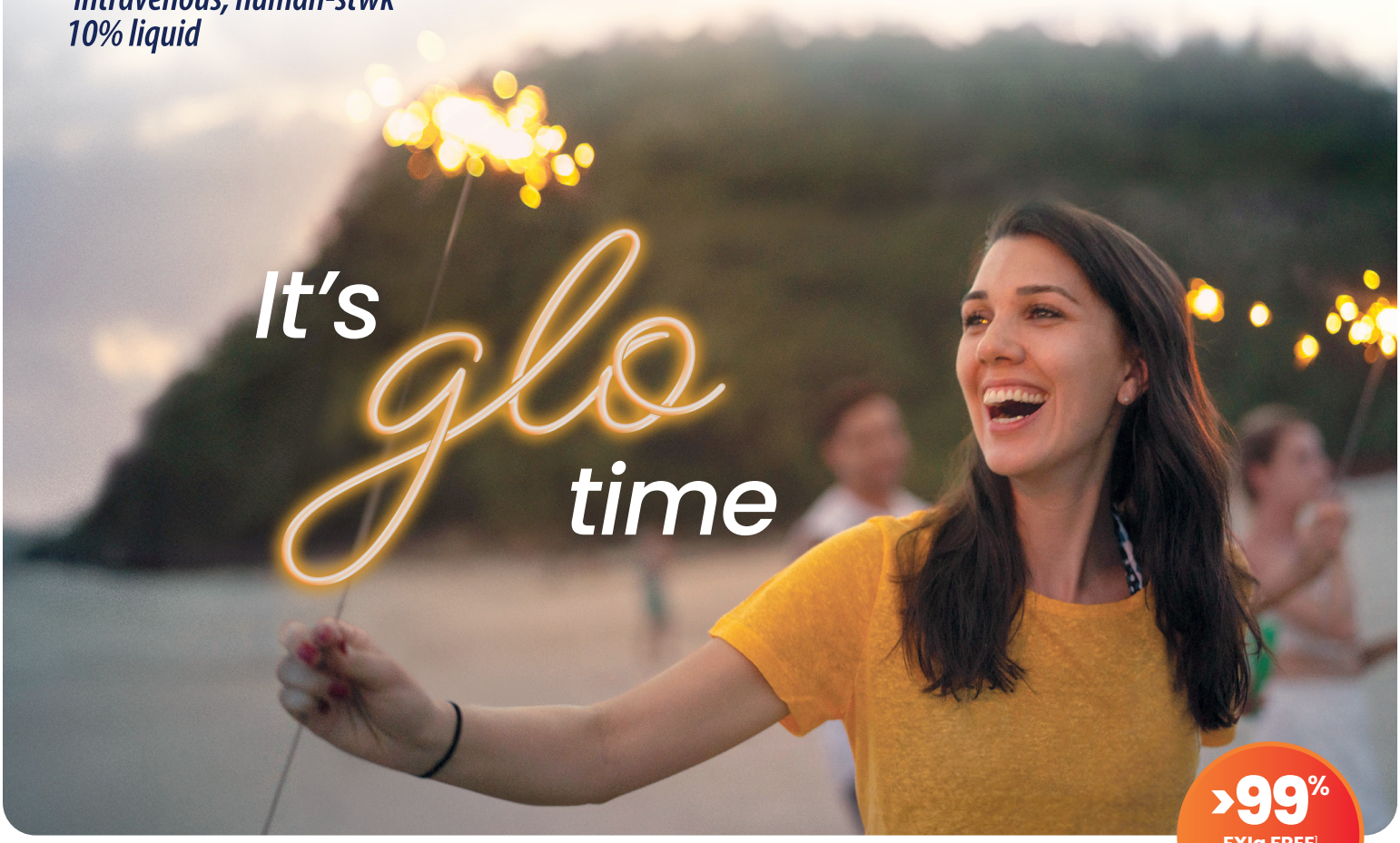
Alyglo®

immune globulin intravenous, human-stwk 10% liquid

You go the **extra step** for patients with primary immunodeficiency (PI). **So do we.**



>99% FXIa FREE[1] (activated coagulation factor XI)

ALYGLO® is a 10% glycine-stabilized intravenous immunoglobulin (IVIG) indicated for the treatment of primary humoral immunodeficiency (PI) in adults aged 17 years and older. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency (CVID), Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS, RENAL DYSFUNCTION and ACUTE RENAL FAILURE

- **Thrombosis may occur with immune globulin intravenous (IGIV) products, including ALYGLO. 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.**
- **Renal dysfunction, acute renal failure, osmotic nephropathy, and death may occur with the administration of IGIV products in predisposed patients.**
- **Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. ALYGLO does not contain sucrose.**
- **For patients at risk of thrombosis, renal dysfunction or renal failure, administer ALYGLO 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 for hyperviscosity.**

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Going the extra step for patients with PI

>99% FXIa FREE

EXTRA PURIFICATION

Manufactured with the extra step of **G-XI™ Technology**

- Utilizes cation exchange (CEX) chromatography to remove activated coagulation factor XI (FXIa)[1]

0.03 ASBIs

PROVEN PROTECTION

In a published study, ALYGLO demonstrated[2,a]:

- 0.03 **acute serious bacterial infections (ASBIs)** per patient year
- Reduced impact on daily living
- Upper one-sided 99% confidence limit was 0.31, which met the predefined success rate of <1 ASBI per patient year (intent-to-treat [ITT] population)

50+ YEARS EXPERTISE IN PLASMA

TRUE PARTNERSHIP

- GC Biopharma has been producing IVIG for more than 50 years, and now distributes to more than 50 countries worldwide

It's time for ALYGLO.

[a]Study design: Efficacy, safety, and tolerability of ALYGLO were evaluated in a prospective, open-label, 12-month study of 33 adults aged 17-70 years. Primary endpoint: ASBIs per patient year with a predefined success rate of <1 ASBI per patient year. Secondary endpoints: annual rate of days of other infection, use of antibiotics, days out of work/school/daycare or unable to perform normal activities due to infection, and days of hospitalization due to infection.

PI, primary immunodeficiency
FXIa, activated coagulation factor XI

IMPORTANT SAFETY INFORMATION, cont.

Contraindications: ALYGLO is contraindicated in patients who have a history of anaphylactic or severe systemic reaction to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity.

Hypersensitivity: In case of hypersensitivity, discontinue infusion immediately and institute appropriate treatment. Epinephrine should be available for immediate treatment of severe acute hypersensitivity reactions.

Hyperproteinemia, Increased Serum Viscosity, and Hyponatremia: Hyperproteinemia, increased serum viscosity, and hyponatremia may occur.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

A brief history:

- **In 2010,** the U.S. Food and Drug Administration (FDA) became aware of a cluster of TEEs associated with FXIa in IVIG[3]
- **In 2013,** the FDA required boxed warnings for the risk of TEEs for all IG products[4]

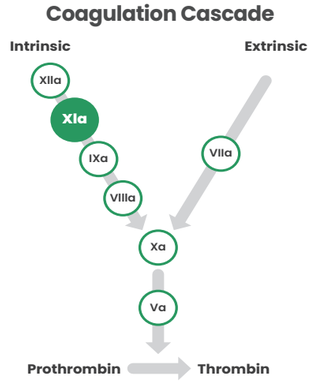
Why FXIa matters in IG treatments

While IG treatment is the gold standard of care for patients with PI and several other diseases, thromboembolic events (TEEs) are a rare but serious potential adverse event.[4]

- For nearly 30 years, it has been known that patients receiving IG treatment are at risk of developing TEEs[5-7]
- The most common IG-related TEEs include stroke and myocardial infarction, usually occurring within 24 hours of IVIG administration[5-7]
- With approximately 500,000 patients in the United States affected by PI,[8] even at a small incidence rate, more patients may be at risk than realized

Activated coagulation factor XI (FXIa) has been identified as one of the root causes of IVIG-related TEEs.[3]

- FXIa plays a key role in the activation of the intrinsic coagulation cascade[9]
- Studies have confirmed that even small quantities of FXIa can result in significant thrombin generation[9]
- Because human IG and FXIa have similar chemical properties, it can be difficult to separate FXIa from IG[1]



An extra step

GC Biopharma's answer to FXIa removal.

About G-XI™ Technology:

1. **Dedicated to FXIa removal,** this extra step in our manufacturing process utilizes cation exchange (CEX) chromatography[1]
2. **Proven in a published study** to reduce activated coagulation factor XI (FXIa) to undetectable limits[1]
3. **Our G-XI Tech Team** is a team of scientists fully dedicated to the oversight of G-XI Technology to ensure product purity
4. **Product end-testing** is conducted to help ensure undetectable levels of FXIa in every lot.

Manufacturing Steps:

- Plasma thawing/cryoprecipitation
- Cohn-Oncley fractionation
- Ultrafiltration/diafiltration
- Anion exchange chromatography
- Viral inactivation: solvent/detergent
- **G-XI Technology**
- Nanofiltration
- Ultrafiltration
- Formulation

IMPORTANT SAFETY INFORMATION, cont.

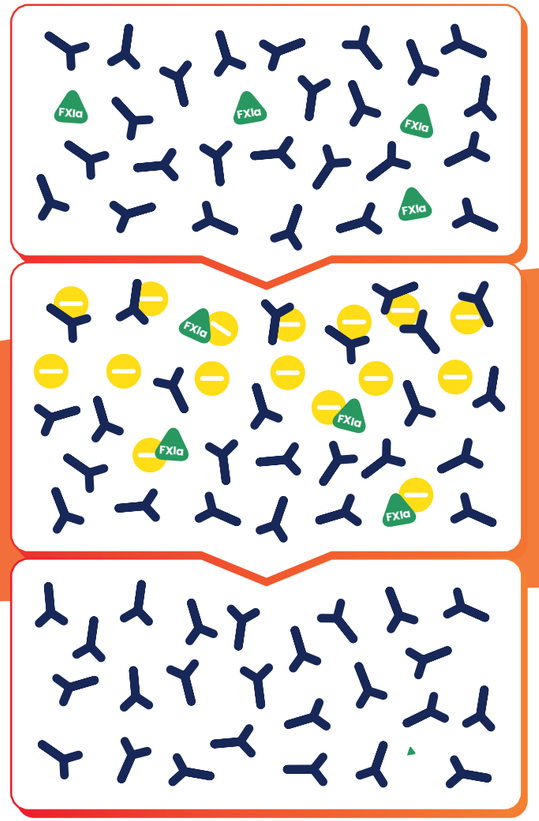
Aseptic Meningitis Syndrome (AMS): Aseptic meningitis syndrome (AMS) may occur, especially with high doses or rapid infusion. AMS usually begins within several hours to 2 days following ALYGLO treatment. Discontinuation of treatment has resulted in remission of AMS within several days without sequelae.

Hemolysis: Delayed hemolytic anemia due to enhanced red blood cell (RBC) sequestration and acute hemolysis consistent with intravascular hemolysis have been reported. Cases of severe hemolysis-related renal dysfunction/failure or disseminated intravascular coagulation have occurred following infusion of IGIV. Closely monitor patients for clinical signs and symptoms of hemolysis, particularly patients with risk factors.

G-XI™ Technology

Reduces activated FXI to undetectable levels.

During this step, **cation exchange (CEX) chromatography** is implemented **using a unique ceramic resin under specific conditions** that aid in the removal of FXIa.[1]



Representation of undetectable limits.

IgG CEX resin FXIa FXIa

Before G-XI

16% FXIa remains

Residual activated coagulation factor XI remained in the solution.[1]

During G-XI

- Positively charged IG and FXIa initially bind to the negatively charged ceramic resin.[1]
- Then, under specific conditions, IG is eluted while the FXIa remains bound to the resin, enabling the IG to effectively separate from FXIa.[1]

After G-XI

>99% FXIa FREE

Once IG is collected, FXIa levels are undetectable in the final IVIG preparations.[1]

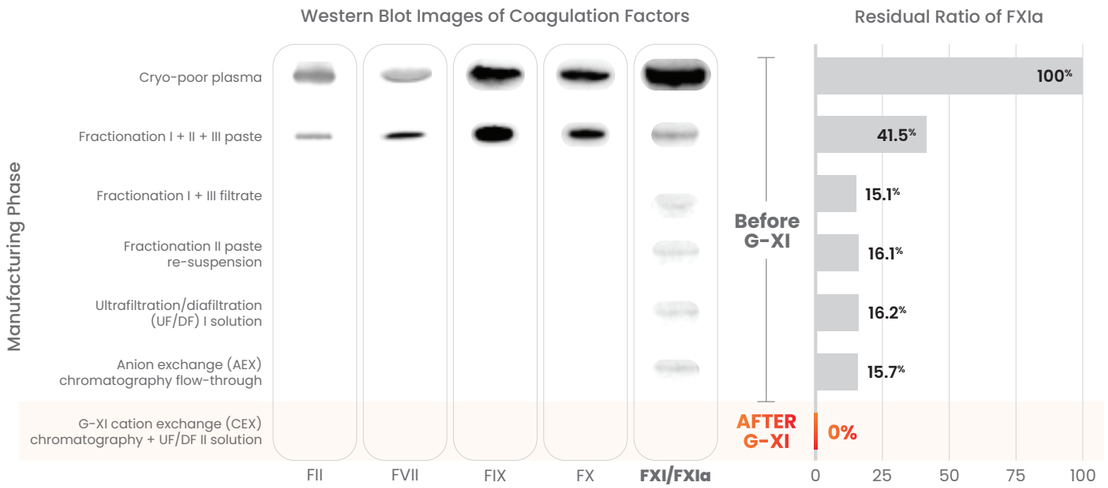
Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

An extra study

G-XI™ Technology was proven to remove >99% of FXIa in a published, multi-step study.[1]

Western blot analysis: Measured coagulation factor levels at each phase of the manufacturing process[1]



Other clotting factors were removed during fractionation but residual FXI/FXIa was present until the G-XI Technology step.[1]

After G-XI Technology, FXIa levels were undetectable.[1]

Spiking study: Examined robustness of G-XI for removing FXIa[1]

Large quantities of activated coagulation factor XI (FXIa) were added to IVIG samples prior to the extra step of G-XI Technology.[1]

FXIa content FXIa/g of IgG	**No spike** 4.13 ng	**32x normal levels** 128.82 ng	**158x normal levels** 643.92 ng
	G-XI Technology		
FXIa content FXIa/g of IgG	0.037 µg	0.11 µg	0.67 µg
Removal ratio	**99.1%**	**99.9%**	**99.9%**

Even in samples spiked >158x normal levels of FXIa protein, G-XI was proven to reduce FXIa below detection limits.[1]

IMPORTANT SAFETY INFORMATION, cont.

Transfusion-Related Acute Lung Injury: Noncardiogenic pulmonary edema (transfusion-related acute lung injury [TRALI]) may occur. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Patients with TRALI may be managed using oxygen therapy with adequate ventilator support. Monitor patients for pulmonary adverse reactions.

Transmissible Infectious Agents: Because ALYGLO is made from human blood, it may carry a risk of transmitting infectious agents (eg, viruses, the variant Creutzfeldt-Jakob disease [vCJD] agent and, theoretically, the Creutzfeldt-Jakob disease [CJD] agent).

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

Proven protection from infection

Clinical study of ALYGLO[2]

- The efficacy, safety, and tolerability of ALYGLO were evaluated in a prospective, open-label, multicenter, single-arm study in 33 adults with PI, aged 17-70 years
- Before enrollment, all subjects were receiving stable doses between 300 and 900 mg/kg of IVIG treatment
- For 12 months, subjects received ALYGLO infusion administered every 21 or 28 days (both the dose and schedule depending on prior therapy)

Proven protection from infection[2]

Primary endpoint was annualized rate of acute serious bacterial infections (ASBIs), defined as bacterial pneumonia, bacteremia/sepsis, bacterial meningitis, visceral abscess, and osteomyelitis/septic arthritis per patient year.

0.03
ASBIs
per patient year

Upper one-sided 99% confidence limit was 0.31, which met the predefined success rate of <1 ASBI per patient year (intent-to-treat [ITT] population)

Reduced impact on daily living[2]

Secondary endpoint was annual rate or days of other infections, use of antibiotics, days out of work/school/daycare or unable to perform normal activities due to infection, and days of hospitalization due to infection.

2.4
other infections
per patient year

6
days of missed work, school, or normal activities
per patient year

0.2
days of hospitalization
per patient year

Safety profile of ALYGLO: common adverse events (AEs)[2]

- **No pre-medications were provided to patients ahead of infusions per study protocol[10]**
- **The majority of adverse events reported during the study (79.1%) were mild in intensity[11]**
- **No adverse events led to withdrawal from the study**

	Total Infusions With AEs (N=427)	Total Patients With AEs (N=33)
Headache	32 (7.5%)	13 (39%)
Nausea/vomiting	20 (4.7%)	11 (33%)
Fatigue	18 (4.2%)	6 (18%)
Nasal/sinus congestion	5 (1.2%)	5 (15%)
Rash	4 (0.9%)	4 (12%)
Arthralgia	4 (0.9%)	3 (9%)
Diarrhea	3 (0.7%)	3 (9%)
Muscle pain/aches	7 (1.6%)	2 (6%)
Infusion site pain/swelling	6 (1.4%)	2 (6%)
Abdominal pain/discomfort	3 (0.7%)	2 (6%)
Cough	2 (0.5%)	2 (6%)
Dizziness	2 (0.5%)	2 (6%)

IMPORTANT SAFETY INFORMATION, cont.

Interference with Laboratory Tests: After infusion of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for a misleading interpretation.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

Patients first, right from the start

ALYGLO administration schedule[2]

After the first infusion, ALYGLO allows for short overall infusion times. If well tolerated, ALYGLO maintenance infusion rates can be doubled every 15 minutes to reach its maximum rate in 30 minutes.

	1st infusion	Subsequent infusions
Dose	**300-800 mg/kg** every 21 or 28 days	**300-800 mg/kg** every 21 or 28 days
Initial infusion rate	**1 mg/kg/min** (0.01 mL/kg/min)	**2 mg/kg/min** (0.02 mL/kg/min)
Maintenance infusion rate	**Double the infusion rate every 30 minutes (if tolerated)** up to 8 mg/kg/min (0.08 mL/kg/min)	**Double the infusion rate every 15 minutes (if tolerated)** up to 8 mg/kg/min (0.08 mL/kg/min)

IMPORTANT SAFETY INFORMATION, cont.

Adverse reactions (observed in ≥ 5% of study subjects) were headache, nausea/vomiting, fatigue, nasal/sinus congestion, rash, arthralgia, diarrhea, muscle pain/aches, infusion site pain/swelling, abdominal pain/discomfort, cough, and dizziness.

It is recommended that ALYGLO be administered separately from other drugs or medications.

Alyglo Assist

YOUR ALLY IN IVIG

ALYGLO CO-PAY PROGRAM

Up to $15,000 per calendar year for ALYGLO deductible, co-pay, and/or coinsurance

Can be used regardless of whether billing is through a major medical plan or pharmacy benefits

ELIGIBLE PATIENTS MAY PAY AS LITTLE AS $0 OUT OF POCKET

Terms, conditions, and eligibility requirements apply. See alyglo.medmonk.com for full details.

Eligibility Criteria for Co-Pay Assistance:

- Patient must be a US resident
- Patient must express financial need
- Assistance is available to commercially insured patients only

Restrictions:

- Assistance covers only out-of-pocket expenses for the drug portion; administration supplies and nursing co-pay costs are not covered through the program
- Patients are ineligible for co-pay assistance if they participate in Medicare, Medicaid, Medigap, Veterans Affairs, Department of Defense, Tricare, or any other federal or state-funded programs.

PRIOR AUTHORIZATION SUPPORT

We can help with prior authorization, which can be complex and time-consuming.

REIMBURSEMENT SUPPORT

Our teams can help with reimbursement claims and guide you through any questions or concerns.

HELP GETTING STARTED

Our team will help establish a connection with care providers for home infusions.

Call **1-888-501-8040** for support

Contraindications: ALYGLO is contraindicated in patients who have a history of anaphylactic or severe systemic reaction to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

About GC Biopharma

- **An established manufacturer** of plasma-derived products for more than 50 years
- **Headquartered in South Korea**, with offices around the world, including the US
- **One of the largest manufacturing facilities** in the world
- **Committed to partnership**, with a leadership team that has been in your shoes and on the front lines of IG treatment and care

ALYGLO® is indicated for the treatment of primary humoral immunodeficiency (PI) in adults aged 17 years and older. This includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency (CVID), Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS, RENAL DYSFUNCTION and ACUTE RENAL FAILURE

- **Thrombosis may occur with immune globulin intravenous (IGIV) products, including ALYGLO. 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.**
- **Renal dysfunction, acute renal failure, osmotic nephropathy, and death may occur with the administration of IGIV products in predisposed patients.**
- **Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. ALYGLO does not contain sucrose.**
- **For patients at risk of thrombosis, renal dysfunction or renal failure, administer ALYGLO 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 for hyperviscosity.**

- **Contraindications:** ALYGLO is contraindicated in patients who have a history of anaphylactic or severe systemic reaction to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and a history of hypersensitivity.
- **Hypersensitivity:** In case of hypersensitivity, discontinue infusion immediately and institute appropriate treatment. Epinephrine should be available for immediate treatment of severe acute hypersensitivity reactions.
- **Hyperproteinemia, Increased Serum Viscosity, and Hyponatremia:** Hyperproteinemia, increased serum viscosity, and hyponatremia may occur.
- **Aseptic Meningitis Syndrome (AMS):** Aseptic meningitis syndrome (AMS) may occur, especially with high doses or rapid infusion. AMS usually begins within several hours to 2 days following ALYGLO treatment. Discontinuation of treatment has resulted in remission of AMS within several days without sequelae.
- **Hemolysis:** Delayed hemolytic anemia due to enhanced red blood cell (RBC) sequestration and acute hemolysis consistent with intravascular hemolysis have been reported. Cases of severe hemolysis-related renal dysfunction/failure or disseminated intravascular coagulation have occurred following infusion of IGIV. Closely monitor patients for clinical signs and symptoms of hemolysis, particularly patients with risk factors.
- **Transfusion-Related Acute Lung Injury:** Noncardiogenic pulmonary edema (transfusion-related acute lung injury [TRALI]) may occur. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Patients with TRALI may be managed using oxygen therapy with adequate ventilator support. Monitor patients for pulmonary adverse reactions.
- **Transmissible Infectious Agents:** Because ALYGLO is made from human blood, it may carry a risk of transmitting infectious agents (eg, viruses, the variant Creutzfeldt-Jakob disease [vCJD] agent and, theoretically, the Creutzfeldt-Jakob disease [CJD] agent).
- **Interference with Laboratory Tests:** After infusion of immunoglobulin, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for a misleading interpretation.
- **Adverse reactions** (observed in ≥ 5% of study subjects) were headache, nausea/vomiting, fatigue, nasal/sinus congestion, rash, arthralgia, diarrhea, muscle pain/aches, infusion site pain/swelling, abdominal pain/discomfort, cough, and dizziness.
- It is recommended that ALYGLO be administered separately from other drugs or medications.

Please see accompanying full Prescribing Information.

Alyglo®
immune globulin intravenous, human-stwk 10% liquid

Alyglo®

immune globulin intravenous, human-stwk 10% liquid

For adult patients 17 and older with primary immunodeficiency

It's time for ALYGLO

G-XI™ Technology
Reduces activated coagulation factor XI to below detection limits[1]

Available in 3 sizes
5, 10, and 20-gram recyclable vials

ALYGLO Assist support
Patient Co-Pay Program, pre-authorization and reimbursement support

100 mg/mL PROTEIN	≥96% IgG	18.8 mg/mL GLYCINE	4.5 – 5.5 pH	≤100 mg/mL IgA

If you would like to speak to a Medical Affairs representative, have an inquiry related to drug safety, or to report adverse events, please contact 1-833-426-6426, or email medicalinfo@gcbiopharmausa.com, or e-fax 1-866-728-7855, or visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

References: 1. Kang GB, Huber A, Lee J, et al. Cation exchange chromatography removes FXIa from a 10% intravenous immunoglobulin preparation. *Front Cardiovasc Med.* 2023;10:1253177. **2.** ALYGLO Prescribing Information. GC Biopharma; 2023. **3.** Ovanesov MV, Menis MD, Scott DE, et al. Association of immune globulin intravenous and thromboembolic adverse events. *Am J Hematol.* 2017;92(4):E44-E45. **4.** Ammann EM, Haskins CB, Fillman KM, et al. Intravenous immune globulin and thromboembolic adverse events: a systematic review and meta-analysis of RCTs. *Am J Hematol.* 2016;91(6):594-605. **5.** Germishuizen WA, Gyure DC, Stubbings D, Burnouf T. Quantifying the thrombogenic potential of human plasma-derived immunoglobulin products. *Biologicals.* 2014;42(5):260-270. **6.** Kapoor M, Spillane J, Englezou C, et al. Thromboembolic risk with IVIg: incidence and risk factors in patients with inflammatory neuropathy. *Neurology.* 2020;94(6):e635-e638. **7.** Funk MB, Gross N, Gross S, et al. Thromboembolic events associated with immunoglobulin treatment. *Vox Sang.* 2013;105(1):54-64. **8.** Primary immune deficiency diseases (PIDDs). National Institute of Allergy and Infectious Diseases. Accessed January 29, 2025. https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pidds **9.** Wolberg AS, Kon RH, Monroe DM, Hoffman M. Coagulation factor XI is a contaminant in intravenous immunoglobulin preparations. *Am J Hematol.* 2000;65(1):30-34. **10.** Data on file. GC Biopharma; 2019. **11.** Perez EE, Hébert J, Ellis AK, et al. Efficacy, safety and tolerability of a new 10% intravenous immunoglobulin for the treatment of primary immunodeficiencies. *Front Immunol.* 2021;12:707463.

IMPORTANT SAFETY INFORMATION, cont.

Adverse reactions (observed in ≥ 5% of study subjects) were headache, nausea/vomiting, fatigue, nasal/sinus congestion, rash, arthralgia, diarrhea, muscle pain/aches, infusion site pain/swelling, abdominal pain/discomfort, cough, and dizziness.

It is recommended that ALYGLO be administered separately from other drugs or medications.

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information.

ALY-C-0099 4/2025

GC Biopharma