Subject: Intravenous Immune Globulin (IVIg) Therapy	**Original Effective Date:** 12/6/2007
Policy Number: MCP-043	**Revision Date(s):** 4/27/2011; 10/22/2013; 3/7/2016; Q3 2019; Q4 2020
Review Date(s): 4/27/2011; 1/22/2013; 12/16/2015; 3/30/2016; 9/19/2017; 7/10/2018; Q3 2020, 1/19/21	
MCPC Approval Date: 7/10/2018	
P&T Approval Date: Q3 2019	

Contents

Disclaimer 1
Summary of Evidence/Position 1
FDA Indications 4
Coverage Criteria for Initial Authorization 7
Coverage Exclusions 41
Background/Summary 42
Definitions 44
Appendix 45
References 48

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 **immune globulin products FDA-approved for intravenous infusion (IVIg)** when appropriate criteria are met.

Abbreviations:

- *Immune globulin, intravenous (human):* 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:* Abbreviated as subcutaneous immune globulin (SCIg)

- This policy only addresses non-specified pooled preparations of intravenous immune globulin. References to immune globulin within this guideline refer to immune globulin refer to IgG. IgG products have been referred to in multiple ways, some of which are: immune globulin (IG), immunoglobulin, gamma globulin, and also by its route of administration - intravenous immune globulin (IVIg), immune globulin intravenous (IGIV), subcutaneous immune globulin (SCIg), immune globulin subcutaneous (IgSC).

- Applications of this product for conditions other than those addressed in this policy are considered **OFF-LABEL** and are not addressed in this policy.

- **This policy DOES NOT address other immunoglobulin preparations that at are specifically used for passive immunization to prevent or attenuate infection with specific viral diseases such as respiratory syncytial virus, cytomegalovirus, or hepatitis B.**

- Refer to **MCP-237 for Intravenous Immune Globulin (IVIg) for Solid Organ Transplantation** requests.

IMMUNE GLOBULIN

Immune globulins are components of the immune system. There are several types of immune globulin produced by the body (e.g., IgA, IgD, IgE, IgG, IgM). Immune globulins are used as replacement therapy to promote passive immunity in patients with primary humoral immunodeficiency diseases. Human immune globulin therapy provides a broad spectrum of opsonizing and neutralizing immunoglobulin G (IgG) antibodies against a wide variety of bacterial and viral antigens. Three formulations of human IgG are available depending on the route of delivery:

- **Intravenous immunoglobulin (IVIg)**
  - Produced by extraction of Ig fractions from blood from at least 1,000 donors; a single infusion of IVIG can be produced from the plasma of 2000 to 60,000 healthy individuals.
  - Affects humoral and cell-based immunity through multiple pathways, without a single dominant mechanism
  - Suppresses antibody production, has anti-idiotype activity, interferes with co-stimulatory molecules including cytokines and chemokines, and inhibits activation of complement and formation of the membrane attack complex
  - Modulates the expression and function of Fc receptors on macrophages and alters the activation, differentiation, and effector functions of T-cells.

- **Subcutaneous infusion (SCIg): Refer to MCP-268 for requests which address the coverage of immune globulin products FDA-approved for subcutaneous infusion for the treatment of primary immune deficiency.**
  SCIg is used for treating patients with primary immunodeficiencies, a genetic basis for more than 80 different types of primary immunodeficiencies has been discovered, the most common being primary antibody deficiency that is associated with low levels or total lack of normal circulating immunoglobulins. With SCIg, it is possible for patients to self-administer the therapy.

- **Intramuscular (IMIg) depot injections** has been largely abandoned in the United States because volume constraints and pain preclude delivery of sufficient products weekly into each buttock to yield therapeutic serum levels of IgG, leaving recipients susceptible to infections. Thus, this policy focuses on intravenous immune globulin for conditions that typically would be treated in an outpatient setting.

- There is robust evidence to support the use of intravenous immunoglobulin G (IVIg) for primary immunodeficiency. This route of administration allows a large volume per infusion, and is administered relatively infrequently (every three to four weeks), however it must be administered by a trained professional, venous access is required, and it is associated with greater fluctuations in IgG levels, potentially resulting in a greater incidence of adverse effects.

- **Currently, there is no evidence of efficacy differences among the different IVIg products.** However, there are potential differences in adverse effects among the different products. Patients with renal dysfunction, diabetes, sepsis, or age >65 years are at increased risk of developing kidney problems if a sucrose-containing product is used. In general, products with higher IgA content are associated with increased adverse effects. There is a higher chance of adverse effects if the IVIg product is switched after establishing therapy with a particular product.

  Immune globulin preparations are available as pre-mixed liquids or lyophilized powders with varying concentrations of IgG. The manufacture of commercial immune globulin products from pooled plasma is a complex multistep process consisting of fractionation, purification, stabilization, virus inactivation, and virus removal and as a result, immune globulin products differ with respect to formulation and composition. Product characteristics such as content (e.g., IgA concentration, stabilizer), volume, and osmolarity may be important considerations for some patients. However, **comparative data are lacking, and it is not known whether one specific product is superior for a particular disease or clinical setting. There is a lack of reliable evidence that any one brand of parenteral immunoglobulin is superior to other brands for medically necessary indications.**

- **For applicable conditions that require use of IVIg due to a rapidly progressive disease:** IVIg should be given along with conventional treatment(s) and used only until conventional therapy could take effect when a patient has a rapidly progressive disease where a clinical response cannot be affected quickly enough using conventional agents. The continued administration of immune globulin is not considered medically necessary once conventional therapy takes effect.

- Immune globulin therapy is derived from the pooled plasma of thousands of donors and contains primarily (>98 %) human immunoglobulin G (IgG) with trace amounts of IgA and IgM. The products differ by route of administration [intravenous (IV) or subcutaneous (SC)], specific titers of each IgG subclass, viral inactivation processes, and additives such as sucrose and sodium. While all immune globulins have comparable efficacy in the treatment of immune deficiencies, the products are not interchangeable. **Selection of product should take into consideration various patient factors including diagnosis, condition and severity, individual comorbidities, available alternative treatments, and previous response to intravenous 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.

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 (5% or 10% when reconstituted)	IV	X	X	X		X	
Gammaplex 5% or 10%	IV	X	X				
Octagam 5%	IV	X					
Octagam 10%	IV		X				
Panzyga 10%	IV	X	X				
Privigen 10%	IV	X	X		X		
Intravenous OR Subcutaneous							
*Gammagard Liquid 10%	IV/SC	X					X
*Gammaked 10%	IV/SC	X	X		X		
*Gamunex-C 10%	IV/SC	X	X		X		
Subcutaneous Immune Globulin (SCIg)							
Hizentra 20%	SQ	X			X		
HyQvia 10%	SQ	X					
Cutaquig 16.5%	SQ	X					
Cuvitru 20%	SQ	X					
Xembify 20%	SQ	X					

PI: Primary Immunodeficiency; ITP: Immune Thrombocytopenia; CIDP: Chronic Inflammatory Demyelinating Polyneuropathy; CLL: Chronic Lymphocytic Leukemia; KD: Kawasaki Disease; MMN: Multifocal Motor Neuropathy

*Gammaked, Gamunex-C, and Gammagard Liquid are approved for both intravenous and subcutaneous use for treatment of PID and when administered subcutaneously, are FDA-approved for the treatment of PID only. NOTE: Gammagard Liquid, Gammaked and Gamunex-C are not approved for SQ 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

Dosage Forms Considerations

- Carimune NF may contain a significant amount of sodium and also contains sucrose.
- Cutaquig and Octagam contains maltose.
- Gammagard S/D may contain a significant amount of sodium and also contains glucose.
- Hyqvia Kit is supplied with a Hyaluronidase (Human Recombinant) component intended for injection prior to Immune Globulin administration to improve dispersion and absorption of the Immune Globulin.

⌘ 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.

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.*

Drug shortages In August 2019, FDA released a statement addressing the issues of product shortages along with a list of the products with limited availability. IG products with a supply that is not able to keep pace as the reason for the shortages. Its recommendations for healthcare providers are to develop a system to determine which patients should receive priority treatment and to consider adding additional products to their formularies to use during times of shortages.

One or more forms of this drug may be in short supply or unavailable. Refer to the following for additional information: ASHP FDA

**Links will be updated with policy with annual review or revision.*

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 IVIg 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.

GENERAL CRITERIA: INITIAL AND REAUTHORIZATION [A AND B]

Intravenous infusion Immune Globulin (IVIg) may be authorized for members who meet **General Requirements [A OR B] AND Condition-Specific Requirements (below 'General Criteria' section)** for member's respective condition:

If coverage criteria are met, authorization may be granted for up to a period of **6 months** *unless a specific authorization period is designated in the condition-based criteria*. Continuation of treatment requires submission of a request with required documentation confirming that current coverage criteria are met and continued IVIg therapy is required and demonstrated clinical benefit.

A. INITIAL THERAPY [ALL]

ALL the following criteria and documentation must be submitted for review: [ALL]

- ❒ Diagnosis: Confirmed by clinical documentation including positive findings on diagnostic testing and/or biopsy results **AND** as specified in the 'Condition-Specific' criteria (as applicable)
  AND
- ❒ Prescribed by, or in consultation with, a board-certified specialist, or physician experienced in the treatment of in the management of the condition being treated. Submit consultation notes if applicable. Specific specialist(s) listed may be listed in the 'Condition-Specific Criteria.' Other Prescribers may be considered on a case-by-case basis by Medical Director.
  AND
- ❒ Documentation Required [ALL APPLICABLE]
  - ❍ History and physical examination documenting the severity of the condition, including frequency and severity of infections where applicable
  - ❍ Laboratory results or diagnostic evidence supporting the indication for which immune globulin is requested [e.g. electromyography (EMG), spinal fluid tests, serum tests and biopsy findings]
  - ❍ Previous treatment failures. EXCEPTION: Primary immunodeficiencies diagnosed at birth do not require documentation of previous treatment failures
  - ❍ Clinical/laboratory monitoring AND any metric assessment utilized for **objective** monitoring of progress, such as (list not all inclusive): Medical Research Council (MRC), INCAT Disability scale, and activities of daily living (ADL) measurements.
    NOTE: Changes in these measures must be clearly documented. Subjective or 'observed' improvement alone is generally insufficient to continue IVIG or to expect coverage.

❒ Contraindications/Exclusions to IVIg therapy
Authorization will not be granted if ANY of the following conditions apply [ANY]
- ❍ IgA deficiency with antibodies to IgA and a history of hypersensitivity
- ❍ History of anaphylaxis or severe systemic reaction to human immune globulin or product components
- ❍ Octagam: Contraindicated in patients with acute hypersensitivity reaction to corn.
- ❍ Privigen: Contraindicated in patients with hyperprolinemia (product contains the stabilizer L-proline)

❒ Administration, Quantity Limit, Authorization Period [ALL]
- ❍ Quantity limit: In accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines AND as indicated in 'Condition-Specific' criteria if applicable
  **Refer to Appendix 2 for information on adjusted body weight dosing*
- ❍ **For dosage/frequency/duration requests that exceed FDA-labeled indication:** Prescriber must submit supporting documentation in accordance to **'Off-Label Use of Drugs and Biologic Agents MCP-162'**
- ❍ Duration of authorization: Every six (6) month review to assess clinical benefit, unless otherwise stated in 'Condition-Specific Criteria' and may be required on a more frequent basis
- ❍ Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11
- ❍ 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.

❒ Continuation of Treatment [ALL]
- ❍ Re-authorization for continuation of treatment is required to determine continued need based on documented positive clinical response. Every six (6) month review to assess clinical benefit, unless otherwise stated in 'Condition-Specific Criteria' and may be required on a more frequent basis
- ❍ Member is closely followed by the prescribing specialist, and treatment response has clearly defined endpoints to measure effectiveness.

❒ **EXCEPTION Criteria for NON-PREFERRED IVIg Products**
If ALL coverage criteria are met, at the discretion of Molina Healthcare, the preferred IVIg product with FDA-labeled indication for member's condition (as applicable) may be authorized. All other IVIg products are not covered unless member meets ANY of the following exception criterion.
Prescriber submit all applicable documentation: [ALL APPLICABLE]
- ❍ IgA deficient member who requires products that are low in IgA content [e.g. Flebogamma or Gammagard S/D (refer to **'Appendix 1' for IgA content FDA-approved IVIg products**)]
- ❍ Objective clinical intolerance to Molina's exclusive IVIg product following 1-2 infusions
- ❍ Failure on an IVIg product previously and currently stable on an existing product
- ❍ Risk factors for volume overload (e.g. congestive heart failure, end stage renal disease and renal dysfunction) and physician's order of fluid volume restriction
- ❍ For emergent administration, e.g. platelets < 30K with bleeding. Authorization for ONE (1) time administration with documentation.

B. REAUTHORIZATIONS/CONTINUATION OF THERAPY REQUESTS [ALL]

Ongoing treatment with immunoglobulin is authorized when ALL the following criteria are met: [ALL]

- ❒ Requested IVIg treatment has not exceeded any applicable 'Condition-Specific Criteria' treatment duration
  AND
- ❒ Chronic medical condition requires maintenance therapy **AND** condition has not been resolved with IVIg
  AND
- ❒ Positive clinical response or sustained clinical benefit to IVIg therapy, including significant improvement in defined clinical endpoints. Continuation of treatment will <u>not</u> be authorized if no positive clinical response.
  AND
- ❒ After 12 months of therapy (on an annual basis): Cessation of IVIg therapy has been attempted or considered **<u>AND</u>** Prescriber/specialist submits the following documentation: [ALL]
  - ❍ Annual review summary with clinical and/or immunological evaluation
    AND
  - ❍ A trial period of cessation of IVIg for the purpose of immunological evaluation has been attempted and has caused (or likely cause) condition to worsen, OR is medically contraindicated. Provide clinical rationale and supporting information for review

- ❒ <u>Administration, Quantity Limit, Authorization Period</u> [ALL]
  - ❍ Prescribed consistent with dose listed in manufacturer package labeling or established clinical literature for the prescribed indication as in the **'Off-Label Use of Drugs and Biologic Agents MCP-162'**
  - ❍ Dose and frequency of immunoglobulin treatment have been titrated to the <u>minimum</u> dose required to achieve/maintain the appropriate clinical outcome. Documentation required.*
    **An attempt should be made to decrease or wean the dosage when clinical improvement has occurred, as appropriate with individual diagnosis and clinical condition. If improvement is sustained with dosage reduction, there should be an attempt to stop administration of IVIg when clinically appropriate.*
  - ❍ Duration of Approval: Up to 6 months, unless otherwise stated in the 'Condition-Specific Criteria'
  - ❍ Refer to MHI Policy & Procedure (P&P): Specialty Medication Administration Site of Care Policy: MHI Pharm 11
  - ❍ 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

CONDITION-SPECIFIC CRITERIA

Intravenous infusion Immune Globulin (IVIg) may be authorized for members who meet the **General Requirements AND Condition-Specific Requirements** for the member's respective condition: [ALL APPLICABLE]

1. Autoimmune Hemolytic Anemia (AIHA)

AIHA is a relatively uncommon disorder caused by antibodies directed against autologous red blood cells. AIHA is classified as warm, cold (which includes cold hemagglutinin disease (CAD) and paroxysmal cold hemoglobinuria) or mixed, according to the thermal range of the autoantibody. AIHA due to the presence of warm agglutinins is almost always due to the presence of IgG antibodies that react with protein antigens on the RBC surface at body temperature.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ***warm-type*** autoimmune hemolytic anemia confirmed by detection of antibody and/or complement components on the surface of the RBC [usually by the direct antiglobulin (Coombs) test[2]]
  AND
- ❒ Refractory to, is intolerant of, or contraindicated to available alternative treatments: [ALL APPLICABLE]
  - ❍ Corticosteroid therapy
    AND
  - ❍ Rituximab

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Use the lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 1,000 mg/kg per day for 5 days
- ❒ Frequency/Quantity Limit: One course per month
- ❒ Duration of Authorization: May authorize up to 6 months (initial therapy and reauthorization)
- ❒ Reauthorization: Documented initial response and recurrence of clinically significant, symptomatic anemia

2. Autoimmune Mucocutaneous Blistering Diseases (AMBDs)

AMBDs are a group of rare, debilitating and possibly fatal disorders caused by antibodies directed against components of the skin. The diseases are characterized by the formation of extensive blisters evolving to painful erosions on the skin and mucous membranes.

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a dermatologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ONE (1) of the following AMBDs: [ONE]
  - ❍ Bullous pemphigoid; OR
  - ❍ Epidermolysis Bullosa Acquisita (EBA); OR
  - ❍ Mucous membrane pemphigoid (also referred to as Cicatrical Pemphigoid); OR
  - ❍ Pemphigus Foliaceus; OR
  - ❍ Pemphigus Vulgaris

  AND
- ❒ Diagnosis confirmed by biopsy
  AND
- ❒ Prescribed for use only for short-term therapy (not as long-term, maintenance therapy)
  AND
- ❒ Member meets ONE (1) of the following criteria: [ONE: A, B, C, OR D]
  - A. Failure of conventional therapy [defined as *failure of disease control after an adequate trial of systemic*] **corticosteroids** (i.e. prednisone, prednisolone, methylprednisolone) AND **immunosuppressive agents** (e.g., azathioprine, cyclophosphamide, methotrexate, or mycophenolate mofetil)
    OR
  - B. Significant adverse effects of conventional/standard treatment (i.e. diabetes or steroid-induced osteoporosis) are potentially life-threatening, cause significant morbidity or inability to cope with activities of daily living, or require the intervention of a physician or drug therapy
    OR
  - C. Contraindication(s) to corticosteroid and immunosuppressive agents. Documentation required: [1 OR 2]
    1) Systemic corticosteroids: existing diabetes, clinically significant osteoporosis, fractures, upper GI bleeding, posterior subcapsular cataracts, pseudotumor cerebri, bone marrow suppression, aplastic anemia, clinically significant psychological changes, steroid myopathy, glaucoma
       OR
    2) Immunosuppressive agents: significant persistent anemia, clinically significant neutropenia, clinically significant abnormal hepatic function, clinically significant impaired renal function, hemorraghic cystitis, clinically significant bone marrow suppression, history of malignancy

    OR

D. Systemic corticosteroid and immunosuppressive agents are inappropriate due to rapid, debilitating or progressive severity of disease.
NOTE: IVIg should be given with conventional treatment(s) and used only until conventional therapy could take effect when a patient has a rapidly progressive disease where a clinical response cannot be affected quickly enough using conventional agents. The continued administration of immune globulin is not considered medically necessary once conventional therapy takes effect.

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. *Use the lowest dose possible that achieves the appropriate clinical outcome.*

- ❒ Recommended Dose: Up to 2 g/kg in divided doses administered over 2-5 days
- ❒ Frequency/Quantity Limit: One course per month. Dose not to exceed 2 g/kg per course of therapy
- ❒ Duration of Authorization: May authorize up to 3 months
- ❒ Reauthorization: IVIg for the treatment of AMBD may be authorized for **short-term therapy** and not as maintenance therapy *(regular use of repeated courses of IVIg for a continuous cycle of exacerbation and remission constitutes maintenance therapy)*

3. B-Cell Chronic Lymphocytic Leukemia (CLL)

CLL is a blood and marrow disorder characterized by increased numbers of CD5-positive B cells. The underlying cause of CLL is unknown, although it is thought to be genetically linked.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, an oncologist, hematologist, or infectious diseases physician. Submit consultation notes if applicable.
  AND
- ❒ Hypogammaglobulinemia defined as an immunoglobulin G (IgG) level of less than 500 mg/dL (5.0 g/L)
  AND
- ❒ Recurrent bacterial infections associated with B-cell CLL: One severe bacterial infection within preceding 6 months **OR** TWO (2) or more bacterial infections in a 1-year period

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Use the lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 100 to 600 mg/kg IV monthly
- ❒ Frequency/Quantity Limit: One dose per month. Dose does not exceed 600 mg/kg every 3 to 4 weeks
- ❒ Duration of Authorization: May authorize up to 6 months (initial therapy and reauthorization)
- ❒ Reauthorization: Positive clinical response to therapy as demonstrated by a reduction in the frequency of bacterial infections since the initiation of IVIg therapy
- ❒ After each 12 months of therapy (on an annual basis): Cessation of IVIg therapy considered and extended as required to enable cessation of therapy **AND** written confirmation from Prescriber/specialist of the following: [ALL]
  - ❍ An annual review with clinical and/or immunological evaluation
  - ❍ Demonstrated clinical benefit, including evidence that treatment has been effective in reducing the number or severity of clinical infections
  - ❍ A trial period of cessation of IVIg for the purpose of immunological evaluation is medically contraindicated or may cause member's condition to worsen

4. Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy

CIDP is a neurological disorder characterized by progressive weakness and impaired sensory function in the legs and arms. The disorder, which is sometimes called chronic relapsing polyneuropathy, is caused by damage to the myelin sheath (the fatty covering that wraps around and protects nerve fibers) of the peripheral nerves. There is evidence of autoimmune dysfunction in CIDP, although the exact cause of the myelin sheath damage is unknown.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a neurologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of CIDP
  AND
- ❒ Symmetric or focal neurologic deficits with slowly progressive or relapsing course over 8 weeks (2 months) or longer (with neurophysiological abnormalities)
  AND
- ❒ ONE (1) of the following clinical/electro-diagnostic criteria are met: [ONE]
  - ❍ Electrodiagnostic evidence of demyelinating neuropathy in at least two limbs, resulting in muscle weakness or sensory dysfunction confirmed by nerve conduction studies (NCS); OR
  - ❍ Results of diagnostic testing meet a recognized set of diagnostic criteria as established by the American Academy of Neurology (AAN), Inflammatory Neuropathy Cause and Treatment (INCAT), or EFNS/PNS guideline

  AND
- ❒ Baseline strength and weakness (and current strength and weakness for continuation requests) documented using an objective clinical measuring tool (e.g. INCAT, MRC, 6-minute timed walking test, Rankin, Modified Rankin)

<u>Administration, Quantity Limit, Authorization Period</u>

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is the lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2,000 mg/kg per month (dose infused over 2 to 5 days; may be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days)
- ❒ Frequency/Quantity Limit: 1 course per month. Dose not to exceed 2,000 mg/kg per course (initial) and 1,000 mg/kg per course (continuation)
- ❒ Duration of Authorization: May authorize up to 3 months (initial therapy); 6 months (continuation of therapy)
- ❒ Reauthorization: [ALL]
  - ❍ Positive clinical response to therapy as measured by an objective scale documented using an objective clinical measuring tool (e.g. INCAT, MRC, 6-minute timed walking test, Rankin, Modified Rankin) compared to baseline
  - ❍ Titration to the minimum dose and frequency needed to maintain sustained clinical effect (attempts to titrate the dose or the interval of therapy result in worsening of symptoms)

5. Dermatomyositis; Polymyositis

Dermatomyositis is an idiopathic inflammatory myopathy that most commonly affects the skin and muscles and may impact joints. Polymyositis is an idiopathic inflammatory myopathy causing muscle weakness, elevated muscle enzyme levels and is similar to dermatomyositis.

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a neurologist or a rheumatologist. Submit consultation notes if applicable.

  AND
- ❒ Diagnosis of dermatomyositis or polymyositis confirmed by ***positive*** **biopsy**

  AND
- ❒ Documentation of the following: [ALL]
  - ❍ Severe active disease state; AND
  - ❍ Muscle weakness in all upper and/or lower limbs

  AND
- ❒ Documented **refractory*** disease that has failed to respond to at least an adequate three (3) month trial of the following first and second-line conventional therapies (unless contraindicated): [1 AND 2]

  **Refractory disease is evidenced by persistently elevated serum creatine kinase and/or lack of improvement on muscle strength improvement scales*
  1) Corticosteroids (e.g., prednisone); AND
  2) Immunosuppressants (e.g., azathioprine, methotrexate, cyclophosphamide, and cyclosporine, Rituxan)

  OR

  EXCEPTION (TO CRITERIA 1 AND 2): Documentation of profound, rapidly progressive and/or potentially life-threatening muscular weakness refractory to prior therapy

  AND
- ❒ A baseline physical examination required. Submit documentation.

  NOTE: Requests for continuation of therapy must demonstrate measurable, objective response within 3 months of initiation (i.e. improvement in CPK levels, increase or stabilization of muscle strength, or EMG abnormalities)

Administration, Quantity Limit, Authorization Period *Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.*

- ❒ Dosing recommendation: [AS APPLICABLE]
  - ❍ Initial dose: 2,000 mg/kg per month; Maintenance dose: 500 – 1,000 mg/kg per month
- ❒ Quantity limit/Frequency: One course per month for 3 months. Dose does not exceed 2,000 mg/kg per month
- ❒ Duration of authorization:
  - ❍ Initial: May authorize up to 3 months; Continuation: May authorize up to 6 months
- ❒ Reauthorization: Continuation of therapy of IVIg is based on objective measures of its sustained effectiveness from baseline as documented by improvements in at least ONE (1) of the following: serum Creatine Kinase (CK) levels, muscle strength, electromyography testing, and/or improvement in rash (for dermatomyositis indication)

6. Fetal or Natal Alloimmune Thrombocytopenia (FAIT/ NAIT)

FAIT/ NAIT is the most common cause of severe thrombocytopenia in the fetus and in otherwise healthy newborn. The mother produces antibodies (IgG) against fetal HPA antigens inherited from the father. These alloantibodies (IgG) can cross the placenta, destroy fetal thrombocytes and may induce severe thrombocytopenia. It is most commonly caused by the HPA-1a antigen (80%).

Member meets ALL the following criteria supported by documentation: [ALL APPLICABLE]

- ❒ Diagnosis of neonatal alloimmune thrombocytopenia (NAIT) or fetal alloimmune thrombocytopenia (FAIT)
  AND
- ❒ Prescribed by, or in consultation with, fetal medicine, obstetrics, or hematology/transfusion medicine. Submit consultation notes if applicable.
  AND
- ❒ ONE (1) of the following: [A OR B]
  - **A.** For fetal alloimmune thrombocytopenia (FAIT), member meets ONE (1) of the following criteria: [ONE]
    - ❍ Previous pregnancy affected by FAIT (previously delivered infants with autoimmune thrombocytopenia); OR
    - ❍ At 20 weeks gestation or later, cordocentesis reveals fetal platelets less than 20,000/ mm^3; or screening reveals platelet alloantibodies

    OR
  - **B.** For neonatal alloimmune thrombocytopenia (NAIT), member must meet **BOTH** of the following criteria: [BOTH]
    - ❍ Member is severely thrombocytopenic (i.e. a platelet count less than 30,000/mm^3) and/or symptomatic; AND
    - ❍ Neonate failed, has a contraindication to, or is intolerant to platelet transfusions

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 1 g/kg/week, increasing to 2 g/kg/week in refractory cases
- ❒ Frequency/Quantity Limit:
  - ❍ **FAIT:** One course per week until delivery. Dose not to exceed 2 g/kg/week once weekly until delivery
  - ❍ **NAIT:** 1 g/kg x 1 dose, may be repeated once if needed; maximum 2 doses
- ❒ Duration of Authorization:
  - ❍ **FAIT:** Until delivery
  - ❍ **NAIT:** Authorization is valid for 1 course (1 month) only and cannot be renewed
- ❒ Reauthorization: No reauthorization. Immune globulin is not authorized for routine use.

7. **Guillain-Barré Syndrome (GBS)** [also referred to as Acute Inflammatory Demyelinating Polyneuropathy (AIDP)]
GBS is an acquired acute peripheral neuropathy causing limb weakness that progresses over a period of days to weeks. The syndrome typically presents with rapidly progressive, relatively symmetrical ascending limb weakness consistent with a polyradiculoneuropathy and often with associated cranial nerve involvement. Motor signs and symptoms usually predominate over sensory signs and symptoms. Major complications include respiratory failure and autonomic dysfunction. The disease is monophasic, reaching its nadir usually within two weeks, although arbitrary definition accepts a limit of four weeks. A plateau phase of variable duration follows the nadir before gradual recovery.

Member meets ALL the following criteria supported by documentation: [ALL]
- ❒ Prescribed by, or in consultation with, a neurologist or a specialist with experience in diagnosing and treating patients with GBS. Submit consultation notes if applicable.
  AND
- ❒ Documented functional disability: ***Severe*** GBS [defined as having significant weakness such as inability to walk or stand without aid, respiratory weakness or bulbar weakness] or Miller-Fisher Syndrome (MFS)
  AND
- ❒ IVIg therapy is initiated ***within 2 weeks*** and no longer than 4 weeks of onset of neuropathic symptoms
  - *IVIg should usually be initiated within 2 weeks and no longer than 4 weeks of onset of neuropathic symptoms for non-ambulatory adult patients with GBS. (AAN, 2013)*

  AND
- ❒ Plasmapheresis is not used concomitantly
  - *The combination of IVIG and plasmapheresis used together is not better than either treatment used alone. Combination therapy with plasma exchange and IVIg was not recommended. (AAN, 2013)*

Administration, Quantity Limit, Authorization Period
Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.
- ❒ Recommended Dose: 2,000 mg/kg per month (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days)
- ❒ Frequency/Quantity Limit: May be approved up to 2 courses for initial month, then 1 course per month. Dose not to exceed 2,000 mg/kg per course (initial) and 1,000 mg/kg per course (continuation)
- ❒ Duration of Authorization: [ONE]
  - ❍ Initial: May authorize up to 2 months
  - ❍ Continuation: May authorize up to 3 months
- ❒ Reauthorization: [ALL]
  - ❍ Documented functional improvement: Positive clinical response to therapy as measured by an objective scale documented using an objective clinical measuring tool (e.g. INCAT, MRC, 6-minute timed walking test, Rankin, Modified Rankin) as compared to baseline
  - ❍ Titration to the minimum dose and frequency needed to maintain sustained clinical effect (attempts to titrate the dose or the interval of therapy result in worsening of symptoms)

Informational Note:

- *Corticosteroids (oral and intravenous) have not been found to have a clinical benefit in GBS. Consequently, this class of drugs is not currently employed in treatment of the syndrome. For adult patients with GBS, glucocorticoids are not recommended for treating.*
- *Immunomodulatory treatment has been used to hasten recovery. IVIg and plasma exchange have proved equally effective. An UpToDate review on "Treatment and prognosis of Guillain-Barré syndrome in adults" (Vriesendorp, 2015) states that "Aside from plasma exchange and IVIg, no other pharmacologic agents have been found to be effective for GBS."*

8. HIV-associated Thrombocytopenia: ADULTS

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, an infectious disease or HIV specialist. Submit consultation notes if applicable.
  AND
- ❒ Current use of combination antiretroviral therapy for HIV infection
  AND
- ❒ Platelet count *less than* is < 20,000/µL **OR** Presence of clinically significant bleeding complications
  AND
- ❒ For Rh-positive patients: Failure of RhIG documented

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Use the lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 400 mg/kg every 2 to 4 weeks
- ❒ Frequency/Quantity Limit: One dose/course per month
- ❒ Duration of Authorization: 3 months
- ❒ Reauthorization: 3 months. The use of IVIG in HIV-infected adults is not definitive to substantiate a positive benefit on overall long-term health outcomes.

9. PEDIATRIC HIV: HIV-infected infants and children to prevent recurrent bacterial infections

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, an infectious disease or HIV specialist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of HIV disease; AND
- ❒ 13 years of age or younger; AND
- ❒ Receiving highly active antiretroviral therapy (HAART); AND
- ❒ Member meets ONE (1) of the following conditions: [ONE]
  - ❍ Hypogammaglobulinemia (pretreatment serum IgG less than 400 mg/dL) **AND** Recurrent serious bacterial infections defined as two (2) or more infections such as bacteremia, meningitis, or pneumonia in a 1-year period; OR
    - *Current guidelines recommend IVIg use among HIV-infected children who have hypogammaglobulinemia (IgG <400 mg/dL) to prevent serious bacterial infections. IVIG is no longer recommended for primary prevention of SBIs in children, unless hypogammaglobulinemia is present.*
  - ❍ Failure to form antibodies to common antigens, such as measles, pneumococcal, and/or Haemophilus influenzae type b vaccine; OR
  - ❍ Reside in areas where measles is highly prevalent and who have not developed an antibody response after TWO doses of measles, mumps, and rubella virus vaccine; OR
  - ❍ Has chronic bronchiectasis that is sub-optimally responsive to antimicrobial and pulmonary therapy

Authorization Limit *Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.*

- ❒ Recommended Dose: Recommended dose for pediatrics: 400 mg/kg every 4 weeks
- ❒ Frequency/Quantity Limit: One dose per month
- ❒ Duration of Authorization: May authorize up to 6 months (initial and continuation)
- ❒ Reauthorization: Documentation of current IgG levels at time of reauthorization request that are in the low to normal range and evidence of clinical improvement (i.e. decreased occurrence of infections)

Immune or Idiopathic Thrombocytopenic Purpura (ITP)

ITP is a reduction in platelet count (thrombocytopenia) resulting from shortened platelet survival due to anti-platelet antibodies. ITP is divided into chronic and acute forms. The goal of medical care for ITP is to increase the platelet count to a safe level, permitting patients to live normal lives while awaiting spontaneous or treatment-induced remission.

10. ADULT: ACUTE ITP

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ITP with duration of illness *less than* 6 months
  AND
- ❒ Prescribed for when a rapid increase in platelet count is necessary (such as in an acute bleeding episode or prior to surgery) or when the platelet count is significantly low is required for ANY of the following conditions: [ONE]
  - ❍ Platelet counts remain persistently at, or below, 30,000/mm^3 despite prior treatment with corticosteroids or splenectomy; OR
  - ❍ To correct thrombocytopenia prior to major, invasive surgical procedures (i.e. splenectomy) when a rapid increase in platelet count is necessary (Platelets less than 100 X 10^9/L); OR
  - ❍ Persistent or potentially life-threatening hemorrhage in members with severe thrombocytopenia (platelet counts less than 20,000/mm^3) considered to be at risk for intracerebral hemorrhage

  AND
- ❒ Diseases known to be associated with "secondary" thrombocytopenia have been ruled out by history, physical examination, complete blood cell count and examination of the peripheral blood smear
  AND
- ❒ Failure or clinically significant adverse effects to systemic corticosteroid (e.g., prednisone)
  NOTE: Rho(D) immune globulin is not necessarily recommended or preferred in place of IVIg; however may be utilized instead in Rho(D) *positive, non-splenectomized* patients, with a *negative* direct antiglobulin test (DAT)

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 1,000 mg/kg body weight given on 1 or 2 consecutive days OR 400 mg/kg body weight given on each of 2 to 5 consecutive days
- ❒ Frequency/Quantity Limit: One dose
- ❒ Duration of Authorization: 5 days
- ❒ Reauthorization: No reauthorization

11. ADULT: CHRONIC idiopathic thrombocytopenic purpura (ITP)

Chronic ITP may relapse and remit spontaneously and the course may be difficult to predict. The goal is to maintain platelet count at a level that prevents spontaneous bleeding or bruising.

Member meets ALL of the following criteria as supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ITP with duration of illness ***greater than 6 months***
  AND
- ❒ No concurrent illness/disease explaining thrombocytopenia
  AND
- ❒ Platelet counts persistently at, or below, 30,000/mm^3
  AND
- ❒ Member is symptomatic, at high risk for bleeding or post-splenectomy sepsis
  AND
- ❒ Prior treatment with systemic corticosteroid (e.g., prednisone), unless failure,* contraindication, or intolerance to corticosteroids. Documentation required.
  **A response may be defined as a platelet count ≥ 30,000/mm^3 and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.*
  **A failure would be defined as a platelet count < 30,000/mm^3 or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.*

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose [Dosing may vary with the product]
  - ❍ Initial: 1 or 2 g/kg total over 2 to 5 days
  - ❍ Maintenance: 800-1,000 mg/kg
- ❒ Frequency/Quantity Limit: every 2 to 6 weeks based on platelet count and dose does not exceed 2 g/kg total (initial) or up to 1,000 mg/kg (maintenance)

- ❒ Duration of Authorization: May authorize up to 6 months
- ❒ Reauthorization: [ALL]
  - ❍ Documented initial response to IVIg therapy
    AND
  - ❍ Continued thrombocytopenia, defined as a platelet count of < 20,000 OR less than 30,000 cells/m^3 and clinically significant bleeding; OR
    Member is scheduled for an invasive procedure with high risk of bleeding

12. PEDIATRIC: Idiopathic thrombocytopenic purpura (ITP)

Chronic ITP may relapse and remit spontaneously and the course may be difficult to predict. The goal is to maintain platelet count at a level that prevents spontaneous bleeding or bruising.

Member meets ALL the following criteria as supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ITP and no concurrent illness/disease explaining thrombocytopenia
  AND
- ❒ Prescribed for ACUTE OR CHRONIC ITP [A OR B]
  - **A.** For ACUTE ITP: [ONE]
    1) Prescribed as initial therapy if platelet count < 20,000/ul; OR
    2) Severe thrombocytopenia (platelet counts less than 20,000/ul) considered to be at risk for intracerebral hemorrhage **NOTE:** IVIg not indicated if only mild manifestations of bleeding
  - **B.** Chronic ITP: [1 AND 2; **OR** 3]
    1) In high risk persons when platelet count low (platelet counts less than 20,000/ul) OR persons symptomatic (*e.g. head trauma or anticipated procedure*); AND
    2) Failure of other therapies

    OR
    3) Member is a high risk for post-splenectomy sepsis

Authorization Limit *Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.* [ONE: ACUTE OR CHRONIC]

- ❒ **ACUTE ITP: [ALL]**
  - ❍ Recommended Dose: 1,000 mg/kg body weight given on 1 or 2 consecutive days OR 400 mg/kg body weight given on each of 2 to 5 consecutive days
  - ❍ Frequency/Quantity Limit: ONE (1) dose
  - ❍ Duration of Authorization: 5 days
  - ❍ Reauthorization: No reauthorization

❒ **CHRONIC ITP: [ALL]**
- ❍ Recommended Dose [Dosing may vary with the product]
  - Initial: 1 or 2 g/kg total over 2 to 5 days
  - Maintenance: 800-1,000 mg/kg
- ❍ Frequency/Quantity Limit: every 2 to 6 weeks based on platelet count and dose does not exceed 2 g/kg total (initial) or up to 1,000 mg/kg (maintenance)
- ❍ Duration of Authorization: May authorize up to 6 months
- ❍ Reauthorization: [ALL]
  - Documented initial response to IVIg therapy
    AND
  - Continued thrombocytopenia, defined as a platelet count of < 20,000 OR less than 30,000 cells/m^3 and clinically significant bleeding
    OR
    Member is scheduled for an invasive procedure with high risk of bleeding.

13. ITP in Pregnancy

The goal of therapy is to minimize the risk of bleeding complications due to thrombocytopenia.
Member meets ALL the following criteria supported by documentation: [ALL]
❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
AND
❒ Member is **pregnant** AND meets ONE (1) of the following criteria supported by documentation: [ONE]
- ❍ Platelet counts less than 10,000/mm^3 in the third trimester, despite an adequate course of corticosteroids, unless use of steroids are contraindicated, or not tolerated; OR
- ❍ Platelet counts < 30,000/mm^3 associated with bleeding before vaginal delivery or C-section; OR
- ❍ Previously delivered infants with autoimmune thrombocytopenia; OR
- ❍ Platelet counts < 55,000/mm^3 during the current pregnancy; OR
- ❍ Past history of splenectomy

Administration, Quantity Limit, Authorization Period
Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.
❒ Recommended Dose: 1,000 mg/kg/day for 1 to 2 days
❒ Frequency/Quantity Limit: One dose per month until the estimated date of delivery
❒ Duration of Authorization: Authorization through delivery as determined necessary by Prescriber
❒ Reauthorization: No reauthorization after term of pregnancy

14. Neonatal hemochromatosis, prophylaxis

Neonatal hemochromatosis is a rare gestational condition in which iron accumulates in the fetal tissues in a distribution like that seen in hereditary hemochromatosis. Extensive liver damage is the dominant clinical feature, with late fetal loss or early neonatal death.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, gastroenterologist, hematologist, and a hepatologist. Submit consultation notes if applicable.
  AND
- ❒ Member is pregnant
  AND
- ❒ History of pregnancy ending with neonatal hemochromatosis

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Use the lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 1,000 mg/kg weekly to pregnant woman (usually from the 18th week until end of gestation);
- ❒ Frequency/Quantity Limit: One dose per week until delivery
- ❒ Duration of Authorization: Until delivery
- ❒ Reauthorization: No reauthorization. Immune globulin is not authorized for routine use.

15. Kawasaki Disease (Mucocutaneous Lymph Node Syndrome)

Kawasaki disease is an acute, febrile, multi-system disease of children and young infants often involving the coronary arteries. Coronary artery aneurysms may occur from the second week of illness during the convalescent stage. The cause of the condition is unknown but there is evidence that the characteristic vasculitis results from an immune reaction characterized by T-cell and macrophage activation to an unknown antigen, secretion of cytokines, polyclonal B-cell hyperactivity, and the formation of autoantibodies to endothelial cells and smooth muscle cells. It is likely that in genetically susceptible individuals, one or more uncharacterized common infectious agents, possibly with super-antigen activity, may trigger the disease.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a pediatric cardiologist or a pediatric infectious diseases physician. Submit consultation notes if applicable.

  AND
- ❒ Diagnosis of Kawasaki Disease or Incomplete (Atypical) Kawasaki Disease

  **Diagnosis must be established; there is no specific lab test; diagnosis is established by meeting the following criteria.*

  AND
- ❒ ONE (1) of the following: **[ONE: A OR B]**
  - **A.** Diagnosis is confirmed by a Cardiologist, Allergist or Rheumatologist
    - *Diagnosis is best confirmed by a clinician experienced in the diagnosis and management of KD so as to avoid misdiagnosis and unnecessary treatment.*[1]

    OR
  - **B.** FOUR of the following five symptoms are present: [FOUR]
    - ❍ Mucous membrane changes such as strawberry tongue and dry fissured lips without discrete lesions
    - ❍ Changes in the extremities such as edema of the hands and feet
    - ❍ Enlarged lymph nodes in the neck
    - ❍ Diffuse red rash covering most of the body
    - ❍ Redness of the eyes

  AND
- ❒ Fever persisting at least 5 days

  AND
- ❒ Treatment is being initiated within ten (10) days of onset of fever

  OR

  Diagnosis *after* ten (10) days of disease onset and member continues to exhibit manifestations of inflammation or evolving coronary artery disease
  - *The effectiveness of IVIg therapy is best established for patients treated within the first 7 to 10 days of illness. The AHA and AAP guidelines recommend that IVIg be administered to children with KD within the first 10 days of illness, and if possible, within the first seven days of illness.*

AND

- ❒ Concomitant aspirin treatment given with immune globulin
  - *Evidence supports IVIg therapy with aspirin. Combination with high-dose aspirin is more effective than aspirin alone in decreasing the risk of CA aneurysms, and there is a dose-response effect of IVIg.*
  - *The AAP, American Heart Association (AHA), and American College of Chest Physicians (ACCP) state that combined therapy with IGIV and aspirin should be administered as soon as possible after Kawasaki disease is diagnosed or strongly suspected (optimally within 7-10 days of disease onset).*[3,4,5]
  - *The AAP and AHA recommend high-dose aspirin (80 to 100 mg/kg/day), but it is not clear that this dose is more effective than the lower doses used in some clinical trials (30 to 50 mg/kg per day).*[1] *The total daily aspirin dose of 30 to 50 mg/kg per day is administered in four divided doses (maximum dose 4 g per day).*

AND

- ❒ Exclusion of other diseases with similar findings, including but not limited to ANY of the following: [ANY]
  - ❍ Viral infections (i.e., measles, adenovirus, enterovirus, Epstein-Barr virus)
  - ❍ Scarlet fever
  - ❍ Staphylococcal scalded skin syndrome
  - ❍ Toxic shock syndrome
  - ❍ Bacterial cervical lymphadenitis
  - ❍ Drug hypersensitivity reactions
  - ❍ Stevens-Johnson syndrome
  - ❍ Juvenile rheumatoid arthritis
  - ❍ Rocky Mountain spotted fever
  - ❍ Leptospirosis
  - ❍ Mercury hypersensitivity reaction (acrodynia)

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: A single dose of intravenous immune globulin (IVIg; 2 g/kg) administered over 8 to 12 hours OR a dose of 400 mg/kg for 4 consecutive days
- ❒ Frequency/Quantity Limit: Single authorization of two (2) doses given *within 10 days* of symptom onset
  NOTE: It is preferable that IVIg be administered within the first 10 days of illness, before aneurysms typically develop, however IVIg may also be administered even beyond this 10-day window in patients with evidence of persistent vasculitis or systemic inflammation (e.g., persistent fever); however there are no studies indicating the benefit of prolonged use after the tenth day.
- ❒ Duration of Authorization: One-time authorization only
- ❒ Reauthorization: No reauthorization

16. Lambert-Eaton Myasthenia Syndrome (LEMS)

LEMS is a rare acquired autoimmune disorder characterized by proximal weakness of extremities, decreased reflexes, and dryness of mouth and eyes. The primary goal of treatment for LEMS is to identify and treat any tumors or other underlying disorders.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a neurologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of LEMS confirmed by electro-physiologic studies
  AND
- ❒ Unresponsive, contraindication, or intolerance to other symptomatic therapies: [ALL APPLICABLE]
  - ❍ Acetylcholinesterase inhibitors (e.g., Mestinon®)
  - ❍ Immunosuppressants (e.g., corticosteriods, azathioprine)
  - ❍ dalfampridine (Ampyra®); Firdapse/Ruzurgi

  AND
- ❒ Immune globulin is used as an alternative to plasma exchange if weakness is severe or when there is difficulty with venous access for plasmapheresis.
  - *Plasmapheresis may be a useful adjunct for patients with severe or rapidly developing neurological deficit (Szczepiorkowski, et al., 2010; National Institutes of Health [NIH], Jul 2012; Smith, et al., 2003).*

  AND
- ❒ Impaired function (e.g., unable to stand or walk without aid), measured by a standard clinical scale and/or objective findings on a physical exam at the time of initial therapy. Documentation required.

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2,000 mg/kg administered over 2 to 5 days; AND
- ❒ Frequency/Quantity Limit: One dose per month for 6 months. Dose does not exceed 2,000 mg/kg per month; AND
- ❒ Duration of Authorization: May authorize up to 6 months; AND
- ❒ Reauthorization: [ALL]
  - ❍ Consult/assessment by a neurologist required (if prescriber is not a neurologist); AND
  - ❍ Documented improvement in muscle function/strength as demonstrated by objective findings of either: [ONE]
    - o Improvement in functional scores activities of daily living (ADL) or quantitative muscle scores or Medical Research Council (MRC) muscle assessment; OR
    - o Stabilization of disease as defined by stable functional scores (ADLs) or quantitative muscle scores or MRC muscle assessment after previous evidence of deterioration in one of these scores

17. Multiple Myeloma (MM)

MM is a malignant tumor of plasma cells associated with impaired function of immunoglobulins, which are an essential component of the immune system. Patients with MM are at increased risk of infection, due to a combination of several factors, including immunoparesis and physical factors.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist, oncologist, or infectious diseases specialist. Submit consultation notes if applicable.
  AND
- ❒ Member in stable, **plateau phase** disease AND (greater than 3 months since diagnosis)
  NOTE: Plateau phase is defined as the time when other causative organisms that may be present due to dysfunction in other immunologic cells besides the B-cell lines of defense are *less likely* to be present. IVIg in any other phase does not meet criteria
  AND
- ❒ Member <u>not</u> undergoing induction chemotherapy or patient is not in relapse phase
  AND
- ❒ Member is at high risk of recurrent infections as evidenced by: **[ONE: 1 OR 2]**
  1) IgG level < 600 mg/dL (normal range IgG=723-1,685 mg/dL); **AND**
     Documentation of life threatening, laboratory-proven bacterial infection within the preceding 6 months
     OR
     Two (2) or more bacterial infections in the preceding year requiring IV antibiotic infusion therapy in the home or in the hospital
  2) Presence of a specific antibody deficiency as evidenced by: [ONE]
     - ❍ Low normal IgG levels during acute sepsis episodes, OR
     - ❍ Failure to mount an appropriate IgG humoral immune response on challenge with pneumococcal vaccine

<u>Administration, Quantity Limit, Authorization Period</u>

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 200-400 mg/kg every 4 to 6 weeks
- ❒ Frequency/Quantity Limit: One dose per month. Dose does not exceed 600 mg/kg per month
- ❒ Duration of Authorization: May authorize up to 6 months (initial and continuation)
- ❒ Reauthorization: Six-month review to assess clinical benefit. Prescriber submit current evidence of clinical improvement, such as decreased occurrence of infections
- ❒ After each 12 months of therapy (on an annual basis): Cessation of IVIg therapy considered and extended as required to enable cessation of therapy **<u>AND</u>** written confirmation from Prescriber/specialist of the following: [ALL]
  - ❍ An annual review with clinical and/or immunological evaluation; AND
  - ❍ Demonstrated clinical benefit, including evidence that treatment has been effective in reducing the number or severity of clinical infections; AND
  - ❍ A trial period of cessation of IVIg for the purpose of immunological evaluation is medically contraindicated or may cause member's condition to worsen

18. Myasthenia Gravis: ACUTE myasthenic crisis, Myasthenic Exacerbation

Myasthenia gravis is an autoimmune disease characterized by autoantibodies directed against the acetylcholine receptors of the muscle end plate that induce muscle weakness and pronounced fatigability. Initial treatment focuses on the use of cholinesterase inhibitors to overcome the post-synaptic blockade.

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a neurologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of myasthenia gravis confirmed by positive serologic test for anti-acetylcholine receptor (AchR) antibodies
  - *Due to its specificity, testing for autoantibodies against the acetylcholine receptor (AChR-Ab) should be performed on all patients. Demonstration of binding antibodies, possible in approximately 85 percent of patients with generalized disease, provides the laboratory confirmation of myasthenia gravis. In select patients, assays for blocking and modulating antibodies may also be helpful. If the AChR-Abs are negative, an assay for antibodies to muscle-specific tyrosine kinase (MuSK) should be performed.*

  AND
- ❒ Prescribed for the treatment of ***ACUTE*** myasthenic crisis in member experiencing disease exacerbation and/or decompensation (e.g. difficulty swallowing, acute respiratory failure, major functional disability responsible for the discontinuation of physical activity; of physical activity, disabling weakness requiring hospital admission)
  - *Myasthenic crisis is a life-threatening condition defined as weakness from acquired myasthenia gravis that is severe enough to necessitate intubation or to delay extubation following surgery. The respiratory failure is due to weakness of respiratory muscles*.

  AND
- ❒ ONE (1) of the following is met. Documentation required: [ONE: 1 OR 2]
  1) History of failure, contraindication, or intolerance to include, but are not limited to: [ALL]
     - ❍ Plasma exchange; AND
     - ❍ Immunomodulator therapy (e.g. corticosteroids, azathioprine, cyclosporine, methotrexate, mycophenolate mofetil, cyclophosphamide)

     OR
  2) Currently receiving immunomodulator therapy (e.g., azathioprine, mycophenolate mofetil, cyclosporine) for long-term management of myasthenia gravis

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: One course of treatment: 1,000-2,000 mg/kg IV divided over 2-5 days
  - *Based largely on the early successful experience of IVIg in idiopathic thrombocytopenic purpura, IVIg is usually given initially at a daily dose of 0.4 gm/kg/d for 5days or 1 gm/kg/d for 2days, depending on local preferences, patient tolerance and IVIg formulations*
- ❒ Frequency/Quantity Limit: One (1) course; 2,000 mg/kg total
- ❒ Initial Authorization/Reauthorization: May authorize up to 3 months. IVIg dose does not exceed 2,000 mg/kg (2 g/kg total) per month. Dosing interval may need to be adjusted in patients with severe comorbidities.

- ❒ Reauthorization for ACUTE myasthenic crisis or exacerbation:
  - ❍ Consult/assessment by a neurologist required (if prescriber is not a neurologist); AND
  - ❍ Evidence of myasthenic exacerbation documented by at least one of the following symptoms within the recent 30 days: difficulty swallowing, acute respiratory failure, major functional disability responsible for the discontinuation of physical activity; of physical activity, disabling weakness requiring hospital admission (not an all-inclusive list)

Informational Note:

- *Maintenance IVIg or plasma exchange: Periodic administration of IVIg or plasma exchange is sometimes used to maintain remission in patients with MG that is not well controlled despite the use of chronic immunomodulating drugs. There are no studies comparing this strategy with other options for refractory disease, however, maintenance IVIg has been noted as necessary and useful in some patients when other strategies have failed (Bird, SJ. 2019).*
- *There are no data from RCTs regarding the value of IVIg as maintenance therapy in MG, either alone or as add-on therapy to IS agents. IVIg has been used chronically as maintenance therapy in individual cases. (Sanders DB, et al. 2016).*
- *Hayes assigned a Rating of "B" for the use of IVIg for the treatment of adult patients with worsening or acute exacerbations of myasthenia gravis without contraindications to IVIg treatment. This Rating reflects moderate-quality evidence that IVIg is at least as efficacious as plasma exchange/plasmapheresis and superior to placebo therapy for improving muscle weakness and other clinical symptoms of MG, and that it is relatively safe for patients without contraindications (Hayes 2019).*

19. Multifocal Motor Neuropathy (MMN)

MMN is a rare neurological disorder characterized by slowly progressive, asymmetric, predominately distal limb weakness without sensory impairment. Weakness often begins in the arms and the combination of weakness, wasting, cramps and fasciculations may suggest a diagnosis of motor neuron disease. However, clinical examination may demonstrate that the pattern of weakness follows the distribution of individual nerves rather than a spinal segmental pattern.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a neurologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of ***progressive, symptomatic*** multifocal motor neuropathy (as characterized by limb weakness or motor involvement having a motor nerve distribution in at least two nerves)
  AND
- ❒ Electrophysiological findings rule out other possible conditions that may not respond to IVIg
  AND
- ❒ Baseline strength and function documented using an objective clinical measuring tool (e.g. INCAT, MRC, 6-minute timed walking test, Rankin, Modified Rankin)

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2,000 mg/kg/month administered over 2 to 5 days
- ❒ Frequency/Quantity Limit: One dose per month for 6 months. Dose does not exceed 2,000 mg/kg per month
- ❒ Duration of Authorization: May authorize up to 6 months (initial and reauthorization)
- ❒ Reauthorization: [ALL]
  - ❍ For stable patients on maintenance treatment, review by a neurologist is required at least annually.
  - ❍ Clinical results document an improvement in strength and function within three weeks of the start of the infusion period. Prescriber submit current strength and function report using an objective clinical measuring tool (e.g. INCAT, MRC, 6-minute timed walking test, Rankin, Modified Rankin)
  - ❍ Continued need is demonstrated by documentation that attempts on an annual basis to titrate the dose or the interval of therapy result in worsening of symptoms

20. Post-Transfusion Purpura (PTP) [Hemolytic Transfusion Reaction]

PTP is a rare bleeding disorder caused by alloantibodies specific to platelet antigens. PTP is characterized by the development of severe, sudden and self-limiting thrombocytopenia occurring 5-10 days after a blood transfusion.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of post-transfusion purpura
  AND
- ❒ Decreased platelet count (*generally* less than 10,000/mm^3)
  AND
- ❒ 2 to 14 days post-transfusion with bleeding **OR** experienced bleeding complications due to thrombocytopenia

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended dose: 400–500 mg/kg per day for 5 days **OR** 1,000 mg/kg per day for 2 days
- ❒ Frequency/Quantity limit: Dose does not exceed 1,000 mg/kg for 2 days
- ❒ Duration of Authorization: One time only for 5 days
- ❒ Continuation of Treatment: No reauthorization

21. Pure Red Blood Cell Aplasia (PRCA): Secondary to Chronic (Persistent) Parvovirus B19 Infection

Parvovirus B19 infects and lyses red cell precursors, which can cause pure red cell aplasia. IVIg therapy is usually reserved for patients with chronic parvovirus infection and chronic anemia.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, an infectious diseases specialist, immunologist, hematologist, or transplant specialist. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of PRCA secondary to parvovirus B19 infection
  AND
- ❒ ***Chronic*** Parvovirus B19 infection with severe anemia associated with bone marrow suppression (i.e., Hgb <10 or Hct < 30)
  AND
- ❒ ***Chronic*** immunodeficient condition (e.g., HIV infection, solid organ transplants [e.g., renal, liver], chemotherapy for hematologic malignancy)
  - *Chronic parvovirus infection with anemia usually occurs in immunocompromised patients. If the immunodeficiency improves, the parvovirus and anemia may spontaneously resolve.*

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2-4 g/kg, divided as 400 mg/kg/day for 5–10 days, 1,000 mg/kg/day for 3 days or 0.5 g/kg weekly for 4 weeks
- ❒ Frequency/Quantity Limit: One dose per month for 6 months
- ❒ Duration of Authorization: May authorize up to 6 months
- ❒ Reauthorization: Documentation of initial response, parvovirus, and recurrence of significant anemia

22. PRIMARY IMMUNODEFICIENCIES (PID)

PID comprise a group of more than 120 separate conditions. Many of these are manifest by failure of protective antibody production. Some PID does not involve antibody failure, such as chronic granulomatous disease and deficiencies of complement components. In these cases, antibody replacement therapy is not justified.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, an allergist, clinical immunologist, otolaryngologist or an infectious disease physician. Submit consultation notes if applicable.
  AND
- ❒ Diagnosis of primary immunodeficiency
  AND
- ❒ Clinically significant functional deficiency of humoral immunity as evidenced by one of the following:
  - ❍ Documented failure to produce antibodies to specific antigens
  - ❍ History of significant recurrent infections

  AND
- ❒ No evidence of renal (nephrotic syndrome) and gastrointestinal (for example, protein losing enteropathy) as causes of hypogammaglobulinemia
  AND
- ❒ Initial, pre-treatment total serum IgG is below the lower limit of the age adjusted laboratory reference range, or more than two standard deviations below the age adjusted mean
  AND
- ❒ Documented diagnosis primary immunodeficiency with laboratory evidence: [ONE]
  - ❍ Autosomal recessive agammaglobulinemia
  - ❍ Autosomal recessive hyperimmunoglobulin M syndrome (HIM)
  - ❍ Bruton's disease
  - ❍ Chronic mucocutaneous moniliasis (CMC or APCED)
  - ❍ Combined immunodeficiency disorders include:
    - o Ataxia-telangiectasia
    - o DiGeorge syndrome
    - o Nuclear factor κB essential modifier deficiency (NEMO)
    - o Nijmegan breakage syndrome
    - o WHIM (warts, hypogammaglobulinemia, immunodeficiency, and myelokathexis) syndrome
    - o Wiskott Aldrich syndrome
  - ❍ Common variable immunodeficiency (CVID)
  - ❍ Congenital hypogammaglobulinemia late onset, ICOS impaired
  - ❍ Congenital / X-linked agammaglobulinemia
  - ❍ Good syndrome (immunodeficiency with thymoma)
  - ❍ Hyperimmunoglobulinemia E syndrome
  - ❍ Hypogammaglobulinemia
  - ❍ ICF syndrome
  - ❍ Polyendocrinopathy and enteropathy (IPEX)
  - ❍ 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

❒ For X-linked agammaglobulinemia (Congenital agammaglobulinemia) ONLY: [ALL]
- ❍ IgA, IgG and IgM levels must be below the normal range (>2 standard deviations below the age-specific mean) on at least two (2) occasions while the member is clear of infections
  AND
- ❍ Documented recurrent bacterial infections resulting from low IgG or serious bacterial infections

❒ For Common variable immunodeficiency (CVID), or Unspecified hypogammaglobulinemia ONLY: [ALL]
- ❍ 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)
  AND
- ❍ Inadequate response or hypersensitivities to prophylaxis/treatment with antibiotics
  AND
- ❍ Lack of, or inadequate response to immunization (for example, but not limited to tetanus or pneumococcal antigen)
  AND
- ❍ Other disorders that may increase susceptibility to infection such as allergy or anatomic defects, have been identified and treated aggressively if present

❒ For combined immunodeficiencies with significant hypogammaglobulinemia or antibody production defect (e.g., ataxia-telangiectasis, DiGeorge syndrome, nuclear factor κB essential modifier deficiency [NEMO]) ONLY: [ONE]
- ❍ Two (2) or more bacterial infections per year due to persistent and significant reduction in total IgG or IgG subclasses, OR
- ❍ Unexplained recurrent or persistent severe bacterial infections, OR
- ❍ Infections that fail to respond adequately to prophylactic antibiotic therapy

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

❒ Recommended Dose: 300-600 mg/kg every 4 weeks, titrated based on individual's response
❒ Frequency/Quantity Limit: One dose per month and dose does not exceed 600 mg/kg
❒ Duration of Authorization: May authorize up to 6 months (initial and continuation of treatment)
❒ Reauthorization: Documented current IgG levels that are in the low to normal range and evidence of clinical improvement, such as reduction of the number and severity of clinical infections

23. Opsoclonus Myoclonus Syndrome (OMS)

Opsoclonus myoclonus is a rare neurological disorder that may occur in association with tumors (paraneoplastic) or viral infections and is characterized by an unsteady, trembling gait, myoclonus and opsoclonus (irregular, rapid eye movements). It is more common in children.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, and treatment monitored by, a neurologist
  AND
- ❒ Member meets ONE (1) of the following sets [A OR B]
  A. Younger than 18 years of age:
     - ❍ Clinical assessment indicates significant disability, as measured by an objective clinical score (i.e. the Cerebellar Functional System Score with a value of at least 2 points)
       NOTE: As there is no validated measure for OMS, the Cerebellar Functional System Score has been selected from the Expanded Disability Status Scale (Kurtzke 1983). Refer to 'Definition' section of MCP for additional information on Cerebellar Functional System Score

  OR

  B. Age 18 and older (adults)
     - ❍ Trial and failure or contraindication to a standard course of corticosteroid therapy
     - ❍ Clinical assessment demonstrates disability (i.e. as measured by the cerebellar functional system score with a value of at least two points)

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 400 – 1,000 mg/kg given monthly
- ❒ Frequency/Quantity Limit: 2,000 mg/kg per month given over 2 to 5 days
- ❒ Duration of Authorization: 6 months (initial and continuation)
- ❒ Reauthorization: Clinical documentation of effectiveness is necessary for continuation of IVIg therapy. Efficacy of Ig treatment is demonstrated by improvement in symptoms of OMS and improvement in, or no deterioration of disability. Documentation of the following required [ALL]
  - ❍ Clinical improvement or stability in opsoclonus symptoms
  - ❍ No further deterioration or some improvement in the degree of disability (i.e. as measured by the Cerebellar Functional System Score)

  NOTE: If there has been no improvement or clinical benefits after six months of treatment, IVIg therapy will not be authorized.

24. Rasmussen Syndrome (RS) [also known as Rasmussen Encephalitis (RE) or Chronic Focal Encephalitis]

RS/RE is a rare neurological, progressive, focal encephalitis that is commonly accompanied by focal seizures, hemiparesis and cognitive decline. It is generally considered to be a disease of childhood, with most cases occurring in children younger than 10 years, although adult onset cases do occur. The precise etiology of RE remains unknown, but immune-mediated injury is considered central in the pathogenesis.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescriber is a neurologist or neurosurgeon
  AND
- ❒ Prescribed for **short-term** amelioration of encephalitis prior to definitive surgical therapy
  NOTE: IVIg is not recommended for long-term therapy for Rasmussen's encephalitis as surgical treatment is the current standard of care.
  AND
- ❒ Intractable focal motor seizures and progressive neurologic deterioration (dementia, hemiparesis)
  AND
- ❒ History of failure, contraindication, or intolerance to antiepileptic drugs and corticosteroids

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2,000 mg/kg (dose infused over 2 to 5 days- can be given as 1,000 mg/kg/day for 2 days, or 400 mg/kg/day for 5 days)
- ❒ Frequency/Quantity Limit: 2,000 mg/kg per month
- ❒ Duration of Authorization: Up to 3 months (or 3 courses of therapy) only
- ❒ Reauthorization: IVIg is not recommended for long-term therapy for Rasmussen's encephalitis as surgical treatment is the current standard of care. Exception for continuation of treatment requires review and determination by a Medical Director. Additional information may be requested and discussion with Prescriber may be necessary.

25. Stiff-Person Syndrome (Moersch-Woltmann Syndrome)

Stiff-person syndrome is a chronic disorder with features of an autoimmune disease involving painful muscle spasms and rigidity. SPS treatments are aimed at symptom relief and/or modulation of the underlying aberrant immune process.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescriber is a neurologist
  AND
- ❒ Diagnosis of Stiff-Person Syndrome (Moersch-Woltmann Syndrome) by supportive testing including EMG findings, anti-glutamic acid decarboxylase antibodies, and/or anti-amphiphysin antibodies
  AND
- ❒ Significant disability as measured by objective scale (i.e. Modified Rankin Functional ADL Score or the Distribution of Stiffness Index)
  AND
- ❒ Baseline physical exam
  AND
- ❒ History of failure, contraindication or intolerance to conventional therapy to at least two (2) of the following treatments: benzodiazepines, baclofen, phenytoin, clonidine and/or tizanidine

<u>Administration, Quantity Limit, Authorization Period</u>

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2g/kg divided over 5 days
- ❒ Frequency/Quantity Limit: 2,000 mg/kg per month
- ❒ Duration of Authorization: May authorize up to 3 months initially and 6 months for continuation of treatment
- ❒ Reauthorization: Clinical documentation of effectiveness demonstrated by objective findings of improvement in symptoms of stiffness. Functional improvement compared to baseline as measured using an objective clinical measuring tool. Prescriber submit documentation of relief of symptoms of stiffness and disability as demonstrated objective findings of improvement in symptoms of stiffness [i.e. Functional Assessment ADL, Modified Rankin Score and a Distribution of Stiffness Index Score (greater than the qualifying baseline scores)]
  NOTE: If there has been no improvement or clinical benefits after six months of treatment, IVIg therapy will not be authorized.

26. Staphylococcal or Streptococcal Toxic Shock Syndrome (TSS) [ALL]

TSS is an acute, multi-system, toxin-mediated illness which may typically result in shock and multi-organ failure early in its clinical course. Causes include toxin-producing strains of Staphylococcus aureus and Invasive Group A Streptococcus (e.g. Streptococcus pyogenes). IVIg is recommended as an adjunctive therapy in children with severe toxin-related infection showing failure to improve despite best standard care.

Member meets ALL of the following criteria supported by documentation: [ALL]

- ❒ Prescribed for severe, life-threatening case of streptococcal or staphylococcal TSS
  AND
- ❒ Failure to achieve rapid improvement with antibiotic therapy and other supportive measures (fluids, inotropes, vasopressors)
  AND
- ❒ Individual is severely ill with ANY ONE of the following: [ANY]
  - ❍ Infection refractory to several hours of aggressive therapy
    - *Intravenous immunoglobulin should be considered in patients in whom there has been no clinical response within the first six hours of aggressive therapy.*
  - ❍ Presence of an undrainable focus
  - ❍ Persistent oliguria with pulmonary edema

Administration, Quantity Limit, Authorization Period

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 2g/kg divided over 5 days x 1 cycle
- ❒ Frequency/Quantity Limit: 2,000 mg/kg dose
- ❒ Duration of Authorization: 1 course (1 month) only. May consider repeat administration after 48 hours if there remains a poor response to treatment.
- ❒ Reauthorization: No reauthorization

TRANSPLANT

26. Allogenic Bone Marrow Transplant (BMT)/Hematopoietic Stem Cell Transplantation (HSCT)

BMT, also referred to as HSCT or hematopoietic cell transplant, is a type of treatment for cancer (and a few other conditions as well). HSCT involves the IV intravenous infusion of autologous or allogeneic stem cells to reestablish hematopoietic function in patients whose bone marrow or immune system is damaged or defective.

Member meets ALL the following criteria supported by documentation: [ALL]

- ❒ Prescribed by, or in consultation with, a hematologist, oncologist or infectious diseases physician. Submit consultation notes if applicable.

  AND
- ❒ Prescribed for ONE (1) of the following:
  - ❍ Prophylaxis of acute graft vs. host disease (GVHD)
  - ❍ Prophylaxis treatment against infection (i.e. cytomegalovirus)

  AND
- ❒ Confirmed **allogeneic** (<u>not</u> autologous) BMT/ HSCT
  - *Routine use of IVIg among autologous recipients is not recommended, according to the Centers for Disease Control and Prevention.*

  AND
- ❒ ONE (1) of the following: [ONE]
  - ❍ *Within* the first 100 days post-transplant

    OR
  - ❍ *After* 100 days or greater post-transplant: Documented *<u>pre-treatment serum</u>* IgG less than 400mg/dL

<u>Administration, Quantity Limit, Authorization Period</u>

Dose and quantity authorized in accordance to FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Goal is lowest dose possible that achieves the appropriate clinical outcome.

- ❒ Recommended Dose: 500mg/kg/week x 90 days, then 500 mg/kg/month up to 360 days post-transplant
- ❒ Frequency/Quantity Limit: Does not exceed 600 mg/kg once weekly for the first 90 days of therapy, then monthly up to 360 days after transplantation. Therapy does not exceed 360 days past patient's allogeneic bone marrow transplantation
- ❒ Duration of Authorization: May only be reauthorized for up to 360 days post-allogeneic bone marrow transplantation. Routine administration of IVIg > 90 days after HSCT is not recommended in absence of hypogammaglobulinemia.
- ❒ Reauthorization: As stated in the 'GENERAL CRITERIA: REAUTHORIZATIONS/CONTINUATION OF THERAPY REQUESTS' criteria

27. Solid Organ Transplantation: Refer to MCP-237 Intravenous Immune Globulin (IVIg) Therapy for Solid Organ Transplant

COVERAGE EXCLUSIONS

All other uses of **Intravenous infusion Immune Globulin (IVIg)** 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.*

- ❒ Experimental/Investigational Use: Indications not supported by CMS recognized compendia or acceptable peer reviewed literature

- ❒ Applications of **IVIg** 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.**

- ❒ Any Ig product for prophylaxis against disease

- ❒ Multiple Sclerosis
  - The American Academy of Neurology (AAN) guideline (Goodin, 2008) *Disease modifying therapies in multiple sclerosis*, addresses IVIg for the treatment of multiple sclerosis and states:
    - The studies of intravenous immunoglobulin (IVIg), to date, have generally involved small numbers of patients, have lacked complete data on clinical and MRI outcomes or have used methods that have been questioned. It is, therefore, only possible that IVIg reduces the attack rate in RRMS (Type C recommendation*). The current evidence suggests that IVIg is of little benefit with regard to slowing disease progression (Type C recommendation: *Possibly effective, ineffective or harmful for the given condition in the specified population.)*
      Reference: Goodin DS, Frohman EM, Garmany GP Jr, et al. Disease modifying therapies in multiple sclerosis: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. Neurology 2002; 58(2):169-178. Reaffirmed July 19, 2008.
  - The current evidence is inadequate to assess the value of IVIG in the treatment of multiple sclerosis. IVIg may be useful in individuals as a second-line therapy in acute relapses of RRMS, but is generally not considered effective for maintenance therapy of MS or in slowing disease progression.

BACKGROUND/SUMMARY

A position statement from the American Academy of Asthma, Allergy and Immunology (Orange, et al., 2005) states that "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.

CLINICAL PRACTICE GUIDELINES

American Academy of Neurology

Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (AAN 2012)

AAN's evidence-based guideline on "Intravenous immunoglobulin in the treatment of neuromuscular disorders" (Patwa et al, 2012) states the following:

- IVIg is as efficacious as plasmapheresis and should be offered for treating Guillain-Barré syndrome (GBS) in adults (Level A)
- IVIg is effective and should be offered in the long-term treatment of chronic inflammatory demyelinating polyneuropathy (Level A)
- IVIg is probably effective and should be considered for treating moderate-to-severe myasthenia gravis and multifocal motor neuropathy (Level B)
- IVIg is possibly effective and may be considered for treating non- responsive dermatomyositis in adults and Lambert-Eaton myasthenic syndrome (Level C)
- Evidence is insufficient to support or refute use of IVIG in the treatment of immunoglobulin M paraprotein-associated neuropathy, inclusion body myositis, polymyositis, diabetic radiculoplexoneuropathy, or Miller Fisher syndrome, or in the routine treatment of post-polio syndrome or in children with GBS (Level U)
- IVIg combined with plasmapheresis should not be considered for treating GBS (Level B). More data are needed regarding IVIG efficacy as compared with other treatments/treatment combinations.

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. 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 regarding 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.

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.

Cerebellar Functional System Score
The cerebellar functional system score was chosen to demonstrate initial disability and response.
Values of the cerebellar functional system score are:

0. Normal: no evidence of cerebellar dysfunction
1. Abnormal signs without disability
2. Mild ataxia
3. Moderate ataxia
4. Severe ataxia (all limbs or gait)
5. Unable to perform coordinated movements due to ataxia

Changes in opsoclonus symptoms will be rated as:

i. Deterioration in symptoms
ii. Symptoms stable
iii. Mild improvement
iv. Moderate improvement
v. Significant improvement

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.

The Inflammatory Neuropathy Cause and Treatment (INCAT) scale is used to access functional disability of both upper and lower extremity components in chronic inflammatory demyelinating polyneuropathy (CIDP). The INCAT scale has upper and lower extremity components, with a maximum of 5 points for the upper extremity (arm disability) and a maximum of 5 points for the lower extremity (leg disability), which add up to a maximum of 10 points (where 0 is normal and 10 is severely incapacitated). The INCAT scores may be used to evaluate the effectiveness and need for IVIG. IVIG may be discontinued when there is a lack of clear clinical improvement (i.e., a decline in INCAT disability score or failure to improve by 1 point at 6 weeks following the initial infusion or return to baseline at any time following initial improvement of 1 point).

The Medical Research Council (MRC) scale is used to grade muscle strength. Scale: 0 = no muscle movement; 1 = flicker of muscle movement; 2 = trace movement but not able to fully overcome gravity; 3 = just able to overcome gravity, but not against resistance; 4 = moves against resistance, but weak; 5 = full strength against resistance.

APPENDIX

Appendix 1: Comparative intravenous immune globulin (IVIg) preparations

Brand Name	Supplied As	IgA Content	Osmolality	Excipient Information	Filtration Requirements	Additional Notes
Bivigam	10% (liquid); 50 mL and 100 mL	≤ 200 mcg/mL	510 mOsm/kg	Glycine, polysorbate 80, NaCl	None	N/A
Carimune NF	3%, 6%, 9%, 12% (lyophilized); 3 g, 6 g, and 12 g	1,000-2,000 mcg/mL	192-1,074 mOsm/kg	Sucrose, NaCl	None	Osmolality varies based on concentration and diluent
Flebogamma DIF	5%, 10% (liquid); 5%: 10 mL, 50 mL, 100 mL, 200 mL, 400 mL; 10%: 50 mL, 100 mL, 200 mL	< 50 mcg/mL (5%); < 32 mcg/mL (10%)	240-370 mOsm/kg	Sorbitol, polyethylene glycol	None	N/A
Gammagard	10% (liquid); 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 300 mL	37 mcg/mL	240-300 mOsm/kg	Glycine	In-line filter optional	N/A
Gammagard S/D	5%, 10% (lyophilized); 2.5 g, 5 g, 10 g	≤ 2.2 mcg/mL or < 1 mcg/mL for 5%	636 mOsm/L (5%)	Glycine, dextrose, albumin, polyethylene glycol, octoxynol-9, polysorbate 80, tributyl phosphate	Supplied with 15 micron filter	2 low-IgA formulations available

Gammaked	10% (liquid); 10 mL, 25 mL, 50 mL, 100 mL, 200 mL	46 mcg/mL	258 mOsm/kg	Glycine, caprylate	None	N/A
Gammaplex	5% (liquid); 50 mL, 100 mL, 200 mL, 400 mL	< 10 mcg/mL	420-500 mOsm/kg	Glycine, polysorbate 80, sorbitol, NaCl, sodium acetate	None	Contraindicated if hereditary intolerance to fructose and in infants and neonates for whom sucrose or fructose intolerance has not been established
Gamunex-C	10% (liquid); 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 400 mL	46 mcg/mL	258 mOsm/kg	Glycine, caprylate	None	N/A
Octagam	5%, 10% (liquid); 5%: 20 mL, 50 mL, 100 mL, 200 mL, 500 mL; 10%: 20 mL, 50 mL, 100 mL, 200 mL	5%: ≤ 200 mcg/mL; 10%: 106 mcg/mL	310-380 mOsm/kg	Maltose, triton X-100, tributyl phosphate	In-line filter optional (0.2-200 microns)	Contraindicated if corn allergy; may falsely elevate glucose levels
Panzyga	10% (liquid): 10 mL, 25 mL, 50 mL, 100 mL, 200 mL, 300 mL	100 mcg/mL (average)	240-310 mOsm/kg	Glycine	Use in-line filter (0.2-200 microns)	Contraindicated in IgA-deficient patients with antibodies against IgA and history of hypersensitivity
Privigen	10% (liquid); 50 mL, 100 mL, 200 mL, 400 mL	≤ 25 mcg/mL	240-440 mOsm/kg	L-proline, albumin	None	Contraindicated in patients with hyperprolinemia

Abbreviation: IgA, immunoglobulin A; N/A, not applicable.

Reference: Table above adapted from DynaMed Plu. Ipswich (MA): EBSCO Information Services. 1995 - Record No. T915089, Comparative intravenous immune globulin (IVIg) preparations; [updated 2018 Dec 04, cited July 2019]. Available from https://www.dynamed.com/topics/dmp~AN~T915089. Registration and login required.

Appendix 2: Adjusted Body Weight Dosing

Dosing for IVIG is highly variable depending on numerous patient specific factors, indication(s), and the specific product selected. For specific dosing regimens refer to current prescribing literature.

Adjusted body weight

Dosing should be calculated using *adjusted* body weight if one or more of the following criteria are met:

- Individual's body mass index (BMI) is 30 kg/m2 or more; OR
- Individual's actual body weight is 20% higher than his or her ideal body weight (IBW)

Adjusted body weight (round dose to nearest 5 gram increment in adult patients) may be calculated with the following dosing formulas:

- BMI = 703 x (weight in pounds/height in inches^2)
- IBW (kg) for males = 50 + [2.3 (height in inches – 60)]
- IBW (kg) for females = 45.5 + [2.3 x (height in inches – 60)]
- Adjusted body weight = IBW + 0.5 (actual body weight – IBW)

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
90283	Immune Globulin (IgIV), human, for intravenous use
J1459	Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin, (Gammaplex), intravenous, non-lyophilized (e.g., liguid), 500 mg
J1561	Injection, immune globulin, (Gamunex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg (Only Carimune NF, Panglobulin NF and Gammagard S/D should be billed using this code)
J1568	Injection, immune globulin, (Octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard), intravenous, non-lyophilized, (e.g., liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1599	Injection, immune globulin, intravenous, non-lyophilized (e.g. liquid), not otherwise specified, 500 mg

J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg (Only Carimune NF, Panglobulin NF and Gammagard S/D should be billed using this code)
J1568	Injection, immune globulin, (Octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard), intravenous, non-lyophilized, (e.g., liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1599	Injection, immune globulin, intravenous, non-lyophilized (e.g. liquid), not otherwise specified, 500 mg

REFERENCES

Package Insert, FDA, Drug Compendia

- Asceniv (immune globulin intravenous [human]) [prescribing information]. Boca Raton, FL: ADMA Biologics; April 2019.
- Bivigam (immune globulin intravenous [human]) [prescribing information]. Boca Raton, FL: Biotest Pharmaceuticals Corporation; July 2019.
- Carimune NF (immune globulin intravenous [human]) [prescribing information]. Kankakee, IL: CSL Behring LLC; May 2018.
- Cutaquig (immune globulin subcutaneous human) [prescribing information]. New York, NY: Pfizer Labs; November 2020.
- Cuvitru (immune globulin subcutaneous [human]) [prescribing information]. Lexington, MA: Baxalta US Inc; May 2019.
- Flebogamma 5% DIF (immune globulin intravenous [human]) [prescribing information]. Barcelona, Spain: Instituto Grifols, SA; September 2019.
- Flebogamma 10% DIF (immune globulin intravenous [human]) [prescribing information]. Barcelona, Spain: Instituto Grifols; September 2019.
- Gammagard Liquid (immune globulin intravenous and subcutaneous [human]) [prescribing information]. Lexington, MA: Baxalta US Inc; July 2017.
- Gammagard S/D (immune globulin intravenous [human]) [prescribing information]. Westlake Village, CA: Baxalta US Inc; March 2017.
- Gammaked (immune globulin intravenous and subcutaneous [human]) [prescribing information]. Fort Lee, NJ: Kedrion Biopharma Inc; June 2018.
- Gammaplex 5% (immune globulin intravenous [human]) [prescribing information]. Durham, NC: BPL, Inc; September 2019.
- Gammaplex 10% (immune globulin intravenous [human]) [prescribing information]. Durham, NC: BPL; received January 2019.
- GamaSTAN (immune globulin intramuscular [human]) [prescribing information]. Research Triangle Park, NC: Grifols Therapeutics Inc; February 2018.
- Gamunex-C (immune globulin [human]) [prescribing information]. Research Triangle Park, NC: Grifols Therapeutics LLC; June 2018.

- Hizentra (immune globulin) [prescribing information]. Kankakee, IL: CSL Behring LLC; March 2020.
- HyQvia (immune globulin infusion 10% [human] with recombinant human hyaluronidase) [prescribing information]. Lexington, MA: Baxalta US Inc; January 2019.
- Octagam 5% (immune globulin intravenous [human]) [prescribing information]. Hoboken, NJ: Octapharma USA; January 2019.
- Octagam 10% (immune globulin intravenous [human]) [prescribing information]. Hoboken, NJ: Octapharma USA; August 2018.
- Panzyga (immune globulin intravenous [human]) [prescribing information]. Hoboken, NJ: Octapharma USA; August 2018.
- Privigen (immune globulin intravenous [human]) [prescribing information]. Kankakee, IL: CSL Behring LLC; March 2019.
- American Hospital Formulary Service (AHFS). Drug Information 2020 [STAT!Ref Web site]. Available at: http://online.statref.com [via subscription only]. Accessed May 2020.
- Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: www.clinicalpharmacology.com [Available with subscription]. Updated periodically. Accessed May 2020.
- Drug Facts and Comparisons. Facts and Comparisons eAnswers [online]. Clinical Drug Information LLC, 2020. Available from Wolters Kluwer Health, Inc. [Available with subscription] Accessed May 2020.
- Micromedex Healthcare Series [database online]. Greenwood Village, CO: Thomson Reuters (Healthcare) Inc. Updated periodically. http://www.thomsonhc.com. [Available with subscription]. Accessed May 2020.

CLINICAL TRIALS, DEFINITIONS, PEER-REVIEWED PUBLICATIONS

Autoimmune Mucocutaneous Blistering Diseases

- Ahmed AR and Dahl MV. Consensus Statement on the Use of Intravenous Immunoglobulin Therapy in the Treatment of Autoimmune Mucocutaneous Blistering Diseases. Arch Dermatol. 2003;139:1051-1059.
- Carlo Brugnara, C and Brodsky, RA. Warm autoimmune hemolytic anemia: Treatment. In: **UpToDate.** Mentzer, WC (Ed). Topic last updated: Aug 07, 2020. Available at: http://www.uptodate.com/contents/warm-autoimmune-hemolytic-anemia-treatment?source=see_link#H20 [via subscription]

Allogenic Bone Marrow Transplant (BMT)/ Allogenic Hematopoietic Stem Cell Transplantation (HSCT)

- Centers for Disease Control and Prevention. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients: recommendations of CDC, the Infectious Disease Society of America, and the American Society of Blood and Marrow Transplantation. MMWR 2000;49(No. RR-10):1-128.

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) or Polyradiculoneuropathy

- Sander HW, Latov N. Research criteria for defining patients with CIDP. Neurology. 2003; 608 (Suppl 3):S8-S15.

Dermatomyositis/Polymyositis

- Wang DX, Shu XM, Tian XL, et al. Intravenous immunoglobulin therapy in adult patients with polymyositis/dermatomyositis: a systematic literature review. Clin Rheumatol. 2012;31(5):801-6. Epub 2012 Jan 26.

Autoimmune Hemolytic Anemia (AIHA)

- Anderson D, Ali K, Blanchette V, et al. Guidelines on the use of intravenous immune globulin for hematologic conditions. Transfus Med Rev. 2007;21(2 Suppl 1):S9-56.

Neonatal hemochromatosis (FAIT/ NAIT)

- Knisely AS, Mieli-Vergani G, Whitington PF. Neonatal hemochromatosis. Gastroenterol Clin North Am. 2003 Sep;32(3):877-89, vi-vii.

Fetal or Natal Alloimmune Thrombocytopenia (FAIT/ NAIT)

- Bertrand G, Drame M, Martageix C, Kaplan C (2011) Prediction of the fetal status in noninvasive management of alloimmune thrombocytopenia. Blood 117: 3209-3213.
- Risson DC, Davies MW, Williams BA (2012) Review of neonatal alloimmune thrombocytopenia. J Paediatr Child Health 48: 816-822.
- American College of Obstetricians and Gynecologists (ACOG). Management of early pregnancy loss. ACOG Bulletin #24. 2001, Feb 12.
- American College of Obstetricians and Gynecologists: Thrombocytopenia in pregnancy. ACOG practice bulletin, Number 6, September 1999. Clinical management guidelines for obstetrician- gynecologists. Int J Gynaecol Obstet 1999 Nov; 67(2): 117-28.
- Fernandes CJ. Neonatal immune-mediated thrombocytopenia. UpToDate.
- Giers G, Wenzel F, Fischer J, et al. Retrospective comparison of maternal vs. HPA-matched donor platelets for treatment of fetal alloimmune thrombocytopenia. Vox Sang. 2010 Apr;98(3 Pt 2):423-30. Epub 2009 Oct 27.
- Paidas MJ. Neonatal alloimmune thrombocytopenia: Parental evaluation and pregnancy management. UpToDate. January 2016.

Guillain-Barre Syndrome (GBS)

- Hughes RA, et al. Intravenous immunoglobulin for Guillain-Barre syndrome. The Cochrane Library. 2004;(1):CD002063.
- Hughes RA, Wijdicks EF, Barohn R, et al. Practice parameter: immunotherapy for Guillain-Barré syndrome: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003; 61:736.
- Vriesendorp FJ. Treatment and prognosis of Guillain-Barré syndrome in adults. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed June 2015.
- Elovaara I, Apostolski S, van Doorn P, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. Eur J Neurol. 2008 Sep;15(9):893-908.

HIV-associated Thrombocytopenia: ADULTS

- Kiehl MG et al. "A controlled trial of intravenous immune globulin for the prevention of serious infections in adults with advanced human immunodeficiency virus infection." Arch Intern Med 1996;156:2545-50.

Pediatric HIV: Bacterial infection in HIV-infected children

- Mofenson, LM, Brady, MT, Danner, SP, et al. Guidelines for the Prevention and Treatment of Opportunistic Infections among HIV-exposed and HIV-infected children: recommendations from CDC, the National Institutes of Health, the HIV Medicine Association of the Infectious Diseases Society of America, the Pediatric Infectious Diseases Society, and the American Academy of Pediatrics. MMWR Recomm Rep. 2009 Sep 4;58(RR-11):1-166. PMID: 19730409
- Panel on Opportunistic Infections in HIV-Exposed and HIV-Infected Children. Guidelines for the prevention and treatment of opportunistic infections in HIV-exposed and HIV-infected children. Department of Health and Human Services. Updated November 2013. Available at: Link

Immune Thrombocytopenia (ITP)

- George J, Arnold D. Immune Thrombocytopenia (ITP) in adults: Initial Treatment and Prognosis. UpToDate. March 04, 2015. Available at: Link
- Bussel J. Immune Thrombocytopenia (ITP) in Children: Initial Management. UpToDate. April 8, 2015. Available at: Link
- Bussel J. Immune Thrombocytopenia (ITP) in Children: Management of Chronic Disease. UpToDate. December 12, 2014. Available at: Link.
- Martí-Carvajal AJ, Peña-Martí GE, Comunián-Carrasco G. Medical treatments for idiopathic thrombocytopenic purpura during pregnancy. Cochrane Database Syst Rev. 2009 Oct 7. CD007722.

Kawaski Disease (KD)

- Sundel, R. Incomplete (atypical) Kawasaki disease. In: UpToDate, Klein-Gitelman, M., UpToDate, Waltham, MA, 2015. Accessed January 2016.
- Sundel, R. Kawasaki disease: Initial treatment and prognosis. In: UpToDate, Klein-Gitelman, M., UpToDate, Waltham, MA, 2015. Accessed January 2016.
- American Academy of Pediatrics. Red Book: 2009 Report of the Committee on Infectious Diseases. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.
- Newburger JW, Takahashi M, Gerber MA et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. *Circulation*. 2004; 110:2747-71.
- Monagle P, Chalmers E, Chan A et al. Antithrombotic therapy in neonates and children: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest. 2008; 133(6 Suppl):887S-968S. [PubMed 18574281]
- Newburger JW, Takahashi M, Gerber MA, et al. Diagnosis, treatment, and long-term management of Kawasaki disease: a statement for health professionals from the Committee on Rheumatic Fever, Endocarditis and Kawasaki Disease, Council on Cardiovascular Disease in the Young, American Heart Association. Circulation 2004; 110:2747.

Lambert-Eaton Myasthenic Syndrome (LEMS)

- Elovaara, I, Apostolski, S, van Doorn, P, et al. European Federation of Neurological Societies (EFNS) guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. Eur J Neurol. 2008 Sep;15(9):893-908. PMID: 18796075
- Patwa, HS, Chaudhry, V, Katzberg, H, Rae-Grant, AD, So, YT. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology (AAN). Neurology. 2012 Mar 27;78(13):1009-15. PMID: 22454268
- Keogh, M, Sedehizadeh, S, Maddison, P. Treatment for Lambert-Eaton myasthenic syndrome. Cochrane Database Syst Rev. 2011(2):CD003279. PMID: 21328260
- Stickler DE, Huff JS, Kleinschmidt P. Lambert-Eaton Myasthenic Syndrome (LEMS) Treatment & Management. Updated: May 23, 2019 Available at: http://emedicine.medscape.com/article/1170810-treatment#showall. http://emedicine.medscape.com/article/1170810-medication

Multifocal Motor Neuropathy (MMN)

- Aminoff MJ, Greenberg DA, Simon RP. Sensory Disorders. In: Aminoff MJ, Greenberg DA, Simon RP, eds. *Clinical Neurology*. 9th ed. New York, NY: MCGraw-Hill; 2015.
- GBS-CIDP Foundation Guidelines. Available at: PTOT Guidelines
- Patwa HS, Chaudhry V, Katzberg H, Rae-Grant AD, So YT. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. *Neurology.* Mar 27 2012;78(13):1009-1015.
- van Schaik IN, van den Berg LH, de Haan R, Vermeulen M. Intravenous immunoglobulin for multifocal motor neuropathy. Cochrane Database Syst Rev. 2005(2):CD004429.

Myasthenia Gravis

- Donofrio PD, Berger A, Brannagan TH, et al. Consensus statement: The use of intravenous immunoglobulin in the treatment of neuromuscular conditions report of the AANEM ad hoc committee. Muscle Nerve. 2009;40:890-900.
- Elovaara I, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. European Journal of Neurology 2008;15(9):893-908.
- Hayes Medical Technology Directory. Intravenous Immunoglobulin for Myasthenia Gravis. Lansdale, PA: Hayes, Inc.; First published on October 5, 2012. Updated on Dec 29, 2016. Annual Review on Dec 17 2018
- Patwa HS, Chaudhry V, Katzberg H, et al. Evidence-based guideline: intravenous immunoglobulin in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2012 Mar 27;78(13):1009-15.
- Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis: Executive summary. Neurology 2016; 87:419.

Multiple Myeloma

- The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (Version 2.2014). © 2013 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org Accessed Feb 2016

Primary Immunodeficiency

- Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.
- Bonilla FA, Bernstein IL, Khan DA, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. Ann Allergy Asthma Immunol. 2005 May;94(5 Suppl 1): S1-63.
- American Academy of Allergy, Asthma, & Immunology. Eight Guiding Principles for Effective Use of IVIG for Patients with Primary Immunodeficiency. December 2011. Available at http://www.aaaai.org/practice-resources?Practice-Tools/ivig-toolkit.aspx.
- Yong PL, Boyle J, Ballow M, et al. Use of intravenous immunoglobulin and adjunctive therapies in the treatment of primary immunodeficiencies: A working group report of and study by the Primary Immunodeficiency Committee of the American Academy of Allergy Asthma and Immunology. Clin Immunol. 2010 May;135(2):255-63. doi: 10.1016/j.clim.2009.10.003. Epub 2009 Nov 14

Post-Transfusion Purpura (hemolytic transfusion reaction)

- Clare Taylor, et. al. Immunological Complications of Blood Transfusion. Transfusion Alter Transfusion Med. 2008;10(3):112-126. Available at: http://www.medscape.com/viewarticle/583195_7

Rasmussen syndrome

- Feasby T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. Transfusion Medicine Reviews 2007;21(2 Suppl 1):S57-107.
- Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.

Stiff-Person Syndrome

- Elovaara I, et al. EFNS guidelines for the use of intravenous immunoglobulin in treatment of neurological diseases: EFNS task force on the use of intravenous immunoglobulin in treatment of neurological diseases. European Journal of Neurology 2008;15(9):893-908.
- Feasby T, et al. Guidelines on the use of intravenous immune globulin for neurologic conditions. Transfusion Medicine Reviews 2007;21(2 Suppl 1):S57-107.
- Orange J, Hossny E, Weiler C, et al. Use of intravenous immunoglobulin in human disease: A review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. J Allergy Clin Immunol 2006;117(4 Suppl): S525-53.
- McKeon A, Robinson MT, McEvoy KM, et al. Stiff-man syndrome and variants: clinical course, treatments, and outcomes. Arch Neurol. 2012 Feb;69(2):230-8. doi: 10.1001/archneurol.2011.991.
- Levy LM, Dalakas MC, Floeter MK. The stiff-person syndrome: an autoimmune disorder affecting neurotransmission of gamma-aminobutyric acid. Ann Intern Med. 1999 Oct 5;131(7):522-30.

Toxic Shock Syndrome (TSS)

- Stevens, DL. Invasive group A streptococcal infection and toxic shock syndrome: Treatment and prevention. In: UpToDate [available via subscription]
- Department of Health Clinical Guidelines for Intravenous Immunoglobulin Use. 2011 Available at: www.ivig.nhs.uk
- Lappin E and Ferguson A. Gram-Positive Toxic Shock Syndromes. Lancet Infect Dis 2009; 9: 281-290

Professional Society Guidelines

Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019 Dec 10. 3 (23):3829-3866. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6963252/

Hallek M, Cheson BD, Catovsky D, et al. CLL International Working Group Guidelines. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018 Jun 21;131(25):2745-2760. doi: 10.1182/blood-2017-09-806398. Epub 2018 Mar 14. PMID: 29540348. Available at: https://ashpublications.org/blood/article/131/25/2745/37141/iwCLL-guidelines-for-diagnosis-indications-for

Policy History	Approval
Policy Developed	MCPC 12/6/2007

Revision* Peer Review. AMR Tracking Num: 257102. 4/23/2011. Board certified in Infectious Disease, Pediatrics Peer Review. AMR Tracking Num: 257109. 4/25/2011. Board certified in Pediatric Infectious Diseases, Pediatrics	MCPC 4/27/2011
Revision* Peer Review. AMR Tracking Num: 359146. 8/24/2012. Board certified in Internal Medicine, Oncology, Hematology	
Revision* Internal Review. Diana Cokingtin, Chair MCPC; MCPC members: M. Bloom MD; D. Green MD; M Siegel MD; B. Schatzman, PharmD.	MCPC 3/7/2016
Revision* Peer Review. AMR Tracking Num: 614710. 7/26/2019. Board certified in Oncology, Hematology Notable revisions: Myasthenia Gravis criterion revised: • Diagnosis criterion: Diagnosis of myasthenia gravis (Added: confirmed by positive serologic test for anti-acetylcholine receptor (AchR) antibodies) • Step/Conservative therapy Criterion: (Added: Currently receiving immunomodulator therapy (e.g., azathioprine, mycophenolate mofetil, cyclosporine) for long-term management of myasthenia gravis) • Reauthorization criterion: Revised from 'no reauthorization' to allow up to '3 months'	P&T Q3 2019
Annual Review* No coverage criteria changes or notable revisions with this annual review. Minor update however no change to intent: Added 'Drug Shortage' section	P&T Q3 2020
Revision* Peer Review. AMR Tracking Num: 1265845. 9/24/2020. Board certified in Oncology, Hematology Revised criteria include: Autoimmune Hemolytic Anemia (AIHA); Autoimmune Mucocutaneous Blistering Diseases (AMBDs); Fetal or Natal Alloimmune Thrombocytopenia (FAIT/ NAIT); Acute ITP in Adults; Chronic ITP in Adults; Lambert-Eaton Myasthenia Syndrome (LEMS); Myasthenia Gravis (Acute myasthenic crisis, Myasthenic Exacerbation); Allogenic Bone Marrow Transplant (BMT)/Hematopoietic Stem Cell Transplantation (HSCT).	Q4 2020

*NOTE: 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 for both 'Annual Reviews' and 'Revisions.' Revisions include notable content updates or revisions that which may have affected criteria or requires review by a practicing specialist, Peer Reviewer. The revisions noted below but may not be all-inclusive of all revised criteria and content in each policy; refer to MCP for all revisions and complete context.