Taking intravenous immune globulin (IVIG) product characteristics into consideration

When prescribing an IVIG therapy, it's important to understand how the formulation, dosing, and packaging vary. The charts below will allow you to differentiate product characteristics but they *do not imply clinical outcomes.*

	Takeda		Bio Products Laboratory
	GAMMAGARD LIQUID® [Immune Globulin Infusion (Human)] 10% Solution[1]	GAMMAGARD S/D [Immune Globulin Intravenous (Human)] IgA <1 µg/mL in a 5% solution[2,3]	GAMMAPLEX 5% [Immune Globulin Intravenous (Human)], 5% Liquid[4]
Usage			
Form	Liquid	Lyophilized	Liquid
Formulation			
IgA content	Average 37µg/mL	<1 µg/mL	<10 µg/mL
Sugar content	No added sugar	Glucose (2 g/dL)	D-sorbitol (5 g/dL)
Sodium content	No added sodium	145 mEq/L	76 mEq/L
Stabilizers	Glycine (250 mM)	Glycine (300 mM); Glucose (2 g/dL)	Glycine (80 mM); D-sorbitol (5 g/dL)
pH range when liquid	4.6-5.1	6.4-7.2 (6.8±0.4)	4.8-5.1
Osmolality/osmolarity (physiologic range: 285-295 mOsmol/kg)[2]	240-300 mOsmol/kg	636 mOsmol/kg[3]	Typically 420-500 mOsmol/kg (>240 mOsmol/kg)
Dedicated viral inactivation/removal steps*	• S/D treatment • 35 nm nanofiltration • Incubation at low pH at elevated temperature (30-32 °C)	• Cold ethanol fractionation • S/D treatment	• S/D treatment • Virus filtration • Low pH incubation
Packaging			
Latex content in packaging	Not made with natural rubber latex	Not made with natural rubber latex	The components used in packaging are not made with natural rubber latex
Shelf life/storage requirements	• 36 months at refrigerated temperature from the date of manufacture: 2-8 °C (36-46 °F) • 24 months at room temperature from the date of manufacture: not to exceed 25 °C (77 °F) • Do not use past expiration date printed on label • Do not freeze	• 24 months at room temperature, not to exceed 25 °C (77 °F) • Do not use past expiration date printed on label • Do not freeze	• 36 months at temperature from 2-25 °C (35.6-77 °F) until expiration date • Protect from light • Do not freeze
Grams of protein per vial	1 g (10 mL) 2.5 g (25 mL) 5 g (50 mL) 10 g (100 mL) 20 g (200 mL) 30 g (300 mL)	5 g 10 g	5 g (100 mL) 10 g (200 mL) 20 g (400 mL)

*Dedicated inactivation/removal steps are introduced into the manufacturing process for the sole purpose of reducing pathogens. Critical parameters can be optimized and standardized to ensure reliable and constant performance across many production runs.

Please see additional Important Safety Information on Page 5 and click for Full Prescribing Information for GAMMAGARD LIQUID and GAMMAGARD S/D including Boxed WARNING regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

Taking intravenous immune globulin (IVIG) product characteristics into consideration

	Bio Products Laboratory	ADMA Biologics	Grifols
	GAMMAPLEX 10% [Immune Globulin Intravenous (Human)], 10% Liquid[5]	BIVIGAM® [Immune Globulin Intravenous (Human)], 10% Liquid[6,7]	FLEBOGAMMA® 5% DIF [Immune Globulin Intravenous (Human)][8]
Usage			
Form	Liquid	Liquid	Liquid
Formulation			
IgA content	<20 µg/mL	≤200µg/mL	Typically <50 µg/mL
Sugar content	No sucrose or maltose	No added sugar	D-sorbitol (5 g/dL)
Sodium content	<30 mEq/L	100-140 mEq/L	Trace amounts
Stabilizers	Glycine (200-300 mM)	Glycine (200-290 mM)	D-sorbitol (5 g/dL)
pH range when liquid	4.9-5.2	4.0-4.6	5.0-6.0
Osmolality/osmolarity (physiologic range: 285-295 mOsmol/kg)[2]	Typically 280 mOsmol/kg (>240mOsmol/kg)	≤510 mOsmol/kg	240-370 mOsmol/kg
Dedicated viral inactivation/removal steps*	• S/D treatment • Virus filtration • Low pH incubation	• Precipitation and removal of fraction III during cold ethanol fractionation • S/D treatment • 35 nm virus filtration	• Pasteurization • S/D treatment • 20 nm nanofiltration • Low pH treatment
Packaging			
Latex content in packaging	The components used in packaging are latex-free	The components used in packaging are not made with natural rubber latex	Not made with natural rubber latex
Shelf life/storage requirements	• 36 months at temperature from 2-25 °C (35.6-77 °F) until expiration date • Protect from light • Do not freeze	• Refrigerate from 2-8 °C (36-46 °F) until expiration date • Do not freeze or heat	• 24 months at room temperature, 2-25 °C (36-77 °F), until expiration date • Do not freeze • Protect from light
Grams of protein per vial (total volume in mL)	5 g (50 mL) 10 g (100 mL) 20 g (200 mL)	5 g (50 mL) 10 g (100 mL)	0.5 g (10 mL) 2.5 g (50 mL) 5 g (100 mL) 10 g (200 mL) 20 g (400 mL)

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Taking intravenous immune globulin (IVIG) product characteristics into consideration

	Grifols		Octapharma
	FLEBOGAMMA® 10% DIF [Immune Globulin Intravenous (Human)][9]	GAMUNEX®-C (immune globulin injection [human], 10% caprylate /chromatography purified)[7,10,11]	OCTAGAM [Immune Globulin Intravenous (Human)] 5% Liquid[12]
Usage			
Form	Liquid	Liquid	Liquid
Formulation			
IgA content	Typically <100 µg/mL	46 µg/mL	≤200 µg/mL
Sugar content	D-sorbitol (5 g/dL)	None[7]	Maltose (10 g/dL)
Sodium content	Trace amounts	Trace amounts[7]	≤30 mEq/L
Stabilizers	D-sorbitol (5 g/dL)	Glycine (160-240 mM)	Maltose (10 g/dL)
pH range when liquid	5.0-6.0	4.0-4.5	5.1-6.0
Osmolality/osmolarity (physiologic range: 285-295 mOsmol/kg)[2]	240-370 mOsmol/kg	258 mOsmol/kg	310-380 mOsmol/kg
Dedicated viral inactivation/removal steps*	• Pasteurization • S/D treatment • 20 mn nanofiltration • Low pH treatment	• Caprylate precipitation • Depth filtration • Low pH incubation	• Cold-ethanol fractionation • S/D treatment • pH 4 treatment
Packaging			
Latex content in packaging	Not made with natural rubber latex	Not made with natural rubber latex	The components used in packaging are not made with natural rubber latex
Shelf life/storage requirements	• 24 months at room temperature, 2-25 °C (36-77 °F), until expiration date • Do not freeze • Protect from light	• 36 months at refrigerated temperature, 2-8 °C (36-46 °F), from the date of manufacture • Up to 6 months not to exceed 25 °C (77 °F) during the 36-month shelf life • Do not freeze	• 24 months at 2-25 °C (36-77 °F) from date of manufacture • Do not freeze
Grams of protein per vial (total volume in mL)	5 g (50 mL) 10 g (100 mL) 20 g (200 mL)	1 g (10 mL) 2.5 g (25 mL) 5 g (50 mL) 10 g (100 mL) 20 g (200 mL) 40 g (400 mL)	1 g (20 mL) 2.5 g (50 mL) 5 g (100 mL) 10 g (200 mL) 25 g (500 mL)

*Dedicated inactivation/removal steps are introduced into the manufacturing process for the sole purpose of reducing pathogens. Critical parameters can be optimized and standardized to ensure reliable and constant performance across many production runs.
†Also distributed by Kedrion as GAMMAKED™ [Immune Globulin Injection (Human)],10% Caprylate/Chromatography Purified.

Taking intravenous immune globulin (IVIG) product characteristics into consideration

	Octapharma		CSL Behring
	OCTAGAM 10% [Immune Globulin Intravenous (Human)][13]	PANZYGA® (immune globulin intravenous, human - ifas) 10% Liquid Preparation[14]	PRIVIGEN® [Immune Globulin Intravenous (Human)] 10%[15]
Usage			
Form	Liquid	Liquid	Liquid
Formulation			
IgA content	Average 106 µg/mL	Average 100 µg/mL	≤25 µg/mL
Sugar content	Maltose (9 g/dL)	No sucrose	No added sugar
Sodium content	≤30 mEq/L	Trace amounts	Trace amounts
Stabilizers	Maltose (9 g/dL)	Glycine (200-260 mM)	L-proline (250 mM)
pH range when liquid	4.5-5.0	4.5-5.0	4.6-5.0
Osmolality/osmolarity (physiologic range: 285-295 mOsmol/kg)[2]	310-380 mOsmol/kg	240-310 mOsmol/kg	~320 mOsmol/kg (240-440 mOsmol/kg)
Dedicated viral inactivation/removal steps*	• Cold-ethanol fractionation • S/D treatment • pH 4 treatment	• S/D treatment • Ion-exchange chromatography • 20 nm nanofiltration	• pH 4 incubation • Virus filtration • Depth filtration
Packaging			
Latex content in packaging	The components used in packaging are not made with natural rubber latex	The components used in packaging are not made with natural rubber latex	The components used in packaging are not made with natural rubber latex
Shelf life/storage requirements	• 24 months at 2-8 °C (36-46 °F) from date of manufacture • Within the first 12 months of this shelf life, the product may be stored up to 9 months at ≤25 °C (77 °F) • Do not freeze	• 24 months at temperature from 2-8 °C (36-46 °F) from date of manufacture • 9 months at temperature of up to 25 °C (77 °F) within shelf-life; use immediately or discard following • Do not use past expiration date • Do not freeze	• 36 months at room temperature, not to exceed 25 °C (77 °F), until expiration date • Do not freeze • Protect from light
Grams of protein per vial (total volume in mL)	2 g (20 mL) 5 g (50 mL) 10 g (100 mL) 20 g (200 mL) 30 g (300 mL)	1 g (10 mL) 2.5 g (25 mL) 5 g (50 mL) 10 g (100 mL) 20 g (200 mL) 30 g (300 mL)	5 g (50 mL) 10 g (100 mL) 20 g (200 mL) 40 g (400 mL)

*Dedicated inactivation/removal steps are introduced into the manufacturing process for the sole purpose of reducing pathogens. Critical parameters can be optimized and standardized to ensure reliable and constant performance across many production runs.

INDICATIONS AND LIMITATION OF USE

GAMMAGARD LIQUID and **GAMMAGARD S/D** are indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients ≥2 years.

GAMMAGARD LIQUID is for intravenous and subcutaneous use.

GAMMAGARD S/D is for intravenous use only.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS

GAMMAGARD LIQUID and GAMMAGARD S/D

- **Thrombosis may occur with immune globulin (IG) products, including GAMMAGARD LIQUID and GAMMAGARD S/D. 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.**
- **For patients at risk of thrombosis, administer GAMMAGARD LIQUID and GAMMAGARD S/D 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.**

WARNING: RENAL DYSFUNCTION and ACUTE RENAL FAILURE

GAMMAGARD LIQUID and GAMMAGARD S/D

- **Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur in predisposed patients with immune globulin intravenous (IGIV) products, including GAMMAGARD LIQUID and GAMMAGARD S/D. 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 and GAMMAGARD S/D do not contain sucrose.**

Contraindications

- **GAMMAGARD LIQUID** is contraindicated in patients with a history of anaphylactic or severe systemic hypersensitivity reactions to human IG, and 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**.
- **GAMMAGARD S/D** is contraindicated in patients with a history of anaphylactic or severe systemic hypersensitivity reactions to the administration of **GAMMAGARD S/D**.

Warnings and Precautions

Hypersensitivity: Severe hypersensitivity reactions may occur, even in patients who have tolerated previous treatment with human IG. Severe hypersensitivity reactions and anaphylactic reactions with a fall in blood pressure have occurred in patients receiving **GAMMAGARD S/D**, including patients who tolerated previous treatments with **GAMMAGARD S/D**, even though it contains low levels of IgA. 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. Acute renal failure has been reported in association with **GAMMAGARD LIQUID** and **GAMMAGARD S/D**. 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 consider lower, more frequent dosing. If renal function deteriorates, consider discontinuation.

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.

Hemolysis: **GAMMAGARD LIQUID** and **GAMMAGARD S/D** contain 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** and **GAMMAGARD S/D** are made from human plasma, they may carry a risk of transmitting infectious agents (e.g., viruses, other pathogens). No confirmed cases of viral transmission of 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 on next Page and click for Full Prescribing Information for GAMMAGARD LIQUID and GAMMAGARD S/D including Boxed WARNING regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

IMPORTANT SAFETY INFORMATION (continued)

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.

Alterations in serum sodium levels (i.e., acute hypernatremia, pseudohyponatremia) may occur with **GAMMAGARD S/D**. In patients on a low sodium diet, calculate the amount of sodium from **GAMMAGARD S/D** when determining dietary sodium intake.

Adverse Reactions

GAMMAGARD LIQUID for PI

IV administration: The serious adverse reaction seen during IV clinical trials was aseptic meningitis. The most common adverse reactions observed in ≥5% of patients in clinical trials were headache, fatigue, pyrexia, nausea, chills, rigors, pain in extremity, diarrhea, migraine, dizziness, vomiting, cough, urticaria, asthma, pharyngolaryngeal pain, rash, arthralgia, myalgia, oedema peripheral, pruritus, and cardiac murmur.

GAMMAGARD S/D

The most common adverse reactions observed in ≥5% of clinical trial patients during or within 48 hours of infusion were headache, nausea, chills, fatigue, pyrexia, upper abdominal pain, diarrhea, back pain, infusion site pain, hyperhidrosis, and flushing.

The most serious adverse reactions reported postmarketing include renal failure, thrombotic events (myocardial infarction, cerebrovascular accidents, and pulmonary embolism), anaphylactic shock, aseptic meningitis, and hemolysis.

Drug Interactions

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

Please click for Full Prescribing Information for GAMMAGARD LIQUID and GAMMAGARD S/D including Boxed WARNING regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

References: 1. GAMMAGARD LIQUID [Prescribing Information]. Lexington, MA: Baxalta US Inc. **2.** GAMMAGARD S/D [Prescribing Information]. Lexington, MA: Baxalta US Inc. **3.** Gelfand EW. Differences between IGIV products: impact on clinical outcome. *Int Immunopharmacol*. 2006;6(4):592-599. **4.** GAMMAPLEX 5% [Prescribing Information]. Elstree, Hertfordshire, UK: Bio Products Laboratory Limited. **5.** GAMMAPLEX 10% [Prescribing Information]. Elstree, Hertfordshire, UK: Bio Products Laboratory Limited. **6.** BIVIGAM [Prescribing Information]. Boca Raton, FL: ADMA Biologics. **7.** Immune Deficiency Foundation. Characteristics of immunoglobulin products used to treat primary immunodeficiency diseases. https://primaryimmune.org/publication/characteristics-ig-products-used-treat-pi-licensed-use-us. Accessed March 15, 2020. **8.** FLEBOGAMMA 5% DIF [Prescribing Information]. Barcelona, Spain: Instituto Grifols, SA. **9.** FLEBOGAMMA 10% DIF [Prescribing Information]. Barcelona, Spain: Instituto Grifols, SA. **10.** GAMUNEX-C [Prescribing Information]. Research Triangle Park, NC: Grifols Therapeutics LLC. **11.** GAMMAKED [Prescribing Information]. Research Triangle Park: Grifols Therapeutics LLC. **12.** OCTAGAM 5% [Prescribing Information]. Hoboken, NJ: Octapharma USA Inc. **13.** OCTAGAM 10% [Prescribing Information]. Hoboken, NJ: Octapharma USA Inc. **14.** PANZYGA [Prescribing Information]. Hoboken, NJ: Octapharma USA Inc. **15.** PRIVIGEN [Prescribing Information]. Bern, Switzerland: CSL Behring AG.

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