

**UNIVERSITY HEALTH CARE  
UNIVERSITY OF UTAH HOSPITALS & CLINICS**

**PHARMACY AND THERAPEUTICS COMMITTEE**

**GUIDELINE**

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**IMMUNE GLOBULIN (IVIG): PART 3 – MONITORING AND ADMINISTRATION**

**Review Date:** 11/15/2006      **Revision Date:** 11/15/2006

**Chapter:** Pharmacy & Therapeutics Committee Guidelines

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**I. PURPOSE:**

- A. To provide guidelines for those who routinely administer IVIG.

**II. GUIDELINE:**

- A. Adverse effects occur in up to 23% of patients receiving IVIG, but are usually mild. The most common reactions include fever, chills, rigors, tremor, flushing, renal dysfunction, headache, nausea, vomiting, diarrhea, back pain, chest pain, chest tightness, malaise, or myalgia.<sup>1-6</sup>
- B. Adverse effects are often associated with rapid infusions of IVIG and will usually resolve with temporary discontinuation or reduction in the infusion rate. Premedication with antihistamines, acetaminophen, or corticosteroids may prevent or alleviate these reactions. Adverse reactions may occur on initial or subsequent infusions.<sup>1-6</sup>
- C. Immune globulin intravenous (human) is contraindicated in patients with selective IgA deficiency or prior anaphylactic reaction to IVIG.<sup>7-13</sup> Patients with selective IgA deficiency have an increased risk of anaphylaxis to IVIG products containing IgA, even when only small concentrations are present. Select a product with lower IgA content (eg, Gammagard S/D, Polygam S/D) if IVIG treatment is necessary for such patients. Use of lower IgA products reduces the risk of adverse reactions, but does not guarantee against them.<sup>7-15</sup> See Table 1 for the IgA content of available products.
- D. The FDA is evaluating the association between IVIG and thrombotic events. Various thrombotic events have been reported including myocardial infarction, cerebral infarction, deep venous thrombosis, and pulmonary embolism. The incidence of thrombotic events is rare and the etiology of these events is unclear. Rapid infusion of IVIG and use of high doses may increase risk by transiently increasing serum viscosity.<sup>4, 6, 16, 17</sup>
- E. Patients at an increased risk for thrombotic events include those with coronary artery disease, hypertension, cerebrovascular disease, and diabetes mellitus. Patients with an increased risk should be carefully evaluated prior to IVIG therapy.<sup>4, 6, 16, 17</sup>
- F. Renal adverse effects may occur although the incidence is low.<sup>3, 4, 6-15, 18</sup> However, significant morbidity and mortality may occur. The exact mechanism is unknown, but may be related to the sucrose content of various products. High doses of sucrose-containing products (eg, Carimune NF) may damage the proximal renal tubules, causing acute renal failure.

- G. Assess baseline renal function (ie, urine output, blood urea nitrogen, serum creatinine) prior to starting IVIG and periodically during administration. Ensure that patients are well-hydrated prior to therapy. If renal function worsens, consider discontinuing therapy or using products without sucrose (eg Flebogamma, Gammagard S/D, Gammagard liquid, Gamunex, Octagam, Polygam S/D), as shown in Table 2.<sup>3, 4, 6-15, 17, 18</sup>
- H. The maltose in Octagam interferes with the University of Utah Hospital's Accucheck Inform Meters resulting in falsely high blood glucose measurements.<sup>19</sup> Patients who receive Octagam should not have their blood glucose measured by the Accucheck Inform Meters. Please note that phlebotomists utilize the Accucheck Inform Meters for point of care blood glucose checks. Blood glucose readings must be performed by ARUP laboratories. WinRho SDF Liquid also contains maltose. When WinRho SDF Liquid is given at the recommended doses, the peak blood maltose concentration is unlikely to interfere with glucose testing using Accucheck Inform Meters.
- I. Table 2 describes the significant adverse effects of IVIG, and gives monitoring and management guidelines. Premedicate all patients with acetaminophen 650 mg and diphenhydramine 25 - 50 mg, given 30 - 60 minutes prior to the IVIG infusion. A glucocorticoid may be given as well. Table 3 compares different glucocorticoids that may be used as premedication for patients receiving IVIG.

**Table 1. Intravenous Immunoglobulin Guidelines for Administration<sup>1, 7-15, 18</sup>**

Product name	Administration rate	Filtration	IgA Content (mcg/mL)	Sugar Content	Storage	Formulary Status
<p>Polygam S/D</p> <p>5 g or 10 g vial of lyophilized powder with Sterile Water for Injection diluent</p> <p>Reconstituted to 5% or 10% solution.</p>	<p>Initial infusion: 0.5 mL/kg/hr, increase as tolerated up to 4 mL/kg/hr maximum (use 5% solution until patient tolerates 4 mL/kg/hr).</p> <p>Subsequent infusions: Patients who tolerate 5% solution at the maximum rate may receive 10% solution, starting at 0.5 mL/kg/hr and increased up to 8 mL/kg/hr.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 4 mL/kg/hr for 5% solution, or 2 mL/kg/hr for 10% solution.</p>	Required, 15 micron	< 2.2	2% glucose	Store at room temperature	Formulary, stock unavailable
<p>Carimune NF</p> <p>3 g, 6 g, or 12 g vial of lyophilized powder for injection</p> <p>Reconstituted to 3%, 6%, or 9% solution</p>	<p>Initial infusion: 3% solution at 0.5-1 mL/min for 15-30 minutes, then increase to 1.5 - 2.5 mL/min.</p> <p>Subsequent infusions: start at 1 - 1.5 mL/min for 15-30 minutes with 3% or 6% solution, then increase up to 2.5 mL/min. May give higher concentrations at same mg/min rate.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 2 mg/kg/min.</p>	Optional, 0.2 micron or greater	720	5% sucrose	Room temperature	Formulary, stock unavailable
<p>Flebogamma</p> <p>5% solution: 0.5/10 mL, 2.5 g/50 mL, 5 g/100 mL, 10 g/200 mL</p>	<p>0.01 mL/kg/min for 30 minutes. If tolerated, gradually increase up to 0.1 mL/kg/min maximum.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 0.06 mL/kg/min.</p>	Optional, 15 to 20 micron	12 to 14	5% D-sorbitol	Store at room temperature or refrigerate	Formulary, stock unavailable
<p>Gammagard S/D</p> <p>2.5 g, 5 g, or 10 g vials of lyophilized powder with Sterile Water for Injection diluent</p> <p>Reconstituted to 5% or 10% solution.</p>	<p>5%: 0.5 mL/kg/hr, increase as tolerated to a maximum of 4 mL/kg/hr. If patient tolerates 5% solution at 4 mL/kg/hr, then can start 10% solution at 0.5 mL/kg/hr and increase as tolerated up to 8 mL/kg/hr.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 4 mL/kg/hr for 5% solution, or 2 mL/kg/hr for 10% solution.</p>	Required, 15 micron	< 2.2	2% glucose	Store at room temperature or refrigerate	Formulary  Consider for patients with hypersensitivity to IgA (IgA content is < 2.2 mcg/m)

**Table 1 Continued. Intravenous Immunoglobulin Guidelines for Administration<sup>1, 7-15, 18</sup>**

Product name	Administration rate	Filtration	IgA Content (mcg/mL)	Sugar Content	Storage	Formulary Status
<p>Gammagard Liquid</p> <p>10% solution 1 g, 2.5 g, 5 g, 10 g, 20 g vials</p> <p>Use solution as supplied, may dilute to 5% with Dextrose 5%</p>	<p>0.5 mL/kg/hour, if increased as tolerated every 30 minutes up to 5 mL/kg/hour</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 2 mL/kg/hr</p>	Optional, in-line filter	37	None, glycine-based	Refrigerate. Length of room temperature storage is based on date of manufacture.	Formulary
<p>Gamunex</p> <p>10% solution: 1 g/10 mL, 2.5 g/25 mL, 5 g/50 mL, 10 g/100 mL, 20 g/200 mL</p>	<p>0.01 mL/kg/min for 30 minutes. If tolerated, may increase up to 0.08 mL/kg/min maximum.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 0.08 mL/kg/min.</p>	Not required	46	None, glycine-based	Refrigerate	Formulary, limited stock available
<p>Octagam</p> <p>5% solution: 1 g/20 mL, 2.5 g/50 mL, 5 g/100 mL, 10 g/200 mL</p>	<p>0.01 mL/kg/min for 30 minutes, then 0.02 mL/kg/min for 30 minutes, then 0.04 mL/kg/min for 30 minutes, then may increase to 0.07 mL/kg/min as tolerated.</p> <p>Patients at high risk for acute renal failure Use lowest infusion rate possible, not to exceed 0.07 mL/kg/min.</p>	Not required	< 200	<p>10% maltose</p> <p>The maltose in this product interferes with Accucheck Inform Meters resulting in falsely high blood glucose measurements</p>	Refrigerate	Formulary, stock unavailable

NOTE: Gammar-P, Iveegam EN and Panglobulin NF are discontinued.

**Table 2. Monitoring for and Management of IVIG Adverse Effects** <sup>1-15, 17, 18, 20</sup>

Possible Adverse Reactions	Monitoring Parameters	Management of Reaction	Comments
<p><i>Infusion-related reactions:</i> Back pain, chest pain, chest tightness or heaviness, fever or chills, rigors, headache, malaise, myalgia, nausea, or vomiting</p>	<p>Vital signs (temperature, blood pressure, pulse rate) and patient symptoms prior to infusion and every 15 minutes for 1 hour after starting infusion or increasing rate; then, monitor periodically during infusion.</p>	<p>Slow infusion rate until symptoms resolve OR stop infusion – contact prescriber. Report adverse event as directed by your health system.</p>	<p>May premedicate patients with acetaminophen 325 mg – 650 mg and diphenhydramine 25 – 50 mg, given 30 minutes to 1 hour prior to infusion.</p> <p>Glucocorticoids may be considered in patients with history of severe reactions.</p>
<p><i>Signs of anaphylaxis:</i> Chest tightness, diaphoresis, hypertension, hypotension, rash, urticaria</p>	<p>Vital signs (temperature, blood pressure, pulse rate) and patient symptoms prior to infusion and every 15 minutes for 1 hour after starting infusion or increasing rate; then, monitor periodically during infusion.</p>	<p>Stop infusion and contact prescriber. Report adverse event as directed by your health system.</p>	<p>Low IgA content products may be appropriate (eg patients with selective IgA deficiency) if IVIG therapy is essential, see Table 2 for IgA content of products.</p>
<p><i>Thrombotic events</i> (eg myocardial infarction, deep vein thrombosis, pulmonary embolism)</p>	<p>Patient symptoms (e.g. calf pain, sudden shortness of breath, chest pain) every 15 minutes for 1 hour; then monitor periodically during infusion.</p>	<p>Slow or stop infusion – contact prescriber; therapy is usually discontinued. Report adverse event as directed by your health system.</p>	<p>Patients at increased risk:</p> <ul style="list-style-type: none"> <li>• Elderly</li> <li>• Overweight</li> <li>• Immobilized</li> <li>• Coronary artery disease</li> <li>• Hypertension</li> <li>• Cerebrovascular disease</li> <li>• Thrombophilic disorders</li> <li>• Diabetes mellitus</li> </ul> <p>In high-risk patients, limit IVIG concentration to 5% or lower and infusion rate to 4 mL/kg/hr or lower.</p>
<p><i>Renal dysfunction or acute renal failure</i></p> <p>More commonly seen with sucrose-containing products (ie Carimune NF, Gammar-P IV, Panglobulin NF)</p>	<p>Assess baseline renal function (urine output, BUN, SCr) prior to initiating infusion and periodically during infusion.</p>	<p>Slow or stop infusion – contact prescriber; therapy is usually discontinued. Report adverse event as directed by your health system.</p>	<p>Patients at increased risk:</p> <ul style="list-style-type: none"> <li>• Pre-existing renal insufficiency</li> <li>• Diabetes mellitus</li> <li>• Age &gt; 65 years</li> <li>• Volume depletion</li> <li>• Sepsis, paraproteinemia</li> <li>• Concomitant nephrotoxic drugs</li> </ul> <p>Consider agents that do not contain sucrose (eg Flebogamma, Gammagard S/D, Gammagard liquid, Gamunex, Octagam, Polygam S/D)</p>

**Table 3. Glucocorticoid Comparison for IVIG Premedication<sup>21, 22</sup>**

Agent	Equivalent dose (approximate mg) administered 30 minutes before IVIG Infusion	Route of administration
Betamethasone	4	IM, PO
Dexamethasone	4	IM, IV, PO
Hydrocortisone	100	IM, IV, PO
Methylprednisolone	20	IM, IV, PO
Prednisolone	25	PO
Prednisone	25	PO

**References**

1. ASHP therapeutic guidelines for intravenous immune globulin. ASHP Commission on Therapeutics. *Clin Pharm.* Feb 1992;11(2):117-136.
2. Anon. Immune globulin intravenous (Human), systemic. *USP DI Volume 1. Drug Information for the Health Care Professional.* 23rd ed. Greenwood Village, CO: Micromedex Thomson Healthcare; 2003:1527-1532.
3. Ballow M. Intravenous immunoglobulins: clinical experience and viral safety. *J Am Pharm Assoc (Wash).* May-Jun 2002;42(3):449-458; quiz 458-449.
4. Knezevic-Maramica I, Kruskall MS. Intravenous immune globulins: an update for clinicians. *Transfusion.* Oct 2003;43(10):1460-1480.
5. Martin TD. Safety and tolerability of intravenous immunoglobulins. *Electroencephalogr Clin Neurophysiol Suppl.* 1999;50:514-520.
6. Pierce LR, Jain N. Risks associated with the use of intravenous immunoglobulin. *Transfus Med Rev.* Oct 2003;17(4):241-251.
7. Baxter. Polygam S/D immune globulin intravenous (Human), solvent/detergent treated package insert. Washington, DC: American Red Cross Blood Services; 2002.
8. Baxter. Gammagard S/D immune globulin intravenous (Human), Solvent Detergent Treated package insert. Westlake Village, CA: Baxter Healthcare Corporation; 2004.
9. Baxter. Gammagard Liquid immune globulin intravenous (Human), package insert. Westlake Village, CA: Baxter Healthcare Corporation; 2005.
10. Bayer. Immune globulin intravenous (Human), 10%, caprylate/chromatography purified (Gamunex) package insert. Elkhart, IN: Bayer Corporation; 2003.
11. Grifols. Flebogamma 5% {immune globulin intravenous (Human)} package insert. Los Angeles, CA: Grifols Biologicals, Inc.; 2004.
12. Octapharma. Immune globulin intravenous (Human) 5%, Solvent/Detergent Treated (Octagam) package insert. Herndon, VA: Octapharma USA, Inc.; 2004.
13. ZLB Behring. Immune globulin intravenous (Human) (Carimune NF Nanofiltered) package insert. Glendale, CA: ZLB Bioplasma Inc.; 2003.
14. Plasma Services. Polygam S/D. Available online at: <http://polygamsd.redcross.org>. Accessed on December 9, 2004. Washington, DC: American Red Cross; 2004.
15. Ratko TA. Other Relevant Issues: Adverse Effects. In: Enman CM, ed. *UHC Clinical Practice Advancement Center Technology Assessment: Intravenous Immunoglobulin Preparations.* Oak Brook, IL: University Hospital Consortium Services Corporation; 1995:139-140.
16. Dalakas MC. High-dose intravenous immunoglobulin and serum viscosity: risk of precipitating thromboembolic events. *Neurology.* Feb 1994;44(2):223-226.
17. Plasma Program. Immune globulin intravenous and serious adverse events. *Plasma Products. Pharmacy Bulletin, First Quarter 2003.* Irving, TX: Novation; 2003:6-9.
18. Siegel J. Immune Globulins: Therapeutic, Pharmaceutical, & Cost Considerations. Available online at: <http://www.pharmacypracticenews.com/index.asp?show=special> Accessed on November 10, 2006. : Pharmacy Practice News.
19. Food and Drug Administration. MedWatch Alert: Parenteral Maltose/Parenteral Galactose/Oral Xylose-Containing Products. Available online at: <http://www.fda.gov/medwatch/safety/2005/safety05.htm#maltose>. Accessed on November 10, 2006. .

20. Meaux JB. Intravenous immunoglobulin: what nurses need to know. *J Perinat Neonatal Nurs*. Mar 1996;9(4):63-69.
21. Glucocorticoids. In: McEvoy GK, Litvak K, Welsh OH, Ford ME, Kester L, eds. *AHFS 2006 Drug Information*. Bethesda, MD: American Society of Health-System Pharmacists; 2006:2974-2987.
22. Adrenocortical Steroids. In: Novak K, ed. *Drug Facts and Comparisons - Updated Monthly* St Louis, MO: Wolters Kluwer Health; 2006:316-331.

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