing renal dysfunction																					
Maximum Rate Remainder of Infusion	5.4 mL/kg/hr	162	189	216	243	270	297	324	351	378	405	432	459	486	513	540	567	594	621	648	675
Indication: Multifocal Motor Neuropathy (MMN)																					
Maximum Rate Remainder of Infusion	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
Following first infusion of this brand, next 3 consecutive infusions																					
Maximum Rate Remainder of Infusion	8.0 mL/kg/hr	240	280	320	360	400	440	480	520	560	600	640	680	720	760	800	840	880	920	960	1000
Per manufacturer's recommended maximum																					
Gammagard Liquid® 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)																			

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***Gammagard S/D® 5 % solution 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	0.5 mL/kg/hr	15	18	20	23	25	28	30	33	35	38	40	43	45	48	50	53	55	58	60	63
Rate next 15 - 30 minutes	1.0 mL/kg/hr	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125
Rate next 15 - 30 minutes	2.0 mL/kg/hr	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
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	3.0 mL/kg/hr	90	105	120	135	150	165	180	195	210	225	240	255	270	285	300	315	330	345	360	375
Maximum Rate Remainder of Infusion For patients judged to be at increased risk for developing renal dysfunction	3.0 mL/kg/hr	90	105	120	135	150	165	180	195	210	225	240	255	270	285	300	315	330	345	360	375
Maximum Rate Remainder of Infusion Following first infusion of this brand, next 3 consecutive infusions	3.0 mL/kg/hr	90	105	120	135	150	165	180	195	210	225	240	255	270	285	300	315	330	345	360	375
Maximum Rate Remainder of Infusion Per manufacturer's recommended maximum	4.0 mL/kg/hr	120	140	160	180	200	220	240	260	280	300	320	340	360	380	400	420	440	460	480	500

* Requires dedicated IV line; can be flushed with 5% dextrose in water (D5W).

* **Infuse with the administration set provided in the packaging** (the required filter is included)

Gammagard S/D® (S/D = solvent detergent treated) is a freeze-dried concentrate form of IVIG. It is reconstituted (diluent, sterile water for injection is included in the packaging), usually as a 5% solution. Refer to the product monograph for detailed information (can also be reconstituted to a 10 % solution).

Gammagard S/D contains only trace amounts of IgA (≤ 2.2 micrograms/mL in a 5% solution).

Contains albumin, glycine (an amino acid) and glucose as stabilizers (does not contain sucrose)

[Gammagard S/D® monograph](#)

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***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	* 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)																				
IGIVnex® monograph																					

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***Octagam® 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 Following first infusion of this brand, next 3 consecutive infusions	6.0 mL/kg/hr	180	210	240	270	300	330	360	390	420	450	480	510	540	570	600	630	660	690	720	750
Maximum Rate Remainder of Infusion Per manufacturer's recommended maximum	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
Octagam® monograph		* Requires dedicated IV line; can be flushed with 5% dextrose in water (D5W) or 0.9 % sodium chloride (NaCl) Contains maltose as a stabilizer (does not contain sucrose)																			

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***Panzyga® 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 Indication: Chronic Immune Thrombocytopenic Purpura (ITP)	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	6.0 mL/kg/hr	180	210	240	270	300	330	360	390	420	450	480	510	540	570	600	630	660	690	720	750
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
Panzyga® 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)																			

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***Privigen® 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	0.3 mL/kg/hr	9	11	12	14	15	17	18	20	21	23	24	26	27	29	30	32	33	35	36	38
Rate next 15 - 30 minutes	1.0 mL/kg/hr	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125
Rate next 15 - 30 minutes	2.0 mL/kg/hr	60	70	80	90	100	110	120	130	140	150	160	170	180	190	200	210	220	230	240	250
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	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 If high dose i.e., ≥ 1g/kg	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	6.0 mL/kg/hr	180	210	240	270	300	330	360	390	420	450	480	510	540	570	600	630	660	690	720	750
Maximum Rate Remainder of Infusion Per manufacturer's recommended maximum	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
Privigen® monograph		* Requires dedicated IV line; can be flushed with 5% dextrose in water (D5W) or 0.9 % sodium chloride (NaCl) Contains L- proline as stabilizer (does not contain sucrose)																			

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Appendix B: IVIG Adverse Reaction Chart (refer to hospital specific policies/procedures)

Immediate Actions if an adverse reaction is suspected:

1. **STOP** the transfusion
2. Maintain **IV access**
3. Check **vital signs**
4. Verify **patient identification** matches transfusion label/tag
5. Notify **prescriber**
6. **Patient care** as ordered; for every reaction **report to TML; document**

Signs & Symptoms	Possible Etiology	Suggested Treatment & Actions; Strategies to Mitigate
Mild Reactions		
Chills/rigors, fever*, flushing, malaise, myalgia, nausea (during or up to 24 hours post-IVIG)	Febrile non-hemolytic reaction	<ul style="list-style-type: none"> ○ Hold the infusion ○ As per prescriber administer antipyretic, analgesic, antihistamine, or non-steroid anti-inflammatory medication (if appropriate for patient [caution elderly, decreased renal function]) ○ As ordered, resume infusion at slow infusion rate ○ If recurrent, consider: <ul style="list-style-type: none"> - Divide high dose (> 1g/kg) infusions over 2 to 5 days - Longer rate increase intervals and slow maximum rate remainder of infusion - Pre-hydration (as per patient clinical status, additional PO fluids several hours prior to and following IVIG or 500 to 1000 mL 0.9 % sodium chloride IV prior to IVIG infusion) - Premedication with anti-pyretic, analgesic, or non-steroid anti-inflammatory medication - If history of migraines, premedicate with anti-migraine medication - If persistently recurrent, change brand of IVIG
Headache Migraine headache can be triggered in patients with history of migraines (during or up to 72 hours post-IVIG)	IVIG headache Most common IVIG reaction	
Itchiness, rash, urticaria (less than 2/3 of body surface), nausea/vomiting, pain - abdominal (during or up to 4 hours post-IVIG)	Minor allergic reaction	<ul style="list-style-type: none"> ○ Hold the infusion ○ As per prescriber administer antihistamine, may require steroid if symptoms slow to resolve ○ If symptoms resolve and product viable, as ordered cautiously resume infusion ○ If recurrent, consider <ul style="list-style-type: none"> - Premedication with antihistamine or steroid - If persistently recurrent, change brand of IVIG

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

Signs & Symptoms	Possible Etiology	Suggested Treatment & Actions; Strategies to Mitigate
Moderate to Severe Reactions		
Airway edema, dyspnea, decreased oxygen saturation, facial and/or tongue swelling, hypotension, itching, nausea/vomiting, rash, tachycardia, urticaria (during or up to 4 hours post-IVIG)	Anaphylaxis/ Anaphylactoid	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Epinephrine ○ Also consider steroid, antihistamine as per prescriber ○ Supportive care per prescriber’s discretion: oxygen, respiratory support, vasopressors ○ Suggest consult Transfusion Medicine physician: explore if indication for <ul style="list-style-type: none"> - TML: Group & Screen, DAT - Haptoglobin - IgA level (ideally pre-transfusion sample available) - Anti-IgA testing (performed via Canadian Blood Services, TML will assist in sending samples) ○ Re-assess indication for IVIG; consider change brand of IVIG to Gammagard S/D, premedication with steroid
Severe persistent headache with eye pain, fever*, lethargy/decreased level of consciousness, nausea/vomiting, neck rigidity/stiffness, photophobia (up to 72 hours post-IVIG)	Aseptic meningitis	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Patients with history of migraines at greater risk ○ Supportive care per prescriber’s discretion: analgesics, anti-emetics, IV fluids, anti-migraine medication ○ Frequently resolves spontaneously within 24 to 48 hours ○ To prevent or decrease incidence: <ul style="list-style-type: none"> - Longer rate increase intervals and slow maximum rate remainder of infusion - Pre-hydration (as per patient clinical status, additional PO fluids several hours prior to and following IVIG or 500 to 1000 mL 0.9 % sodium chloride IV prior to IVIG infusion) - Premedication with analgesic (acetaminophen) or antihistamine - If history of migraines, premedicate with anti-migraine medication
Fever* with dyspnea, hypotension, tachycardia or High-risk fever alone (greater than 38.9 ° C) (during or up to 4 hours post-IVIG)	Bacterial contamination Occurs extremely rarely	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Patient blood culture (from a different peripheral site) ○ Broad spectrum IV antibiotics; DO NOT wait for culture results ○ Return IVIG to TML for product culture ○ Supportive care per physician’s discretion: vasopressors, oxygen, respiratory support ○ Serious reaction, call TML immediately

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

<p>Acute: fever*, dyspnea, hypotension, pain (back, IV site), tachycardia, urine - red/brown or tea coloured (during or up to 24 hours post-IVIG)</p> <p>Delayed: back pain, decreased hemoglobin, fever*, fatigue - extreme/unexpected/unexplained, jaundice, tachycardia, urine - red/brown or tea coloured (24 hours to 10 days post-IVIG)</p>	<p>Hemolysis: acute or delayed Defined as: 10 g/L or greater decrease in hemoglobin, positive direct antiglobulin test (DAT) AND at least two of the following: increased reticulocyte count, increased lactate dehydrogenase, low haptoglobin, hyperbilirubinemia, hemoglobinemia, hemoglobinuria</p>	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Supportive care per physician’s discretion: IV fluid (aggressive hydration; maintain good urine output), vasopressors, oxygen, respiratory support ○ TML: Group & Screen, DAT ○ Urinalysis (first void post-reaction) ○ Hemolysis work-up: CBC, bilirubin, LDH, AST, haptoglobin, reticulocyte count, blood film ○ If indicated, assess for <ul style="list-style-type: none"> - AKI (Acute Kidney Injury): electrolytes, creatinine - DIC (Disseminated Intravascular Coagulation): INR, PTT, fibrinogen, D-dimer - Thrombosis ○ Severity is variable (self-limiting to requiring RBC transfusion support); steroid treatment has been utilized ○ Consider: pause IVIG treatment, avoid implicated lot number of IVIG, change brand of IVIG ○ Educate patient regarding signs and symptoms; if noted, notify prescriber promptly ○ Most often occurs with first treatment, blood group AB, A, B patients receiving high dose IVIG; mechanism of hemolysis not clearly differentiated (IVIG contains anti-A and anti-B antibodies)
<p>Edema (periorbital, peripheral), hematuria, hypertension, pain (back, flank), serum creatinine – increased, urination - decreased (oliguria) (1 to 10 days post-IVIG)</p>	<p>Renal Failure</p>	<ul style="list-style-type: none"> ○ IVIG-related renal impairment has been related to IVIG stabilized with sucrose (at this time, these brands are not licenced in Canada) ○ Renal impairment has also been reported in patients receiving sucrose-free IVIG ○ All patients receiving IVIG <ul style="list-style-type: none"> - should be screened for renal disease risk factors (pre-existing renal insufficiency, diabetes mellitus, hypertension, age greater than 64 years, volume depletion, sepsis, paraproteinemia, or receiving known nephrotoxic drugs) - serum creatinine should be monitored at baseline ○ For patients with renal insufficiency or with risk factors: <ul style="list-style-type: none"> - Longer rate increase intervals and slow maximum rate remainder of infusion - Pre-hydration (as per patient clinical status, additional PO fluids several hours prior to and following IVIG or 500 to 1000 mL 0.9 % sodium chloride IV prior to IVIG infusion) - Close monitoring (interval serum creatinine testing) ○ If renal function declines, discontinuation of IVIG should be considered; SCIG might be an alternative (dose administered per infusion is lower)

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

<p>Dyspnea, hypertension, increased jugular venous pressure, orthopnea, tachycardia, (during or up to 12 hours post-IVIG)</p>	<p>Transfusion Associated Circulatory Overload (TACO)</p>	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Oxygen, high fowler’s position, diuretics (document fluid balance) ○ Consider chest x-ray; Findings - pulmonary edema, Kerley B lines, peri bronchial cuffing, may be pleural fluid ○ Future infusion/prevention strategies: <ul style="list-style-type: none"> - Slow maximum rate remainder of infusion - Pre-infusion diuretic ** - Divide infusion of high doses/high volumes over more than 1 day ○ Prevention: <ul style="list-style-type: none"> - Assess all patients for TACO risk factors (advanced age, history of heart failure or myocardial infarction, left ventricular dysfunction, renal dysfunction, positive fluid balance) - If risk identified, review with prescriber for prevention strategies (infuse slowly over longer time period; administer pre-transfusion diuretic**)
<p>Acute dyspnea with decreased oxygen saturation, hypotension, tachycardia, +/- *fever (during or up to 6 hours post-IVIG)</p>	<p>Transfusion Related Acute Lung Injury (TRALI) Occurs extremely rarely</p>	<ul style="list-style-type: none"> ○ DO NOT resume infusion ○ Supportive care per physician’s discretion: oxygen, respiratory support, vasopressors (benefit uncertain for diuretics [document fluid balance], steroids, and bronchodilators) ○ Chest x-ray: Findings – bilateral interstitial/alveolar infiltrates without elevated pulmonary pressures ○ If also hypoxia: blood gases ○ Canadian Blood Services requires follow up information & patient blood tests, contact TML, will assist in sending samples ○ Serious reaction, call TML immediately
<p>Symptoms related to deep vein thrombosis, myocardial infarction, pulmonary embolism, stroke, transient ischemic attack (within 24 hours to days to weeks post-IVIG)</p>	<p>Thromboembolic events</p>	<ul style="list-style-type: none"> ○ Proposed possible mechanisms of IVIG-related thrombotic events include <ul style="list-style-type: none"> - Increase in plasma viscosity due to IVIG’s high protein load and protein polymerization - Pro-coagulant potential (presence of contaminants in IVIG i.e., activated coagulation factor XI, factor XII, pre-kallikrein, antiphospholipid antibodies) - Increased platelet count and aggregation activity ○ All patients receiving IVIG should be screened for thromboembolic event risk factors (including but not limited to) <ul style="list-style-type: none"> - Advanced age - Pre-existing atherosclerotic disease (hypertension, diabetes mellitus, hypercholesterolemia, smoking, previous history of stroke, carotid artery stenosis, myocardial infarction/coronary disease, obesity) - Previous/current venous thrombosis or pulmonary embolism

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

		<ul style="list-style-type: none"> - Immobilization - Hereditary hypercoagulable state (antithrombin III, protein C or S deficiency, factor V Leiden or prothrombin mutation) - Increased serum viscosity (monoclonal gammopathy, polycythemia, thrombocythemia) - Permanent indwelling venous catheter - Medications (estrogen, steroids, antineoplastics, diuretics) o IVIG-related thromboembolic events have been reported in the absence of patient risk factors o For patients with risk factors: <ul style="list-style-type: none"> - Slow maximum rate remainder of infusion - Pre-hydration (as per patient clinical status, additional PO fluids several hours prior to and following IVIG or 500 to 1000 mL 0.9 % sodium chloride IV prior to IVIG infusion) - Divide infusion of high doses (> 1g/kg) over 2 to 5 days (viscous effect is dose dependant) - Close monitoring and educate patient regarding signs and symptoms; if evident, patient should notify prescriber promptly o IVIG should be administered via infusion pumps to promote mobility and minimize period restricted to bed/chair o If thromboembolic event occurs, IVIG should be discontinued; SCIG might be an alternative (dose administered per infusion is lower)
<p>* Fever: Temperature of at least 38° C and an increase of at least 1° C from pre-transfusion</p>		
<p>** Pre-infusion diuretic: Furosemide PO: onset 30 to 60 minutes, maximal effect 1-2 hours, effect persists about 6-8 hours Furosemide IV: onset 5 minutes, maximal effect 20-60 minutes, effect persists about 2 hours</p>		

IVIG (Intravenous Immune Globulin) Infusion Guide and Adverse Reaction Chart for Ontario

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