

IG Treatment Guide for Your Patients With Pl

Familiarize yourself with Takeda IG therapy options and how to help your patients with primary immunodeficiency (PI) get the care they deserve.



Discussing IG options with your patients with PI

Putting patients with PI at the center of their care is important.^{1,2} But no two patients are the same. That's why it's essential to match a patient's treatment with their administration preferences.



IG therapy options

In order for patients to make an educated decision, they must first understand the different IG therapy options that are available to them:

	Intravenous immune globulin therapy (IVIG)	Subcutaneous immune globulin therapy (SCIG)	Facilitated immune globulin therapy
Route of administration	IG treatment administered directly into a vein	IG treatment that is infused under the skin	IG treatment infused under the skin and facilitated with hyaluronidase to increase dispersion and absorption of IG
Frequency	Every 3 or 4 weeks	Daily to every 2 weeks	Every 3 or 4 weeks
Average infusion time*	-2 hours	-1 to 2 hours	~2 hours
Infusion time range*	~1 to 2 hours	~5 minutes to 2 hours	~1 to 2 hours
Mode	IV	subQ	subQ
How administered	Nurse-administered	Self-administered after training by an HCP	Nurse-administered or self-administered after training by an HCP
Location	Home, HCP office, hospital, infusion center	Home	Home, HCP office, hospital, infusion center

^{*}Infusion times may vary based on frequency, dose, volume, number of needlesticks, and tolerability.

Other factors to consider

Once a patient understands the different IG therapy options at a high level and how they compare to each other, there are several other factors that may lead to one option being more suitable for the patient.

To help you both make a more educated therapy decision, discuss topics such as:

What is the patient's age?

2-16 years

Not all IG therapies are indicated for patients ages 2-16

17-65 years

Older patients may prefer assistance due to dexterity issues and other factors or comorbidities

Does the patient prefer nurseadministration or self-administration?

Self-administration

Some patients prefer to administer on their own

Nurse-administration

Some patients may prefer assisted administration by a trained medical professional

What number of needlesticks is the patient comfortable with?

More

Prefer more needles in a single infusion to reduce infusion time

Fewer

Prefer to minimize the number of needlesticks per infusion

INDICATIONS

CUVITRU® [Immune Globulin Subcutaneous (Human)] 20% Solution, GAMMAGARD LIQUID® [Immune Globulin Infusion (Human)] 10% Solution, and GAMMAGARD® S/D [Immune Globulin Intravenous (Human)] IgA less than 1 µg/mL in a 5% solution are indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients ≥2 years.

HYQVIA* [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] Solution is indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients two years of age and older.

CUVITRU and **HYQVIA** are for subcutaneous use only.

GAMMAGARD LIQUID is for intravenous and subcutaneous use.

GAMMAGARD S/D is for intravenous use only.

Other factors to consider (continued)

Once a patient understands the different IG therapy options at a high level and how they compare to each other, there are several other factors that may lead to one option being more suitable for the patient.

To help you both make a more educated therapy decision, discuss topics such as:

Where is the closest hospital or infusion center?

Far

If a patient lives far away from an infusion center, they may want to administer at home to avoid the long commute

Near

If a patient lives close to an infusion center and prefers nurse-administration, they may prefer to do their infusions at an infusion center

Daily

Every 2 weeks

Monthly

How does the patient feel about duration of treatment?

More time

Less time

The answers to these questions will help you and your patient determine appropriate therapy options.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS

CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D

- Thrombosis may occur with immune globulin (IG) products, including CUVITRU, HYQVIA, 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 CUVITRU, HYQVIA, 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.

Choosing an appropriate therapy

Takeda has the broadest portfolio of IG therapies, designed to help a wide range of PI patients.³ Keeping in mind your patient's preferences that you uncovered during your conversations, you can now begin to explore therapy options.

Takeda's four distinct IG therapies give you the ability to offer people with PI a product that fits their administration preferences⁴⁻⁷:

		Patient's age		Can be self-administered after training by an HCP	Can be nurse-administered
		2-16 years	17-65 years		
IVIG	GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10%	~	~		~
	GAMMAGARD S/D [Immune Globulin Intravenous (Human)] IgA less than 1 μg/mL in a 5% solution	~	~		✓
SCIG	Cuvitru [Immune Globulin Subcutaneous (Human)] 20%	~	~	~	✓
fSCIG	HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]	~	~	~	✓

fSCIG = facilitated subcutaneous immune globulin therapy.

IMPORTANT SAFETY INFORMATION (continued)

Contraindications

- CUVITRU, HYQVIA, and GAMMAGARD LIQUID are 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.
- Additionally, HYQVIA is contraindicated in patients with known systemic hypersensitivity to hyaluronidase including Recombinant Human Hyaluronidase of HYQVIA, and known systemic hypersensitivity to human albumin (in the hyaluronidase solution).
- **GAMMAGARD S/D** is contraindicated in patients with a history of anaphylactic or severe systemic hypersensitivity reactions to the administration of **GAMMAGARD S/D**.

Choosing an appropriate therapy (continued)

Takeda has the broadest portfolio of IG therapies, designed to help a wide range of PI patients.³ Keeping in mind your patient's preferences that you uncovered during your conversations, you can now begin to explore therapy options.

Takeda's four distinct IG therapies give you the ability to offer people with PI a product that fits their administration preferences⁴⁻⁷:

		Treatment frequency		Number of needlesticks can be customized*	Treatment duration can be customized	
		Daily	Every 2 weeks	Monthly		
n//c	GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10%			~		
IVIG -	GAMMAGARD S/D [Immune Globulin Intravenous (Human)] IgA less than 1 µg/mL in a 5% solution			~		
scig	Cuvitru [Immune Blobulin Subcutaneous (Human)] 20%	~	~		✓	✓
fSCIG	Hyovia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]			every 3-4 weeks	~	~

^{*}Number of needlesticks may vary based on patient weight, dose, volume, and tolerability. fSCIG = facilitated subcutaneous immune globulin therapy.

IMPORTANT SAFETY INFORMATION (continued)

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.

Free trial programs



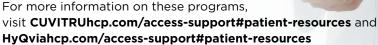
HelloHYQVIA

If you are unsure about which treatment option may be right for your eligible PI patient, the HelloCUVITRU and HelloHYQVIA free trial programs may help you decide.

For eligible patients, both free trial programs cover the entire cost of:

- First 4 CUVITRU infusions or the first 3 HyQvia infusions
- Ancillary supplies, pump, and administration

At minimum, eligible patients must have an ICD-10 verified diagnosis of PI and be a new patient not currently enrolled in the HELLO program. Additional terms and conditions apply.





Warnings and Precautions (continued)

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.



Getting started

Now that you're ready to get your patient started on a Takeda IG therapy, you can either work directly with your specialty pharmacy or send a Start Form to Takeda Patient Support:

Specialty pharmacy

For more information about the specialty pharmacy process and to access a list of specialty pharmacies that are authorized to provide Takeda IG therapies, visit:

- CUVITRUhcp.com/starting-patients
- · HyQviahcp.com/starting-hyqvia
- GAMMAGARD.com/hcp/pi-resources

Once you have chosen a specialty pharmacy provider, visit their website and then navigate to and complete the referral form.

When completing the referral form, to prevent substitution, remember to specify the preferred branded product.

Takeda Patient Support



When your patient enrolls, we're here to help them gain access to their prescribed Takeda medication. Our dedicated specialists provide several services, including:

- Benefits investigation to help determine your patient's insurance benefits
- Prior authorization (PA), reauthorization, and appeals information in coordination with your patient's insurance company to determine any requirements
- Financial assistance options including the Takeda Patient Support Co-Pay Assistance Program. The program may cover up to 100% of your patient's out-of-pocket co-pay costs, if they're eligible '
- Education and training about their prescribed Takeda treatment or condition from nursing professionals. Our nurses cannot provide medical advice
- Specialty pharmacy triage, coordination, and more^t

Need assistance?

Our support specialists are never more than a tap or call away — 1-866-861-1750, Monday through Friday, 8 AM to 8 PM ET.

Need to enroll your patient?

Visit our convenient online enrollment portal at TakedaPatientSupport.com/hcp.

You can also enroll your patient by faxing the completed Start Form to 1-866-861-1752.

If English is not your patient's preferred language, we can assist them in a language of their choosing.

*Must meet eligibility requirements.

IMPORTANT NOTICE: The Takeda Patient Support 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 patient's insurance situation changes, they must notify the Program immediately at 1-866-861-1750. Coverage of certain administration charges will not apply for patients residing in states where it is prohibited by law. Takeda reserves the right to rescind, revoke, or amend the Program at any time without notice.

¹If your patients' medication is dispensed by specialty pharmacy.

Indications and Important Safety Information

INDICATIONS

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HYQVIA* [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] Solution is indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients two years of age and older.

CUVITRU and **HYQVIA** are for subcutaneous use only. **GAMMAGARD LIQUID** is for intravenous and subcutaneous use. **GAMMAGARD S/D** is for intravenous use only.

IMPORTANT SAFETY INFORMATION

WARNING: THROMBOSIS

CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D

- Thrombosis may occur with immune globulin (IG) products, including CUVITRU, HYQVIA, 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 CUVITRU, HYQVIA, 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

- CUVITRU, HYQVIA, and GAMMAGARD LIQUID are 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.
- Additionally, HYQVIA is contraindicated in patients with known systemic hypersensitivity to hyaluronidase including Recombinant Human Hyaluronidase of HYQVIA, and known systemic hypersensitivity to human albumin (in the hyaluronidase solution).
- **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: Has been reported to occur following treatment with IG products, including **HYQVIA** 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, including **CUVITRU** and **HYQVIA** 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. The syndrome usually begins within several hours to two days following IG treatment.

Indications and Important Safety Information (continued)

Warnings and Precautions (continued)

Hemolysis: CUVITRU, HYQVIA, 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 has been reported with IV-administered IG, including **GAMMAGARD LIQUID**. 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 CUVITRU, HYQVIA, 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 CUVITRU or GAMMAGARD LIQUID, and no cases have been associated with HYQVIA.

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.

Additional Warnings and Precautions for HYQVIA

Immunogenicity of Recombinant Human Hyaluronidase (rHuPH20): Non-neutralizing antibodies to the Recombinant Human Hyaluronidase component can develop. The clinical significance of these antibodies or whether they interfere with fertilization in humans is unknown.

Spread of Localized Infection: Do not infuse **HYQVIA** into or around an infected area due to potential risk of spreading a localized infection.

Additional Warnings and Precautions for GAMMAGARD LIQUID and GAMMAGARD S/D

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

CUVITRU

The most common adverse reactions observed in ≥5% of patients in clinical trials were local adverse reactions including

mild or moderate pain, erythema, and pruritus, and systemic adverse reactions including headache, nausea, fatigue, diarrhea, and vomiting.

HYQVIA

The most common adverse reactions observed in >5% of patients in clinical trials were local adverse reactions including pain, erythema, edema, and pruritus, and systemic adverse reactions including headache, antibody formation against Recombinant Human Hyaluronidase (rHuPH20), fatigue, nausea, pyrexia, and vomiting.

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.

<u>Subcutaneous administration</u>: The most common adverse reactions observed in ≥5% of patients in clinical trials 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.

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).

Use In Specific Populations

Pregnancy: Limited human data are available on the use of **HYQVIA** during pregnancy. The effects of antibodies to the Recombinant Human Hyaluronidase on the human embryo or fetal development are unknown. It is not known whether **HYQVIA** can cause fetal harm when administered to a pregnant woman or if it can affect reproductive capacity. **HYQVIA** should be given to a pregnant woman only if clearly needed.

Please click for Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D, including BOXED WARNINGS regarding Thrombosis, Renal Dysfunction, and Acute Renal Failure.

PI educational resources for patients



my Ig source

MylgSource is committed to providing education and peer-to-peer support to help people manage life with primary immunodeficiency. MylgSource is open to all, regardless of treatment. Living with PI can be challenging, but often easier when you feel connected to people who understand. MylgSource offers many ways to connect and engage, including virtual events, a robust and active online community, one-on-one calls with the Ig Community Support Team, and more.



Learn more at MylgSource.com

References: 1. Hartog NL, Williams KW, Abraham RS. "The State of the Union": current and future perspectives on patient-centric care for primary immunodeficiencies and immune dysregulatory diseases. Front Immunol. 2019;10:1783. 2. World PI Week. Our 2019 Campaign. Accessed May 4, 2022. http://www.worldpiweek.org/resources/campaign-materials/2019-campaign/ 3. Marketing Research Bureau. The Plasma Proteins Market in the United States—2018. Revised 2019:1-298. 4. CUVITRU. Prescribing information. Takeda Pharmaceuticals U.S.A., Inc.; 2023. 5. HYQVIA. Prescribing information. Takeda Pharmaceuticals U.S.A., Inc.; 2024. 7. GAMMAGARD S/D. Prescribing information. Takeda Pharmaceuticals U.S.A., Inc.; 2023. 5. Hygvia U.S.A., Inc.; 2024. 7. GAMMAGARD S/D. Prescribing information. Takeda Pharmaceuticals U.S.A., Inc.; 2023. 5.

