Considerations for administration

of IVIG in adults with multifocal motor neuropathy (MMN)

Not all IVIG formulations are interchangeable[1-3]

The final formulation can differ among IVIGs, meaning they are not interchangeable.[1-3]

When selecting an IVIG treatment, individual patient characteristics should be considered.[2]

IVIG, intravenous immune globulin.

INDICATION

GAMMAGARD LIQUID is indicated as a maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy (MMN). GAMMAGARD LIQUID for MMN is for intravenous use only.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS, RENAL DYSFUNCTION, and ACUTE RENAL FAILURE

- **Thrombosis may occur with immune globulin (IG) products, including GAMMAGARD LIQUID. Risk factors may include advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors.**
- **Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur in predisposed patients with immune globulin intravenous (IGIV) products. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMMAGARD LIQUID does not contain sucrose.**
- **For patients at risk of thrombosis, administer GAMMAGARD LIQUID at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity.**

Contraindications

- History of anaphylactic or severe systemic hypersensitivity reactions to human IG
- IgA-deficient patients with antibodies to IgA and a history of hypersensitivity to human IG. Anaphylaxis has been reported with intravenous (IV) use of GAMMAGARD LIQUID.

Please see additional Important Safety Information throughout and click for Full Prescribing Information.

Not all IVIG formulations are interchangeable[1-3]

IVIG treatments are distinct plasma products that are not interchangeable, with patient tolerance differing from one brand to another. Not all IVIG treatments are equivalent, and caution should be used when changing products.[1-3]

Please see table below for patient conditions and risk factors to consider with IVIG administration.

Patient condition	Patient risk factors (This is not an all-inclusive list)	IVIG risk factors[1,4]				
		Sodium content	Sugar content	Osmolality	IgA	Volume load
Predisposition for renal insufficiency[1,5-7]	• Diabetes mellitus • Elderly • Hypovolemia • Sepsis • Paraproteinemia • Concomitant therapy with nephrotoxic drugs	✓	✓	✓		✓
Heart disease[1,8-10]	• Thromboembolic risk factors • Coronary artery disease • Heart failure • Hypertension • Hyperlipidemia • Cardiovascular risk factors	✓		✓		✓
Diabetes mellitus, pre-diabetes[6]	• Type 1 • Type 2		✓			
Elderly[1,11]	• Generally considered as >65 years of age	✓	✓	✓		✓
IgA deficiency[1]	• IgA-deficient patients with antibodies to IgA and a history of hypersensitivity • All patients, since an IgA concentration that will provoke a reaction is unknown; even trace amounts of IgA present a risk for anaphylaxis				✓	
Volume intake restrictions[1,9]	• Hyperviscosity risk factors • Cardiac impairment • Renal impairment • Pulmonary edema • Hypertension • Elderly	✓	✓	✓		✓

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions

Hypersensitivity: Severe hypersensitivity reactions may occur, even in patients who have tolerated previous treatment with human IG. If a hypersensitivity reaction occurs, discontinue infusion immediately and institute appropriate treatment. IgA-deficient patients with antibodies to IgA are at greater risk of developing potentially severe hypersensitivity reactions, including anaphylaxis.

Renal Dysfunction/Failure: Acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, and death may occur with IV use of IG products, especially those containing sucrose. Ensure patients are not volume depleted prior to infusion. In patients at risk due to pre-existing renal insufficiency or predisposition to acute renal failure, assess renal function before initiation and throughout treatment, and use the minimum infusion rate practicable for IV administration. If renal function deteriorates, consider discontinuation.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur. It is critical to distinguish true hyponatremia from a pseudohyponatremia because certain treatments may lead to volume depletion, a further increase in serum viscosity, and a predisposition to thromboembolic events.

Thrombosis: May occur following treatment with IG products and in the absence of known risk factors. In patients at risk, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Aseptic Meningitis Syndrome: Has been reported with use of IG and may occur more frequently in females. Conduct a thorough neurological exam on patients exhibiting signs and symptoms, to rule out other causes of meningitis. Discontinuing IG treatment has resulted in remission within several days without sequelae.

GAMMAGARD LIQUID is the first and only FDA-approved treatment for MMN[12]

GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10%

Characteristics of GAMMAGARD LIQUID	
Formulation	
Sodium content	No added sodium[12]
Sugar content	No sucrose or added sugar[12]
Preservatives	No added preservatives[12]
Stabilizer	0.25M glycine[12]
Osmolality	240-300 mOsmol/kg (similar to physiologic osmolality: 285-295 mOsmol/kg)[12]
IgA concentration	Average concentration of 37 µg/mL[12]
pH range	4.6-5.1[12]
Dosage for MMN	
Dose	Range: 0.5-2.4 g/kg/mo (based on clinical response)[12]
Infusion rate – initial	0.5 mL/kg/hr (0.8 mg/kg/min)[12]
Infusion rate – maintenance	If tolerated, up to a maximum rate of 5.4 mL/kg/hr (9 mg/kg/min)[12]
Packaging	
Latex content in packaging	The packaging is not made with natural rubber latex.[12]
Vial sizes (grams protein)	10 mL (1 g), 25 mL (2.5 g), 50 mL (5 g), 100 mL (10 g), 200 mL (20 g), 300 mL (30 g)[12]
Shelf life/storage requirements	• Up to 36 months at refrigerated temperature: 2 °C-8 °C (36 °F-46 °F)[12] • Up to 24 months at room temperature: 25 °C (77 °F)[12] • Do not use past expiration date printed on label[12] • Do not freeze[12]

IMPORTANT SAFETY INFORMATION (continued)

Warnings and Precautions (continued)

Hemolysis: GAMMAGARD LIQUID contains blood group antibodies, which may cause a positive direct antiglobulin reaction and hemolysis. Monitor patients for signs and symptoms of hemolysis and delayed hemolytic anemia and, if present, perform appropriate confirmatory lab testing.

Transfusion-Related Acute Lung Injury: Non-cardiogenic pulmonary edema may occur with IV administered IG. Monitor patients for pulmonary adverse reactions. If suspected, perform appropriate tests for presence of anti-neutrophil and anti-HLA antibodies in both product and patient serum. May be managed using oxygen therapy with adequate ventilatory support.

Transmittable Infectious Agents: Because GAMMAGARD LIQUID is made from human plasma, it may carry a risk of transmitting infectious agents (e.g., viruses, other pathogens). No confirmed cases of viral transmission or variant Creutzfeldt-Jakob disease (vCJD) have been associated with GAMMAGARD LIQUID.

Interference with Lab Tests: False positive serological test results and certain assay readings, with the potential for misleading interpretation, may occur as the result of passively transferred antibodies.

Please see additional Important Safety Information throughout and click for Full Prescribing Information, including Boxed Warning regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

Consider GAMMAGARD LIQUID for IVIG administration in adults with MMN[12]

GAMMAGARD LIQUID
[Immune Globulin Infusion (Human)] 10%

Vial size	NDC number
1 g (10 mL)	0944-2700-02
2.5 g (25 mL)	0944-2700-03
5 g (50 mL)	0944-2700-04
10 g (100 mL)	0944-2700-05
20 g (200 mL)	0944-2700-06
30 g (300 mL)	0944-2700-07

Use diagnosis code **ICD-10-CM G61.82** when prescribing GAMMAGARD LIQUID for MMN patients

PREVENT SUBSTITUTIONS
write "Dispense as Written"

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

The serious adverse reactions in the clinical study for MMN were pulmonary embolism and blurred vision. The most common adverse reactions observed in ≥5% of subjects were headache, chest discomfort, muscle spasms, muscular weakness, nausea, oropharyngeal pain, and pain in extremity.

Drug Interactions

Passive transfer of antibodies may transiently interfere with immune responses to live attenuated virus vaccines (e.g., measles, mumps, rubella, and varicella).

Please see additional Important Safety Information throughout and click for Full Prescribing Information, including Boxed Warning regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

References: 1. Gelfand EW. Differences between IGIV products: impact on clinical outcome. *Int Immunopharmacol.* 2006;6(4):592-599. **2.** Ballow M. Safety of IGIV therapy and infusion-related adverse events. *Immunol Res.* 2007;38(1-3):122-132. **3.** American Academy of Allergy Asthma & Immunology. Eight guiding principles for effective use of IVIG for patients with primary immunodeficiency. 2011. Accessed June 22, 2020. http://primaryimmune.org/wp-content/uploads/2011/11/Guiding-Principles-I.pdf **4.** Siegel J. Tailoring IVIG therapy to the individual patient: considerations for pharmacy practice. *Pharm Pract News.* 2007. Accessed June 22, 2020. http://pharmacypracticenews.com/download/07015SR-FINALWM.pdf **5.** Gurcan HM, Keskin DB, Ahmed AR. Information for healthcare providers on general features of IGIV with emphasis on differences between commercially available products. *Autoimmun Rev.* 2010;9(8):553-559. **6.** Ochs HD, Siegel J. Stabilizers used in intravenous immune globulin products: a comparative review. *Pharm Pract News.* 2010. Accessed June 22, 2020. http://www.pharmacypracticenews.com/download/SR1019_Stabl_IVIG_WM.pdf **7.** US Food and Drug Administration. Important drug warning: potential risk of acute renal failure reported to be associated with administration of Immune Globulin Intravenous (Human). Accessed June 22, 2020. http://www.fda. gov/BiologicsBloodVaccines/SafetyAvailability/ucm105901.htm **8.** Brown HC, Ballas ZK. Acute thromboembolic events associated with intravenous immunoglobulin infusion in antibody-deficient patients. *J Allergy Clin Immunol.* 2003;112(4):797-799. **9.** Lemm G. Composition and properties of IVIg preparations that affect tolerability and therapeutic efficacy. *Neurology.* 2002;59(12 suppl 6):S28-S32. **10.** Paran D, Herishanu Y, Elkayam O, Shopin L, Ben-Ami R. Venous and arterial thrombosis following administration of intravenous immunoglobulins. *Blood Coagul Fibrinolysis.* 2005;16(5):313-318. **11.** Cheng MJ, Christmas C. Special considerations with the use of intravenous immunoglobulin in older persons. *Drugs Aging.* 2011;28(9):729-736. **12.** GAMMAGARD LIQUID. Prescribing information. Baxalta US Inc.

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