Subject: Subcutaneous Immune Globulin (SCIg)	**Original Effective Date:** 2/2016
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DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP document and provide the directive for all Medicare members.

SUMMARY OF EVIDENCE/POSITION

This policy addresses the coverage of **immune globulin products FDA-approved for subcutaneous infusion (SCIg)** for the treatment of **primary immune deficiency** when appropriate criteria are met with consideration for members in whom IVIg has failed, is not tolerated, and contraindicated or for members already stable on a SCIg product.

The intent of this coverage policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical studies, nationally recognized authoritative references and current peer-reviewed scientific literature. The information outlined in the Molina Clinical Policy includes but is not limited to a review of evidence based information obtained from the following sources Evaluation of New and Existing Technologies (UM 10). This policy is intended to address coverage criteria that are appropriate for the majority of individuals/members with a particular disease, illness, or condition. Each member's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.

Abbreviations:

- *Immune globulin, intravenous (human)* will be referred to as IVIg since this term is commonly used by clinicians, although the abbreviation used by industry and various regulatory agencies is IGIV
- *Immune globulin, subcutaneous* will be abbreviated as subcutaneous immune globulin (SCIg)

⌘ Subcutaneous immune globulin (SCIg) is a protein solution that contains at least 98% immunoglobulin G (IgG). It is used in the treatment of primary immunoglobulin deficiency (PID). For individuals with immunodeficiencies, both IVIg and SCIg are effective. Use of SCIg for the treatment of primary immunodeficiencies was approved by the FDA based on an open-label, nonrandomized, prospective, multicenter study.

SCIg products are indicated for replacement therapy in patients with PID, including but not limited to the humoral defect in the following conditions: common variable immunodeficiency (CVID), X-lined agammaglobulinemia (XLA), Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (SCID). [Clinical Pharmacology, 2019]

- The exact mechanism of SCIg in PID is not fully understood.

- Immune globulin may be administered subcutaneously by three methods which differ in the frequency and how the SCIG is given: traditional, facilitated subcutaneous, and subcutaneous rapid-push.
    - Traditional: uses infusion pumps to give predominantly weekly infusions
    - Rapid-push SC: administered using only a syringe and butterfly needle at frequencies from several times per week to daily
    - Hyaluronidase-facilitated SCIg (fSCIg): A two-step delivery system of recombinant human hyaluronidase (rHuPH20) and a 10% immune globulin preparation, human hyaluronidase (rHuPH20) given immediately before the immune globulin, to allow up to a full monthly dose to be given in a single SC infusion. The hyaluronidase is drawn up into a separate single syringe and infused alone by manual push from the syringe before the SCIG is given. Generally administered every three to four weeks
- SCIg has a lower bioavailability than IVIg, so must be given in higher doses to achieve the same serum IgG concentrations. However, subcutaneous delivery may result in higher steady-state IgG levels due to less variation in IgG levels.

- **For SCIg requests of an FDA-approved product that is not addressed in this policy, the criteria outlined within this policy, product labeling, clinical studies, nationally recognized authoritative references and current peer-reviewed scientific literature will be applied.**

- Applications of Subcutaneous Immune Globulin (SCIg) for conditions other than primary immunodeficiencies are considered not addressed in this policy. Conditions that are off-label may be addressed by Molina Healthcare's off-label coverage for prescription drugs and biologics policy, **Off-Label Use of Drugs and Biologic Agents MCP-162.**

- Molina Healthcare does not cover subcutaneous immune globulin (SCIg) for non-FDA approved conditions, including but not limited to conditions when its use is considered investigational or unproven, and is not supported by evidence-based literature.

- Refer to **Intravenous Immune Globulin (IVIg) MCP-043** for immune globulin products FDA-approved for intravenous infusion (IVIg)

- Comparison of SCIg with IVIg
    - Immune globulin products specifically intended for subcutaneous (SC) and intramuscular (IM) administration are generally more concentrated than those designed for intravenous (IV) use, allowing more immune globulin to be administered in lower volumes.
        - Generally, many 10% IVIg solutions can be administered subcutaneously or intravenously, but more concentrated products (e.g., 20%) should not be given intravenously. The subcutaneous route is associated with fewer systemic adverse events and provides more stable serum IgG levels. In contrast, SCIG has not been studied as extensively in autoimmune and inflammatory disorders.
        - IVIg is used when high doses are desired (e.g., 2 g/kg) in acute situations, such as in the management of Kawasaki disease, Guillain-Barré syndrome, and immune thrombocytopenia.
    - IVIg infusions may be preferable for patients who require faster increase of trough level at initiation
    - SCIg is associated with more stable serum Ig concentrations and advantageous for patients with poor venous access due to no need for indwelling venous catheter, particularly in patients with poor venous access
    - Appendix 1: Comparison of IV and Subcutaneous Immunoglobulin Therapy

- **Similar clinical efficacy of SCIg replacement therapy versus IVIg**

  Subcutaneous and intravenous immune globulin are similarly effective at preventing infections.
  - In 2013, Lingman-Framme and Fasth published a systematic review of the literature on SCIg compared with IVIg for treatment of primary and secondary immunodeficiencies (Lingman-Framme J, 2013). The authors identified 20 studies; 2 were RCTs, and 19 included patients with primary immunodeficiencies. The primary outcome of interest was the number of serious bacterial infections, defined as bacterial pneumonia, meningitis, osteomyelitis, septicemia, and peritonitis. Only 3 studies reported on serious bacterial infections during both SCIg and IVIg administration, and no serious bacterial infections were identified. Five studies reported the annual number of infections (bacterial and/or viral), and no significant difference was found in infection rates associated with SCIg and IVIg. Four studies compared health-related quality of life in patients who changed the route of administration from IV to subcutaneous. All four of these studies found that patients reported a better quality of life with home-based SCIg compared with hospital-based IVIg. Moreover, all 11 studies that reported IgG trough levels found higher levels with SCIg compared with IVIg.
  - The similar clinical efficacy of SCIg replacement therapy versus IVIg, in the context of more favorable pharmacokinetic parameters and a simpler delivery method for chronic therapy, suggests SCIg treatment may be considered medically necessary in the place of IVIg to prevent recurrent infections in patients with primary immunodeficiencies PID who require lifelong immunoglobulin replacement therapy.

- There are no head-to-head studies comparing concentrated SCIg to IVIg in PID and no evidence-based reviews demonstrating that SCIg is more effective than IVIg to improve and maintain immune globulin levels. **Therefore, unless contraindicated, a trial of IVIg is required before SCIg products will be considered for authorization.**

- There is robust evidence to support the use of subcutaneous IgG (SCIg) for primary immunodeficiency. The SCIg formulation may be appealing to patients due to a lack of requirement of venous access, a perceived sense of independence associated with self-administration, and more consistent serum IgG levels. However, limitations of SCIg include increased dosing frequency, requirement of multiple dosing sites, and the need for competent and adherent patients.
  - There is no strong evidence that indicates a preferential route of administration of IgG. Systematic reviews indicate that there is **no difference in efficacy** between IVIg and SCIg products. Products with low IgA counts may be preferable to those who experience infusion reactions. (Lingman-Framme J, et al; Abolhassani H, et al.; Chapel HM, et al)
  - There is **no strong evidence that shows that the differences in the pharmacokinetic profiles** of IVIg and SCIg translate to meaningful improvements in patient outcomes. While some studies showed a lower incidence of adverse events in SCIg versus IVIg, the 20% SCIG formulation has not been directly compared to IVIg. (Lingman-Framme J, et al; Abolhassani H, et al.; Chapel HM, et al)

- Adjustments of dosage, frequency, site of administration, and duration of therapy must be consistent and supported by FDA-approved labeling for member's condition and severity, availability of alternative treatments, and prior response to immune globulin therapy.

FDA INDICATIONS

FDA-approved indication does not, in itself, dictate coverage. Molina coverage Policy may not recommend coverage for all FDA-approved indications. Please review this Policy in its entirety for indications covered by Molina Healthcare.

The covered FDA-approved indications are conditions that are considered medically necessary; however it is not inclusive of all conditions which may be approved by the Medical Reviewer. At the discretion of the Medical Director and on a case-by-case basis, Molina Healthcare may consider authorization of the biologic therapy addressed in this Policy for members with exceptional circumstances and for members with severe disease who may fall outside of the defined criteria.

Molina Healthcare reserves the right to update this Policy and revise coverage criteria to include or omit any off-label condition(s) as necessary based on medical literature and clinical studies that may become available.

FDA-APPROVED PRODUCTS AND INDICATIONS

BRAND NAME	ROUTE	PID	ITP	CLL	CIDP	KD	MMN
Intravenous							
Asceniv (FDA-approved April 2019)	IV	X					
Bivigam	IV	X					
Carimune NF	IV	X	X				
Flebogamma 5% DIF	IV	X					
Flebogamma 10% DIF	IV	X	X				
Gammagard S/D	IV	X	X	X		X	
Gammaplex	IV	X	X				
Octagam 5%	IV	X					
Octagam 10%	IV		X				
Panzyga	IV	X	X				
Privigen	IV	X	X		X		
Xembify (FDA-approved July 2019)	IV	X					
Intravenous OR Subcutaneous							
*Gammagard Liquid	IV/SC	X					X
*Gammaked	IV/SC	X	X		X		
*Gamunex-C	IV/SC	X	X		X		
Subcutaneous Immune Globulin (SCIg)							
Hizentra	SQ	X			X		
HyQvia	SQ	X					
Cutaquig	SQ	**X**					
Cuvitru	SQ	X					

Abbreviations: Primary immunodeficiency diseases (PID), idiopathic thrombocytopenic purpura (ITP), B-cell chronic lymphocytic leukemia (CLL), chronic inflammatory demyelinating polyneuropathy (CIDP), Kawasaki disease and /or multifocal motor neuropath (MMN)

**Gammaked, Gamunex-C, and Gammagard Liquid are approved for both intravenous and subcutaneous use for treatment of PID. Gammagard Liquid, Gammaked and Gamunex-C, when administered subcutaneously, are FDA-approved for the treatment of PID. All three are available as a 10% solution. NOTE: Gammagard Liquid, Gammaked and Gamunex-C are not approved for subcutaneous use in patients with ITP or CIDP.*

[§]The following products do not contain sucrose: Gammaplex, Bivigam, Octagam 10%, Gamunex-C, Gammagard Liquid, Gammagard S/D, Gammaked, Flebogamma 5% DIF, Flebogamma 10% DIF, Privigen, and Hizentra

- Each product varies with FDA-approved indications.
  - Currently there are six (6) indications that are FDA approved for specific Ig products:
    - Primary Immunodeficiency Diseases (PID) [includes, but are not limited to, the humoral immune defect in common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies]
    - Idiopathic thrombocytopenic purpura (ITP)
    - B-cell chronic lymphocytic leukemia (CLL)
    - Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
    - Kawasaki Disease (KD)
    - Multifocal Motor Neuropath (MMN)
  - **SCIg products are currently only FDA approved for the treatment of PID and CIDP (Hizentra only)**
    - **Hizentra is the first and only SCIg approved for the treatment of CIDP** (March 2018)
  - All conditions are FDA approved for the intravenous route
  - IVIg products will not be approved for subcutaneous use, unless FDA approved for that route of administration.

- All available immune globulin replacement products are FDA-approved for use in primary immunodeficiency (PID).
  - Immune globulin is the standard treatment for PID. PID includes, but are not limited to, the humoral immune defect in common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

- All Ig products (IVIg and SCIg) are FDA approved for the indication of PID. However, only PID is FDA-approved for the subcutaneous route (SC).

Black Box Warnings

Thrombosis *may occur with immune globulin products. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. For patients at risk of thrombosis, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.*

Renal dysfunction and acute renal failure (excluding Cuvitru, Hizentra, HyQvia, and GamaSTAN S/D) *may occur in predisposed patients with immune globulin intravenous IV products. Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65 years, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving immune globulin IV products containing sucrose. (**Note:** The following products do not contain sucrose: Bivigam, Flebogamma DIF, Gammagard Liquid, Gammagard S/D, Gammaked, Gammaplex, Gamunex-C, Octagam 5%, Octagam 10%, Panzyga, and Privigen.) For patients at risk of renal dysfunction or acute renal failure, administer immune globulin IV products at the minimum concentration dose and infusion rate practicable. Ensure adequate hydration in patients before administration.*

CLASSIFICATION: Immunoglobulins

COVERAGE CRITERIA FOR INITIAL AUTHORIZATION

This policy is intended to address coverage criteria that are appropriate for the majority of individuals/members with a particular disease, illness, or condition. Each member's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.

Molina Healthcare encourages the Prescriber to reserve prescribing of subcutaneous and intravenous immune globulin for members with severe immune deficiency and who have low antibody levels or for those whom have other well-established indications for therapy with IVIg as described within this policy.

Subcutaneously administered immunoglobulin (SCIg) as an alternative to intravenous immunoglobulin therapy may be considered for members who meet ALL of the following criteria **[ALL]**

1. **Prescriber specialty [ONE]**

   ❒ Prescribed by, or in consultation with, a board-certified immunologist, an infectious diseases physician who treats patients with primary immune deficiencies, or a physician who has specialized expertise in managing patients on immune globulin therapy (e.g., immunologist, hematologist, neurologist, etc.). Submit consultation notes if applicable.

   NOTE: Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.

   Clinical Rationale: Due to the expertise required for evaluation and diagnosis of patients treated with SCIg, in addition to the monitoring required for adverse events and long-term efficacy, authorization requires SCIg to be prescribed by or in consultation with a physician who specializes in the condition being treated.

2. **Diagnosis/Indication [ALL]**
   Clinically documented diagnosis (*includes chart notes, applicable lab values and/or tests, adverse outcomes, treatment failures, or any other additional clinical information or clinical notes from the member's medical records supporting the diagnosis*) of: [A OR B]

   ❒ A definitive diagnosis of ONE (1) of the following. Documentation required. **[A OR B]**

   A. Primary immunodeficiency (PID)/Wiskott-Aldrich syndrome (list may not be all-inclusive): [ONE]
   - ❍ Autosomal recessive agammaglobinulinemia
   - ❍ Autosomal recessive hyperimmunoglobulin M syndrome (HIM)
   - ❍ Combined immunodeficiency disorders
   - ❍ Ataxia-telangiectasia
   - ❍ DiGeorge syndrome
   - ❍ Nijmegan breakage syndrome
   - ❍ WHIM (warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis) syndrome
   - ❍ Wiskott Aldrich syndrome
   - ❍ Common variable immunodeficiency [CVID; acquired hypogammaglobulinemia; adult onset hypogammaglobulinemia; dysgammaglobulinemia]
   - ❍ Congenital hypogammaglobulinemia late onset, ICOS impaired
   - ❍ Congenital/X-linked agammaglobulinemia (XLA or Bruton's agammaglobulinemia)
   - ❍ Good syndrome (immunodeficiency with thymoma)
   - ❍ Hyperimmunoglobulinemia E syndrome
   - ❍ Hypogammaglobulinemia

- ❍ ICF syndrome
- ❍ Selective IgG subclass deficiencies (persistent absence of IgG1, IgG2, and/or IgG3)
- ❍ Selective IgM deficiency
- ❍ Severe combined immunodeficiency
- ❍ Specific antibody deficiency
- ❍ Transient hypogammaglobulinemia of infancy, short-term treatment of recurrent severe bacterial infections
- ❍ X-linked immunodeficiency with hyperimmunoglobulin M

B. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [Hizentra ONLY]
NOTE: Member must be 18 years or older to meet age criterion for Hizentra

- ❍ Diagnosis of CIDP as per criteria established by American Academy of Neurology (AAN 1991) or European Federation of Neurological Societies and the Peripheral Nerve Society (EFNS/PNS, 2006; updated in 2010)
  AND
- ❍ Prescribed as initial maintenance therapy for prevention of disease relapses after treatment and stabilization with intravenous immunoglobulin (IVIg);
  OR
  For re-initiation of maintenance therapy after experiencing a relapse and requiring re-induction therapy with IVIg
  AND
- ❍ Baseline disease severity utilizing an objective measure/tool. Submit documentation.

❒ **EXCEPTION to criterion [A and B above]**
SCIg may be authorized for members who meet **ALL** of the following criteria (without meeting additional criteria). Prescriber submit required documentation to Pharmacy/Medical Director for review: **[ALL]**

- ❍ Risk factors for volume overload (e.g. congestive heart failure, end stage renal disease and renal dysfunction). Documentation required.
  AND
- ❍ Prescriber/Physician's order of fluid volume restriction. Documentation required.

❒ ALL of the following criteria for treatment with immune globulin: A) Laboratory evidence of immunoglobulin deficiency, B) Inability to mount an adequate immunologic response to inciting antigens, **AND** C) Persistent and severe infections despite treatment with prophylactic antibiotics. Documentation required. **[A, B, AND C]**

A. Laboratory evidence of immunoglobulin deficiency [ONE]
Abnormalities of serum immune globulin concentration as indicated by ONE (1) of the following laboratory evidence of the immunoglobulin deficiency: [ONE]

- ❍ Laboratory evidence such as absence of B lymphocytes that supports evidence of immunoglobulin deficiency
- ❍ Common variable immunodeficiency (CVID): total IgG < 400mg/dL, or at least 2 standard deviations below normal, on at least 2 occasions
- ❍ Congenital agammaglobulinemia (X-linked or autosomal recessive): total IgG less than 200 mg/dL
- ❍ Persistent hypogammaglobulinemia: Total IgG less than 400 mg/dL, or at least two standard deviations below normal, on at least two occasions

NOTE: Immunoglobulin reference ranges vary depending on the age of the patient and the particular assay method utilized. The reference ranges from the respective laboratories should be used, where available. If the laboratory's reference ranges are not submitted with the immunoglobulin level results, the following standard reference ranges may be applied.

B. Inability to mount an adequate immunologic response to inciting antigens as evidenced by ONE (1) of the following examples (list not all inclusive). Documentation required: [ONE]

- ❍ Markedly impaired antibody response to protein (e.g., tetanus, diphtheria) antigen OR antibody testing with a polysaccharide antigen (pneumococcus) can be used instead of a protein if the patient already has antibodies to tetanus and diphtheria. **An abnormal response is defined as less than a four-fold rise in antibody titer*
- ❍ Lack of appropriate rise in antibody titer following provocation with a polysaccharide antigen such as pneumococcal vaccine (abnormal response is defined as less than a four-fold rise in antibody titer)

NOTE: The diagnosis of immunodeficiency and post immunization titers must be taken in context with the clinical presentation of the patient, and may vary dependent on the type of vaccine given and the prior immunization history of the patient. The parameters listed above are examples of criteria for diagnosis of the primary immunodeficiency syndromes and therefore not an all-inclusive list.

C. Clinical history of significant recurrent infections meeting ONE (1) of the following criteria: Documentation required. [AT LEAST ONE]

- ❍ Two or more bacterial infections per year due to persistent and significant reduction in total IgG or IgG subclasses
- ❍ Unexplained recurrent or persistent severe bacterial infections despite antibiotic therapy
- ❍ Infections are responding inadequately to treatment with antibiotics and/or appropriate prophylaxis with antibiotics OR the member has multiple antibiotic hypersensitivities that interfere with treatment
- ❍ History of significant recurrent or persistent, severe bacterial infections (such as recurrent pneumonias, frequent episodes of bacterial infections such as sinusitis, otitis, bronchitis, skin structure infections, or infections of the gastrointestinal tract)
- ❍ For total IgG level is < 200mg/dL or infants with BTK gene or absence of B lymphocytes: Documentation of an infection history not required.

- *Rationale for criteria A, B, and C: Per the American Academy of Allergy, Asthma and Immunology (AAAAI) Position Paper: Use of IVIG January 2005, the decision to treat with Ig should be based on: 1) abnormalities of serum immune globulin concentration, 2) clinical history of infections, and when appropriate and 3) the demonstrated inability to produce antibody normally following antigenic stimulation.*

3. Age/Gender/Other restrictions [ALL APPLICABLE]

❒ Member meets age recommendation of SCIg product requested: [ONE]

- ❍ Hizentra; Cuvitru; Gammagard Liquid 10%; Gammaplex 5% Liquid: 2 years and older
  - *The safety and efficacy were not established in pediatric patients younger than 2 years.*
- ❍ HyQvia and Cutaquig: 18 years and older
  - *Efficacy and safety in pediatric patients using the subcutaneous route of administration have not been established.*

❒ Other disorders that may increase susceptibility to infection such as allergy or anatomic defects, have been sought out and treated aggressively if present

4. Step/Conservative Therapy/Other condition Requirements [ALL]

- ❒ Subcutaneous immunoglobulin required due to inability to continue receiving IVIg, such as but not limited to ONE (1) of the following: [ONE]
  - ❍ Trial, intolerance, or other clinical rationale explaining the inappropriateness to IVIg
    - *There is no medical evidence which demonstrates that SCIg is more effective than IVIg to improve and maintain immune globulin levels. Therefore, unless contraindicated, a trial of IVIG is required before SCIg products will be considered for authorization.*
  - ❍ Poor venous access
    - *SCIg products are often utilized in infants and children because of difficulty of intravenous (IV) access.*
  - ❍ Infusion reactions not controlled by infusion rate adjustments or access site issues that are ongoing and unresolved by traditional means

5. Contraindications*/Exclusions/Discontinuations

Authorization will not be granted if ANY of the following conditions apply [ANY]

- ❒ Non-FDA approved indications
- ❒ Hypersensitivity to immune globulin or any component of the formulation
- ❒ IgA deficiency (with anti-IgA antibodies and history of hypersensitivity [excluding Gammagard S/D])
- ❒ Hyperprolinemia (Hizentra, Privigen)
- ❒ Severe thrombocytopenia or coagulation disorders where IM injections are contraindicated (GamaSTAN S/D)
- ❒ Hypersensitivity to hyaluronidase, human albumin, or any component of the hyaluronidase formulation (HyQvia)

  Note: Documentation of allergenic cross-reactivity for immune globulins is limited. However, because of similarities in chemical structure and/or pharmacologic actions, the possibility of cross-sensitivity cannot be ruled out with certainty.

6. Labs/Reports/Documentation required [ALL]

All documentation for determination of medical necessity must be submitted for review. Prescriber to submit documentation as indicated in the criteria above, including but not limited to chart notes, applicable lab values and/or tests, adverse outcomes, treatment failures, or any other additional clinical information or clinical notes from the member's medical records supporting the diagnosis. Letters of support and/or explanation are often useful, but are not sufficient documentation unless ALL specific information required by this MCP are included.

NOTE: Additional documentation, rationale, and/or supporting evidence may be requested for review as deemed necessary or appropriate by Molina Medical/Pharmacy staff.

REAUTHORIZATION /CONTINUATION OF THERAPY

Subcutaneous Immune Globulin (SCIg) may be authorized for continuation of therapy if meet **ALL** of the following criteria are met: **[ALL]**

1. Initial Coverage Criteria

- ❑ Member currently meets ALL initial coverage criteria
- ❑ Consultation notes must be submitted for initial request and for continuation of treatment requests at least ONCE annually.

2. Compliance: N/A

3. Labs/Reports/Documentation required [ALL APPLICABLE]

- ❒ Sustained clinical benefit of SCIg treatment as evidenced by at least ONE (1) of the following. Documentation required: [AT LEAST ONE]
  - ❍ Objective monitoring of progress using metric assessment such as: Inflammatory Neuropathy Cause and Treatment (INCAT) scale, the Medical Research Council (MRC) scale, and activities of daily living (ADL) measurements
  - ❍ Medical Research Council (MRC) scale, Rankin score, Activities of Daily Living (ADL) scores
  - ❍ Objective findings on physical exam
  - ❍ Lab values showing normalized trough IgG (ideally greater than 600 mg/dL)
    NOTE: Serum immunoglobulin G (IgG) levels can be drawn at any time relative to infusions once steady-state has been reached, which is usually after 6 to 12 weeks of SCIG therapy. The member's clinical condition should be the main determinant of the necessary IgG level, and different patients may require very different IgG levels to remain infection-free.
    - *Rationale: According to a 2010 national guideline from Canada on immune globulin for primary immune deficiency, although higher trough levels of IVIg may be associated with clinical response; the goal of IVIg dose increases should be to improve clinical effectiveness and not merely to increase trough levels.*
  - ❍ Reduction/elimination of persistent bacterial infections
  - ❍ Reduction/elimination of hospitalization related to infectious illness
  - ❍ Stable disease or maintenance of desired clinical outcome documented by chart notes and medical records for member's disease and specific condition

NOTE: Subjective improvement is insufficient to continue immune globulin treatment. If an objective clinical improvement does not occur, continued administration may not be considered medically necessary.

NOTE: Clinical monitoring may take precedence over laboratory monitoring. If clinical improvement is evident, then laboratory monitoring solely to guide immune globulin therapy is not necessary.[D]

- *According to a 2010 national guideline from Canada on immune globulin for primary immune deficiency, although higher trough levels of IVIg may be associated with clinical response; the goal of IVIg dose increases should be to improve clinical effectiveness and not merely to increase trough levels.*

- ❒ Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) [For Hizentra ONLY]

  Member must meet ALL of the following: [ALL]

  - ❍ Sustained clinical benefit to maintenance therapy, without relapses, based on an objective clinical measurements (as indicated in the above criterion)
    OR
    Member experienced a relapse while on Hizentra and re-initiating maintenance therapy

    AND

  - ❍ Improvement and stabilization are observed while on IVIg treatment previously. Documentation required
    - *If CIDP symptoms worsen on the 0.4 g/kg body weight per week dose, consider re- initiating therapy with an IVIg while discontinuing Hizentra. If improvement and stabilization are observed during IVIg treatment, consider reinitiating Hizentra at the dose of 0.4 g/kg body weight per week, administered in 2 sessions per week over 1 or 2 consecutive days, while discontinuing IVIg.*

    AND

  - ❍ Member was NOT receiving maximum dosing of Hizentra prior to relapse
    NOTE: Recommended subcutaneous dose is 0.2 g/kg (1 mL/kg) body weight per week, administered in 1 or 2 sessions over 1 or 2 consecutive days

- ❒ Requested dosing remains within FDA-labeled recommendations for respective indication
  AND
  Minimum effective dose being utilized for maintenance therapy (by decreasing the dose, increasing the frequency of administration, or implementing both strategies

4. Discontinuation of Treatment [ANY]

Discontinue treatment if ANY of the following conditions applies: [ANY]

- ❑ Intolerable adverse effects or drug toxicity
- ❑ Persistent and uncorrectable problems with adherence to treatment
- ❑ Poor response to treatment as evidenced by physical findings and/or clinical symptoms
- ❑ Contraindications/Exclusions to therapy
  - ❍ Non-FDA approved indications
  - ❍ Hypersensitivity to immune globulin or any component of the formulation
  - ❍ IgA deficiency (with anti–IgA antibodies and history of hypersensitivity)
  - ❍ Hyperprolinemia (type I or II); Hizentra contains the stabilizer L-proline

ADMINISTRATION, QUANTITY LIMITATIONS, AND AUTHORIZATION PERIOD

1. Recommended Dosage [ALL]

- ❒ Dosage, frequency, site of administration, and duration of therapy is consistent with FDA-approved labeling in accordance to member's specific condition. SCIg dosage must be individualized and is highly variable depending on the nature and severity of the disease and on the individual patient response. There is no absolute maximum dosage. Refer to FDA-approved labeling for dosage recommendations.

  NOTE: Not all products are interchangeable with regards to route of administration; consult manufacturers' labeling for additional information. Product-specific dosing is provided where applicable; some clinicians use ideal body weight or an adjusted ideal body weight in morbidly-obese patients to calculate an IVIG dose.Ref Dosage expressed as mg/kg or mL/kg and is dependent upon route of administration; use extra precaution to ensure accuracy. [National Health Service. Clinical Guidelines for the Use of Immunoglobulin Use: Second Edition Update, July 2011]

- ❒ **Adjustment(s) of dosage, frequency, site of administration, and duration of therapy** must be reasonable and appropriate based on condition and severity, alternative available treatments, and previous response to intravenous immune globulin therapy.

- ❒ **Conversion from IVIG**: To convert a patient from intravenous immune globulin (IVIg) to SCIg (by pump or rapid-push), the total monthly intravenous (IV) dose given is divided by four and given weekly. This approach will, after several months, result in steady-state immunoglobulin G (IgG) levels equivalent or higher than the levels achieved with an equivalent dose of IVIG. A dose of 100 mg/kg per week may be a good starting dose for most patients (adults and children).

- ❒ **For dosage or duration outside of outside of the FDA-labeled indication:** Prescriber must submit supporting documentation in accordance to Molina Healthcare's recognized pharmacology compendia and criteria for peer-reviewed clinical research for review. Refer to **Off-Label Use of Drugs and Biologic Agents MCP-162.**

2. Authorization Limit [ALL]

- ❒ Quantity limit: [BOTH]
  - ❍ One dose per month
  - ❍ Authorization dosing and quantity in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

- ❒ Duration of initial authorization: **6 months**

- ❒ Continuation of treatment: Re-authorization for continuation of treatment is required every **12 months** to determine continued need based on documented positive clinical response

3. Route of Administration [ALL]

- ❒ SCIg is administered subcutaneously and is considered a **self-administered drug** via a subcutaneous injection via a small, portable pump. Many patients can be readily trained to infuse subcutaneous immune globulin (SCIg) themselves at home, or parents may administer the infusions to their children. This is true in many older adults (>75 years) as well, including those on anticoagulant and/or platelet-inhibitor therapy. Adult patients can self-administer the infusion without the need to train another family member or schedule a home care visit.

- ❒ Per the manufacturer this drug may be administered at the patient's convenience. Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility will not be authorized.

- ❒ If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare. Self-administered medications may not be dispensed for self-administration and billed through the medical benefit by a provider; they must be dispensed through a participating pharmacy.

COVERAGE EXCLUSIONS

All other uses of Subcutaneous Immune Globulin (SCIg) that are not an FDA-approved indication or not included in the 'Coverage Criteria' section of this policy or supported as an accepted off-label use, as defined in the Company medical policy on off-label coverage will not be authorized by this policy. *This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.*

- ⌘ Applications of Subcutaneous Immune Globulin (SCIg) for conditions other than primary immunodeficiencies are considered off-label in the United States and are not addressed in this policy. Refer to the off-label coverage for prescription drugs and biologics policy for complete criteria: **Off-Label Use of Drugs and Biologic Agents MCP-162.**

BACKGROUND/SUMMARY

Primary Humoral Immune Deficiency

Primary humoral immune deficiencies, a group of chronic disorders, are an FDA-approved indication for immune globulin therapy. Immune globulin is the standard treatment for primary immunodeficiency diseases (PI). Primary immunodeficiency diseases includes, but are not limited to, the humoral immune defect in common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

Other FDA-approved indications for immune globulin include idiopathic thrombocytopenic purpura (ITP), B-cell chronic lymphocytic leukemia (CLL), chronic inflammatory demyelinating polyneuropathy (CIDP), and Kawasaki syndrome as outlined above. In addition, in clinical practice, immune globulin is frequently used for treating a variety of off-label conditions in various therapeutic areas such as neurology, hematology, infectious disease, stem cell transplant, dermatology, and rheumatology. However, many of these off-label or proposed uses lack quality evidence of clinical benefit. Given the increasing demand and limited supply of immune globulin, along with the potential risks and relatively high cost of therapy, the indications for use of immune globulin require judicious consideration.

- ⌘ Safety and efficacy of Gammagard Liquid 10% administered subcutaneously for replacement therapy in adults and children with primary immunodeficiency were evaluated in an open-label, prospective multicenter US study in 49 adult and pediatric patients, including those who had been receiving IGIV or another subcutaneous immune globulin preparation. All patients (regardless of their prior regimen) received an initial IV regimen of Gammagard Liquid 10% (IV once every 3 or 4 weeks for 12 weeks) before being switched to subcutaneous Gammagard Liquid 10%. The median duration of subcutaneous Gammagard Liquid 10% therapy was 379 days (range 57-477 days). The annual rate of acute serious bacterial infections while patients were receiving subcutaneous Gammagard® Liquid 10% was 0.067 infections per patient per year and the annual rate of any infection (including viral and fungal infections) was 4.1 infections per patient per year. [Per American Hospital Formulary Service (AHFS). Drug Information 2019. Immune Globulin]

- ⌘ Safety and efficacy of Hizentra 20% immune globulin subcutaneous for replacement therapy in patients with primary immune deficiency were evaluated in an open-label, prospective, multicenter US study that included 49 adult and pediatric patients who were previously receiving a once-monthly regimen of IGIV and were switched to a once-weekly regimen of subcutaneous Hizentra 20% given for 15 months. After a 3-month wash-in/wash-out period, the Hizentra

20% dose was adjusted individually to achieve an IgG area under the concentration-time curve (AUC) that was equivalent to that attained with their previous IVIg therapy and the next 12 months of therapy was considered the efficacy period. In the modified intention-to-treat (MITT) population (38 patients who completed the 3-month wash-in/wash-out period and received at least 1 subcutaneous infusion of Hizentra 20%), there were no serious bacterial infections (defined as bacterial pneumonia, bacteremia/septicemia, osteomyelitis/septic arthritis, bacterial meningitis, and visceral abscess) and the annual rate of any infection was 2.76 infections per patient per year.

- Safety and efficacy of Hizentra 20% immune globulin subcutaneous also has been evaluated in a 40-week prospective, open-label, multicenter, single-arm, phase 3 study, enrolled 51 patients with PI in a multicenter study in Europe. Study participants, 51 adult and pediatric patients with primary immunodeficiency, who were previously receiving once-monthly IVIg (31 patients) or once-weekly immune globulin subcutaneous (20 patients) and were switched to once-weekly Hizentra 20%. Participants were switched from their current IV or SC regimens to weekly SC infusions of Hizentra at equivalent doses. Primary efficacy was measured as IgG levels prior to next infusion. IgG trough levels maintained similar concentrations between both the pre-study and efficacy portion of the study (7.49 [SD, 1.57] and 8.1 [SD, 1.34], respectively). Secondary efficacy was determined by the rate of serious bacterial infections (SBIs). No SBIs were identified during the efficacy period. For non-SBI infections, participants experienced a rate of 5.18 infections/patient/year (95% confidence interval [CI], 4.305 to 6.171). No serious adverse events were reported. Given the study design, extrapolation cannot be done to determine superiority. (AHFS 2019)

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

CIDP is an acquired immune-mediated disease that evolves in a progressive or relapsing pattern over months to years. Although "typical" CIDP is characterized by symmetric proximal and distal motor and sensory deficits, it is now recognized that multifocal (asymmetric), distally predominant, pure sensory, and pure motor variants also fall within the CIDP spectrum. First-line treatment options for CIDP include corticosteroids, IVIg, and plasmapheresis (plasma exchange). For patients refractory to first-line options or those chronically dependent on high-dose first-line therapy, no evidence-based treatment recommendations exist. (Gorson KC, 2012) (Allen, JA et al. 2017)

- Subcutaneous immunoglobulin for maintenance treatment in CIDP (PATH): a randomized, double-blind, placebo-controlled, phase 3 trial (van Schaik et al. 2018)

  The 172-patient trial tested a high and low dose of SCIg over the course of 25 weeks to determine their effect on the primary outcome of CIDP relapse or withdrawal from treatment for any reason. In this evaluation of using SCIg for maintenance of response, relapses or treatment withdrawal occurred in 63% with placebo, 39% with low dose SCIg (0.2 g/kg weekly), and 33% with high dose (0.4 g/kg weekly).

  Patients were randomized in a 1:1:1 ratio to a placebo group (n=57 [33%]), a low-dose group (n=57 [33%]), and a high-dose group (n=57 [33%]). The trial found that both SCIg doses were effective and well-tolerated, suggesting that can be used as maintenance treatment for CIDP. Seventy-seven patients withdrew from the trial due to relapse- or other reasons: 36 (63%; 95% CI, 50% to 74%) placebo patients, 22 (39%; 95% CI, 27% to 52) low-dose SCIg patients, and 19 (33%; 95% CI, [22% to 46) high-dose patients ($p<0.001$).

  This study, at the time it was conducted, was the largest trial of CIDP to date and the first to study two administrations of immunoglobulins and two doses, showed that both doses of 20% SCIg solution were efficacious and well-tolerated, suggesting that SCIg can be used as a maintenance treatment for CIDP.

  Conclusion: The use of SCIg for the maintenance of CIPD might be effective, with relatively low adverse events, however the trial was limited by a high withdrawal (45% subjects withdrew from the trial) missing patient data and inadequate follow-up of those who withdrew. The evidence is insufficient to determine the effects of the technology on health outcomes.

- One crossover RCT comparing IVIg and SCIg for CIDP was identified (Markvardsen et al. 2017). 20 patients underwent 10 weeks of treatment with SCIg and IVIg, in random order, for a total intervention duration of 20 weeks. The primary efficacy outcome was change in isokinetic muscle strength. Fourteen (20%) of 20 patients completed the trial. Isokinetic muscle strength increased by 7.4% with SCIG and 14% with IVIg; the difference between groups was not statistically significant. Conclusions about the relative efficacy of SCIg and IVIg cannot be drawn from this trial due to the small sample size, high dropout rate, short-term follow-up, and the crossover design without a washout period.

Clinical Practice Guidelines

- The Immune Deficiency Foundation (IDF) Guidelines

  In 2011, the Immune Deficiency Foundation (IDF) published guidelines on diagnosis and clinical care for primary immunodeficiency diseases. The guidelines support clinicians determine the possible type of PI and the screening diagnostic tests that should be ordered based on the site of infection. Although there are several different types of PI, the types that result in antibody production defects are those that are eligible for IgG therapy.
  - The IDF recommends regular IgG therapy for patients with identified antibody deficiency disorders.
  - The guidelines state the IVIG product should be dosed every 2-4 weeks and SCIG should be given every 1-14 days.
  - **It is recommended that an immunologist should participate in the determination of the proper dose and interval for IgG therapy in each patient.**
  - **Should IgG treatment be required IV or SC administration are both recommended, and one product is not preferentially recommended over any other product.**

- Canadian Blood Services and Canada's National Advisory Committee Guidelines

  The Canadian Blood Services and Canada's National Advisory Committee on Blood and Blood Products led a joint initiative to create guidelines for treatment of PI with immunoglobulin therapy. While the guidelines are primarily intended for health care professionals in Canada, many of their recommendations may be applied in other parts of the world, including the United States.

  The National Advisory Committee on Blood and Blood Products and Canadian Blood Services issued practice guidelines on the use of IVIg in primary immune deficiency in 2010 (Shehata N, et al.) The recommendations were based on interpretation of available evidence and where evidence was lacking, consensus of expert clinical opinion. The guidelines were constructed from an expert panel consisting of physicians from large pediatric and adult tertiary care centers who frequently cared for patients with primary immune deficiency, methodology experts, and members from the National Advisory Committee on Blood and Blood Products. The levels of evidence and grades used for each recommendation were adapted from the Canadian Task Force on Preventative Health Care. The levels of evidence describe the methodological rigor of the study, and the grades of recommendation comprise the level of evidence and clinical expertise. Relevant recommendations include the following:
  - Give immunoglobulin to patients with primary antibody deficiency to reduce infections. (Level of evidence: I, Grade of recommendation: A)
  - Give immunoglobulin to reduce hospitalization and organ damage. (I, A)
  - Give immunoglobulin to improve survival and quality of life. (III, A)
  - **With respect to clinical efficacy and adverse events, there is insufficient evidence to recommend one manufacturer of IG over another for currently available products. (I to II-2, I)**
  - **With respect to clinical efficacy for reducing infections, IVIg and SCIg preparations should be considered equivalent. (I and II, B)**
  - Do not give IMIG for replacement therapy for primary immune deficiency. (I, D)
  - Start IVIG at a dose of 400 to 600 mg/kg per 4 weeks or SCIg at a dose of 100 to 150 mg/kg per week in most patients. (III, B)
  - Patient and practitioners should be aware that patients with primary immune deficiency may require immunoglobulin replacement therapy indefinitely. (II-3, A)

Other recommendations in the 2010 guideline in regards to IVIg treatment of primary immune deficiencies include:

- If there is end-organ damage, the dose and/or frequency of immune globulin can be increased.
- Patients with primary immune deficiency may require immune globulin therapy indefinitely.
- Although higher trough levels of IVIg may be associated with clinical response; the goal of IVIg dose increases should be to improve clinical effectiveness and not merely to increase trough levels.

- American Academy of Asthma, Allergy and Immunology
  - A position statement from the American Academy of Asthma, Allergy and Immunology (Orange, et al., 2005) states: the decision to administer IVIg to patients with primary deficiencies in antibody production should be based on: 1) abnormalities of serum immunoglobulin concentrations; 2) clinical history of infections; and, when appropriate, 3) the demonstrated inability to produce antibody normally following antigenic stimulation.
  - Guidelines from the American Academy of Asthma, Allergy & Immunology (Orange, et al., 2006) state; "Reduced levels of serum immunoglobulin in patients with recurrent bacterial infections coupled with a lack of response to protein or polysaccharide vaccine challenges (i.e., patients who cannot make IgG antibody against diphtheria and tetanus toxoids, pneumococcal polysaccharide vaccine, or both) is a clear indication for IgG replacement.

DEFINITIONS

Antibody: Specialized gamma globulin proteins found in the blood or lymph that act as an immune defense against foreign agents (antigens).

Antigen: A substance, that when introduced into the body stimulates the production of an antibody. Antigens include toxins, bacteria, foreign blood cells, and the cells of transplanted organs.

Immune globulin: Replacement therapy for primary immunodeficiency; IgG antibodies against bacterial and viral agents; spectrum of antibodies that interact with and alter the activity immune system cells; antibodies capable of reacting with cells such as erythrocytes.

Intravenous infusion immune globulin (IVIg) is an antibody-containing solution obtained from the pooled plasma of healthy blood donors that contains antibodies to greater than 10 million antigens. IVIg has been used to correct immune deficiencies in patients with either inherited or acquired immunodeficiencies and has also been investigated as an immunomodulator in diseases thought to have an autoimmune basis. Several IVIg products are available for clinical use in the United States.

APPENDIX

Appendix 1: Comparison of IV and Subcutaneous Immunoglobulin Therapy

Comparison of IV and Subcutaneous Immunoglobulin Therapy

Therapy Comparison	IV	Subcutaneous
Administration and frequency	▪ Administered every 3-4 weeks ▪ Faster increase of trough level at initiation ▪ Requires venous access	▪ Administered weekly or biweekly ▪ Self-administered ▪ Portable (suitable for patients who travel ▪ Advantageous for venous access
Duration of infusion	2-4 hours	▪ 60-90 minutes with conventional infusions ▪ 5-20 minutes with push method
Adverse events	▪ Systemic reactions are possible, especially on first infusion ▪ Usually no local reactions (such as redness and swelling)	▪ Rare systemic reactions ▪ Local reactions may include redness and itching, but these diminish after repeated infusions ▪ May be better for patients with renal or cardiac insufficiency
Monitoring requirements	Close monitoring required	Less monitoring required
Other considerations	High dose therapy possible	More stable Ig levels

Abbreviation: Ig, immunoglobulin

Reference: Albin S, Cunningham-Rundles C. An update on the use of immunoglobulin for the treatment of immunodeficiency disorders. Immunotherapy. 2014;6(10):1113-26

Appendix 2: **Validated scales suitable for use in CIDP (list may not be all-inclusive)**

Scale	Number of Items	Scoring Range	Estimated Time to Complete	Key Measures	Patient vs. Physician-Reported
INCAT	10	0 to 10	3–5 min	Arm and leg disabilities scores, overall score is sum of the two	Patient
ODSS	10	0 to 5 (upper limb) and 0 to 7 (lower limb)	3 min	Arm and leg disabilities scores, overall score is sum of the two	Patient
ONLS	13	0 to 5 (upper limb) and 0 to 7 (lower limb)	3 min	Same as ODSS, but question "Does the patient have difficulty walking?" has been changed to "Does the patient have difficulty running or climbing stairs?"	Patient
RODS	24	Raw RODS score (0–48) transformed to final score 0–100	3–5 min	Upper and lower limb disability, questions range from ability to "read a book," "eat," or "brush teeth" to "dance", "stand for hours," and "run." Participants are asked to indicate if they can easily perform the task, perform it with difficulty, or are unable to perform the task at all	Patient
GAITrite®	NA	Percentage scores recorded	*	Gait parameters: Velocity, cadence, swing phase, double support time, stance phase	Physician
TUG	NA	Timed activity test	2–3 min	Time taken to stand up from a chair, walk a short distance, turn around, return, and sit down again	Physician
10-meter walk test	NA	Timed activity test	*	Time taken to walk 10 meters	Physician
Grip strength	NA	Instrument-based scale	3–5 min	Grip strength	Physician
FSS	9	9–63	3–5 min	Questions relating to fatigue severity and the impact of fatigue on activities and lifestyle	Patient
Rasch-based FSS	7		2–3 min	As in FSS but with 4 response categories	Patient
SF-36	36	8 scaled scores, each directly transformed into a 0–100 scale	*	Physical functioning (10 items), role functioning— physical (4), role functioning— emotional (3), social functioning (2), body pain (2), mental health (5), vitality (4), general health perception (5), and change in health	Patient
CAP-PRI	15	Single score comprising 4 life domains	5–10 min	Physical function, social function, pain, emotional well-being	Patient

**No estimated time given although most assessments will be finished in approximately 5 minutes. The exact time taken to perform tests depends on the severity of a patient and the experience of the practitioner collecting the measure. CAP-PRI: Chronic Acquired Polyneuropathy Patient-reported Index; CIDP = chronic inflammatory demyelinating polyneuropathy; FSS: Fatigue Severity Scale; ICE: Immune Globulin Intravenous CIDP Efficacy; INCAT = Inflammatory Neuropathy Cause and Treatment; MMN: multifocal motor neuropathy; ODSS: INCAT overall disability sum score; ONLS: Overall Neuropathy Limitations Scale; RODS: Rasch-built Overall Disability Scale; TUG: Timed Up and Go; SF-36: Short Form–36.*

Table above adapted from Allen, JA et al. Optimizing the Use of Outcome Measures in Chronic Inflammatory Demyelinating Polyneuropathy. US Neurology, 2017;13(1):26–34. DOI: https://doi.org/10.17925/USN.2017.13.01.26

CODING INFORMATION: THE CODES LISTED IN THIS CLINICAL POLICY ARE FOR INFORMATIONAL PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS A COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE AND INCLUSION OR EXCLUSION OF ANY CODES DOES NOT GUARANTEE COVERAGE. PROVIDERS SHOULD REFERENCE THE MOST UP-TO-DATE SOURCES OF PROFESSIONAL CODING GUIDANCE PRIOR TO THE SUBMISSION OF CLAIMS FOR REIMBURSEMENT OF COVERED SERVICES.

CPT	Description

HCPCS	Description
J1559	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin, (Gamunex/Gamunex-C/Gammaked), nonlyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), nonlyophilized, (e.g., liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase, (hyqvia), 100 mg immunoglobulin
J1555	Injection, Immune Globulin (Cuvitru), 100mg
J3490/ J3590	Injection, immune globulin (Cutaquig), human, for SC use

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Policy History	MCPC
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Policy Revised Peer Review: AMR Peer Review Network. 7/31/2019. Practicing Physician. Board certified Neurology All content, clinical evidence, coverage criteria, practice guidelines, appendices and reference sections were reviewed and revised with the most recent medical literature and available evidence. Coverage criteria for Initial and Continuation of Therapy were revised/updated as appropriate. Notable revisions: Added initial/continuation criteria for 'Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)' and relevant clinical evidence for CIDP in background/summary section of policy. Updated policy to included available products since last revision (Cuvitru; Cutaquig). Updated tables and content in 'Appendix.'	7/_/2019

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