# Payer Denials and Appeals Resource

To Support Patients' Access to Takeda Immune Globulin Therapies

ENTER

Takeda

01

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# Introduction

The purpose of this resource is to equip healthcare providers (HCPs), institutions, specialty pharmacy providers (SPPs), and home infusion pharmacies with information to help respond to denials for immune globulin (IG) coverage. This resource includes brief explanations of some common reasons for coverage denial, a checklist for information to include when appealing specific denials, and specific references to support treatment with a Takeda IG product. The information included in this resource is meant to help navigate the appeals process for access to the Takeda IG portfolio. Please note that third-party payment for medical products and services is affected by numerous factors, and Takeda cannot promise success in obtaining insurance payments for IG therapies.

**Not all Takeda therapies are indicated for all mentioned disease states.**

# Takeda IG Products

## INDICATIONS[1-4]

| | |
|---|---|
| Cuvitru [Immune Globulin Subcutaneous (Human)] 20%<br>HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]<br>GAMMAGARD LIQUID [Immune Globulin Infusion (Human)] 10% | CUVITRU, GAMMAGARD LIQUID, and GAMMAGARD S/D are indicated as replacement therapy for primary humoral immunodeficiency (PI) in adult and pediatric patients ≥2 years.<br>HYQVIA is indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients two years of age and older and for chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment in adults.<br>GAMMAGARD LIQUID is also indicated as a maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy (MMN) and as a therapy to improve neuromuscular disability and impairment in adult patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).<br>LIMITATIONS OF USE (CIDP): GAMMAGARD LIQUID has not been studied in immunoglobulin-naive patients with CIDP. GAMMAGARD LIQUID maintenance therapy in CIDP has not been studied for periods longer than 6 months. After responding during an initial treatment period, not all patients require indefinite maintenance therapy with GAMMAGARD LIQUID in order to remain free of CIDP symptoms. Individualize the duration of any treatment beyond 6 months based upon the patient's response and demonstrated need for continued therapy. |
| GAMMAGARD S/D [Immune Globulin Intravenous (Human)] IgA less than 1 µg/mL in a 5% solution | GAMMAGARD S/D is also indicated for the prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia (CLL), prevention and/or control of bleeding in adult chronic idiopathic thrombocytopenic purpura (ITP) patients, and prevention of coronary artery aneurysms associated with Kawasaki syndrome in pediatric patients.<br>CUVITRU and HYQVIA are for subcutaneous use only.<br>GAMMAGARD LIQUID for PI is for intravenous or subcutaneous use.<br>GAMMAGARD LIQUID for MMN and CIDP is for intravenous use only.<br>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.**

***Please see additional Important Safety Information on pages 35-38 and click for Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

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# Common Denial Scenarios

- Prior Authorization
- Step Therapy
- Formulary Exclusion
- Site of Care Requirement
- Coding Error
- Out-of-Network Pharmacy
- High-Dollar-Amount Edits
- Incorrect Benefit
- Medicare-Specific Reimbursement Challenges

# Prior Authorization (PA)

PA is a **management tool** that requires the prescribing physician to justify the clinical need and therapeutic rationale for the prescribed medication before the health plan will process the prescription or reimburse the claim.[5]

**There are a number of reasons why a drug may require a PA.**

LEARN MORE

**When a PA is required, the prescribing physician may submit the PA directly to the payer, or the pharmacy may complete the PA on behalf of the prescriber before the plan will cover the medication.**

References

# Prior Authorization (PA)
(Continued)

**Reasons why a drug would require a PA:**

1. A need for additional clinical patient information to determine if coverage is appropriate[5]
2. Prevention of drug misuse or inappropriate use[5]
3. Administration of step therapy[5]
   **More information**
4. Administration of quantity limits or management rules[5]
5. Exception process for a closed formulary[5]
   **More information**

**When a PA is required, the prescribing physician may submit the PA directly to the payer, or the pharmacy may complete the PA on behalf of the prescriber before the plan will cover the medication.**

References

# Prior Authorization (PA)
(Continued)

PA criteria vary from plan to plan; however, the following criteria are commonly found across top payer types and may be required for IG therapy. These criteria should be considered when drafting a PA request form:

**FOR PATIENTS WITH PRIMARY IMMUNODEFICIENCY (PI)[6,7]**

LEARN MORE

**FOR PATIENTS WITH MULTIFOCAL MOTOR NEUROPATHY (MMN)[6,7]**

LEARN MORE

**FOR PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)[6,7]**

LEARN MORE

GO TO PA REQUEST FORM CHECKLIST

GO TO PA APPEALS LETTER CHECKLIST

References

# Prior Authorization (PA)
(Continued)

## FOR PATIENTS WITH PRIMARY IMMUNODEFICIENCY (PI)[6,7]

### Disease History

- Clinical diagnosis of PI
- Patient's medical records, including a history of infections and antibiotics
- ICD-10 codes
- Laboratory results
  - — CBC with differential
  - — Total IG levels (IgG, IgM, IgA)
  - — Pre- and postvaccination titers
  - — Genetic testing confirming the diagnosis

### Treatment History

- Previous therapies and response
- Hospitalizations due to infection

### Other

- Physician specialty (i.e., allergist/immunologist)
- Physician's case notes
  - — Family history of PI
  - — Control of underlying conditions

### Clinical Guidance

- Laboratory evidence of IG deficiency
  - — IgG <200 mg/dL
- Laboratory evidence of the inability to mount an adequate response to inciting antigens
- Patient history of multiple hard-to-treat infections, which may be indicated by at least 1 of the following:
  - — 4 or more ear infections within 1 year
  - — 2 or more serious sinus infections within 1 year
  - — 2 or more months of antibiotics with little effect
  - — 2 or more pneumonias within 1 year
  - — Recurrent or deep skin abscesses
  - — Need for IV antibiotics to clear infections
  - — 2 or more deep-seated infections, including septicemia

CBC=complete blood count; ICD-10=International Statistical Classification of Diseases, Tenth Revision; IG=immune globulin; IgA=immunoglobulin A; IgG=immunoglobulin G; IgM=immunoglobulin M; IV=intravenous.

# Prior Authorization (PA)
(Continued)

## FOR PATIENTS WITH MULTIFOCAL MOTOR NEUROPATHY (MMN)[6,7]

### Disease History

- Clinical diagnosis of MMN
- Patient medical records, including any clinical signs and symptoms associated with MMN
- ICD-10 codes
- Laboratory results
  - Anti-GM1 antibodies
  - Electromyography
  - Nerve conduction study
- MRI results

### Treatment History

- Previous therapies and response
- Hospitalizations due to MMN or any associated clinical symptoms due to MMN

### Other

- Physician specialty (i.e., neurologist/neuromuscular specialists)
- Physician's case notes
  - An accurate weight in kilograms (the dosage is based on mg/kg)

### Clinical Guidance

- Detailed patient history
- Evidence of conduction block (e.g., demyelination)
- Presence of anti-GM1 antibodies
- Consultation from a neurologist or neuromuscular specialist who is an expert in the field of MMN

GM1=ganglioside-monosialic acid; ICD-10=International Statistical Classification of Diseases, Tenth Revision; MRI=magnetic resonance imaging.

# Prior Authorization (PA)
(Continued)

## FOR PATIENTS WITH CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)[6-10]

### Disease History

- Clinical diagnosis of CIDP
- History of symptoms and medical interventions
- ICD-10 codes
- Laboratory results
  - CSF analysis
  - CBC with differential
  - ESR
  - CRP
- Pre- and posttreatment assessments
- MRI of the spinal cord and other nerve regions
- NCS and EMG findings

### Treatment History

- Previous therapies and response

### Other

- Physician specialty (i.e., neurologist or rheumatologist)
- Thorough history and examination
  - Biopsy when necessary

### Clinical Guidance

- Progressive or relapsing/remitting disease course for ≥2 months
- Abnormal or absent deep tendon reflexes in upper or lower limbs
- Electrodiagnostic testing indicative of demyelination
- Refractory or intolerant to corticosteroids
- Reduced conduction velocity in at least 2 motor nerves

CBC=complete blood count; CRP=C-reactive protein; CSF=cerebrospinal fluid; EMG=electromyography; ESR=erythrocyte sedimentation rate; ICD-10=International Statistical Classification of Diseases, Tenth Revision; MRI=magnetic resonance imaging; NCS=nerve conduction study.

References

# Prior Authorization (PA)
(Continued)

**Unfortunately, a PA request may not always be approved.**

In this scenario, the prescribing physician will need to **prepare additional information to appeal the decision**.

There are numerous reasons why a PA could be denied, some of which are described on the following pages, but a common reason for a PA denial is **incomplete information**. It is crucial for the physician or specialty pharmacy completing the PA request to include all relevant diagnostic and patient information, including the prescribing physician's case notes.

When a PA request is denied, whether for incomplete information or a different reason, an appeal will need to:

- **Include additional support for why the medication is clinically necessary for the patient**
- **Be submitted in the time frame specified by the patient's insurance**

# Step Therapy

Step therapy, or fail-first, is a management tool frequently included in a PA that requires a trial of one or more preferred medications before a nonpreferred medication is covered. In IG, there are **2 kinds of step therapy** that could affect a patient's access to their prescribed medication.

01

Some plans may require **trial and failure** of a 5% or 10% IG product before covering a 20% IG product, or require use of a 10% IG product that may be IV or SC before covering a subcutaneous IG (SCIG)–only product.

02

Step through a **preferred product/ preferred drug list (PDL)** – plan might have preferred IG products that a patient must try and fail before a different, nonpreferred option is covered.

A PA denial due to step therapy may be appealed. Some plans require a **letter or statement of medical necessity (LMN, SMN)** to be submitted along with the PA appeals letter to support the IG product choice.

GO TO PA APPEALS LETTER CHECKLIST

GO TO LMN/SMN CHECKLIST

GO TO SUPPORTING REFERENCES TABLE

# Formulary Exclusion

There are **2 basic types of formularies** a health plan can have.

01

**OPEN**

An open formulary pharmacy benefit provides coverage at the point of sale for all medications covered under the prescription benefit, even those not listed on the formulary.[5]

02

**CLOSED**

Under a closed formulary pharmacy benefit, only the drugs listed on the formulary are covered at the point of sale.[5] Nonformulary medications can only be obtained via a formulary exception process.

The PA process can be used to request coverage for Takeda IG products that are covered under the pharmacy benefit but are not included on a plan's formulary. A formulary exception request form prepared by the prescribing physician should be submitted to the patient's health plan as part of this process.

**Note:** Restricted formularies may also be available whereby coverage is contingent on a set of criteria. See the "Prior Authorization" section starting on page 7 for more information.

**GO TO FORMULARY EXCEPTION REQUEST FORM CHECKLIST**

# Site of Care Requirement

Some health plans have a site-of-care policy for specific injectable or infused drugs. For the initial infusion of IG, reinitiation of IG therapy after more than 6 months off therapy, or the change of an IG product, health plans will generally cover the physician's site of care of choice, including a hospital.[11,12]

For subsequent infusions, health plans may not cover infusions in the hospital setting unless the physician provides evidence of medical necessity.[11,12]

Health plans will have their own specific site-of-care policies, but in general, it may be considered medically necessary for patients receiving IG to **receive their infusion in an outpatient hospital or in a home care setting**.

If the site of care that the patient and the patient's physician have agreed upon is **not covered by the patient's insurance**, it may be necessary to **submit an LMN/SMN** outlining the reasons why the chosen site of care is medically necessary.

GO TO LMN/SMN CHECKLIST

GO TO SUPPORTING REFERENCES TABLE

# Coding Error

**What Happens If A Claim Is Denied**

**Incorrect code**
submitted in claim

Prescribing physician must
**identify the correct code**

**Reopen the claim**

A patient's **access**
to necessary medication
is **delayed**

If the **incorrect** diagnosis code, National Drug Code (NDC), Healthcare Common Procedure Coding System (HCPCS) code, or Current Procedural Terminology (CPT®) code is submitted in the claim, the **claim may be denied**.[13] The prescribing physician will then have to identify the correct code before reopening the claim, possibly delaying a patient's access to necessary medication.

**To help prevent coding errors, Takeda provides coding guides for all of the IG products in its portfolio.**

# Out-of-Network Pharmacy

If the physician sends the prescription for a Takeda IG product to a **pharmacy that is not in the plan's specialty pharmacy network**, the claim will not be processed. The out-of-network pharmacy may contact the provider's office to note the issue or may transfer the prescription to an in-network pharmacy directly.

The out-of-network pharmacy may also get an **exception to fill the prescription,** and the patient may choose to pay out of pocket.

**Health plans may provide information on preferred specialty pharmacies in provider newsletters or via publication of specialty drug lists.**

# High-Dollar-Amount Edits

**All IG products require weight-based dosing, leading to a large variation in cost from patient to patient.**

Patients who require a larger amount of IG may experience a delay in their claim approval due to a high-dollar-amount edit. This issue may be resolved with the submission of an LMN/SMN that includes details such as the patient's height and weight, and information from the product's Prescribing Information or treatment guidelines to support why the prescribed dose is appropriate.

GO TO LMN/SMN CHECKLIST

GO TO SUPPORTING REFERENCES TABLE

# Incorrect Benefit

Takeda's IG portfolio includes intravenous IG (IVIG) and SCIG products, and there is some variance in how the different products are billed to commercial health plans. IVIG products and the associated support staff and medical equipment are generally covered under the medical benefit. For SCIG, the product itself is usually covered under the pharmacy benefit, but other items necessary for administration may be covered under the medical benefit. Additionally, the initial dose of a Takeda SCIG product may be administered in a hospital outpatient facility or an infusion center, in which case the product itself may be covered under the medical benefit. A home nursing visit to assist with administration may also be covered under the medical benefit.

**If a patient's claim is rejected due to billing to the incorrect benefit**, the HCP should work with the dispensing pharmacy to correct the error, and the dispensing pharmacy should resubmit the claim to the appropriate benefit.

# Medicare-Specific Reimbursement Challenges

IG therapy for PI, MMN, or CIDP, whether it is IVIG or SCIG, is ~80% covered under Medicare Part B.[14] If the IVIG/SCIG service claim is submitted under Part D when it should be under Part B, the HCP will need to resubmit the claim through the appropriate benefit.[15]

The following conditions must be met for IVIG and SCIG to be covered under Medicare Part B in the home setting[16]:

- **Patient is diagnosed with PI, MMN, or CIDP**
- **Physician determines that administration of IVIG in the home is medically appropriate**

It is important to note the specifics of Medicare Part B coverage for at-home IVIG administration.

- Coverage is provided for SCIG products
- Coverage is not provided for items or services related to IVIG administration (i.e., in-home nursing professionals)[16]

LEARN MORE

**For detailed information on the Medicare appeals process for drugs covered under Part B and Part D, please refer to the official Medicare Appeals booklet**

References

# The following diagnosis codes are approvable under Medicare Part B[16]:

| ICD-10[17] | | | |
|---|---|---|---|
| **G11.3** | Cerebellar ataxia with defective DNA repair | **D81.7** | Major histocompatibility complex class II deficiency |
| **D80.0** | Hereditary hypogammaglobulinemia | **D81.89** | Combined immunodeficiency, unspecified; SCID NOS |
| **D80.2** | Selective deficiency of immunoglobulin A [IgA] | **D82.0** | Wiskott-Aldrich syndrome |
| **D80.3** | Selective deficiency of immunoglobulin G [IgG] subclasses | **D82.1** | DiGeorge syndrome |
| | | **D82.4** | Hyperimmunoglobulin E [IgE] syndrome |
| **D80.4** | Selective deficiency of immunoglobulin M [IgM] | **D83.0** | Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function |
| **D80.5** | Immunodeficiency with increased IgM | | |
| **D80.6** | Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia | **D83.1** | Common variable immunodeficiency with predominant immunoregulatory T-cell disorders |
| **D80.7** | Transient hypogammaglobulinemia of infancy | **D83.2** | Common variable immunodeficiency with autoantibodies to B- or T-cells |
| **D81.0** | SCID with reticular dysgenesis | **D83.8** | Other common variable immunodeficiencies |
| **D81.1** | SCID with low T- and B-cell numbers | **D83.9** | Common variable immunodeficiency, unspecified |
| **D81.2** | SCID with low or normal B-cell numbers | **G61.81** | Chronic inflammatory demyelinating polyneuritis |
| **D81.5** | Purine nucleoside phosphorylase [PNP] deficiency | **G61.82** | Multifocal motor neuropathy [MMN] |
| **D81.6** | Major histocompatibility complex class I deficiency | | |

DNA=deoxyribonucleic acid; NOS=not otherwise specified; SCID=severe combined immunodeficiency.

***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

04

# Actions to Support Effective Appeals

# PA Request Form Checklist

## PA Request Form Checklist

- ○ Be sure to fill in as much information on the form as possible. Incomplete information can lead to a PA denial
- ○ Include the patient's name, policy number, ID number, group number, and date of birth
- ○ Include the prescribing physician's name, specialty, and NPI number
- ○ Include the phone numbers for the prescribing physician and patient if the health plan requires any additional information to support the appeal
- ○ Include specific billing codes where appropriate
  - Include the ICD-10 code, and relevant HCPCS code and NDC code, if applicable
- ○ If the patient is currently receiving an IG product, include the product name, manufacturer name, and dose
  - Include specific measures of clinical benefit seen in the patient with the IG product
- ○ Include the prescribed dose and patient weight
- ○ If the PA includes preferred products, include content from the **Additional considerations for a formulary exception request form**

**Include additional clinical information, if applicable**

- ✓ Setting of care
- ✓ Date of service
- ✓ Diagnosis codes and descriptions (ICD-10-CM)
- ✓ NDCs, procedure/service requested
- ✓ HCPCS/CPT codes and descriptions
- ✓ Diagnostic criteria

**LEARN MORE**

Please do not share with your Takeda representative any documentation of labs, clinical history, or other patient-specific information.

ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; ID=identification; NPI=National Provider Identifier.

# PA Request Form Checklist

## DIAGNOSTIC CRITERIA

### For PI

Lab tests that confirm a diagnosis, such as quantitative serum IG levels, CBC differential, ESR, quantification of blood T- and B-cell subpopulations, and/or other relevant antibody tests

### For MMN

Lab tests that confirm a diagnosis, such as electromyography, nerve conduction studies, nerve ultrasound, or MRI

- Antibody results, such as IgM Anti-GM1 titers

### For CIDP

- Tests that confirm a diagnosis, such as electromyography, nerve conduction studies, CSF analysis, or nerve biopsy
- If requested, include the patient's medical records and all of the documents listed or referenced in the PA request form when it is sent to the patient's insurance provider
- Signature from the prescribing physician

### Formulary Exception Request Form

In addition to the information listed in the **PA request form checklist**, consider including the following items in a formulary exception request form:

- Be sure to fill in as much information on the form as possible. Incomplete information can lead to a denial
- Clearly state the rationale for prescribing an IG product that is not on formulary and why the formulary agents are not appropriate. Possible reasons include:
  - Patient comorbidities
  - Previous infusion-related adverse reactions
  - Patient is currently stable on drug that is not on formulary
  - Limited availability of formulary alternatives
  - Prior therapeutic failure on formulary agent
  - Volume limitations

# Additional Considerations for a PA Appeals Letter

**In addition to the information listed in the PA request form checklist, consider including the following items in a PA appeals letter:**

- Review the reason for the denial, if supplied
- If information (dose, indicated use, etc.) was missing from original PA request that may have led to the denial, include that information in the appeal
- Confirm the timeline and process for appeals
- Confirm where the appeal is to be sent; it may differ from the original PA request
- Provide well-accepted diagnostic studies and standards of practical criteria to support the laboratory studies, if applicable
- Include an LMN or SMN if required by the patient's health plan
- Include the names of immunologists who have completed the scientific research on the diagnosis in question, should the health plan request a peer review

Please do not share with your Takeda representative any documentation of labs, clinical history, or other patient-specific information.

GO TO SUPPORTING REFERENCES TABLE

ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification; NPI=National Provider Identifier.

# Appeals Review

**Consider the following to help prepare for a successful peer-to-peer review in the appeal process:**

- Clinical rationale supported by medical history or publications are the most compelling, but quality of life rationale may also be considered
- Submit an LMN or SMN in writing prior to the peer-to-peer review
- Request a like specialist (e.g., allergist/immunologist, clinical immunologist)
- Refer to and have relevant documents and lab results available during the discussion (e.g., diagnosis, case notes, medical history)
- Refer to supporting references and publications to support rationale for a particular product
- Discuss the results of a successful trial of product, if available
- Discuss the potential consequences of a denial for the patient
- Discuss patient's adverse events with previously trialed products, if appropriate
- Be available during the call window; missing the peer-to-peer review can result in automatic denials
- If denial is the final outcome of the review, ask for the peer's name and license number to be noted in the chart

Please do not share with your Takeda representative any documentation of labs, clinical history, or other patient-specific information.

GO TO SUPPORTING REFERENCES TABLE

# Letter or Statement of Medical Necessity (LMN, SMN)

An LMN/SMN is a critical component of appealing a coverage denial or requesting a formulary exception. The LMN/SMN is the prescribing physician's opportunity to present all of the rationale for why a certain Takeda IG product is clinically necessary for the patient. It is important to note that LMNs/SMNs should be concise while making as strong an argument as possible, and should be drafted on official letterhead stationery.

**In addition to the information listed in the PA request form checklist, consider including the following items in an LMN/SMN:**

- Clearly state the rationale for treatment with the relevant Takeda IG product and why it is appropriate for the patient
  - Include support for the treatment recommendation
    - Citing published trials can be impactful. See the updated guidelines on the use of immunoglobulin in human disease
  - Specify if patient is already on a Takeda IG product and is clinically stable, and include specific measures of clinical benefit
  - Explain why the formulary-preferred agents, if applicable, are not appropriate (e.g., patient's comorbidities, previous infusion-related adverse reaction, etc.)
  - Outline implications if patient goes without treatment
- If applicable, include the product name, duration of treatment, and reason for discontinuation for any previous IG treatments

LEARN MORE

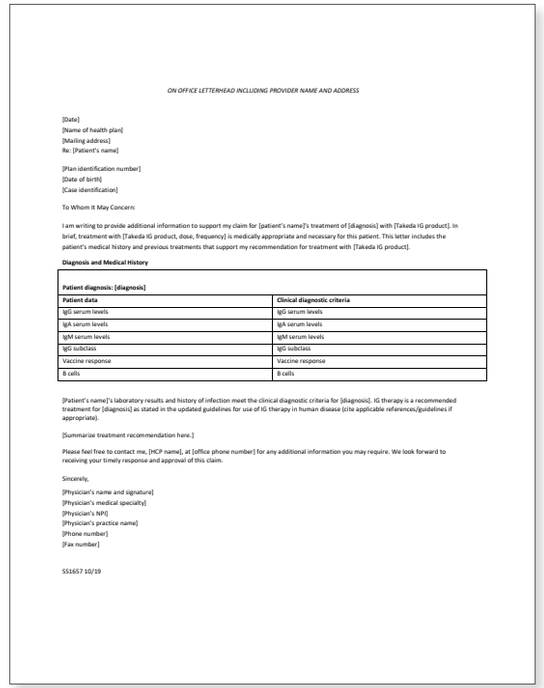
Please do not share with your Takeda representative any documentation of labs, clinical history, or other patient-specific information.

GO TO SUPPORTING REFERENCES TABLE

## ADDITIONAL CONSIDERATIONS

**Important information to consider including in a LMN/SMN letter when prescribing Takeda IG products not on formulary or on the preferred drug list:**

- Evidence of clinical benefit seen with Takeda IG treatment. Can include pre- and posttreatment laboratory results in the above table to demonstrate clinical benefit
- Patient-specific reasons for prescribing an IG product that is not preferred or on formulary (patient comorbidities, history of adverse reactions to formulary agent, etc.)
- Rationale against switching IG products
- Reasons why IG products are not interchangeable
- Clinical implications if treatment with the Takeda IG product is interrupted
- For patients prescribed SCIG, include rationale for SCIG treatment
- For patients whose chosen site of care is not covered, include rationale to support site of care



*ON OFFICE LETTERHEAD INCLUDING PROVIDER NAME AND ADDRESS*

[Date]
[Name of health plan]
[Mailing address]
Re: [Patient's name]

[Plan identification number]
[Date of birth]
[Case identification]

To Whom It May Concern:

I am writing to provide additional information to support my claim for [patient's name]'s treatment of [diagnosis] with [Takeda IG product]. In brief, treatment with [Takeda IG product, dose, frequency] is medically appropriate and necessary for this patient. This letter includes the patient's medical history and previous treatments that support my recommendation for treatment with [Takeda IG product].

**Diagnosis and Medical History**

| **Patient diagnosis: [diagnosis]** | |
|---|---|
| **Patient data** | **Clinical diagnostic criteria** |
| IgG serum levels | IgG serum levels |
| IgA serum levels | IgA serum levels |
| IgM serum levels | IgM serum levels |
| IgG subclass | IgG subclass |
| Vaccine response | Vaccine response |
| B cells | B cells |

[Patient's name]'s laboratory results and history of infection meet the clinical diagnostic criteria for [diagnosis]. IG therapy is a recommended treatment for [diagnosis] as stated in the updated guidelines for use of IG therapy in human disease (cite applicable references/guidelines if appropriate).

[Summarize treatment recommendation here.]

Please feel free to contact me, [HCP name], at [office phone number] for any additional information you may require. We look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI]
[Physician's practice name]
[Phone number]
[Fax number]

SS1657 10/19

*Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.*

References

05

# Billing and Coding Information

# Support References

Please refer to the below support information for treatment with a Takeda IG product, which may be included in a PA request form or appeals letter, an LMN/SMN, or a formulary exception request form to further support the case.

| Support | Reference Citation |
|---|---|
| **Support for Indication/Appropriate Use of IG[18,19]** | |
| Recommendations and rationale for use of IG in specific disease states are included in the updated guidelines on the use of IG in human disease | Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol*. 2017;139(3 suppl):S1-S46. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. |
| A summary of disease-specific diagnostic criteria can be found in the 2015 practice parameter for the diagnosis and management of PI: | Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*. 2015;136(5):1186-1205. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/PID-Nov-2015.pdf**. |
| **Rationale Against Switching IG Products[18,20]** | |
| Significant adverse reactions occur in approximately 15%-18% of patients when switching IVIG products | Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol*. 2017;139(3 suppl):S1-S46. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. |
| The *AAAAI Guiding Principles* state that a patient stabilized on a particular product should be maintained on that particular therapy | American Academy of Allergy, Asthma & Immunology. Eight guiding principles for effective use of IVIG for patients with primary immunodeficiency. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/IVIG-guiding-principles.pdf**. December 2011. Accessed January 3, 2024. |

**This is not an exhaustive list of references that may be helpful to support treatment with a Takeda IG product in the context of a denial and appeal or formulary exception request.**

Each insurer and/or patient may need different information to support the appeal or formulary exception process. Carefully review the insurer guidelines and denial, if applicable, to determine what information should be included in your submission.

# Support References
(Continued)

Please refer to the below support information for treatment with a Takeda IG product, which may be included in a PA request form or appeals letter, an LMN/SMN, or a formulary exception request form to further support the case.

| Support | Reference Citation |
|---|---|
| **Reasons Why IG Products Are Not Interchangeable[20-22]** | |
| The *AAAAI Guiding Principles* state that the various IG products that are indicated for the treatment of PI diseases "are not generic and there are notable differences amongst them"<br>• A patient with diabetes should not use an IG product that uses glucose as a stabilizer<br>• IG products with a higher sodium content would not be appropriate to use in patients with cardiac conditions | American Academy of Allergy, Asthma & Immunology. Eight guiding principles for effective use of IVIG for patients with primary immunodeficiency. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/IVIG-guiding-principles.pdf**. December 2011. Accessed January 3, 2024. |
| IG products are not interchangeable, and patients can have varying reactions to seemingly similar products. The 2018 IDF treatment survey found that many PI patients who have been on more than one IG product tolerate some IG products better than others | Immune Deficiency Foundation. 2018 IDF national treatment survey. **https://primaryimmune.org/sites/default/files/IDF-2018-Treatment-Survey_0.pdf**. Accessed January 3, 2024. |
| Patient tolerance or responsiveness can vary across IG products. Poorly tolerated therapies adversely affect patient outcomes and may also require the use of additional therapies, which can increase costs. Taking cost-effectiveness into consideration, physicians should have the flexibility to prescribe appropriate therapies based on the patient's individual needs | Grabowski H, Manning R. Key economic and value considerations in the U.S. market for plasma protein therapies. Bates White Economic Consulting. February 2018. **https://www.bateswhite.com/media/publication/154_Plasma_Protein_Therapies_paper.pdf**. Accessed January 3, 2024. |

**This is not an exhaustive list of references that may be helpful to support treatment with a Takeda IG product in the context of a denial and appeal or formulary exception request.**

Each insurer and/or patient may need different information to support the appeal or formulary exception process. Carefully review the insurer guidelines and denial, if applicable, to determine what information should be included in your submission.

IDF=Immune Deficiency Foundation.

# Support References
(Continued)

Please refer to the below support information for treatment with a Takeda IG product, which may be included in a PA request form or appeals letter, an LMN/SMN, or a formulary exception request form to further support the case.

| Support | Reference Citation |
|---|---|
| **Rationale to Support SCIG[18,20]** | |
| Subcutaneous IG therapy presents numerous benefits for patients experiencing severe or difficult-to-control adverse events related to intravenous IG infusion<br><br>**NOTE:** The physician may need to list patient-specific benefits of SCIG therapy and include documentation of the IVIG adverse events to demonstrate clinical need | American Academy of Allergy, Asthma & Immunology. Eight guiding principles for effective use of IVIG for patients with primary immunodeficiency. **https://www.aaaai.org/Aaaai/media/Media-Library-PDFs/Practice%20Management/Practice%20Tools/IVIG-guiding-principles.pdf**. December 2011. Accessed January 3, 2024. |
| Patients with poor venous access may require SCIG<br><br>**NOTE:** The physician will need to provide documentation of the reason for poor venous access (i.e., type of VAD, prior VAD infections, etc.) | American Academy of Allergy, Asthma & Immunology. Eight guiding principles for effective use of IVIG for patients with primary immunodeficiency. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/IVIG-guiding-principles.pdf**. December 2011. Accessed January 3, 2024. |
| With SCIG, patients reach steady-state IgG levels, so the withdrawal effects (e.g., malaise or symptoms of infection) that patients may experience in the week preceding the next IVIG infusion are minimal<br><br>**NOTE:** The physician may need to provide documentation and attest to the patient's withdrawal symptoms | Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol.* 2017;139(3 suppl):S1-S46. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. |

**This is not an exhaustive list of references that may be helpful to support treatment with a Takeda IG product in the context of a denial and appeal or formulary exception request.**

Each insurer and/or patient may need different information to support the appeal or formulary exception process. Carefully review the insurer guidelines and denial, if applicable, to determine what information should be included in your submission.

VAD=vascular access device.

# Support References
(Continued)

Please refer to the below support information for treatment with a Takeda IG product, which may be included in a PA request form or appeals letter, an LMN/SMN, or a formulary exception request form to further support the case.

| Support | Reference Citation |
|---|---|
| **Rationale to Support IVIG Site of Care[23]** | |
| Certain patients require higher levels of monitoring and intervention during IVIG infusions. If infusion-related adverse events are concerning to the physician, medical supervision should be available.<br><br>**NOTE:** The physician will also need to include patient-specific information to demonstrate clinical need for increased monitoring | American Academy of Allergy, Asthma & Immunology. Guidelines for site of care for administration of IVIG therapy. **www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. Accessed January 3, 2024. |
| Some patients with PI may require frequent follow-up visits with physicians because of disease-related complications (chronic bronchitis, inflammatory bowel disease, etc.) or to ensure appropriate management of the underlying disease. In some cases, considerable savings in time and costs can be achieved by having physician follow-up visits at the same time and place as the IVIG infusions. | American Academy of Allergy, Asthma & Immunology. Guidelines for site of care for administration of IVIG therapy. **https://www.aaaai.org/Aaaai/media/Media-Library-PDFs/Practice%20Management/Practice%20Tools/Guidelines-for-the-site-of-care-for-administration-of-IGIV-therapy.pdf**. Accessed January 3, 2024. |
| **Rationale to Support Prescribed Dose[18]** | |
| Defining "adequate" treatment by using only the standard of minimal or suboptimal IgG levels can potentially harm patients. Treatment regimens should be individualized for each patient. | Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol*. 2017;139(3 suppl):S1-S46. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. |
| For patients switching from IVIG to SCIG, dose may need to be adjusted beyond the conversion factor of 1.37 for patients with a very low or very high BMI. Studies of 16% and 20% SCIG formulations have suggested that subjects with a high BMI might require higher dose adjustments when switching for IVIG to SCIG. | Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol*. 2017;139(3 suppl):S1-S46. **https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20and%20Parameters/IVIG-March-2017.pdf**. |

**This is not an exhaustive list of references that may be helpful to support treatment with a Takeda IG product in the context of a denial and appeal or formulary exception request.**

Each insurer and/or patient may need different information to support the appeal or formulary exception process. Carefully review the insurer guidelines and denial, if applicable, to determine what information should be included in your submission.

BMI=body mass index.

# PI, MMN, and CIDP ICD-10 Diagnosis Codes[17]

CUVITRU [Immune Globulin Subcutaneous (Human)] 20% Solution, HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] 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

| D80 | Immunodeficiency With Predominantly Antibody Defects |
|---|---|
| **D80.0** | Hereditary hypogammaglobulinemia<br>Autosomal recessive agammaglobulinemia (Swiss type)<br>X-linked agammaglobulinemia [Bruton] (with growth hormone deficiency) |
| **D80.1** | Nonfamilial hypogammaglobulinemia<br>Agammaglobulinemia with immunoglobulin-bearing B-lymphocytes<br>Common variable agammaglobulinemia [CVAgamma]<br>Hypogammaglobulinemia NOS |
| **D80.3** | Selective deficiency of immunoglobulin G [IgG] subclasses |
| **D80.4** | Selective deficiency of immunoglobulin M [IgM] |
| **D80.5** | Immunodeficiency with increased immunoglobulin M [IgM] |
| **D80.6** | Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinemia |
| **D80.7** | Transient hypogammaglobulinemia of infancy |
| **D80.8** | Other immunodeficiencies with predominantly antibody defects<br>Kappa light chain deficiency |
| **D80.9** | Immunodeficiency with predominantly antibody defects, unspecified |

| D81 | Combined Immunodeficiencies |
|---|---|
| **D81.0** | Severe combined immunodeficiency [SCID] with reticular dysgenesis |
| **D81.1** | Severe combined immunodeficiency [SCID] with low T- and B-cell numbers |
| **D81.2** | Severe combined immunodeficiency [SCID] with low or normal B-cell numbers |
| **D81.4** | Nezelof syndrome |
| **D81.6** | Major histocompatibility complex class I deficiency<br>Bare lymphocyte syndrome |
| **D81.7** | Major histocompatibility complex class II deficiency |
| **D81.89** | Other combined immunodeficiencies |
| **D81.9** | Combined immunodeficiency, unspecified\<br>Severe combined immunodeficiency disorder [SCID] NOS |

***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

# PI, MMN, and CIDP ICD-10 Diagnosis Codes[17]
(Continued)

CUVITRU [Immune Globulin Subcutaneous (Human)] 20% Solution, HYQVIA [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase] 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

| D82 | Immunodeficiency Associated With Other Major Defects |
|---|---|
| **D82.0** | Wiskott-Aldrich syndrome<br>Immunodeficiency with thrombocytopenia and eczema |
| **D82.1** | DiGeorge syndrome<br>Pharyngeal pouch syndrome<br>Thymic alymphoplasia<br>Thymic aplasia or hypoplasia with immunodeficiency |
| **D82.2** | Immunodeficiency with short-limbed stature |
| **D82.3** | Immunodeficiency following hereditary defective response to Epstein-Barr virus<br>X-linked lymphoproliferative disease |
| **D82.4** | Hyperimmunoglobulin E [IgE] syndrome |
| **D82.8** | Immunodeficiency associated with other specified major defects |
| **D82.9** | Immunodeficiency associated with major defect, unspecified |

| D83 | Common Variable Immunodeficiency |
|---|---|
| **D83.0** | Common variable immunodeficiency with predominant abnormalities of B-cell numbers and function |
| **D83.1** | Common variable immunodeficiency with predominant immunoregulatory T-cell disorders |
| **D83.2** | Common variable immunodeficiency with autoantibodies to B- or T-cells |
| **D83.8** | Other common variable immunodeficiencies |
| **D83.9** | Common variable immunodeficiency, unspecified |

| G61 | Inflammatory Polyneuropathy |
|---|---|
| **G61.81** | Chronic inflammatory demyelinating polyneuritis |
| **G61.82** | Multifocal motor neuropathy [MMN] |

***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

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# CUVITRU Billing Codes

Cuvitru [Immune Globulin Subcutaneous (Human)] 20%

Takeda

The provider is responsible for ensuring accurate and appropriate diagnostic coding to obtain reimbursement.

| Applicable HCPCS Codes[24] | |
|---|---|
| **HCPCS Code** | **Description** |
| **J1555** | Injection, immune globulin (CUVITRU), 100 mg |

| External Infusion Pump | |
|---|---|
| **HCPCS Code** | **Description** |
| **E0779** | Ambulatory infusion pump, mechanical, reusable, for infusion 8 hours or greater |
| **E0780** | Ambulatory infusion pump, mechanical, for infusion less than 8 hours |
| **E0781** | Ambulatory infusion pump, single or multiple channels, electric or battery operated, with administrative equipment, worn by patient |
| **E0791** | Parenteral infusion pump, stationary, single, or multichannel |

| External Infusion Pump Supplies | |
|---|---|
| **A4221** | Supplies for maintenance of drug infusion catheter, per week (list drugs separately) |
| **A4222** | Infusion supplies for external drug infusion pump, per cassette or bag |
| **K0552** | Supplies for external drug infusion pump, syringe type cartridge, sterile, each |

| CUVITRU NDC Numbers[1] | | | |
|---|---|---|---|
| **NDC Number** | | **Grams Protein** [Immune Globulin Subcutaneous (Human) 20%] | **J1555-Billing Units** [Injection, immune globulin (CUVITRU), 100 mg] |
| **0944-2850-01** | 5 mL | 1.0 | 10 units |
| **0944-2850-03** | 10 mL | 2.0 | 20 units |
| **0944-2850-05** | 20 mL | 4.0 | 40 units |
| **0944-2850-07** | 40 mL | 8.0 | 80 units |
| **0944-2850-09** | 50 mL | 10.0 | 100 units |

| CPT Codes[25] | |
|---|---|
| **Subcutaneous Administration**<br>The following CPT codes apply to administration services performed by a healthcare provider concurrent with infusion. | |
| **CPT Code** | **Description** |
| **96369** | Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s) |
| **96370** | Each additional hour (list separately in addition to code for primary procedure) |

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***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

# HYQVIA Billing Codes

HyQvia [Immune Globulin Infusion 10% (Human) with Recombinant Human Hyaluronidase]

Takeda

The provider is responsible for ensuring accurate and appropriate diagnostic coding to obtain reimbursement.

| Applicable HCPCS Codes[24] | |
|---|---|
| **HCPCS Code** | **Description** |
| **J1575** | Injection, immune globulin/hyaluronidase, (HYQVIA), 100 mg immune globulin |

| DME and Supply Codes | |
|---|---|
| **HCPCS Code** | **Description** |
| **E0779** | Ambulatory infusion pump, mechanical, reusable, for infusion 8 hours or greater |
| **E0780** | Ambulatory infusion pump, mechanical, for infusion less than 8 hours |
| **E0781** | Ambulatory infusion pump, single or multiple channels, electric or battery operated, with administrative equipment, worn by patient |
| **E0791** | Parenteral infusion pump, stationary, single, or multichannel |
| **A4221** | Supplies for maintenance of drug infusion catheter, per week (list drugs separately) |
| **K0552** | Supplies for external drug infusion pump, syringe type cartridge, sterile, each |

| Home Infusion Therapy | |
|---|---|
| **S9338** | Home infusion therapy, immunotherapy, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem |

| CPT Codes[25] | |
|---|---|
| **Subcutaneous Administration** | |
| **CPT Code** | **Description** |
| **96369** | Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s) |
| **96370** | Each additional hour (list separately in addition to code for primary procedure) |
| **96371** | Additional pump set-up with establishment of new subcutaneous infusion site(s) (list separately in addition to code for primary procedure) |

| NDC Numbers[2] | | | |
|---|---|---|---|
| **NDC Number** | **Volume** | **Grams Protein** [Immune Globulin 10% (Human)] | **J1575-Billing Units[a]** [Injection, immune globulin/ hyaluronidase, (HYQVIA) 100 mg immune globulin] |
| **0944-2510-02** | 25 mL | 2.5 | 25 mL |
| **0944-2511-02** | 50 mL | 5.0 | 50 mL |
| **0944-2512-02** | 100 mL | 10.0 | 100 mL |
| **0944-2513-02** | 200 mL | 20.0 | 200 mL |
| **0944-2514-02** | 300 mL | 30.0 | 300 mL |

[a]HYQVIA is supplied in a dual-vial unit of 2 single-use vials containing the labeled amount of functionally active Immune Globulin Infusion 10% (Human) and Recombinant Human Hyaluronidase.

***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

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# GAMMAGARD LIQUID Billing Codes

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

The provider is responsible for ensuring accurate and appropriate diagnostic coding to obtain reimbursement.

**HCPCS Codes[24]** [Immune Globulin Infusion (Human)] 10%

| HCPCS Code | Description |
|---|---|
| **J1569[a]** | Injection, immune globulin (GAMMAGARD LIQUID), intravenous, non-lyophilized (e.g., liquid), 500 mg |
| **J1569JB[b]** | |

[a]The HCPCS code currently assigned to GAMMAGARD LIQUID, J1569, only describes the IV route of administration. Providers are advised to contact the payer for the appropriate HCPCS code when GAMMAGARD LIQUID is administered subcutaneously.

[b]Medicare DME MAC coding guidance for GAMMAGARD LIQUID with the SC route of administration via a pump.

**NDC Numbers[3]**

| NDC Number | Grams |
|---|---|
| **0944-2700-02** | 1.0 |
| **0944-2700-03** | 2.5 |
| **0944-2700-04** | 5.0 |
| **0944-2700-05** | 10.0 |
| **0944-2700-06** | 20.0 |
| **0944-2700-07** | 30.0 |

**Home Infusion Therapy (for IVIG or SCIG)[24]**

| HCPCS Code | Description |
|---|---|
| **S9338** | Home infusion therapy, immunotherapy, administrative services, professional pharmacy services, care coordination and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem |

HCPs should contact payers for guidance on appropriate coding.

**Hospital Revenue Code**

| Code | Description |
|---|---|
| **0636** | Pharmacy, drugs requiring detailed coding |

DME=durable medical equipment; MAC=Medicare administrative contractor; SC=subcutaneous.

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***Please click for Indications and Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

References

# GAMMAGARD LIQUID Billing Codes
(Continued)

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

The provider is responsible for ensuring accurate and appropriate diagnostic coding to obtain reimbursement.

| CPT Codes[25] | |
|---|---|
| **Intravenous Administration** | |
| **CPT Code** | **Description** |
| **96365** | IV infusion for therapy, prophylaxis, or diagnosis; initial, up to 1 hour |
| **96366** (add-on code) | IV infusion for therapy, prophylaxis, or diagnosis; each additional hour (list separately in addition to code for primary procedure) |
| **96367** (add-on code) | IV infusion for therapy, prophylaxis, or diagnosis; additional sequential infusion, up to 1 hour (list separately in addition to code for primary procedure) |
| **96368** (add-on code) | IV infusion for therapy, prophylaxis, or diagnosis; concurrent infusion (list separately in addition to code for primary procedure) |

| CPT Codes[25] | |
|---|---|
| **Subcutaneous Administration** | |
| **CPT Code** | **Description** |
| **96369** | Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s). Excludes infusions of 15 minutes or less (96372) |
| **96370** | Each additional hour (list separately in addition to code for primary procedure). Includes infusions of more than 30 minutes beyond 1 hour |
| **96371** | Additional pump set-up with establishment of new subcutaneous infusion site(s) (list separately in addition to code for primary procedure) |

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References

# GAMMAGARD S/D Billing Codes



The provider is responsible for ensuring accurate and appropriate diagnostic coding to obtain reimbursement.

| HCPCS Codes and Descriptions[24] | |
|---|---|
| **Drug-specific HCPCS Code** | |
| **Code** | **Description** |
| **J1566** | Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg |
| **DME and Supply Codes** | |
| **S9338** | Home infusion therapy, immunotherapy, administrative services, professional pharmacy services, care coordination, and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem |

| CPT Codes and Descriptions[25] | |
|---|---|
| **Code** | **Description** |
| **96365** | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour |
| **96366** | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (list separately in addition to code for primary procedure) |
| **96367** | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (list separately in addition to code for primary procedure) |
| **96368** | Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (list separately in addition to code for primary procedure) |
| **NDC Number[4]** | **Grams Protein** |
| **0944-2656-03** | 5 g |
| **0944-2658-04** | 10 g |

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06

# Indications and Important Safety Information

# Indications and Important Safety Information

**INDICATIONS**

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

HYQVIA is indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients two years of age and older and for chronic inflammatory demyelinating polyneuropathy (CIDP) as maintenance therapy to prevent relapse of neuromuscular disability and impairment in adults.

GAMMAGARD LIQUID is also indicated as a maintenance therapy to improve muscle strength and disability in adult patients with Multifocal Motor Neuropathy (MMN) and as a therapy to improve neuromuscular disability and impairment in adult patients with Chronic Inflammatory Demyelinating Polyneuropathy (CIDP).

LIMITATIONS OF USE (CIDP): GAMMAGARD LIQUID has not been studied in immunoglobulin-naive patients with CIDP. GAMMAGARD LIQUID maintenance therapy in CIDP has not been studied for periods longer than 6 months. After responding during an initial treatment period, not all patients require indefinite maintenance therapy with GAMMAGARD LIQUID in order to remain free of CIDP symptoms. Individualize the duration of any treatment beyond 6 months based upon the patient's response and demonstrated need for continued therapy.

GAMMAGARD S/D is also indicated for the prevention of bacterial infections in hypogammaglobulinemia and/or recurrent bacterial infections associated with B-cell chronic lymphocytic leukemia (CLL), prevention and/or control of bleeding in adult chronic idiopathic thrombocytopenic purpura (ITP) patients, and prevention of coronary artery aneurysms associated with Kawasaki syndrome in pediatric patients.

CUVITRU and HYQVIA are for subcutaneous use only.

GAMMAGARD LIQUID for PI is for intravenous or subcutaneous use.

GAMMAGARD LIQUID for MMN and CIDP is for intravenous use only.

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.**

*Please see additional Important Safety Information on pages 35-38 and click for Full Prescribing Information for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.*

References

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# Indications and 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**.

## 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.

***Please see additional Important Safety Information on pages 35-38 and click for Full Prescribing Information, including Boxed Warnings regarding Thrombosis, Renal Dysfunction, and Acute Renal Failure, for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

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# 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.

***Please see additional Important Safety Information on pages 35-38 and click for Full Prescribing Information, including Boxed Warnings regarding Thrombosis, Renal Dysfunction, and Acute Renal Failure, for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

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# Indications and Important Safety Information (Continued)

**Adverse Reactions (Continued)**

**HYQVIA**

The most common adverse reactions observed in >5% of patients in clinical trials were:

PI: 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.

CIDP: local reactions, headache, pyrexia, nausea, fatigue, erythema, pruritus, increased lipase, abdominal pain, back pain, and pain in extremity.

**GAMMAGARD LIQUID**

The serious adverse reactions observed in clinical studies in PI was aseptic meningitis, and in MMN were pulmonary embolism and blurred vision.

The most common adverse reactions observed in ≥5% of patients were:

IV administration for PI: 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: 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.

IV administration for MMN: headache, chest discomfort, muscle spasms, muscular weakness, nausea, oropharyngeal pain, and pain in extremity.

IV administration for CIDP: Headache, pyrexia, anemia, leukopenia, neutropenia, illness, blood creatinine increased, dizziness, migraine, somnolence, tremor, nasal dryness, abdominal pain upper, vomiting, chills, nasopharyngitis, 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 see additional Important Safety Information on pages 35-38 and click for Full Prescribing Information, including Boxed Warnings regarding Thrombosis, Renal Dysfunction, and Acute Renal Failure, for CUVITRU, HYQVIA, GAMMAGARD LIQUID, and GAMMAGARD S/D.***

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US-XMP-2440v3.0 06/24