ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Gammagard S/D ®
Immune Globulin Intravenous (Human)

APPLICABILITY: This document applies to all APL, AHS, Covenant Health, and all other health care professionals involved in the transfusion of blood components and products in Alberta.	***Other Names:*** *Intravenous Immune Globulin, IVIG* ***Company:*** *Takeda Canada Inc* ***Class:*** *Manufactured blood product, derived from human plasma*

In the event of discrepancy between APL Monograph and Manufacturer's documentation or patient resources, the APL Monograph will take precedence.

	INTRAVENOUS			OTHER		
ROUTES	**DIRECT IV**	**IV Infusion**	**Continuous Infusion**	**SC**	**IM**	**OTHER**
Acceptable Routes*	No	Yes	No	No	No	N/A

* Administration of blood components and blood products is a restricted activity. For specific conditions that apply to a profession's authorization to administer blood components and blood products, consult the applicable discipline-specific regulation under the Health Professions Act (Alberta). Health care professionals with this authorization require the applicable education, training and competency.

** Direct IV administration of blood products may be performed by health care professionals that have authorization of administration of blood products within their scope of practice.

DESCRIPTION:

- Gammagard S/D® is a sterile, lyophilized freeze-dried preparation of highly purified immune globulin G (IgG) derived from large pools of human plasma.
- Manufactured by the Cohn-Oncley cold alcohol fractionation procedure followed by ultrafiltration and ion exchange chromatography.
- Solvent/detergent treated.
- Available in 5g vial size of which 90% (4.5g) is gamma globulin and less than or equal to 2.2 mcg/mL is IgA in a 5% solution.
- Vials are reconstituted with sterile water for injection to a 5% or 10% solution.
- pH is 6.4 – 7.2
- Also contains albumin, glycine, glucose, PEG, tri(n-butyl) phosphate, octoxynol-9 and polysorbate-80.
- Latex-free.

AVAILABILITY

- Supplied by Canadian Blood Services.
- Gammagard S/D® is primarily reserved for patients with documented anti-IgA antibodies and IgA deficiency.
- Requests for IVIG must meet approved indications. An IVIG request form may need to be completed for initial approval and renewal unless ordered through Connect Care.
- Contact your local laboratory/transfusion service regarding stock availability on site.

INDICATIONS FOR USE:

- IVIG may be appropriate in a number of clinical indications. Refer to the Prairie Collaborative Criteria for the Clinical Use of Immune Globulin.

CONTRAINDICATIONS:

- Patients who are hypersensitive to human immune globulin, or any ingredient in the formulation or component of the container.
- In patients with selective IgA deficiency where it is the only abnormality of concern.

WARNINGS:

- May impair the efficacy of live attenuated virus vaccines. Refer to the Canadian National Advisory Committee on Immunization for further recommendations.
- IVIG has been reported to be associated with renal dysfunction. The minimum concentration and the minimum rate of infusion practicable should be used.
- There is evidence of an association between IVIG administration and thromboembolic events in patients with pre-existing risk factors for thrombotic events including: obesity, advanced age, diabetes mellitus, history of vascular disease or thrombotic episodes, acquired or inherited thrombophilic disorders, patients with prolonged periods of immobilization, severe hypovolemia and patients with disease states that increase blood viscosity.
- IVIG can contain blood group antibodies which may act as hemolysins and induce in vivo coating of red blood cells with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, clinically significant hemolysis.
- Gammagard S/D® contains 850 mg/L of sodium at 5% concentration. This should be considered for patients on a low sodium diet.

DOSE:

- Use the lowest dose for the shortest duration required to achieve clinical efficacy.
- Use adjusted body weight dosing for adult patients with a height of greater than 152 cm and a weight of 20 – 400 kg. Body weight adjusted dose calculator is available at IVIG Dosing based on Adjusted Body Weight Calculation (albertahealthservices.ca)
- If IVIG is being used for immune replacement therapy (primary or secondary), monitoring trough levels is recommended.
- IVIG dose will be rounded to the nearest available vial size.
- Refer to the Prairie Collaborative Criteria for the Clinical Use of Immune Globulin. for dosing recommendations.

ADMINISTRATION:

Confirm signed consent has been obtained and documented prior to requesting blood components or products (human-source) from lab/transfusion service where possible.

Pre-Infusion:

- Ensure recent patient weight and height is on file
- Ensure pertinent labs are available as required (i.e. trough IgG, IgA, CBC)
- Ensure any ordered premedications have been given (antihistamines, antipyretics prn).
- Perform pre-transfusion checks per AHS Transfusion Policy and Procedure
- Report any new onset acute illness to MD/authorized prescriber prior to commencing infusion.

Access:

- Gammagard S/D® can be given via CVAD or peripheral venous line

Reconstitution:

- Refer to Gammagard S/D® Reconstitution Instructions
- After reconstitution, Gammagard S/D® should be clear or slightly opalescent and colorless or pale yellow
- Gammagard S/D® should be visually inspected for particulate matter and discoloration prior to administration. Do not use if particulate matter is observed.
- Gammagard S/D® should be administered as soon as possible (within 12 hours) after reconstitution.

Compatible IV Solutions:

- Compatible with D5W.
- Do not mix with other products, medications, or solutions.
- Normal saline may be used to prime and flush the line.

Administration Supplies:

- Gammagard S/D® should only be given using a vented, 15 micron filtered set.

Administration:

- Visually inspect the product prior to administration. Do not use products that are cloudy or contain particulates.
- Allow IVIG time to come to room temperature where possible.
- Be careful not to shake the IVIG vial.
- If multiple vials sizes will be infused, start with the smallest vial first.
- Ensure the vent is open to ensure a steady flow of IVIG
- Use of a syringe pump is acceptable.
- IVIG vials should be infused within 4 hours of spiking
- Flush the line to ensure all product is infused

Infusion Rate:

- Subsequent vials may be infused at the same maximum rate as tolerated by the patient on previous vials (i.e.. new vials do not have to be restarted at initial rate)

- **10% solutions:**
  - When switching from the 5% solution to the 10% solution, the rate of the 10% solution should be initially reduced to keep the rate of IgG protein administration comparable.
  - Patients should be infused at a lower infusion rate if:
    - This is their initial treatment with the particular IVIG brand.
    - It has been more than 8 weeks since the last IVIG treatment
    - The patient has renal impairment, risk of thrombosis, or is >65 years old
    - The patient does not tolerate a faster infusion rate.
  - For adult infusions, please refer to the following table: IVIG Infusion Rate Table - Adult (albertahealthservices.ca)
    For pediatric infusions, please refer to following table: Peds IVIG Infusion Rate Table (albertahealthservices.ca)

- **5% solutions:**

Initial Infusion **More than 8 weeks since last IVIG dose**				
Rate calculation: Rate (mL/h) = Pt Weight (kg) x Desired Rate (mL/kg/h) = mL/h				
Patient weight: _____(kg)	Initial Rate:	Then:	Then:	Then: **MAX RATE**
	0.5 mL/kg/h **X 15 min**	**1mL/kg/h** **X 45 min**	**2mL/kg/h** **X 30 min**	**4 mL/kg/h** For remainder of infusion
	_____mL/h	_____mL/h	_____mL/h	_____mL/h

Subsequent IVIG infusion **Less than 8 weeks since last IVIG dose*** **					
Rate calculation: Rate (mL/h) = Pt Weight (kg) x Desired Rate (mL/kg/h) = mL/h					
Patient weight: _____(kg)	Initial Rate:	Then:	Then:	Then: **MAX RATE** For patients with renal impairment, risk of thrombus, or greater than 65 years old	Then: **MAX RATE***** if 4 mL/kg/h tolerated for 30 min
	0.5 mL/kg/h X 15 min	**1.5 mL/kg/h** X 15 min	**3mL/kg/h** X 30 min	**4 mL/kg/h** X 30 min	**8 mL/kg/h** For remainder of infusion
	_____ mL/h	_____ mL/h	_____ mL/h	_____ mL/h	_____ mL/h

Infusion Rate (mL/h) = Pt Weight (kg) x Desired Rate (mL/kg/h) = mL/h

Patients at risk for renal impairment, elderly patients, or those with a history of hypertension, cardiovascular disease, previous thrombotic events or dehydration maximum infusion rate is 4 mL/kg/h as they are at increased risk of thrombus formation.

***The decision to use this maximum rate is at the discretion of the MRHP but should only be used if the patient has had previous exposure to IVIG infusion and demonstrated tolerability on more than one occasion. In these chronic infusion situations, the MRHP may eliminate some intervening rate increases or alter the time intervals between rate escalation if close monitoring for adverse events is available.

NURSING IMPLICATIONS:

Patient Monitoring:

- Vital Signs: Pre-administration**,** on completion of dose, and as patient condition requires.
- If the patient has experienced previous adverse reaction to product transfusion, or this is the first transfusion of product for patient, monitor for 30-60 minutes post.

	Pre-transfusion	At each rate increase (to assess tolerability)	Remainder of transfusion	Post transfusion
ADULTS and PEDIATRICS	**Yes**	**Yes**	**q1h**	**20-30 min post, then PRN**

Note: Vital signs/patient monitoring may be conducted more frequently as determined by clinical condition of patient.

Patients receiving blood product transfusions must be observed closely for signs of any unexpected or untoward reactions. These reactions may occur during or after the infusion of blood or blood products. For follow up to a transfusion reaction see Transfusion Reactions | Alberta Health Services. Notify the transfusion service as soon as possible that an adverse reaction has occurred.

Documentation:

- Ensure documentation is completed as per the AHS Transfusion of Blood Components and Products Policy
- Start and stop time of infusion and assessment of patient tolerability should be documented in appropriate flow chart or clinical record (electronic or paper).
- Document vital signs as required in the appropriate flow chart or clinical record (electronic or paper).
- Provide patient notification of transfusion documentation where required.

Laboratory Monitoring:

- High doses of IVIG (i.e. 2 g/kg) or consecutive days of IVIG therapy may cause temporary increases in serum and urine glucose.
- False positive results in serological tests may occur (e.g. CMV serology, Direct Antiglobulin Test, etc.).

POTENTIAL HAZARDS WITH PARENTERAL ADMINISTRATION:

Adverse Events

- Potential adverse events related to a blood product transfusion range in severity from minor with no sequelae to life-threatening.
- All adverse events occurring during a transfusion should be evaluated to determine whether or not the transfusion can be safely continued/restarted.
- All adverse events suspected to be related to a product transfusion (whether during or after a transfusion) must be reported to your local transfusion service.
- Most reactions to IVIG are due to serum osmolarity changes and are rate related reactions (vs. reactions to a single donor in a pool of IVIG).
- Slower infusion rates will diminish rate related symptoms such as headache, shivering, tachycardia and blood pressure alterations.
- Some patients may require pretreatment with antihistamines, anti-inflammatories and corticosteroids, particularly if they have a past history of reaction
- Serious but rare complications of IVIG include anaphylaxis, hemolytic anemia (delayed reaction up to 10 days later), thromboembolic events, aseptic meningitis and renal failure (with older sucrose containing IVIG preparations). These reactions are reportable to Transfusion Medicine/lab.
- Patients with antibodies to IgA or with IgA deficiencies may be at increased risk of anaphylactic reaction.

Minor IVIG Reactions	
If patient experiences:	**Then:**
• Skin rash • Dizziness • Mild headache (not improved with rate decrease) • Flushing • Muscle pain and arthralgia • RR 30% increase over baseline (e.g. RR of 18 increasing to 24) • HR 15% increase over baseline (e.g. HR of 60 increasing to 70) • Diastolic BP 15% change from baseline • Temperature increase less than 1.0°C	1. Decrease infusion rate to highest previously tolerated rate. 2. Recheck vitals within 5 minutes. 3. Continue new rate, if tolerated. 4. Recheck vital signs after 10 minutes. 5. Continue at new rate. Progressively increase vital signs and rate increase schedule, restarting at q15 minutes x 2, for remainder of infusion. 6. Notify authorized prescriber and Transfusion Medicine lab after completion of infusion. 7. Document transfusion reaction and care provided in patient health record 8. Complete transfusion reaction notification and forward to Transfusion Medicine lab

Major IVIG Reactions	
If patient experiences:	**Then:**
• RR 60% increase over baseline (e.g. RR of 18 increasing to 28) • HR 30% increase over baseline (e.g. HR of 60 increasing to 78) • Systolic or diastolic BP 30% change from baseline • Temperature increase more than 1.0°C • Chills, rigors, diaphoresis • SOB, wheezing • Severe headache and meningeal signs • Anaphylaxis • Chest or abdominal pain	**1. Stop infusion** 2. Assess vitals and ABCs (airway, breathing, circulation) 3. Notify authorized prescriber and Transfusion Medicine lab 4. Disconnect IV tubing at a point closest to patient. 5. Flush IV site with 0.9% normal saline 6. Infuse 0.9% normal saline at a rate equal to current IVIG rate 7. Administer emergency medications as ordered. 8. Closely monitor patient 9. Document transfusion reaction and care provided in patient health record 10. Complete transfusion reaction notification 11. Forward transfusion reaction notification and remaining unused product to Transfusion Medicine lab.

STORAGE & STABILITY:

- Lyophilized product is stored up to 25°C
- Do not freeze
- Do not use expired product.

Contact Information

Approved By: APL Transfusion Medicine Discipline Council

For questions or comments regarding this document please contact: Transfusion.SafetyTeam@aplabs.ca

REFERENCES:

Gammagard S/D® manufacturer monograph. Available from GAMMAGARD S/D - Drug and Health Products Portal (hpfb-dgpsa.ca)

Prairie Collaborative Immune Globulin Utilization Management Framework Project. *Criteria for the clinical use of immune globulin, 2nd edition*. Alberta Ministry of Health, Shared Health Manitoba, and Saskatchewan Ministry of Health; March 2022. Available from www.ihe.ca

Canadian National Advisory Committee on Immunization