IV administration with a proven history of clinical use[1]

The most utilized IG product in the United States[1-3]

- 12 years of real-world experience
- 92,205 patients*
- 1,106,465 infusions*

GAMMAGARD LIQUID® [Immune Globulin Infusion (Human)] 10% Solution intravenous (IV) can help you and your patients feel at ease with a supervised and trusted primary immunodeficiency (PI) treatment experience

Patients may prefer IV administration for:

- Peace of mind that comes from receiving care from a trained healthcare professional
- Supervised check-ins at each infusion to help monitor adherence
- Flexibility to administer at the physician's office or at home with nurse assistance

INDICATION

GAMMAGARD LIQUID is indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients ≥2 years.

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.**

*Calculations based on units of GAMMAGARD LIQUID sold from 2006-2017, assuming an average utilization of 450 g/y/patient with PI.[1]

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

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

Links to: https://www.shirecontent.com/PI/PDFs/GAMLIQUID_USA_ENG.pdf

Takeda

Established efficacy[4,5]

GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10% Solution sustained protection against infection in the IV clinical trial

0 **No cases of validated acute serious bacterial infections***
Validated acute serious bacterial infections include bacteremia/sepsis, bacterial meningitis, osteomyelitis/septic arthritis, bacterial pneumonia, and visceral abscess.

0 **No hospitalizations secondary to validated bacterial infections**

4 **Four validated other bacterial infections**
Validated other bacterial infections included 1 urinary tract infection, 1 gastroenteritis, and 2 otitis media.

The rate of all clinically defined but nonvalidated infections was 3.4 infections per subject per year (n=61).

*The rate of validated ASBIs (95% CI: 0.000-0.064; *P*<0.0001) was significantly lower than the rate of <1 per subject per year, which was set by the FDA.

IMPORTANT SAFETY INFORMATION (continued)

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.

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.

Established safety profile[4]

GAMMAGARD LIQUID provided a tolerable profile in the IV clinical trial

- During more than 1800 infusions, the most common systemic adverse reaction per infusion was headaches at a rate of 5.2% (94/1812)
- 15 adverse reactions in 8 subjects were serious. Of these, 2 serious reactions occurred (2 episodes of aseptic meningitis in 1 patient) and were deemed to be possibly related to the infusion of GAMMAGARD LIQUID
- An adverse reaction is defined as an event occurring during or within 72 hours of infusion or any causally related event occurring within the study period

Systemic adverse reactions that occurred in ≥10% of subjects

SYSTEMIC ADVERSE REACTIONS	PER INFUSION N (%) (N=1812 infusions)	PER SUBJECT N (%) (N=61 subjects)
Headache	94 (5.2%)	29 (47.5%)
Fatigue	33 (1.8%)	14 (23.0%)
Pyrexia	28 (1.5%)	17 (27.9%)
Nausea	17 (0.9%)	11 (18.0%)
Chills	14 (0.8%)	8 (13.1%)
Rigors	14 (0.8%)	8 (13.1%)
Pain in extremity	13 (0.7%)	7 (11.5%)
Diarrhea	12 (0.7%)	9 (14.8%)
Dizziness	11 (0.6%)	8 (13.1%)
Vomiting	11 (0.6%)	9 (14.8%)
Cough	9 (0.5%)	8 (13.1%)

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 here for Full Prescribing Information, including Boxed Warning regarding Thrombosis, Renal Dysfunction and Acute Renal Failure.

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

OnePath product support for your patients

Takeda's OnePath program offers product support for your patients prescribed GAMMAGARD LIQUID

Through OnePath, eligible patients are connected with a Patient Support Manager who can assist them by:

- Facilitating an insurance benefits investigation
- Working with specialty pharmacies to coordinate treatment access — if applicable
- Enrolling eligible* patients in the **OnePath Co-Pay Assistance Program** or providing information about other financial assistance options
- Informing patients and caregivers about educational resources available to them

OnePath Co-Pay Assistance Program

The OnePath Co-Pay Assistance Program helps eligible patients cover certain out-of-pocket treatment costs.†

To enroll a patient in OnePath, complete a GAMMAGARD LIQUID Start Form with your patient and fax it to 1-833-388-5467.

*At a minimum to be eligible, patients must be enrolled in OnePath and have commercial insurance. Other terms and conditions apply. Contact OnePath for more information.

†IMPORTANT NOTICE: The OnePath Co-Pay Assistance Program (the Program) is not valid for prescriptions eligible to be reimbursed, in whole or in part, by Medicaid, Medicare (including Medicare Part D), Tricare, Medigap, VA, DoD, or other federal or state programs (including any medical or state prescription drug assistance programs). No claim for reimbursement of the out-of-pocket expense amount covered by the Program shall be submitted to any third party payer, whether public or private. The Program cannot be combined with any other rebate/coupon, free trial, or similar offer. Copayment assistance under the Program is not transferable. The Program only applies in the United States, including Puerto Rico and other U.S. territories, and does not apply where prohibited by law, taxed, or restricted. This does not constitute health insurance. Void where use is prohibited by your insurance provider. If your insurance situation changes you must notify the Program immediately at 1-866-888-0660. Coverage of certain administration charges does not apply for patients residing in Massachusetts, Michigan, Minnesota, Rhode Island, and Vermont. Takeda reserves the right to rescind, revoke, or amend the Program at any time without notice.

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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.

Adverse Reactions

IV administration for PI: The serious adverse reaction seen during IV clinical studies was aseptic meningitis. The most common adverse reactions observed in ≥5% of subjects 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.

Subcutaneous administration for PI: The most common adverse reactions observed in ≥5% of subjects were infusion site (local) event (rash, erythema, edema, hemorrhage, and irritation), headache, fatigue, heart rate increased, pyrexia, abdominal pain upper, nausea, vomiting, asthma, blood pressure systolic increased, diarrhea, ear pain, aphthous stomatitis, migraine, 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 click here for Full Prescribing Information.

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

Formulated with patient needs in mind

GAMMAGARD LIQUID is formulated with no added sugars, no added sodium, no preservatives, and no proline or sucrose stabilizers[4-6]

- Osmolality (240-300 mOsmol/kg) is similar to physiological osmolality (285-295 mOsmol/kg)[4]
- The packaging is not made with natural rubber latex[4]
- The product has been stabilized and buffered with glycine[4]

Intravenous dosage and administration in PI[4]

DOSE*	INITIAL INFUSION RATE	MAINTENANCE INFUSION RATE
300-600 mg/kg every 3 to 4 weeks based on clinical response	0.5 mL/kg/hr (0.8 mg/kg/min) for 30 minutes	Increase every 30 minutes (if tolerated) up to 5 mL/kg/hr (8 mg/kg/min)

*Adjust dose according to IgG levels and clinical response, as the frequency and dose of immune globulin may vary from patient to patient.

IMPORTANT SAFETY INFORMATION (continued)

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References: 1. Data on file. Takeda. 2017. **2.** Data on file. Analysis of potential vial reduction 30g size. Baxter Healthcare Corporation. **3.** Market Research Bureau. The plasma proteins market in the United States 2015. Published July 2016. **4.** GAMMAGARD LIQUID [Prescribing Information]. Westlake Village, CA: Baxalta, US Inc. **5.** Church JA, Leibl H, Stein MR, et al. Efficacy, safety and tolerability of a new 10% liquid intravenous immune globulin [IVIG 10%] in patients with primary immunodeficiency. *J Clin Immunol.* 2006;26(4):388-395. **6.** Sun A, Teschner W, Yel L. Improving patient tolerability in immunoglobulin treatment: focus on stabilizer effects. *Expert Rev Clin Immunol.* 2013;9(6):577-587.

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