Clinical Policy: Immune Globulins

Reference Number: LA.PHAR.103
Effective Date:
Last Review Date: 01.21
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are immune globulins requiring prior authorization: Asceniv™, Bivigam®, Carimune® NF, Cutaquig®, Cuvitru™, Flebogamma® DIF, GamaSTAN®, GamaSTAN® S/D, Gammagard®liquid, Gammagard® S/D, Gammaked™, Gammaplex®, Gamunex®-C, Hizentra®, HyQvia®, Octagam®, Panzyga®, Privigen®, and Xembify®.

FDA Approved Indication(s)

Brand Name	ROA	PI	ITP	CIDP	KS	MMN	CLL	VPPX
Asceniv	IV	x						
Bivigam	IV	x						
Carimune NF	IV	x	x					
Cutaquig	SC	x						
Cuvitru	SC	x						
Flebogamma DIF	IV	x	x (10% only)					
GamaSTAN, GamaSTAN S/D	IM							x
Gammagard Liquid	IV, SC	x				x (IV only)		
Gammagard S/D	IV	x	x		x		x	
Gammaked	IV, SC	x	x (IV only)	x (IV only)				
Gammaplex	IV	x	x					
Gamunex-C	IV, SC	x	x (IV only)	x (IV only)				
Hizentra	SC	x		x				
HyQvia	SC	x						
Octagam	IV	x (5% only)	x (10% only)					
Panzyga	IV	x	x					
Privigen	IV	x	x	x				
Xembify	SC	x						

ROA = route of administration; CIDP = chronic inflammatory demyelinating polyneuropathy; CLL = B-cell chronic lymphocytic leukemia; ITP = idiopathic thrombocytopenic purpura; KS = Kawasaki syndrome; MMN = multifocal motor neuropathy; PI = primary humoral immunodeficiency; VPPX = viral prophylaxis (for hepatitis A, measles, varicella, rubella)

CLINICAL POLICY
Immune Globulins

Contents:

Policy/Criteria

Prior authorization is required. Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections that immune globulins are medically necessary when the following criteria are met:

I. Initial Approval Criteria

A. B-Cell Chronic Lymphocytic Leukemia Infection Prophylaxis (must meet all):

1. **Diagnosis of B-cell CLL;**
2. **Prescribed by or in consultation with a hematologist, oncologist, or immunologist;**
3. **Current (within the last 6 months) hypogammaglobulinemia as evidenced by two separate measurements of immunoglobulin G (IgG) level less than 500 mg/dL;**

4. **Member has had recurrent serious bacterial infections (e.g., requiring IV antibiotics, hospitalization, or consultation with an infectious disease specialist) within the past 12 months;**
5. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
6. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on total body weight (TBW) or ideal body weight (IBW), whichever is less. For obese members, use adjusted body weight (adjBW). *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 400 mg per kg IV every 3 to 4 weeks;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

B. **Dermatomyositis, Polymyositis (off-label) (must meet all):**
1. **Diagnosis of dermatomyositis (DM) or polymyositis (PM);**
2. **Prescribed by or in consultation with a dermatologist, rheumatologist, neurologist, or neuromuscular specialist;**
3. **Failure of a 4-month trial of a systemic corticosteroid (e.g., prednisone) in combination with one of the following immunosuppressive agents, both at up to maximally indicated doses unless clinically significant adverse effects are experienced or all are contraindicated: methotrexate, azathioprine, cyclophosphamide, mycophenolate mofetil, tacrolimus, cyclosporine (*see Appendix D*);**
4. **For dermatomyositis requests only: Failure of a trial of rituximab, unless contraindicated, clinically significant adverse effects are experienced, or the member is diagnosed with juvenile dermatomyositis plus calcinosis;**
5. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
6. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2 g per kg IV per month;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

C. **Fetal/Neonatal Alloimmune Thrombocytopenia (off-label) (must meet all):**
1. **Diagnosis of fetal/neonatal alloimmune thrombocytopenia (FNAIT);**

2. **Prescribed by or in consultation with a hematologist, immunologist, perinatologist, or neonatologist;**
3. **Meets one of the following (a, b, c, or d):**
   a. **Previous pregnancy affected by FNAIT;**
   b. **Serological confirmation of FNAIT as evidenced by maternal-fetal HPA incompatibility;**
   c. **Nadir platelet count < 100 x 10^9/L at birth or within 7 days after birth of the affected child;**
   d. **Fetal intracranial hemorrhage;**
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a or b):**
   a. **Dose does not exceed 2 g per kg IV per week;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

D. Inflammatory Demyelinating Polyneuropathy (Acute/Guillain-Barre Syndrome or Chronic) (must meet all):

1. **Diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP)/Guillain-Barre Syndrome (GBS) or CIDP;**
2. **Prescribed by or in consultation with a neurologist or neuromuscular specialist;**
3. **Member meets one of the following (a – h):**
   a. **Inability to stand or walk at least 30 feet without assistance;**
   b. **ICU admission required for aspiration or mechanical ventilation;**
   c. **Miller-Fisher syndrome;**
   d. **Inability to raise head against gravity;**
   e. **Severe bulbar palsy (e.g., impaired gag reflex, dysarthria and/or dysphagia);**
   f. **Bilateral facial weakness;**
   g. **Autonomic dysfunction (e.g., unexplained dysrhythmia, blood pressure fluctuations, significant bowel or bladder involvement);**
   h. **Disease is progressive or relapsing for more than 2 months;**
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a, b, c, or d) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **For AIDP/GB: Dose does not exceed 0.4 g per kg per day IV for 5 days;**

b. **For CIDP: Dose does not exceed a loading dose of 2 g per kg IV given in divided doses over two to five consecutive days, following by maintenance dose of 1 g per kg IV every 3 weeks;**
c. **For CIDP: Dose does not exceed Hizentra 0.2 g per kg body weight SC per week, starting 1 week after last IVIG infusion or 0.4 g per kg body weight SC per week if evidence is submitted demonstrating worsening symptoms;**
d. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

E. Idiopathic Thrombocytopenic Purpura (Acute or Chronic) (must meet all):
1. **Diagnosis of acute or chronic ITP;**
2. **Prescribed by or in consultation with a hematologist;**
3. **Member meets one of the following (a or b):**
   a. **Failure of one of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated (i or ii):**
      i. **Systemic corticosteroids (e.g., prednisone);**
      i. **Rh_0(D) immune globulin (RhIG);**
      Prior authorization may be required for RhIG
   b. **Pregnant;**
4. **Member meets one of the following (a – e):**
   a. **Current (within the last 30 days) platelet count less than 30,000/µL;**
   b. **Actively bleeding;**
   c. **High risk of life-threatening hemorrhage;**
   d. **Splenectomy is scheduled;**
   e. **Pregnant;**
5. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
6. **Request meets one of the following (a, b, c, or d) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 1 g per kg IV for 1 to 2 days;**
   b. **Dose does not exceed 400 mg per kg per day IV for up to 5 days;**
   c. **For Gammagard S/D: Dose does not exceed 1 g per kg for up to 3 total doses QOD;**
   d. **Dose is supported by practice guidelines or peer-reviewed literatures for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

F. Kawasaki Syndrome Aneurysm Prevention (must meet all):

1. **Diagnosis of Kawasaki syndrome or incomplete (atypical) Kawasaki disease;**
2. **Prescribed by or in consultation with a cardiologist, allergist, immunologist, infectious disease specialist, or rheumatologist;**
3. **Prescribed concurrently with aspirin therapy, unless contraindicated or clinically significant adverse effects are experienced;**
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a, b, c, or d):**
   a. **Dose does not exceed 1 g per kg IV as a single infusion;**
   b. **Dose does not exceed 400 mg per kg IV daily for 4 consecutive days;**
   c. **Dose does not exceed 2 g per kg IV as a single infusion;**
   d. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration: One time approval (1 month)

G. Kidney Transplant (off-label) (must meet all):

1. **Member meets one of the following (a or b):**
   a. **If prescribed prior to kidney transplant, member has high levels of "anti-donor" antibodies (i.e., member is highly sensitized to the tissue of the majority of living or cadaveric donors because of "non-self" human leukocyte antigen (HLA) or ABO incompatibility);**
   b. **If prescribed following kidney transplant, used for the treatment of antibody-mediated rejection;**
2. **Prescribed by or in consultation with a nephrologist, transplant specialist, or hematologist;**
3. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
4. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 140 g IV per infusion;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

H. Multifocal Motor Neuropathy (must meet all):

1. **Diagnosis of MMN;**
2. **Prescribed by or in consultation with a neurologist or neuromuscular specialist;**
3. **Member meets one of the following (a or b):**

a. **Request is for Gammagard;**
b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**

4. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2.4 g per kg IV per month;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

I. **Multiple Myeloma Infection Prophylaxis (off-label) (must meet all):**
1. **Diagnosis of multiple myeloma (MM) with stable plateau phase disease;**
2. **Prescribed by or in consultation with an hematologist, oncologist, or immunologist;**
3. **Current (within the last 6 months) hypogammaglobulinemia as evidenced by two separate measurements of immunoglobulin G (IgG) level less than 600 mg/dL;**
4. **Member has had recurrent serious bacterial infections (e.g., requiring IV antibiotics, hospitalization, or consultation with an infectious disease specialist) within the past 12 months;**
5. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
6. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 400 mg per kg IV every 3 weeks;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

J. **Multiple Sclerosis (off-label) (must meet all):**
1. **Diagnosis of relapsing-remitting multiple sclerosis (MS);**
2. **Prescribed by or in consultation with a neurologist;**
3. **Failure of three FDA-approved disease-modifying MS therapies (e.g., Avonex, Aubagio, Betaseron, Rebif, Copaxone, Tecfidera, Gilenya) at up to maximally indicated doses, unless clinically significant side effects are experienced or all are contraindicated;**
   Prior authorization may be required for MS therapies
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**

b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**

5. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed an initial loading dose of 400 mg per kg IV for 5 days, followed by maintenance dose of 1 g per kg IV per month;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

K. **Myasthenia Gravis (MG)/Lambert Eaton Myasthenic Syndrome (LEMS) (off-label) (must meet all):**
1. **Diagnosis of myasthenia gravis (MG) or Lambert Eaton myasthenic syndrome (LEMS);**
2. **Prescribed by or in consultation with a neurologist or neuromuscular specialist;**
3. **Member meets one of the following (a, b, or c):**
   a. **Acute crisis (e.g., vital capacity less than 1 L/min, inability to walk 100 ft without assistance, intubation, dysphagia with aspiration, mechanical ventilation);**
   b. **Thymectomy surgery is scheduled;**
   c. **Failure of both of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated (i and ii):**
      i. **Amifampridine (for LEMS) or a cholinesterase inhibitor (e.g., pyridostigmine; for MG);**
      ii. **Systemic corticosteroid (e.g., prednisone) or immunosuppressant (e.g., azathioprine);**

   Prior authorization may be required for amifampridine
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2 g per kg IV for 2 to 5 days per treatment course;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

L. **Paraneoplastic Neurological Syndrome (off-label) (must meet all):**

1. **Diagnosis of one of the following subtypes of paraneoplastic neurological syndrome (a or b):**
   a. **Opsoclonus-myoclonus syndrome;**
   b. **Anti-NMDA encephalitis;**
2. **Prescribed by or in consultation with a neurologist, neuromuscular specialist, or oncologist;**
3. **For opsoclonus-myoclonus syndrome: Failure of at least one systemic corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;**
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a, b, c, or d) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2 g per kg IV per month;**
   b. **Dose does not exceed 0.4 g per kg IV per day;**
   c. **Dose does not exceed 200 mg per kg SC per week;**
   d. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

M. Parvovirus B19 Infection and Anemia (off-label) (must meet all):

1. **Diagnosis of anemia secondary to chronic parvovirus B19 infection;**
2. **Prescribed by or in consultation with a hematologist, infectious disease specialist, or immunologist;**
3. **Current (within the last 30 days) severe anemia (i.e., Hgb <10 or Hct < 30) due to bone marrow suppression;**
4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed an initial dose of 2 g per kg per day for up to 5 days, followed by maintenance dose of 400 mg per kg IV every 4 weeks;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

N. Pediatric Human Immunodeficiency Virus (HIV) Infection Prophylaxis (off-label) (must meet all):

1. **Prescribed for prophylaxis of serious bacterial infection in a child who has human immunodeficiency virus (HIV);**
2. **Prescribed by or in consultation with an HIV or infectious disease specialist;**
3. **Current (within the last 6 months) hypogammaglobulinemia as evidenced by two separate measurements of serum IgG concentration less than 400 mg/dL;**
4. **Member meets one of the following (a – e):**
   a. **Recurrent serious bacterial infections (defined as two or more infections such as bacteremia, meningitis, or pneumonia in a 12-month period);**
   b. **Inadequate antibody response to protein/polysaccharide antigens (e.g., measles, pneumococcal, and/or *Haemophilus influenzae* type b);**
   c. **Lives in an area where measles is highly prevalent and has not developed an antibody response after two doses of measles, mumps, and rubella virus live vaccine;**
   d. **Exposure to measles (requires a single dose);**
   e. **Chronic bronchiectasis that is suboptimally responsive to antimicrobial and pulmonary therapy;**
5. **Member meets one of the following (a or b):**
   a. Request is for Gammagard;
   b. Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;
6. **Request meets one of the following (a or b):**
   a. **Dose does not exceed 400 mg per kg IV every 2 to 4 weeks;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

O. Pemphigus Vulgaris, Pemphigus Foliaceus, Bullous Pemphigoid, Mucous Membrane Pemphigoid (a.k.a. Cicatricial Pemphigoid), Epidermolysis Bullosa Acquisita (off-label) (must meet all):

1. **Diagnosis of one of the following (a, b, c, d, or e):**
   a. **Pemphigus vulgaris;**
   b. **Pemphigus foliaceus;**
   c. **Bullous pemphigoid;**
   d. **Mucous membrane pemphigoid (a.k.a. cicatricial pemphigoid);**
   e. **Epidermolysis bullosa acquisita;**
2. **Prescribed by or in consultation with a dermatologist;**
3. **Failure of at least one corticosteroid (e.g., prednisone) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;**
4. **Failure of at least one immunosuppressive agent (e.g., cyclophosphamide, azathioprine, mycophenolate mofetil) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;**

5. **Failure of rituximab unless contraindicated or clinically significant adverse effects are experienced;**
   Prior authorization may be required for rituximab
6. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
7. **Request meets one of the following (a, b, c, or d) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2 gm per kg IV every 4 weeks;**
   b. **Dose does not exceed 400 mg per kg per day IV for 5 days (1 cycle only; may repeat up to three times in a 6-month period);**
   c. **Dose does not exceed 300 mg per kg per day IV for 5 days at monthly intervals (for up to 3 cycles);**
   d. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

P. Primary Immunodeficiencies (must meet all):
1. **Diagnosis of primary immunodeficiencies (PI), including any of the following (a – h):**
   a. Agammaglobulinemia (e.g., X-linked, congenital);
   b. Common variable immunodeficiency (CVID);
   c. Congenital hypogammaglobulinemia;
   d. Immunodeficiency with near/normal IgM (absent IgG, IgA) (also known as Hyper IgM syndrome);
   e. Selective immunodeficiency (e.g., selective IgA, IgM, or IgG subclass);
   f. Severe combined immunodeficiency disorders (SCID) (e.g., X-SCID, jak3, ZAP70, adenosine deaminase (ADA) deficiency, PNP, RAG defects, Ataxia Telangiectasia, Wiskott-Aldrich syndrome, DiGeorge syndrome);
   g. Subclass deficiency (*see Appendix D*);
   h. Functional/specific antibody deficiency (*see Appendix D*);
2. **Prescribed by or in consultation with an immunologist or hematologist;**
3. **Member meets one of the following (a or b):**
   a. **For functional/specific antibody deficiency, meets all of the following (i, ii, and iii):**
      i. Normal immune globulin levels;
      ii. Inadequate antibody response to polysaccharide antigens (e.g., pneumococcal);
      iii. Recurrent serious bacterial infections (e.g., requiring IV antibiotics, hospitalization, or consultation with an infectious disease specialist) within the past 12 months;

b. **Current (within the last 6 months) total or subclass immune globulin deficiency (below normal for age) as evidenced by two separate measurements of immunoglobulin level (*see Appendix E*) and one of the following (i, ii, iii, or iv):**
   i. **For ADA-SCID: failure (defined as experiencing continued recurrent serious bacterial infections) of Adagen®, Revcovi™, or hematopoietic stem cell transplant, unless contraindicated or clinically significant adverse effects are experienced;**
   Prior authorization may be required for Adagen and Revcovi
   ii. **SCID (not including ADA-SCID);**
   iii. **Recurrent serious bacterial infections (e.g., requiring IV antibiotics, hospitalization, or consultation with an infectious disease specialist) within the past 12 months;**
   iv. **Inadequate antibody response to protein/polysaccharide antigens (e.g., tetanus, diphtheria, pneumococcal);**

4. **Member meets one of the following (a or b):**
   a. **Request is for Gammagard;**
   b. **Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;**
5. **Request meets one of the following (a, b, c, or d) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. Dose does not exceed 800 mg per kg IV every 3 to 4 weeks;
   b. Dose does not exceed 600 mg per kg SC every 3 to 4 weeks;
   c. Dose does not exceed SC: initial dose of 1.37 x previous initial IV dose given 1 week after last IVIG infusion (*refer to section V. for product-specific dosing frequency*);
   d. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid– 6 months

Q. Stiff Person Syndrome (off-label) (must meet all):
1. **Diagnosis of stiff person syndrome (also known as Moersch-Woltmann syndrome);**
2. **Prescribed by or in consultation with a neurologist or neuromuscular specialist;**
3. **Failure of a benzodiazepine (e.g., diazepam) or baclofen at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;**
4. **Member meets one of the following (a or b):**
   a. Request is for Gammagard;
   b. Failure of Gammagard unless contraindicated or clinically significant adverse effects are experienced;

5. **Request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose does not exceed 2 g per kg IV for 2 to 5 days per treatment course;**
   b. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

R. Viral Prophylaxis for Hepatitis A, Measles, Varicella, Rubella Viruses (must meet all):
1. **Request is for intramuscular formulation;**
2. **Request is for one of the following indications (a, b, c, or d):**
   a. **Hepatitis A post-exposure/high-risk prophylaxis and meets both of the following (i and ii):**
      i. **Hepatitis A exposure or at high risk for exposure as evidenced by (a or b):**
         a) **Exposure to hepatitis A in the past 2 weeks (e.g., household contact, sexual contact, sharing illicit drugs with someone positive for hepatitis A, regular babysitters/caretakers, food handlers at the same establishment as one who is positive for hepatitis A) AND does not have clinical manifestations of hepatitis A;**
         b) **Traveling to or working in an area endemic for hepatitis A;**
      ii. **Meets at least one of the following (a, b, or c):**
         a) Hepatitis A vaccine is locally unavailable;
         b) History of severe allergic reaction (anaphylaxis) to the hepatitis A vaccine;
         c) If either exposed to the virus or traveling in ≤ 2 weeks to an area endemic for hepatitis A, then (1, 2, or 3):
            1) Age < 1 year or > 40 years;
            2) Chronic liver disease or other chronic medical condition;
            3) Immunocompromised;
   b. **Measles (rubeola) post-exposure prophylaxis and meets all of the following (i, ii, iii, and iv):**
      i. **Exposure to measles within the past 6 days;**
      ii. **Member has not previously received a measles vaccine;**
      iii. **Member has not previously had measles;**
      iv. **Meets at least one of the following (a – f):**
         a) **Measles vaccine is locally unavailable;**
         b) **History of severe allergic reaction (anaphylaxis) to the measles vaccine;**
         c) **Pregnancy;**
         d) **Immunocompromised;**
         e) **Has been > 3 days since exposure;**
         f) **Age < 12 months;**

c. **Chickenpox (varicella) post-exposure prophylaxis and meets all of the following (i, ii, iii, and iv):**
   i. **Exposure to varicella within the past 10 days;**
   ii. **Member lacks immunity to varicella;**
   iii. **Varicella zoster immune globulin (VZIG) is currently unavailable;**
   iv. **Meets any of the following (a – e):**
      a) **Varicella vaccine is locally unavailable;**
      b) **History of a severe allergic reaction (anaphylaxis) to the varicella vaccine;**
      c) **Pregnancy;**
      d) **Immunocompromised;**
      e) **Newborn of mother who had varicella from 5 days before to 2 days after delivery;**

d. **Rubella post-exposure prophylaxis (i and ii):**
   i. **Recent exposure to rubella;**
   ii. **Member is pregnant;**

2. **Request meets one of the following (a – e) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Hepatitis A (i, ii, or iii): Dose does not exceed:**
      i. **0.1 mL/kg IM once;**
      ii. **For anticipated exposure up to 2 months: 0.2 mL/kg IM once;**
      iii. **For anticipated exposure 2 months or longer: 0.2 mL/kg IM every 2 months;**
   b. **Measles: Dose does not exceed 15 mL IM once;**
   c. **Varicella: Dose does not exceed 1.2 mL/kg IM once;**
   d. **Rubella: Dose does not exceed 0.55 mL/kg IM once;**
   e. **Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Hepatitis A: Up to 6 months
All other indications: One time approval (1 month)

S. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.

II. Continued Therapy
A. Kawasaki Syndrome/Incomplete (Atypical) Kawasaki Disease, Viral Prophylaxis (Hep A, Measles, Varicella, Rubella)
1. **Re-authorization is not permitted. Members must meet the initial approval criteria.**

Approval duration: Not applicable

B. All Other Indications in Section I (must meet all):
1. **Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;**
2. **Member is responding positively to therapy (*see Appendix D for examples*);**
3. **If request is for a dose increase, request meets one of the following (a or b) [Note: for adults, calculate dosing based on TBW or IBW, whichever is less. For obese members, use adjBW. *(See Appendix F for weight-based dosing calculations.)*]:**
   a. **Dose titration or conversion is appropriate per package insert labeling;**
   b. **New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).**

Approval duration:
Medicaid– 6 months

C. Other diagnoses/indications (must meet 1 or 2):
1. **Currently receiving medication via Louisiana Healthcare Connections benefit and documentation supports positive response to therapy.**
   Approval duration: Duration of request or 6 months (whichever is less); or
2. **Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): LA.PMN.53 for Medicaid.**

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use LA.PMN.53 for Medicaid, or evidence of coverage documents;

B. The following are conditions for which treatment with immune globulins is considered not medically necessary:
1. **Acquired factor VIII inhibitors;**
2. **Adrenoleukodystrophy;**
3. **Alzheimers Disease;**
4. **Amyotrophic lateral sclerosis;**
5. **Angioedema;**
6. **Antiphospholipid syndrome;**
7. **Aplastic anemia;**
8. **Asthma;**
9. **Autism;**
10. **Autoimmune chronic urticaria;**
11. **Behçet's syndrome;**
12. **Cardiomyopathy, acute;**
13. **Chronic fatigue syndrome;**
14. **Chronic sinusitis;**
15. **Complex pain regional syndrome (CPRS);**
16. **Congenital heart block;**
17. **Critical illness myopathy (necrotizing myopathy) (ICD10: G7281);**

18. **Cystic fibrosis;**
19. **Dermatosis, autoimmune blistering;**
20. **Diabetes mellitus;**
21. **Diamond-Blackfan anemia;**
22. **Dysautonomia, acute idiopathic;**
23. **Eczema;**
24. **Encephalopathy, acute;**
25. **Endotoxemia;**
26. **Epilepsy;**
27. **Goodpasture's syndrome;**
28. **Hemolytic transfusion reaction;**
29. **Hemolytic-uremic syndrome;**
30. **Hemophagocytic syndrome;**
31. **Idiopathic lumbosacral flexopathy;**
32. **Idiopathic progressive neuropathy (ICD10: G603);**
33. **Immune-mediated neutropenia;**
34. **Inclusion body myositis;**
35. **Infection prevention and control in newborns;**
36. **Intractable seizures;**
37. **Iridocyclitis, unspecified (ICD10: H209);**
38. **Leukemia, acute lymphoblastic;**
39. **Lower motor neuron syndrome;**
40. **Multiple sclerosis - primary progressive or secondary types;**
41. **Myalgia, myositis, unspecified;**
42. **Myelopathy, HTLV-I associated;**
43. **Nephropathy, membranous;**
44. **Nephrotic syndrome;**
45. **Non-immune thrombocytopenia;**
46. **Ophthalmopathy, euthyroid;**
47. **Oral use;**
48. **Orbital myositis, bilateral (ICD10: H05123);**
49. **Other diseases of capillaries [Clarkson disease (systemic capillary leak syndrome)] (ICD10: I788);**
50. **Otitis media, recurrent;**
51. **Paraneoplastic cerebellar degeneration;**
52. **Paraproteinemic neuropathy;**
53. **Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS) [note: coverage exclusion of PANDAS does not apply to requests from Illinois, Indiana, and New Hampshire];**
54. **POEMS syndrome (see General Information – Section IV for definition);**
55. **Polyarteritis nodosa;**
56. **Progressive lumbosacral plexopathy;**
57. **Radiculoneuritis, Lyme;**
58. **Rasmussen's syndrome;**
59. **Recurrent otitis media;**

60. **Recurrent spontaneous pregnancy loss;**
61. **Refractoriness to platelet transfusion;**
62. **Reiter's syndrome;**
63. **Renal failure, acute;**
64. **Rheumatoid arthritis (adult and juvenile);**
65. **Scleroderma;**
66. **Secondary immunodeficiencies induced by biologic therapies;**
67. **Sensory neuropathy;**
68. **Systemic lupus erythematosis;**
69. **Systemic vasculitides;**
70. **Thrombocytopenia (non-immune);**
71. **Vasculitis associated with other connective tissue diseases;**
72. **Vogt-Koyanagi-Harada syndrome;**
73. **Wegener's granulomatosis.**

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACTH: adrenocorticotropic hormone
ADA: adenosine deaminase
adjBW: adjusted body weight
AIDP: acute inflammatory demyelinating polyneuropathy
CIDP: chronic inflammatory demyelinating polyneuropathy
CLL: chronic lymphocytic leukemia
CVID: common variable immunodeficiency
DIF: dual inactivation plus nanofiltration
FNAIT: fetal/neonatal alloimmune thrombocytopenia
FDA: Food and Drug Administration
GBS: Guillain Barre Syndrome
HIV: human immunodeficiency virus
HLA: human leukocyte antigen
HPA: human platelet antigen
IBW: ideal body weight
IG: immune globulin
IgA: immune globulin A
IgG: immune globulin G
IgM: immune globulin M
IMIG: intramuscular immune globulin
ITP: immune thrombocytopenic purpura
IVIG: intravenous immune globulin
MMN: multifocal motor neuropathy
NAIT: neonatal alloimmune thrombocytopenia
NF: nanofiltered
NMDA: N-methyl D-aspartate
PI: primary [humoral] immunodeficiency
POEMS: polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes
RhIG: Rh_0(D) immune globulin
SC: subcutaneous
SCID: severe combined immunodeficiency disorders
SCIG: subcutaneous immune globulin
S/D: solvent/detergent treated
TBW: total body weight
VZIG: varicella zoster immune globulin

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Adagen® (pegademase bovine)	ADA-SCID Initial: 10 U/kg IM for the first dose, 15 U/kg for the second dose, 20 U/kg for the third dose (each dose is given 7 days apart) Maintenance: 20 U/kg IM per week	20 U/kg/week
baclofen (Lioresal®)	Stiff Person Syndrome* 20 mg PO BID or TID, or 50 to 1,600 mcg/day intrathecally	PO: 80 mg/day IT: 1600 mcg/day
diazepam (Valium®)	Stiff Person Syndrome* 20 to 80 mg/day PO (given in divided doses)	Daily doses needed to control the disease can be as high as 100 to 200 mg/day in some patients
Firdapse® (amifampridine)	Lambert-Eaton Myasthenic Syndrome *Adults:* 15 mg to 30 mg PO in 3 to 4 divided doses daily. Dose can be increased by 5 mg daily every 3 to 4 days.	80 mg/day (20 mg/dose)
Ruzurgi® (amifampridine)	Lambert-Eaton Myasthenic Syndrome *Pediatric (age 6 to <17 years) and weight ≥ 45 kg:* 15 to 30 mg PO in 2 to 3 divided doses. Dose can be increased by 5 mg to 10 mg increments daily, divided in up to 5 doses per day. *Pediatric (age 6 to <17 years) and weight < 45 kg:* 7.5 mg to 15 mg PO in 2 to 3 divided doses. Dose can be increased by 2.5 mg to 5 mg increments daily, divided in up to 5 doses per day.	100 mg/day (30 mg/dose) for weight ≥ 45 kg; 50 mg/day (15 mg/dose) for weight < 45 kg)
pyridostigmine (Mestinon®); Mestinon® Timespan (pyridostigmine extended release)	Myasthenia Gravis Immediate Release (IR) tablets and syrup *Adults*: 60 to 1,500 mg PO daily in divided doses (avg 600 mg PO daily) *Pediatrics**: 1 mg/kg PO Q4 to 6 hrs Extended Release 180 to 540 mg PO QD or BID	IR: 1,500 mg/day (adults) or 7 mg/kg/day (pediatrics) ER: 1,080 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Revcovi™ (elapegademase-lvlr)	ADA-SCID Adagen-naïve: 0.2 mg/kg twice a week IM Transitioning from Adagen: 0.2 mg/kg weekly IM	0.4 mg/kg/week
Rhophylac, WinRho SDF (Rh_0(D) immune globulin)	Idiopathic Thrombocytopenic Purpura in non-splenectomized, Rh_0(D) antigen positive patients Initial: 50 mcg/kg IV Maintenance Therapy: 25 to 60 mcg/kg IV	75 mcg/kg*
Rituxan® (rituximab)	Pemphigus Vulgaris Initial: Two-1000 mg IV infusions separated by 2 weeks in combination with a tapering course of glucocorticoids Maintenance Therapy: 500 mg IV at month 12 and every 6 months thereafter Dermatomyositis/Polymyositis* 1,000 mg/m^2 IV weekly x 2 weeks	500 mg/6 months
Immunosuppressive agents		
azathioprine (Imuran®)	Dermatomyositis/Polymyositis*, Myasthenia Gravis* 2 mg/kg PO QD or 50 mg/day PO up to 2 to 3 mg/kg/day Pemphigus vulgaris and associated conditions* 2 to 3 mg/kg/day PO	3 mg/kg/day
cyclophosphamide (Cytoxan®)	Dermatomyositis/Polymyositis* 1 to 3 mg/kg/day PO QD or 500 mg IV every 2 weeks for 6 doses Pemphigus vulgaris and associated conditions* 50 to 75 mg/day PO or pulsed regimen of 500 mg IV on day, and then every 4 weeks thereafter in combination with oral cyclophosphamide and dexamethasone	Not applicable

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cyclosporine (Gengraf®, Neoral®, Sandimmune®)	Dermatomyositis/Polymyositis* 5 to 10 mg/kg/day PO	Not applicable
methotrexate (Rheumatrex®)	Dermatomyositis/Polymyositis* 10 to 25 mg/week PO/IV	50 mg/week
mycophenolate mofetil (Cellcept®)	Dermatomyositis/Polymyositis* 250 to 500 mg PO BID, increasing to a target dose of 1,500-3,000 mg/day Pemphigus vulgaris and associated conditions* 35 to 45 mg/kg/day PO or 1 g PO BID	DM/PM: 3 g/day PV, etc: 2 g/day
tacrolimus (Prograf®)	Dermatomyositis/Polymyositis* 0.075mg/kg/day PO BID OR begin at 1 mg PO BID, increase to reach trough of 5-10 ng/ml	Not applicable
Systemic corticosteroids (e.g., prednisone, prednisolone, methylprednisolone)	An equivalent dose of prednisone 1 mg/kg/day (with or without tapering)	2 mg/kg/day
Disease-modifying therapies for relapsing remitting MS		
Aubagio® (teriflunomide)	7 or 14 mg PO QD	14 mg/day
Avonex®, Rebif® (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Betaseron®, Extavia® (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone®, Glatopa®)	*Copaxone*: 20 mg SC QD or 40 mg SC TIW *Glatopa*: 20 mg SC QD	*Copaxone*: 20 mg/day or 40 mg TIW *Glatopa*: 20 mg/day
Gilenya™ (fingolimod)	0.5 mg PO QD	0.5 mg/day
Lemtrada® (alemtuzumab)	IV infusion for 2 treatment courses: • First course: 12 mg/day on 5 consecutive days	See regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	• Second course: 12 mg/day on 3 consecutive days 12 months after first course	
Novantrone® (mitoxantrone)	12 mg/m^2 given as a short (approximately 5 to 15 minutes) IV every 3 months	Cumulative lifetime dose of ≥ 140 mg/m^2
Ocrevus™ (ocreliuzmab)	Initial: 300 mg IV, then 300 mg IV 2 weeks later Maintenance: 600 mg IV every 6 months	600 mg/6 months
Plegridy® (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Tecfidera® (dimethyl fumarate)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day
Tysabri® (natalizumab)	300 mg IV every 4 weeks	300 mg/4 weeks
Zinbryta® (daclizumab)	150 mg SC once monthly	150 mg/month

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
****Off-label***

Appendix C: Contraindications/Boxed Warnings

- **Contraindication(s):**
  - **History of anaphylactic or severe systemic reactions to human immune globulin**
  - **IgA-deficient patients with antibodies against IgA and a history of hypersensitivity**
- **Boxed warning(s): thrombosis, renal dysfunction, and acute renal failure**

Appendix D: General Information

- **CLL:**
  - **These patients have a pattern of infection caused by encapsulated bacteria (*Haemophilus influenzae*, pneumococci, streptococci) which tends to be chronic and/or recurrent and does not demonstrate improvement with an adequate course of PO antibiotics and/or prophylactic antibiotics. Recurrent infections may include sinus infections, otitis media, bronchiectasis and pyogenic pneumonias.**
- **Dermatomyositis, Polymyositis:**
  - **Per the 2020 American Academy of Dermatology treatment guidelines for dermatomyositis, in cases where a combination of systemic corticosteroids and**

an oral immunosuppressant fail, rituximab is the appropriate next step in therapy. In individuals with vasculopathic or calcinotic lesions, adults with anti-MDA5 positivity, or children with NXP-2 positivity, rituximab plus systemic corticosteroids can be considered first-line treatment. Additionally, patients with juvenile dermatomyositis and calcinosis should be preferentially treated with IVIG because it has the best data supporting its use for calcinosis specifically.

- **IVIG may be medically necessary after less than 4 months trial of prednisone or prednisone combination therapies if the patient has profound, rapidly progressive and/or potentially life threatening muscular weakness (e.g., life-threatening aggressive disease with involvement of respiratory musculature, possibly requiring hospitalization, elective intubation and mechanical ventilatory support) and is refractory to or intolerant of previous therapy.**
- **Failure or clinically significant adverse effects to continual high dose steroids in combination with other immunosuppressive agents is defined as the patient being unresponsive or poorly responsive to therapy (persistently elevated serum creatine kinase (CK) levels and/or lack of improvement on muscle strength improvement scales) or intolerant of therapy (i.e., steroid myopathy or severe osteoporosis).**
- **Inclusion body myositis (IBM) is classified as one of the idiopathic inflammatory myopathies. However, despite some histologic similarities, the clinical manifestations, treatment and prognosis are different from DM and PM. IBM is relatively resistant to standard immunosuppressive therapy. In two clinical studies, IVIG was unable demonstrate objective improvement in the treatment of IBM.**

- **ITP:**
  - **Definitions of acute vs. chronic ITP:**
    - **Per an International Working Group consensus panel of ITP experts, ITP is defined as newly diagnosed (diagnosis to 3 months), persistent (3 to 12 months from diagnosis), or chronic (lasting for more than 12 months). Although not formally validated, these definitions are supported and used by the American Society of Hematology (ASH).**
    - **In clinical trials evaluating the efficacy and safety of IVIG in ITP, acute ITP was defined as condition duration of up to 6 months while chronic ITP was defined as condition duration of greater than 12 months.**
  - **Per the 2011 ASH guidelines, response to treatment was defined by the following:**
    - **A response would be defined as a platelet count ≥ 30,000/µL 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/µL 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.**
  - **There have been reports of fatal intravascular hemolysis with Rho(D) immune globulin and specific monitoring is required. This therapy is not necessarily recommended over IVIG but can be used instead in patients who are Rh**

positive, have a negative direct antiglobulin test (DAT), and have not had a splenectomy.
  - **For acute ITP, a single dose of IVIG is used as first line treatment. For adults, a second dose may be given if necessary.**
- **(Acute) Inflammatory Demyelinating Polyneuropathy or GBS:**
  - **GBS subtypes include the following: Acute inflammatory demyelinating polyneuropathy (AIDP), Acute motor axonal neuropathy (AMAN), Acute motor-sensory axonal neuropathy (AMSAN), and Miller Fisher Syndrome (MFS).**
  - **Miller Fisher syndrome is a rare, acute polyneuropathy characterized by ataxia (abnormal muscle coordination), ophthalmoplegia (paralysis of the eye muscles), and areflexia (absence of the reflexes).**
  - **Elevated CSF protein, with a normal CSF white blood cell count, is often present; fifty to 66 percent the first week of symptoms and ≥75 percent the third week.**
  - **GBS and AIDP typically progresses over 2 weeks, and the majority of patients achieve nadir of the disease by four weeks.**
  - **Initiation of IVIG within 2 weeks of symptom onset appears to be as effective as plasma exchange (PE).**
  - **The combination of IVIG and plasmaphoresis used together is not better than either treatment used alone.**
  - **The combination of IVIG and IV methylprednisolone was not more effective than IVIG alone.**
  - **Immunoabsorption is an alternative technique to PE that removes immunoglobulins. There is insufficient evidence to recommend the use of immunoabsorption for GBS.**
  - **CSF filtration is as effective as PE for treatment of GBS.**
  - **Pulmonary function risk factors include one or more of the following:**
    - **Forced vital capacity < 20 mL/kg**
    - **Maximal inspiratory pressure < 30 cm H2O**
    - **Maximal inspiratory pressure < 40 cm H2O**
    - **30% reduction in vital capacity from baseline**
- **(Chronic) Inflammatory Demyelinating Polyneuropathy or CIDP:**
  - **The definition of CIDP includes multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) variant or when Sensory CIDP exists with other causes of neuropathy such as diabetes and Charcot-Marie-Tooth (CMT), as evidenced by superimposed features of CIDP.**
  - **IVIG, corticosteroids, and plasmapheresis are all considered first-line treatments for patients with moderate to severe disability. Patient-specific factors may determine the appropriate choice of therapy.**
  - **As evidence of progression is more significant than the level of disability, mild cases of CIDP may not need to be treated aggressively if they are stable, but any signs of progression warrants effective treatment with IVIG to begin immediately.**

- **Plasmapheresis has not been shown to be more effective than IVIG, however, it may be used in patients who are unresponsive to both IVIG and corticosteroid therapy.**

- **Kawasaki:**
  - **The efficacy of IVIG administered in the acute phase of Kawasaki disease in reducing the prevalence of coronary artery abnormalities is well-established. The mechanism of action of IVIG in treating Kawasaki disease is unknown; however IVIG appears to have a generalized anti-inflammatory effect.**
  - **For patients with persistent or recurrent fever after initial IVIG infusion, IVIG retreatment may be useful. Failure to respond usually is defined as persistent or recrudescent fever ≥36 hours after completion of the initial IVIG infusion. Most experts recommend retreatment with IVIG, 2 g/kg. The putative dose-response effect of IVIG forms the theoretical basis for this approach.**
- **Kidney Transplant:**
  - **Louisiana Healthcare Connections considers the combination of IVIG and Rituxan (rituximab) for desensitization prior to renal transplantation, investigational at this time. Larger, prospective, randomized controlled trials are needed to evaluate the long-term efficacy and safety of this treatment and to compare this protocol with the current treatment of IVIG alone.**
  - **In a retrospective analysis of 50 kidney transplant patients at Johns Hopkins Hospital, all patients were live donor HLA incompatible recipients. Desensitization included plasmapheresis with low dose IVIG, mycophenolate and tacrolimus, and intraoperative induction therapy with anti-IL2 receptor antibodies. Twenty five of the higher risk patients also received rituximab (375 mg/m^2) the day prior to transplant. There was no significant difference in the incidence of acute rejection within the first 3 months of transplant between the two groups. Further randomized, controlled trials are still needed.**
- **MMN:**
  - **Although not required for diagnosis, the presence of a high titer (>1:1000) of serum Immunoglobulin M (IgM) antibody directed against ganglioside-monodialic acid (IgM Anti-GM1 antibodies) provides independent support for MMN (> 80% of patients).**
  - **Although no reports exist of controlled trials of immunosuppressive drugs in patients with multifocal motor neuropathy, there are a series of anecdotal reports of patients who transiently responded to oral or pulsed doses of cyclophosphamide, however, this treatment was associated with significant side effects, related in part to the cumulative dose of cyclophosphamide.**
- **MM:**
  - **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 is considered not medically necessary.**
  - **These patients have a pattern of infection caused by encapsulated bacteria (Haemophilus influenzae, pneumococci, streptococci) which tends to be chronic**

and/or recurrent and does not demonstrate improvement with an adequate course of PO antibiotics and/or prophylactic antibiotics. Recurrent infections may include sinus infections, otitis media, bronchiectasis and pyogenic pneumonias.

- **MS:**
  - **The clinical course of MS usually falls within one of the following categories, with the potential for progression from one pattern to a more serious one:**
    - **Relapsing-remitting MS: This form of MS is characterized by clearly defined acute attacks with full recovery or with some remaining neurological signs/symptoms and residual deficit upon recovery. The periods between disease relapses are characterized by a lack of disease progression.**
    - **Secondary progressive MS: The disease begins with an initial relapsing-remitting course, followed by progression at a variable rate that may also include occasional relapses and minor remissions.**
    - **Progressive-relapsing MS: Persons with progressive-relapsing MS experience progressive disease from onset, with clear, acute relapses that may or may not resolve with full recovery. Unlike relapsing-remitting MS, the periods between relapses are characterized by continuing disease progression.**
    - **Primary progressive MS: The disease shows gradual progression of disability from its onset, without plateaus or remissions or with occasional plateaus and temporary minor improvements.**
- **MG:**
  - **Myasthenia gravis (MG) is a disorder of neuromuscular function that is characterized by fatigue and weakness of the muscular system without atrophy or sensory deficits.**
  - **Myasthenia "Crisis" refers to exacerbation sufficient to endanger life, and usually involves respiratory failure in MG, therefore would not include disabled patients who are able to walk with or without assistance.**
  - **Intravenous Immunoglobulin (IVIG) has not been shown to be superior to plasmapheresis in the treatment of life-threatening myasthenia gravis.**
  - **High-dose IVIG may temporarily modify the immune system and suppress autoantibody production to improve severe myasthenia gravis symptoms. The effect of IVIG is seen typically in less than a week, and the benefit can last for three to six weeks. IVIG is used to quickly reverse an exacerbation of myasthenia.**
  - **According to the European Federation of Neurological Studies (EFNS) guidelines on the use of intravenous immunoglobulin in treatment of neurological diseases, the efficacy of IVIG has been proven acute exacerbations of myasthenia gravis and short-term treatment of severe MG (level A recommendation).**
  - **A small clinical trial conducted by Wegner and Ahmed showed that long-term IVIG was effective. This trial included six patients who were anti-AChR-Ab-positive. These patients received IVIG at a dosage of 400 mg/kg/day for 5 days then a maintenance therapy of 400 mg/kg for 1 day every 3 to 4 months. After a**

2 year follow up, all patients maintained a good functional status and side effects from IVIG did not increase.

- **NAIT:**
  - **NAIT is caused by maternal alloantibodies directed against fetal (paternally inherited) platelet antigens as a result of feto-maternal transplacental passage of incompatible platelets during pregnancy.**
  - **HPA-1a is the platelet-specific antigen implicated in most cases of neonatal alloimmune thrombocytopenia.**
  - **Administering IVIG to the mother during pregnancy is the most successful strategy for increasing the fetal platelet count and has become the recommended standard treatment of known fetal alloimmune thrombocytopenia.**
  - **Studies have shown that weekly infusions (1 g/kg maternal body weight) beginning at 20 to 24 weeks' gestation stabilize or increase the fetal platelet count in fetuses with documented alloimmune thrombocytopenia.**
  - **In very high-risk pregnancies (intracranial hemorrhage in a previous sibling before 30 weeks' gestation), some investigators recommend starting IVIG therapy as early as 12 to 14 weeks' gestation.**
  - **Although the mechanism of action of IVIG in FAIT is not clearly defined, it is postulated that IVIG decreases maternal alloantibodies and may also block transplacental transport of maternal antiplatelet antibodies.**
  - **There is still no consensus on the optimal protocol for managing IVIG after it is begun.**
- **Paraneoplastic Syndromes**
  - **Paraneoplastic syndromes are the remote effects of a cancer unrelated to the effects of the tumor or its metastasis. Sometimes they are associated with low immune globulin values and sometimes they are associated with autoantibodies.**
  - **The combination of IVIG, cyclophosphamide, and methylprednisolone in patients with paraneoplastic cerebellar degeneration and antineuronal antibodies in is not effective.**
  - **Anti-NMDA encephalitis**
    - **Although no standard of care for anti-NMDA encephalitis exists, on the basis of data from the reviews completed, concurrent IVIG (0.4 g/kg per day for 5 days) and methylprednisolone (1 g/day for 5 days) is preferred over plasma exchange.**
    - **If no response is seen after 10 days, a second-line therapy is started.**
    - **Although there is a paucity of randomized controlled and comparative trials regarding the use of IVIG for this disorder, because of the severity of anti-NMDA encephalitis and on the basis of data from the completed reviews and case series, it has been noted that individuals who received early tumor treatment (usually with immunotherapy) had better outcome and fewer neurological relapses than the rest of the patients,**
    - **IVIG given concurrently with corticosteroids has been determined to assist with full or substantial recovery in approximately 75% of the individuals with anti-NMDA encephalitis.**

- **Opsoclonus-myoclonus-syndrome or "dancing eyes-dancing feet" syndrome is a rare neurological disorder that affects infants and young children and has been described in adult patients with cancer**
  - **The current therapeutic strategies for OMS provide a broad spectrum of nonselective immunotherapies, including noncytotoxic and cytotoxic drugs, intravenous immunoglobulins, ACTH and plasma exchange**
  - **Intravenous immunoglobulin G is occasionally used as an alternative to ACTH.**
  - **Altogether, the available evidence suggests that IVIG may be an effective treatment in parainfectious and idiopathic OMS.**
  - **Treatment with IVIG has been reported in a few idiopathic adult-onset OMS cases in literature and they have concluded that idiopathic OMS presents an age dependent prognosis and immunotherapy. IVIG seems to be associated with a faster recovery.**
  - **Trends in the standard of care of OMS report that ACTH, prednisone, and intravenous immunoglobulin were used with equal frequency, but ACTH was associated with the best early response**

- **Parvovirus B19 Infection**
  - **Human parvovirus B19 infection can give rise to the loss of mature red blood cells, severe anemia and the formation of immune complexes.**
  - **A robust antibody response is necessary for virus clearance and control of the infection.**
  - **IVIG has been shown to be effective in recurrent infection in augmenting the inadequate humoral immune response. Based on the evidence available, IVIG therapy has become the standard of care if the aplastic crisis becomes prolonged, even though there are no definitive clinical trials demonstrating the efficacy of HPV B19-induced anemia.**
  - **Use of IVIG for treatment in parvovirus B19 infection is a category 2A NCCN recommendation**
  - **IVIG dose adjustments:**
    - **Adjustment of the IVIG dose and time interval between doses should be based on trough levels measured every month for the first three months of therapy and again at six months**
    - **Adjustments to infusion rates and measuring of serum IgG levels may be needed during infections or in persons who have a high catabolism of infused IgG**
    - **To reduce infection frequency in immunodeficient patients, serum trough levels should be maintained at 670-730 mg/dl, a value close to the lower limit of normal. All IgG trough levels outside of the low normal range of 6.7-7.3 mg/dl require dosage adjustment.**
- **Pemphigus Vulgaris and related conditions:**
  - **IVIG therapy for Pemphigus Vulgaris must be used only for short-term therapy and not as a maintenance therapy.**
  - **IVIG dose adjustments:**

- **Adjustment of the IVIG dose and time interval between doses should be based on trough levels measured every month for the first three months of therapy and again at six months**
- **Adjustments to infusion rates and measuring of serum (immunoglobulin G) IgG levels may be needed during infections or in persons who have a high catabolism of infused IgG**
- **To reduce infection frequency in immunodeficient patients, serum trough levels should be maintained at 670-730 mg/dl, a value close to the lower limit of normal. All IgG trough levels outside of the low normal range of 6.7-7.3 mg/dl require dosage adjustment.**

o **For Pemphigus Vulgaris, Pemphigus Foliaceus, Bullous Pemphigoid, Mucous Membrane Pemphigoid (a.k.a. Cicatricial Pemphigoid), Epidermolysis Bullosa Acquisita: the treatment is considered complete when the patient is free of disease after a 16-week interval between the last two infusion cycles;**

o **Examples of clinically significant adverse effects to corticosteroids, immunosuppressive agents (e.g., cyclophosphamide, azathioprine, mycophenolate mofetil) are diabetes or fractures from chronic steroid use.**

- **PI:**
  - o **Common variable immunodeficiency (CVID), the most frequently diagnosed primary immunodeficiency, is characterized by a low serum IgG level antibody deficiency at least 2 SDs below the mean for age, with most patients having concurrent deficiencies of IgA and IgM. Many Patients with CVID have IgG levels below 639 that require IVIG. However, there are rare instances when a patient will have normal IgG levels. The serum immunoglobulin measurement alone does not establish a diagnosis of CVID. A definitive diagnosis of CVID is established when a patient does not demonstrate a prolonged antibody response to immunization with protein antigens (e.g., tetanus) or carbohydrate antigens (e.g., pneumococcal capsular polysaccharides such as pneumovax).**
  - o **Subclass deficiency or IgG subclass deficiency (IGGSD) is diagnosed in patients with recurrent infections, deficiency in one or more IgG subclass levels (less than the 5th percentile or 2 standard deviations below), and normal total concentrations of IgG, IgM, and IgA.**
  - o **Specific antigen deficiency or functional antibody deficiency is diagnosed in patients 2 years and older who present with recurrent respiratory tract infections, normal immunoglobulin and IgG subclass levels, and impaired IgG response to pneumococcal capsular polysaccharide.**
  - o **The gamma globulin band consists of 5 immunoglobulins: about 80% immunoglobulin G (IgG), 15% immunoglobulin A (IgA), 5% immunoglobulin M (IgM), 0.2% immunoglobulin D (IgD), and a trace of immunoglobulin E (IgE).**
  - o **The use of intravenous immune globulin should be reserved for patients with serious defects of antibody function. All immune deficiency conditions require ongoing monitoring of the patient's clinical condition with measurement of pre-infusion (trough) serum IgG levels.**

- **For lifelong treatment serum trough IgG levels should be measured before the infusion, and then monitored every 3 months to maintain low normal level (usually 400 – 600 mg/dl).**
- **See Appendix E: Reference Ranges for Immune Globulin Levels**

- **Stiff person syndrome**
  - **Stiff person syndrome (also known as Moersch-Woltmann syndrome) is a rare progressive neurological disorder characterized by progressive rigidity and stiffness of the axial musculature, associated with painful spasms, primarily in the lower limbs, neck and trunk.**
  - **Symptoms are related to autoantibodies directed against glutamic acid decarboxylase in the nervous system called anti-GAD antibodies. This antibody marker, which is an antibody to an enzyme found both in the pancreas and in nerve tissue, is found in high concentrations in classical Stiff-man syndrome.**
  - **In most cases, improvement in symptoms occurs with combinations of diazepam and baclofen, often in reasonably high dosage. Where all drug treatments fail to give sufficient relief from spasms and pain, treatment is directed against the underlying immunologic condition with drug choices consisting of steroids (either intravenous or orally), plasma exchange or pooled IVIG.**
  - **Current treatments do not offer or lead to a cure. However, they are able to control symptoms in the majority of patients.**
- **Coverage is excluded for the following indications. The use of immune globulins for these indications is considered investigational due to lack of conclusive, evidence-based data with randomized controlled trials. As such, alternative therapies for these indications include:**
  - **Critical illness myopathy (necrotizing myopathy): corticosteroids (e.g., prednisone, methylprednisolone), immunosuppressive agents (e.g., cyclophosphamide, methotrexate, azathioprine)**
  - **Idiopathic progressive neuropathy: corticosteroids**
  - **Iridocyclitis, unspecified: corticosteroids**
  - **Orbital myositis, bilateral: corticosteroids**
  - **Other diseases of capillaries [Clarkson disease (systemic capillary leak syndrome)]: corticosteroids**

Appendix E: Reference Ranges for Immune Globulin Levels

- **The Mayo Clinic suggests the following reference ranges of immune globulins:**

Age	Total IgG	Total IgA	Total IgM
0 to < 5 months	100-334 mg/dL	7-37 mg/dL	26-122 mg/dL
5 to < 9 months	164-588 mg/dL	16-50 mg/dL	32-132 mg/dL
9 to < 15 months	246-904 mg/dL	27-66 mg/dL	40-143 mg/dL
15 to < 24 months	313-1,170 mg/dL	36-79 mg/dL	46-152 mg/dL
2 to < 4 years	295-1,156 mg/dL	27-246 mg/dL	37-184 mg/dL
4 to < 7 years	386-1,470 mg/dL	29-256 mg/dL	37-224 mg/dL
7 to < 10 years	462-1,682 mg/dL	34-274 mg/dL	38-251 mg/dL
10 to < 13 years	503-1,719 mg/dL	42-295 mg/dL	41-255 mg/dL

Age	Total IgG	Total IgA	Total IgM
13 to < 16 years	509-1,580 mg/dL	52-319 mg/dL	45-244 mg/dL
16 to < 18 years	487-1,327 mg/dL	60-337 mg/dL	49-201 mg/dL
≥ 18 years	767-1,590 mg/dL	61-356 mg/dL	37-286 mg/dL

- Some primary immunodeficiency disorders, such as functional antibody deficiency or specific antibody deficiency exhibit normal total IgG concentration but deficiencies in one or more IgG subclasses. The Mayo Clinic suggests the following references ranges:

Age	IgG1	IgG2	IgG3	IgG4
0 to < 5 months	56-215 mg/dL	≤ 82 mg/dL	7.6-82.3 mg/dL	≤ 19.8 mg/dL
5 to < 9 months	102-369 mg/dL	≤ 89 mg/dL	11.9-74.0 mg/dL	≤ 20.8 mg/dL
9 to < 15 months	160-562 mg/dL	24-98 mg/dL	17.3-63.7 mg/dL	≤ 22.0 mg/dL
15 to < 24 months	209-724 mg/dL	35-105 mg/dL	21.9-55.0 mg/dL	≤ 23.0 mg/dL
2 to < 4 years	158-721 mg/dL	39-176 mg/dL	17.0-84.7 mg/dL	0.4-49.1 mg/dL
4 to < 7 years	209-902 mg/dL	44-316 mg/dL	10.8-102.6 mg/dL	0.8-81.9 mg/dL
7 to < 10 years	253-1,019 mg/dL	54-435 mg/dL	8.5-102.6 mg/dL	1.0-108.7 mg/dL
10 to < 13 years	280-1,030 mg/dL	66-502 mg/dL	11.5-105.3 mg/dL	1.0-121.9 mg/dL
13 to < 16 years	289-934 mg/dL	82-516 mg/dL	20.0-103.2 mg/dL	0.7-121.7 mg/dL
16 to < 18 years	283-772 mg/dL	98-486 mg/dL	31.3-97.6 mg/dL	0.3-111.0 mg/dL
≥ 18 years	341-894 mg/dL	171-632 mg/dL	18.4-106.0 mg/dL	2.4-121.0 mg/dL

Appendix F: Weight-based Dose Calculations

- Cost-effective dosing of immune globulins is achieved by dosing based on the lesser of either total body weight (TBW; i.e., actual body weight) or ideal body weight (IBW).
  - IBW for males: 50 kg + (2.3 x inches over 5 feet)
  - IBW for females: 45.5 kg + (2.3 x inches over 5 feet)
- For obese members (e.g., BMI is ≥ 30 kg/m^2 or TBW is > 20-30% over IBW), adjusted body weight (adjBW) should be used for dose calculations.
  - AdjBW = IBW + [0.4 x (TBW-IBW)]
- Online adult IBW and adjBW calculator: https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight

- **Online BMI calculator:**
  https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

V. Dosage and Administration

Refer to full prescribing information for specific dosage instructions. Dosage must be individualized and is highly variable depending on the nature and severity of the disease and on the individual patient response (e.g., serum IgG trough levels). There is no absolute maximum dosage of immune globulin or hyaluronidase.

Drug Name	Indication	Dosing Regimen	Maximum Dose
Asceniv	PI	300 to 800 mg/kg IV every 3 to 4 weeks [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
Bivigam	PI	Initial: 300 to 800 mg/kg IV every 3 to 4 weeks Maintenance: IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
Carimune NF	ITP	Initial: 0.4 g/kg IV QD on 2 to 5 consecutive days Maintenance: 0.4 g/kg as a single IV infusion; if an adequate response does not result, the dose can be increased to 0.8-1 g/kg IV as a single infusion [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable

Drug Name	Indication	Dosing Regimen	Maximum Dose
	PI	**Initial: 0.4 to 0.8 g/kg IV every 3 to 4 weeks** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Cutaquig	**PI**	**Previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.40. Prorate the weekly dose and give SC at regular intervals QD to every 2 weeks beginning 1 to 2 weeks after last IV or SC dose depending on dosing regimen.** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Cuvitru	**PI**	**Initial: Previous IGIV/HyQvia dose in grams divided by number of weeks between IV doses and multiplied by 1.30. Prorate the weekly dose and give SC at regular intervals QD to every 2 weeks beginning 1 week after last IV or HyQvia dose.** **[Use TBW or IBW, whichever is *less*; if**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		member is obese, use adjBW – see *Appendix F*.]	
Flebogamma 5%	**PI**	**Initial: 300 to 600 mg/kg IV every 3 to 4 weeks** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Flebogamma 10%	**ITP**	**1 g/kg IV QD for 2 consecutive days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial: 300 to 600 mg/kg IV every 3 to 4 weeks** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Gamastan, Gamastan S/D	**Hepatitis A prophylaxis**	**Household and institutional case contacts: 0.1 mL/kg IM once** **Travel to Hepatitis A-endemic areas:** **Up to 1 month stay: 0.1 mL/kg IM once**	**0.1 mL/kg as a single dose or 0.2 mL/kg every 2 months**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Up to 2 months stay: 0.2 mL/kg IM once **2 months or longer stay: 0.2 mL/kg IM every 2 months** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	
	Measles postexposure prophylaxis	**0.25 mL/kg IM once** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**0.25 mL/kg**
	Rubella postexposure prophylaxis	**0.55 mL/kg IM once** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**0.55 mL/kg**
	Varicella postexposure prophylaxis	**0.6 to 1.2 mL/kg IM once** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**1.2 mL/kg**
Gammagard Liquid	**MMN**	**0.5 to 2.4 g/kg/month IV** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial:** **IV: 300 to 600 mg/kg every 3 to 4 weeks** **SC: Previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.37**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Maintenance: **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **SC: given once weekly with dose adjusted per PI** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	
Gammagard S/D	**CLL**	**400 mg/kg IV every 3 to 4 weeks** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	ITP	**1 g/kg IV, up to 3 doses on alternate days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	KS	**1 g/kg IV single dose or 400 mg/kg IV QD for four consecutive days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial:** **IV: 300 to 600 mg/kg every 3 to 4 weeks** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		per serum IgG level and clinical response [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	
Gammaked	CIDP	Loading dose: 2 g/kg IV given in divided doses over 2 to 4 consecutive days Maintenance dose: 1 g/kg IV every 3 weeks [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
	ITP	1 g/kg IV QD given on 2 consecutive days or 0.4 g/kg IV QD given on 5 consecutive days [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
	PI	Initial: IV: 300 to 600 mg/kg every 3 to 4 weeks SC: Previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.37 Maintenance: IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response SC: given once weekly with dose adjusted per PI	Not applicable

Drug Name	Indication	Dosing Regimen	Maximum Dose
		[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	
Gammaplex	**ITP**	**1 g/kg IV QD for 2 consecutive days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial: 300 to 800 mg/kg IV every 3 to 4 weeks** **Maintenance: IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Gamunex-C	**CIDP**	**Initial: 2 g/kg IV given in divided doses over 2 to 4 consecutive days** **Maintenance: 1 g/kg IV on one day or 0.5 g/kg IV on two consecutive days, every 3 weeks** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	ITP	**1 g/kg IV QD on 2 consecutive days, or 0.4 g/kg IV QD given on 5 consecutive days**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	
	PI	**Initial:** **IV: 300 to 600 mg/kg every 3 to 4 weeks** **SC: Previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.37** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response** **SC: given once weekly with dose adjusted per PI** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Hizentra	**CIDP**	**0.2 to 0.4 g/kg SC per week** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial weekly dose: previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.37. Prorate the weekly dose to give SC at regular intervals QD to every 2 weeks beginning 1 to 2 weeks after last IV or SC**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		dose depending on dosing regimen. [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	
HyQvia	PI	If IG therapy naïve or switching from IGSC: 300 to 600 mg/kg every 3 to 4 weeks after initial ramp-up (see manufacturer labeling) If switching from IGIV therapy: Give SC at same dose and frequency as previous IV therapy after initial ramp-up (see manufacturer labeling) [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
Octagam 5%	PI	Initial: 300 to 600 mg/kg IV every 3 to 4 weeks Maintenance: IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response [Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	Not applicable
Octagam 10%	ITP	1 g/kg IV QD for 2 consecutive days [Use TBW or IBW, whichever is *less*; if	Not applicable

Drug Name	Indication	Dosing Regimen	Maximum Dose
		member is obese, use adjBW – see *Appendix F*.]	
Panzyga	**PI**	**300 to 600 mg/kg IV every 3 to 4 weeks** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	ITP	**1g/kg IV QD for 2 consecutive days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
Privigen	**CIDP**	**Loading dose: 2 g/kg IV in divided doses over 2 to 5 consecutive days** **Maintenance dose: 1 g/kg IV every 3 weeks** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	ITP	**1 g/kg IV QD for 2 consecutive days** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**
	PI	**Initial: 200 to 800 mg/kg IV every 3 to 4 weeks** **Maintenance:** **IV: given every 3 to 4 weeks with dose adjusted per serum IgG level and clinical response**	**Not applicable**

Drug Name	Indication	Dosing Regimen	Maximum Dose
		[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]	
Xembify	**PI**	**Previous IGIV dose in grams divided by number of weeks between IV doses and multiplied by 1.37. Prorate the weekly dose and give SC at regular intervals QD to every week beginning 1 week after last IV dose.** **Or** **Previous SC weekly dose administered in regular intervals with prorated doses QD to every week.** **[Use TBW or IBW, whichever is *less*; if member is obese, use adjBW – see *Appendix F*.]**	**Not applicable**

VI. Product Availability

Drug	Availability
IV administration - ready to use	
Asceniv (10%)	**Single-use vial: 5 gram**
Bivigam (10%)	**Single-use vial: 5, 10 gram**
Flebogamma DIF (5%)	**Single-use vial: 0.5, 2.5, 5, 10, 20 gram**
Flebogamma DIF (10%)	**Single-use vial: 5, 10, 20 gram**
Gammaplex (5%)	**Single-use bottle: 5, 10, 20 gram**
Gammaplex (10%)	**Single-use bottle: 5, 10, 20 gram**
Octagam (5%)	**Single-use bottle: 1, 2.5, 5, 10, 25 gram**
Octagam (10%)	**Single-use bottle: 2, 5, 10, 20, 30 gram**
Panzyga (10%)	**Single-use bottle: 1, 2.5, 5, 10, 20, 30 gram**
Privigen (10%)	**Single-use vial: 5, 10, 20, 40 gram**
IV administration - lyophilized powder for reconstitution	
Carimune NF	**Single-use vial: 6, 12 gram**
IV administration - freeze dried for reconstitution	
Gammagard S/D	**5% single-use bottle: 5 gram** **10% single-use bottle: 10 gram**
IV or SC administration - ready to use	

Drug	Availability
Gammagard Liquid (10%)	Single-use bottle: 1, 2.5, 5, 10, 20, 30 gram
Gammaked (10%)	Single-use bottle: 1, 2.5, 5, 10, 20 gram
Gamunex-C (10%)	Single-use vial: 1, 2.5, 5, 10, 20, 40 gram
SC administration - ready to use	
Cutaquig (16.5%)	Single-use vial: 165 mg/mL
Cuvitru (20%)	Single-use vial: 1, 2, 4, 8, 10 gram
Hizentra (20%)	Single-use vial: 1, 2, 4, 10 gram Single-use prefilled syringe: 1, 2, 4 gram
HyQvia (10%) IgG and 160 U/mL recombinant human hyaluronidase* *Hyaluronidase increases permeability of the local SC tissue for approximately 24 to 48 hours.	Single-use dual vial set: 2.5 g/25 mL, 5 g/50 mL, 10 g/100 mL, 20 g/200 mL, 30 g/300 mL
Xembify (20%)	Single-use vial: 1, 2, 4, 10 gram
IM administration – ready to use	
GamaSTAN (16.5%)	Single-use vial: 2 mL and 10 mL
GamaSTAN S/D (15-18%)	Single-use vial: 2 mL and 10 mL

VII. References

1. Asceniv Prescribing Information. Boca Raton, FL: ADMA Biologics; April 2019. Available at: https://www.fda.gov/media/122525/download. Accessed May 6, 2020.
2. Bivigam Prescribing Information. Boca Raton, FL: Biotest Pharmaceuticals Corporation; July 2019. Available at: http://www.bivigam.com/clientuploads/pdfs/Prescribing_Information.pdf. Accessed May 6, 2020.
3. Carimune NF Prescribing Information. Kankakee, IL: CSL Behring, LLC; May 2018. Available at: http://labeling.cslbehring.com/PI/US/Carimune%20NF/EN/Carimune%20NF-Prescribing-Information.pdf. Accessed May 6, 2020.
4. Cutaquig Prescribing Information. Hoboken, NJ: Octapharma USA, Inc; November 2019. Available at: https://www.fda.gov/media/119234/download. Accessed May 6, 2020.
5. Cuvitru Prescribing Information. Westlake Village, CA: Baxalta US, Inc.; May 2019. Available at: http://www.shirecontent.com/PI/PDFS/Cuvitru_USA_ENG.PDF. Accessed May 6, 2020.
6. Flebogamma 10% DIF Prescribing Information. Los Angeles, CA: Grifols Biologicals, Inc.; September 2019. Available at: https://www.grifols.com/documents/10192/63615/flebo10-ft-us-en/f477695f-32d7-4d2b-bdb6-85f49d8eab67. Accessed May 6, 2020.
7. Flebogamma 5% DIF Prescribing Information. Los Angeles, CA: Grifols Biologicals, Inc.; September 2019. Available at: http://www.grifols.com/documents/10192/69257/ft_flebogamma_5_dif_eeuu_EN/2224ef9e-34e5-4808-afde-d470dba5825d. Accessed May 6, 2020.

8. **GamaSTAN Prescribing Information. Research Triangle Park, NC: Grifolis Therapeutics, Inc.; February 2018. Available at: https://www.hypermunes.com/documents/31474919/31475109/Prescribing+Information+GamaSTAN/d04d3e20-f4ee-48c6-9bce-7f29f6eb39ab. Accessed May 6, 2020.**
9. **GamaSTAN S/D Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; February 2018. Available at: http://www.grifolsusa.com/documents/10192/61676/ft_gamastan_s_d_immune_globulin_eeuu.en/01c7af9f-49f6-4b84-9c36-5593d06bb9fc. Accessed May 21, 2019.**
10. **Gammagard Liquid Prescribing Information. Westlake Village, CA: Baxalta US Inc.; June 2016. Available at: http://www.gammagard.com/MMN/prescribing-information.html. Accessed May 6, 2020.**
11. **Gammagard S/D Prescribing Information. Westlake Village, CA: Baxalta US Inc.; August 2017. Available at: http://www.baxter.nl/downloads/healthcare_professionals/products/GGSD_Low_IgA_PI.pdf. Accessed May 6, 2020.**
12. **Gammaked Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics Inc.; June 2018. Available at: http://www.gammaked.com/. Accessed May 6, 2020.**
13. **Gammaplex 5% Prescribing Information. Durham, NC: BPL Inc.; September 2019. Available at: http://www.gammaplex.com/. Accessed May 6, 2020.**
14. **Gammaplex 10% Prescribing Information. Durham, NC: BPL Inc.; September 2019. Available at: http://www.gammaplex.com/. Accessed May 6, 2020.**
15. **Gamunex-C Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics, Inc.; January 2020. Available at: http://www.gamunex-c.com/en/web/gamunex/hcp/home. Accessed May 6, 2020.**
16. **Hizentra Prescribing Information. Kankakee, IL: CSL Behring LLC; March 2020. Available at: http://www.hizentra.com/professional/prescribing-information.aspx. Accessed May 6, 2020.**
17. **HyQvia Prescribing Information. Westlake Village, CA: Baxalta US Inc.; February 2020. Available at: http://www.hyqvia.com/. Accessed May 6, 2020.**
18. **Octagam 5% Prescribing Information. Hoboken, NJ: Octapharma USA, Inc.; September 2019. Available at: http://www.octagamus.net/B.840.014.USA_420x340_02_2014.pdf. Accessed May 6, 2020.**
19. **Octagam 10% Prescribing Information. Hoboken, NJ: Octapharma USA, Inc.; August 2018. Available at: http://www.octagamus.net/. Accessed May 6, 2020.**
20. **Panzyga Prescribing Information. Hoboken, NJ: Octapharma; August 2019. Available at: https://www.fda.gov/files/vaccines,%20blood%20&%20biologics/published/Package-Insert---PANZYGA.pdf. Accessed May 6, 2020.**
21. **Privigen Prescribing Information. Kankakee, IL: CSL Behring, LLC; March 2019. Available at: http://labeling.cslbehring.com/PI/US/Privigen/EN/Privigen-Prescribing-Information.pdf. Accessed May 6, 2020.**

22. **Xembify Prescribing Information. Research Triangle Park, NC: Grifols Therapeutics LLC; July 2019. Available at: https://www.fda.gov/media/128601/download. Accessed May 6, 2020.**
23. **Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 6, 2020.**
24. **Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/.**

B-Cell Chronic Lymphocytic Leukemia Infection Prophylaxis

25. **Hallek M, Cheson BD, Catovsky D, et al. iwCLL guidelines for diagnosis, indications for treatment, response assessment, and supportive management of CLL. Blood. 2018. 131(25):2745-2760.**
26. **National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2019. Available at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed May 21, 2019.**
27. **Raanani P, Gafter-Gvili A, Paul M, et al. Immunoglobulin prophylaxis in chronic lymphocytic leukemia and multiple myeloma: a systematic review and meta-analysis. Leuk Lymphoma. 2009; 50:764.**

Dermatomyositis/Polymyositis

28. **Dalakas MC, Koffman B, Fujii M, Spector S, Sivakumar K, Cupler E. A controlled study of intravenous immunoglobulin combined with prednisone in the treatment of IBM. Neurology 2001;56:323-7.**
29. **Dalakas MC, Sonies B, Dambrosia J, Sekul E, Cupler E, Sivakumar K. Treatment of inclusion-body myositis with IVIG: a double-blind, placebo-controlled study. Neurology 1997;48:712-6.**
30. **Lam CG, Manlhiot C, Pullenayegum EM, Feldman BM. Efficacy of intravenous Ig therapy in juvenile dermatomyositis. Ann Rheum Dis 2011 Dec;70(12):2089-94.**
31. **Marie I, Mouthon L. Therapy of polymyositis and dermatomyositis. Autoimmun Rev. 2011 Nov;11(1):6-13.**
32. **Miyasaka N, Hara M, Koike T, et al. Effects of intravenous immunoglobulin therapy in Japanese patients with polymyositis and dermatomyositis resistant to corticosteroids: a randomized double-blind placebo-controlled trial. Mod Rheumatol 2012;22(3):382-93.**
33. **Patwa HS, Chaudhry V, So YT, 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. Available at: http://www.guideline.gov/content.aspx?id=36895&search=inflammatory+demyelinating. Accessed May 15, 2018.**
34. **Waldman R, DeWane ME, Lu J. Dermatomyositis: diagnosis and treatment. J Am Acad Dermatol. 2020;82:283-96.**
35. **Oddis CV, Reed AM, Aggarwal R, et al. Rituximab in the treatment of refractory adult and juvenile dermatomyositis and adult polymyositis: a randomized, placebo-phase trial. Arthritis Rheum. 2013 February;65(2):314-24.**

Fetal/Neonatal Alloimmune Thrombocytopenia

36. **Brojer E, Husebekk A, Debska M, et al. Fetal/neonatal alloimmune thrombocytopenia: pathogenesis, diagnostics and prevention. Arch Immunol Ther Exp. 2016;64:279-290.**

37. **Pacheco LD, Berkowitz RL, Moise KJ Jr, et al. Fetal and neonatal alloimmune thrombocytopenia: a management algorithm based on risk stratification. Obstet Gynecol. 2011;118(5):1157-63.**
38. **Petermann R, Bakchoul T, Curtis BR, et al. Investigations for fetal and neonatal alloimmune thrombocytopenia: communication from the SSC of the ISTH. Journal of Thrombosis and Haemostasis. 2018; 16:2526-9.**
39. **Peterson JA, McFarland JG, Curtis BR, Aster R. Neonatal alloimmune thrombocytopenia: pathogenesis, diagnosis, and management. British Journal of Haematology. 2013;161:3-14.**

Inflammatory Demyelinating Polyneuropathy (Acute/Guillain-Barre Syndrome)

40. **El-Bayoumi MA, El-Refaey AM, Abdelkader AM, et al. Comparison of intravenous immunoglobulin and plasma exchange in treatment of mechanically ventilated children with Guillain Barré syndrome: a randomized study. Crit Care 2011 Jul 11;15(4):R164.**
41. **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.**
42. **Hughes RAC, Wijdicks EFM, Barohn R, et al. Practice parameter: immunotherapy for Guillain-Barre syndrome. Report of the Quality Standards subcommittee of the American Academy of Neurology. AAN. 2003;61(6).**
43. **Koler RC, Montemarano A. Dermatomyositis. Am Fam Physician. 2001 Nov 1;64(9):1565-1573. Available at: http://www.aafp.org/afp/20011101/1565.html.**

Inflammatory Demyelinating Polyneuropathy (Chronic)

44. **Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society–First Revision. European Journal of Neurology. 2010;17: 356-363. Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1468-1331.2009.02930.x/epdf15.**
45. **Sander HW, Latov N. Chronic Inflammatory Demyelinating Polyradiculoneuropathy Neurology. 2003 Apr 1; 60(8 Suppl 3): S8-15. Available at: http://www.cidpusa.org/P/VARIANTA.htm. Accessed May 15, 2018.**

Idiopathic Thrombocytopenic Purpura (Acute or Chronic)

46. **George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guidelines developed by explicit methods for the American Society of Hematology. Blood 1996;88(1):3-40.**
47. **Neunert C, Lim W, Crowther M, et al. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood 2011;117(16):4190-4207.**
48. **Portielje JEA, Westendorp RGJ, Kluin-Nelemans HC, Brand A. Morbidity and mortality in adults with idiopathic thrombocytopenic purpura. Blood 2001;97(9):2549-2554.**
49. **Provan D, Stasi R, Newland AC, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. Blood. 2010;115(2):168-86.**

Kawasaki Syndrome or Incomplete (Atypical) Kawasaki Disease

50. **McCrindle B, Rowley AH, Newburger JW, et al. Diagnosis, treatment, and long-term management of Kawasaki disease. Circulation. 2017;135:e927-e999.**

Kidney Transplant

51. **Habicht A, Bröker V, Blume C, et al. Increase of infectious complications in ABO-incompatible kidney transplant recipients–a single centre experience. Nephrol Dial Transplant. 2011 Dec;26(12):4124-31. Epub 2011 May 28.**
52. **Jordan SC, Toyoda M, Kahwaji J, et al. Clinical aspects of intravenous immunoglobulin use in solid organ transplant recipients. Am J Transplant. 2011 Feb;11(2):196-202. Epub 2011 Jan 10.**
53. **KDIGO 2009 guidelines for Kidney transplant.**
54. **Taal: Brenner and Rector's The Kidney, 9th ed. 2011 Saunders, An Imprint of Elsevier. Kidney Transplantation.**
55. **Vo AA. Use of intravenous immune globulin and rituximab for desensitization of highly HLA-sensitized patients awaiting kidney transplantation. Transplantation. May 15, 2010; 89 (9): 1095-102.**
56. **Jordan SC, Vo AA, Peng A, et al. Intravenous Gammaglobulin (IVIG): A Novel Approach to Improve Transplant Rates and Outcomes in Highly HLA-Sensitized Patients. American Journal of Transplantation 2006;6: 459-466. Available at: http://www.blackwell-synergy.com/doi/pdf/10.1111/j.1600-6143.2005.01214.x?cookieSet=1**
57. **Clinicaltrials.gov. Desensitization of Highly Sensitized Deceased Donor Renal Transplantation Candidates. ClinicalTrials.gov Identifier: NCT00986947. Available at: http://www.clinicaltrials.gov/ct2/show/NCT00986947?term=Rituximab+and+Intravenous+Immunoglobulin+%28IVIG%29+for+Desensitization+in+Renal+Transplantation&rank=3. Accessed January 24, 2017**
58. **Clinicaltrials.gov. Rituximab + Immune Globulin Intravenous (IVIG) for Desensitization. ClinicalTrials.gov Identifier: NCT01178216. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01178216?term=Rituximab+and+Intravenous+Immunoglobulin+%28IVIG%29+for+Desensitization+in+Renal+Transplantation&rank=2. Accessed January 24, 2017**
59. **Clinicaltrials.gov. Desensitization Protocol for Highly Sensitized Patients on the Waiting List for Kidney Transplant. ClinicalTrials.gov Identifier: NCT01502267. Available at: http://www.clinicaltrials.gov/ct2/show/NCT01502267?term=Rituximab+and+Intravenous+Immunoglobulin+%28IVIG%29+for+Desensitization+in+Renal+Transplantation&rank=4. Accessed January 24, 2017**

Multifocal Motor Neuropathy

60. **Azulay JP, Blin O, Pouget J, et al. Intravenous immunoglobulin treatment in patients with motor neuron syndromes associated with anti-GM1 antibodies: a double-blind, placebo-controlled study. Neurology 1994;44(3 Pt 1):429-32.**
61. **Harbo T, Andersen H, Jakobsen J. Long-term therapy with high doses of subcutaneous immunoglobulin in multifocal motor neuropathy. Neurology 2010;75(15):1377-80.**

62. **Lehmann HC, Hartung HP. Plasma exchange and intravenous immunoglobulins: mechanism of action in immune-mediated neuropathies. J Neuroimmunol 2011;231(1-2):61-9.**
63. **Olney RK, Lewis RA, Putnam TD, Campellone JV Jr. Consensus criteria for the diagnosis of multifocal motor neuropathy. Muscle Nerve 2003;27:117-121. National Guideline Clearinghouse. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of paraproteinemic demyelinating neuropathies. Report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society. J Peripher Nerv Syst 2006;11(1):9-19.**

Multiple Myeloma

64. **Blombery P, Prince HM, Worth LJ, et al. Prophylactic intravenous immunoglobulin during autologous haemopoietic stem cell transplantation for multiple myeloma is not associated with reduced infectious complications. Ann Hematol. 2011 Oct;90(10):1167-72.**
65. **Chapel HM, Hargreaves R, et al. Randomized trial of intravenous immunoglobulin as prophylaxis against infection in plateau-phase multiple myeloma. Lancet. 1994; 343: 1059-1063.**
66. **National Comprehensive Cancer Network. Multiple Myeloma Version 2.2019. Available at http://www.nccn.org. Accessed May 21, 2019.**
67. **National Comprehensive Cancer Network. Prevention and Treatment of Cancer-Related Infections Version 1.2019. Available at http://www.nccn.org. Accessed May 21, 2019.**
68. **Musto P, Brugiatelli M, Carotenuto M. Prophylaxis against infections with intravenous immunoglobulins in multiple myeloma. Br J Haematol. 1995 Apr;89(4):945-6**

Multiple Sclerosis

69. **Blombery P, Prince HM, Worth LJ, et al. Prophylactic intravenous immunoglobulin during autologous haemopoietic stem cell transplantation for multiple myeloma is not associated with reduced infectious complications. Ann Hematol. 2011 Oct;90(10):1167-72.**
70. **Clerico M, Rivoiro C, Contessa G, et al. The therapy of multiple sclerosis with immune-modulating or immunosuppressive drug: a critical evaluation based upon evidence based parameters and published systematic reviews. Clin Neurol Neurosurg. 2008;110(9):878-85**
71. **Engelhardt B, Kappos L. Natalizumab: targeting alpha4-integrins in multiple sclerosis. Buttmann M, Rieckmann P. Treating multiple sclerosis with monoclonal antibodies. Expert Rev Neurother. 2008 Mar;8(3):433-55.**
72. **Fiore D. Multiple sclerosis and Natalizumab. Am J Ther. 2007 Nov-Dec;14(6):555-60.**
73. **Greenberg BM, Balcer L, Calabresi PA, et al. Interferon Beta Use and Disability Prevention in Relapsing-Remitting Multiple Sclerosis. Arch Neurol. 2012 Nov 5:1-4.**
74. **Horga A, Horga de la Parte JF. Natalizumab in the treatment of multiple sclerosis. Rev Neurol. 2007 Sep 1-15;45(5):293-303.**
75. **Mareckova H, Havrdova E, Krasulova E, et al. Natalizumab in the treatment of patients with multiple sclerosis: first experience. Ann N Y Acad Sci. 2007 Sep;1110:465-73.**

76. **Miller AE, Rhoades RW. Treatment of relapsing-remitting multiple sclerosis: current approaches and unmet needs. Curr Opin Neurol. 2012 Feb;25 Suppl:S4-10**
77. **Zohren F, Toutzaris D, Klärner V, et al. The monoclonal anti-VLA-4 antibody natalizumab mobilizes CD34+ hematopoietic progenitor cells in humans. Blood. 2008 Apr 1;111(7):3893-5.**

Myasthenia Gravis (MG) and Lambert Eaton Myasthenic Syndrome (LEMS)

78. **Barth D, Nabavi Nouri M, Ng E, Nwe P, Bril V. Comparison of IVIg and PLEX in patients with myasthenia gravis. Neurology. 2011 Jun 7;76(23):2017-23.**
79. **Gilhus NE, Owe JF, Hoff JM, et al. Myasthenia gravis: a review of available treatment approaches. Autoimmune Dis. 2011;2011:847393.**
80. **Keogh M, Sedehizadeh S, Maddison P. Treatment for Lambert-Eaton myasthenic syndrome. Cochrane Database Syst Rev. 2011 Feb 16;(2):CD003279**
81. **Kim JY, Park KD, Richman DP. Treatment of myasthenia gravis based on its immunopathogenesis. J Clin Neurol. 2011 Dec;7(4):173-83.**
82. **Lindquist S, Stangel M. Update on treatment options for Lambert–Eaton myasthenic syndrome: focus on use of AP. Neuropsychiatr Dis Treat 2011; 7: 341–349.**
83. **Sanders DB, Wolfe GI, Benatar M, et al. International consensus guidance for management of myasthenia gravis. Neurology. 2016;87(4): 419-425.**

Parvovirus B19 Infection and Anemia

84. **Crabol Y, Terrier B, Rozenberg F, et al. Intravenous immunoglobulin therapy for pure red cell aplasia related to human parvovirus b19 infection: a retrospective study of 10 patients and review of the literature. Clin Infect Dis. 2013;56(7);968-77.**
85. **Frickhofen N, Abkowitz JL, Safford M, et al. Persistent B19 parvovirus infection in patients infected with human immunodeficiency virus type 1 (HIV-1): a treatable cause of anemia in AIDS. Ann Intern Med. 1990;113(12):926-33.**
86. **Koduri PR. Parvovirus B19-related anemia in HIV-infected patients. AIDS Patient Care STDS. 2000;14(1):7-11.**
87. **Moudgil A, Shidban H, Nast CC, et al. Parvovirus B19 infection-related complications in renal transplant recipients: treatment with intravenous immunoglobulin. Transplantation. 1997;64(12):1847-50.**

Pediatric Human Immunodeficiency Virus (HIV) Infection Prophylaxis

88. **Falloon J, Eddy J, Wiener L, Pizzo PA. Human immunodeficiency virus infection in children. J Pediatr. 1989 Jan;114(1):1-30.**
89. **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. 2009; 55(RR11);1-166.**
90. **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. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf. Bacterial Infections Section accessed May 21, 2019.**

91. **Pastori D, Esposito A, Mezzaroma I. Immunomodulatory effects of intravenous immunoglobulins (IVIGs) in HIV-1 disease: a systematic review. Int Rev Immunol. 2011 Feb;30(1):44-66**
92. **The National Institute of Child Health and Human Developments Intravenous Immunoglobulin Study Group. Intravenous immune globulin for the prevention of bacterial infections in children with symptomatic human immunodeficiency virus infection. N Engl J Med. Jul 11 1991;325(2):73-80..**

Pemphigus Disorders

93. **Ahmed A. IVIG therapy in the treatment of patients with bullous pemphigus unresponsive to conventional immunosuppressive treatment. J Am Acad. Derm. 2001;45:1.**
94. **Bystryn JC, Jiao D, Natow S. Treatment of pemphigus with intravenous immunoglobulin. J Am Acad Dermatol. 2002;47(3):358-63.**
95. **Harman KE, Albert S, Black MM. Guidelines for the management of pemphigus vulgaris. Br J Dermatol 2003 Nov;149(5):926-37. Available at: http://www.bad.org.uk/library-media%5Cdocuments%5CPemphigus_vulgaris_2003.pdf. Accessed January 13, 2017.**
96. **Ishii N, Hashimoto T, Zillikens D, et al. High-dose intravenous immunoglobulin (IVIG) therapy in autoimmune skin blistering diseases. Clin Rev Allergy Immunol 2010; 38:186.**
97. **Murrell DF, Pena S, Joly P, et al. Diagnosis and management of pemphigus: recommendations by an international panel of experts. J Am Acad Dermatol. 2018 Feb 10. Pii: S0190-9622(18)30207-X. doi: 10.1016/j.jaad.2018.02.021. [Epub ahead of print]**
98. **Sami N, Qureshi A, Ruocco E, Ahmed AR. Corticosteroid-sparing effect of intravenous immunoglobulin therapy in patients with pemphigus vulgaris. Arch Dermatol. 2002;138(9):1158-62.**

Primary Immunodeficiencies

99. **Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015;136(5):1186-1205.e78**
100. **Calvelli TA, Rubinstein A. Intravenous gamma-globulin in infant acquired immunodeficiency syndrome. Pediatr Infect Dis. 1986 May-Jun;5(3 Suppl):S207-10.**
101. **Eijkhout HW, van Der Meer JW, Kallenberg CG, et al. The effect of two different dosages of intravenous immunoglobulin on the incidence of recurrent infections in patients with primary hypogammaglobulinemia. A randomized, double-blind, multicenter crossover trial. Ann Intern Med. 2001 Aug 7;135(3):165-74.**
102. **Kohn DB, Hershfield MS, Puck JM, et al. Consensus approach for the management of severe combined immune deficiency caused by adenosine deaminase deficiency. J Allergy Clin Immunol. 2019;143(3):852. Epub 2018 Sep 5.**
103. **Stiehm ER. Human intravenous immunoglobulin in primary and secondary antibody deficiencies. Pediatr Infect Dis J. 1997 Jul;16(7):696-707.**

Stiff Person Syndrome

104. **Gnanapavan S, Vincent A, Giovannoni G. Surviving stiff-person syndrome: a case report. J Neurol. 2011 Oct;258(10):1898-900.**

Viral Prophylaxis for Hepatitis A, Measles, Varicella, Rubella Viruses

105. **Chart of contraindications and precautions to commonly used vaccines (childhood and adult vaccines). In: Centers for Disease Control. Available at: https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/contraindications.html. Last reviewed July 12, 2017; last updated May 10, 2019. Accessed May 21, 2019.**
106. **Control and Prevention of Rubella: Evaluation and Management of Suspected Outbreaks, Rubella in pregnant women, and surveillance for congenital rubella syndrome. In: Centers for Disease Control, MMWR Recomm Rep. 2001; 50(RR-12):1-23. Available at: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5012a1.htm. Accessed May 15, 2018.**
107. **Measles (Rubeola). In: Centers for Disease Control. Available at: http://www.cdc.gov/measles/hcp/. Last reviewed February 5, 2018/updated May 8, 2018. Accessed May 15, 2018.**
108. **Viral Hepatitis – Hepatitis A Information. In: Centers for Disease Control. Available at http://www.cdc.gov/hepatitis/hav/havfaq.htm. Last reviewed/updated May 8, 2019. Accessed May 21, 2019.**

Multiple Indications

109. **Agarwal S, Cunningham-Rundles C. Assessment and clinical interpretation of reduced IgG values. Annals of Allergy, Asthma and Immunology Sept 2007 99;3:281-283**
110. **Agrawal RV, Murthy S, Sangwan V, Biswas J. Current approach in diagnosis and management of anterior uveitis. Indian J Ophthalmol. 2010;58(1):11–19. Doi:10.4103/0301-4738.58468**
111. **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.**
112. **Kirch W, Gold R, Hensel M, et al. Assessment of immunoglobulins in a long-term non-interventional study (SIGNS Study). Rationale, design, and methods. Med Klin (Munich). 2010 Sep;105(9):647-51.**
113. **Kubota T. Orbital myositis. In: Idiopathic Inflammatory Myopathies – Recent Developments. JT Gran, ed. Rijeka, Croatia; InTech Europe; September 2011. Available at: http://www.intechopen.com/books/idiopathic-inflammatory-myopathies-recent-developments/orbital-myositis. Accessed January 20, 2020.**
114. **Liu X, Treister R, Lang M, Oaklander AL. IVIg for apparently autoimmune small-fiber polyneuropathy: first analysis of efficacy and safety. Ther Adv Neurol Disord. 2018;11:1756285617744484.**
115. **Mayo Clinic immune globulin lab values accessed at: http://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/8156.**
116. **Ramanathan S, Langguth D, Hardy TA, et al. Clinical course and treatment of anti-HMGCR antibody-associated necrotizing autoimmune myopathy. Neurol Neuroimmunol Neuroinflamm. 2015;2(3):e96.**
117. **Patil AK, Prabhakar AT, Sivadasan A, et al. An unusual case of inflammatory necrotizing myopathy and neuropathy with pipestem capillaries. Neurol India. 2015;63(1):72-76.**

118. **Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. J Allergy Clin Immunol. March 2017;139(3):S1-S46.**
119. **Petiot P, Choumert A, Hamelin L, et al. Necrotizing autoimmune myopathies. Rev Neurol (Paris). 2013;169(8-9):650-655.**
120. **Shinder R, Nasser QJ, Brejt S, et al. Idiopathic inflammation of the orbit and contiguous structures. Ophthal Plast Reconstr Surg. 2012;28(4):10.**
121. **Szenborn L. The use of immunoglobulins in the treatment of infectious diseases. Pol Merkur Lekarski. 2011 Jun;30(180):441-7.**
122. **Xie Z, Chan EC, Long LM, Nelson C, Druey KM. High-dose intravenous immunoglobulin therapy for systemic capillary leak syndrome (Clarkson disease). Am J Med. 2015 Jan;128(1):91-5.**

Weight-based Dosing

123. **Grindeland JW, Grindeland CJ, Moen C, et al. Outcomes associated with standardized ideal body weight dosing of intrevenous immune globulin in hospitalized patients: a multicenter study. Ann Pharmacother. Mar 2020;54(3):205-12.**
124. **Stump SE, Schepers AJ, Jones AR, et al. Comparison of weight-based dosing strategies for intravenous immunoglobulin in patients with hematologic malignancies. Pharmacotherapy. Dec 2017;37(12):1530-6.**
125. **Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. J Allergy Clin Immunol. 2017;139:S1-46.**
126. **Figgins BS, Aitken SL, Whited LK. Optimization of intravenous immune globulin use at a comprehensive cancer center. AJHP. Dec 2019;76(Suppl 4):S102-6.**
127. **Fouche A, Oprica C, Sankaranarayanan J, et al. Retrospective evalulation of IVIG use: appropriateness and potential cost savings from body-weight dosing at a Northeastern tertiary hospital in the United States. RRJHCP. Sep 2016;2(3):19-26.**
128. **Anderson CR, Olson JA. Correlation of weight-based i.v. immune globulin doses with changes in serum immunoglobulin G levels. Am J Health-Syst Pharm. Feb 2015;72:285-9.**

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. 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.

HCPCS Codes	Description
C9270	Injection, immune globulin (Gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1459	Injection, immune globulin (Privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1555	Injection, immune globulin (Cuvitru), 100 mg
J1556	Injection, immune globulin (Bivigam), 500 mg
J1557	Injection, immune globulin (Gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg

HCPCS Codes	Description
J1559	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin (Gamunex-C/Gammaked), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1566	Injection, immune globulin, intravenous, lyophilized (e.g., powder), not otherwise specified, 500 mg
J1568	Injection, immune globulin (Octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin (Gammagard liquid), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1572	Injection, immune globulin (Flebogamma/Flebogamma DIF), intravenous, non-lyophilized (e.g., liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase (Hyqvia), 100 mg immunoglobulin
J1599	Injection, immune globulin, intravenous, nonlyophilized (e.g., liquid), not otherwise specified, 500 mg

Reviews, Revisions, and Approvals	Date
Converted corporate to local policy	01.21

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or

regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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