Intravenous Immune Globulin (IVIG) Therapy

NDC CODE(S)  59730-6502-XX - Bivigam 5 g protein
             59730-6503-XX - Bivigam 10 g protein
             44206-0416-XX - Carimune NF 3 g protein
             44206-0417-XX - Carimune 6 g protein
             44206-0418-XX - Carimune 12 g protein
             61953-0005-XX - Flebogamma 10% DIF 5, 10, 20 g protein
             61953-0004-XX - Flebogamma 5% DIF 2.5, 5, 10, 20 g protein
             13533-0800-XX - Gamunex-C 1, 2.5, 5, 10, 20, 40 g protein
             00944-2700-XX - Gammagard Liquid - 1, 2.5, 5, 10, 20, 30 g protein
             00944-2656-XX - Gammagard S/D 5 g protein
             00944-2658-XX - Gammagard S/D 10 g protein
             76125-0900-XX - Gammaked 1, 2.5, 5, 10, 20 g protein
             64208-8234-XX - Gammaplex 2.5, 5, 10, 20 g protein
             68982-0850-XX - Octagam 10% 2, 5, 10, 20 g protein
             67467-0843-XX - Octagam 5% 1, 5 g protein
             44206-0436-XX - Privigen 5 g protein
             44206-0437-XX - Privigen 10 g protein
             44206-0438-XX - Privigen 20 g protein
             44206-0439-XX - Privigen 40 g protein

DESCRIPTION

Immune globulins or immunoglobulins (Ig) are specialized glycoproteins which function in the body as antibodies in the immune system. Produced by plasma cells, there are five human isotypes of immunoglobulins, IgA, IgD, IgE, IgG and IgM. Of these, IgG, IgA and IgM are referred to as natural antibodies as they are produced without deliberate immunization or antigen exposure. IgD and IgE are generally produced in response to the introduction of foreign antigens to which they bind and deactivate. Together, all immunoglobulin isotypes are vital components of the body’s immune response.

IgG is the most common of the immunoglobulins. It has multiple functions including placental antibody transfer, phagocytic cell surface binding and the activation of complement. Commercial preparations of intravenous immune globulins (IVIGs) are sterile, highly purified IgG products manufactured from large pools of human plasma, typically from 1000 or more healthy blood donors. They contain more than 95% unmodified IgG but only trace amounts of IgA and/or IgM. IVIG products are used in the treatment of multiple conditions.

POLICY

- Intravenous immune globulin (IVIG) therapy for the treatment of the following is considered medically necessary if the medical appropriateness criteria are met. (See Medical Appropriateness below.)
  - Acquired Immune Deficiency secondary to Acute Lymphoblastic Leukemia
  - Acquired Immune Deficiency secondary to Chronic lymphocytic leukemia or Multiple Myeloma
  - Ataxic neuropathies
  - Autoimmune mucocutaneous blistering diseases
  - Chronic Inflammatory/Immune Demyelinating Polyneuropathy
  - Dermatomyositis/Polymyositis

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o Fetal alloimmune thrombocytopenia (FAIT)
o Guillain-Barré syndrome (GBS)
o Hemolytic disease of the newborn
o Immune/idiopathic thrombocytic purpura (ITP)
o Kawasaki disease
o Lambert-Eaton myasthenic syndrome
o Management of Immune-Checkpoint-Inhibitor Related Toxicity
o Measles postexposure
o Multifocal motor neuropathy (MMN)
o Multiple sclerosis
o Myasthenia gravis
o Neonatal Alloimmune Thrombocytopenia
o Primary Immunodeficiency
o Parvovirus B19
o Stiff person syndrome (SPS)
o Tetanus postexposure
o Toxic shock syndrome
o Transplant recipient

• Intravenous immune globulin (IVIG) therapy for the prevention of the following is considered medically necessary if the medical appropriateness criteria are met. (See Medical Appropriateness below.)
  o Bacterial infections
  o Graft-versus-host disease
  o Measles postexposure
  o Varicella postexposure

• Intravenous immune globulin (IVIG) therapy for the treatment or prevention of other conditions/diseases is considered investigational.

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

• Intravenous immune globulin (IVIG) therapy is considered medically appropriate if ALL of the following criteria are met:
  o Baseline BUN (blood urea nitrogen) and serum creatinine values obtained within 30 days
  o Diagnosis of ANY ONE of the following:
    ▪ Acquired Immune Deficiency secondary to Acute Lymphoblastic Leukemia (ALL) and ALL of the following:
      • Used for prevention of infection
      • Individual is less than 18 years old
      • IgG level is less than 400 mg/dL
    ▪ Acquired Immune Deficiency secondary to chronic lymphocytic leukemia or multiple myeloma, if individual has ANY ONE of the following:
      • IgG level < 200 mg/dL
      • Individual has a deficiency in producing antibodies in response to vaccination and titers were drawn before challenging with vaccination and titers were drawn between 4 and 8 weeks of vaccination AND individual has a history of recurrent infections that include a minimum of one of the following:
        o Four or more ear infections within 1 year
        o Two or more serious sinus infections within 1 year
        o Two or more months of antibiotics with little effect
        o Two or more pneumonias within 1 year
        o Recurrent or deep skin abscesses
Need for intravenous antibiotics to clear infections
Two or more deep-seated infections including septicaemia
Other secondary immunodeficiencies resulting in hypogammaglobulinemia and/or B-cell aplasia will be evaluated on a case-by-case basis

- Allogeneic Bone Marrow or Stem Cell Transplant and **ALL** of the following:
  - Used for prevention of acute Graft-Versus-Host-Disease (aGvHD) or infection
  - Individuals **BMT** was allogeneic
  - Individuals IgG level is less than 400 mg/dL
  - Initial authorization is valid for 3 months

- Ataxic neuropathies associated with anti-GD1b IgM antibodies considered to be chronic disease

- Autoimmune mucocutaneous blistering diseases if **ALL** of the following:
  - Diagnosis of **ANY ONE** of the following:
    - Pemphigus vulgaris
    - Pemphigus foliaceus
    - Bullous pemphigoid
    - Mucous membrane pemphigoid
    - Epidermolysis bullosa acquisita
    - Pemphigus gestationis (Herpes gestationis)
    - Linear IgA dermatosis
  - Disease is **ALL** of the following:
    - Confirmed by biopsy
    - Severe, debilitating and extensive
    - Progressive
    - Refractory to trial of conventional therapy with corticosteroids and concurrent immnosuppressive treatment (e.g., azathioprine, cyclophosphamide, mycophenolate mofetil, etc.)
  - Individual has a documented baseline on physical exam

- Bacterial infections associated with neonates, as treatment or prevention, if therapy is adjunctive (i.e., to increase efficacy of primary treatment)

- Chronic Inflammatory/Immune Demyelinating Polyneuropathy (CIDP) if **ALL** of the following:
  - Disease course is progressive or relapsing/remitting for 2 months or longer
  - Individual has abnormal or absent deep tendon reflexes in upper or lower limbs
  - Electrodiagnostic testing indicates demyelination by **ANY ONE** of the following:
    - Partial motor conduction block in at least two motor nerves or in 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve
    - Distal CMAP duration increase in at least 1 nerve plus one other demyelination criterion listed here in at least 1 other nerve
    - Abnormal temporal dispersion conduction must be present in at least 2 motor nerves
    - Reduced conduction velocity in at least 2 motor nerves
    - Prolonged distal motor latency in at least 2 motor nerves
    - Absent F wave in at least two motor nerves plus one other demyelination criterion listed here in at least 1 other nerve
    - Prolonged F wave latency in at least 2 motor nerves
  - Cerebrospinal fluid analysis indicates white cell count of <10 cells/mm3, CSF protein is elevated
  - Individual is intolerant of or refractory to corticosteroids (e.g. prednisolone, prednisone) given in therapeutic doses over at least three months
  - Initial approval will be for 3 months
  - Initial authorization is valid for 3 months
- Complications of transplanted solid organ (kidney, liver, lung, heart, pancreas) or bone marrow transplant if ANY ONE of the following (list not all inclusive):
  - Suppression of panel reactive anti-human leukocyte antigen (HLA) antibodies prior to transplantation
  - Post solid organ transplant for treatment of an antibody-mediated rejection
  - Prevention or treatment of viral infections (e.g., cytomegalovirus, Parvo B-19 virus, and Polyoma BK virus)
- Dermatomyositis/Polymyositis if ALL of the following:
  - Individual has failed corticosteroid therapy (i.e., prednisone) or corticosteroid therapy is contraindicated
  - Individual has failed a trial of immunosuppressants, e.g. methotrexate, azathioprine, etc.
  - Severe active disease state with proximal weakness in upper and/or lower limbs
  - Diagnosis has been confirmed by muscle biopsy
  - Must be used as part of combination therapy with other agents
  - Documented baseline per physical exam and muscular strength/function
  - Initial approval valid for 3 months
- Fetal alloimmune thrombocytopenia (FAIT) for authorization until delivery date if ANY ONE of the following:
  - Individual has a history of a prior FAIT pregnancy
  - There is family history of the disease
  - Screening reveals platelet alloantibodies
- Guillain-Barré Syndrome (GBS) (Acute inflammatory polyneuropathy) if ALL of the following:
  - Disease is severe (individual requires assistance to walk)
  - Onset of symptoms are recent (less than 1 month)
  - Individual has abnormal or absent deep tendon reflexes in upper or lower limbs
  - Diagnosis is confirmed using a cerebrospinal fluid analysis
  - Approval will be granted for a maximum of 2 rounds of therapy within 6 weeks on onset
  - Authorization is valid for 2 months only
- Immune thrombocytopenia / idiopathic thrombocytic purpura (ITP) for ANY ONE of the following:
  - Acute disease state and ANY ONE of the following with authorization valid for one month only:
    - Manage acute bleeding due to severe thrombocytopenia (e.g., platelet counts less than 30 x 10^9/L)
    - Increase platelet counts prior to invasive surgical procedure, e.g., splenectomy, (platelets less than 100 x 10^9/L)
    - Severe thrombocytopenia (platelet count less than 20 x 10^9/L) and considered to be at risk for intracerebral hemorrhage
  - Chronic immune thrombocytopenia (CIT) if ALL of the following:
    - Increased risk for bleeding with platelet count less than 30 x 10^9/L
    - History of failure of, contraindication to or intolerance to corticosteroids
    - Duration of illness > 6 months
    - Individual ≥ 2 years of age
- Kawasaki disease
  - Authorization is valid for one course one (1 month only)
- Lambert-Eaton Myasthenic Syndrome if the individual has failed conventional therapy
- Management of Immune-Checkpoint-Inhibitor Related Toxicity if ALL of the following:
  - Individual has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, etc.)
  - Individual has ANY ONE of the following toxicities related to their immunotherapy:
    - Myasthenia gravis refractory to high-dose corticosteroids
    - Severe transverse myelitis
Measles postexposure for **ANY ONE** of the following:
- Pregnant woman without evidence of measles immunity
- Severely immunocompromised person (e.g., individual with severe primary immunodeficiency, bone marrow or stem cell transplant recipient, receiving treatment for acute lymphocytic leukemia, diagnosed with AIDS or HIV)

Multifocal motor neuropathy if **ALL** of the following:
- Individual has progressive multi-focal weakness (without sensory symptoms)
- Complete or partial conduction block or abnormal temporal dispersion conduction present in at least 2 nerves with accompanying normal sensory nerve conduction study across the same nerve that demonstrated the conduction block
- Baseline in strength/weakness documented using objective clinical measurement tool (e.g., INCAT, Medical Research Council (MRC) muscle strength, 6 MWT, Rankin, Modified Rankin)
- Initial authorization length is valid for 3 months

Multiple sclerosis if **ALL** of the following:
- Disease is relapsing-remitting
- As second-line therapy (i.e., after failure of initial treatment of choice)

Myasthenia gravis with **ALL** of the following:
- Individual has a positive serologic test for anti-acetylcholine receptor (AchR) antibodies
- Individual has an acute exacerbation resulting in impending myasthenic crisis (impending, i.e., respiratory compromise, acute respiratory failure, and/or bulbar compromise)
- Failure of conventional immunosuppressant therapy alone (corticosteroids, azathioprine, cyclosporine, mycophenolate, methotrexate, tacrolimus, cyclophosphamide etc.)
- Treatment will include combination therapy with corticosteroids or other immunosuppressant (e.g. azathioprine, mycophenolate, cyclosporine, methotrexate, tacrolimus, cyclophosphamide, etc.)
- Authorization length is 1 course (1 month) only

Neonatal Alloimmune Thrombocytopenia and authorization is valid for 1 course (1 month) only

Parvovirus B19 if **ALL** the following:
- Disease is chronic
- Individual with severe anemia secondary to bone marrow suppression

Pediatric HIV for control or prevention of bacterial infection and IgG level is less than 400 mg/dL

Primary immunodeficiencies (PID)/Wiskott-Aldrich syndrome (i.e., x-linked agammaglobulinemia, common variable immunodeficiency, transient hypogammaglobulinemia of infancy, IgG subclass deficiency with or without IgA deficiency, antibody deficiency with near normal immunoglobulin levels) and combined deficiencies (severe combined immunodeficiencies, ataxia-telangiectasia, x-linked lymphoproliferative syndrome) [list not all inclusive] if **ANY ONE** of the following:
- Individual with IgG level < 200 mg/dL
- Deficiency in producing antibodies in response to vaccination with titers drawn before challenging with vaccination and titers drawn between 4 and 8 weeks of vaccination and individual has history of multiple hard to treat infections with **ALL ANY ONE** of the following:
  - Four or more ear infections within 1 year
  - Two or more serious sinus infections within 1 year
  - Two or more months of antibiotics with little effect
  - Two or more pneumonias within 1 year
  - Recurrent or deep skin abscesses
  - Need for intravenous antibiotics to clear infections
  - Two or more deep-seated infections including septicemia

**Stiff person syndrome if ALL** of the following:
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- Individual positive for anti-glutamic acid decarboxylase (GAD) antibodies
- Individual has documented baseline on physical exam
- Failure of a minimum of two of the following therapies:
  - Benzodiazepines
  - Baclofen
  - Gabapentin
  - Valproate
  - Tiagabine
  - Levetiracetam
- Tetanus postexposure when tetanus immune globulin (TIG) is unavailable
- Toxic shock syndrome and authorization is valid for 1 course (1 month) only

RENEWAL CRITERIA

- Intravenous immune globulin (IVIG) therapy is considered medically appropriate for renewal therapy if ALL of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Absence of unacceptable toxicity from the agent e.g., acute kidney injury, thrombosis, hemolysis, hypersensitivity, pulmonary adverse reactions, volume overload, etc.
  - BUN and serum creatinine obtained within the last 6 months and the concentration and rate of infusion adjusted accordingly
  - Renewal authorization is appropriate for ANY ONE of the following indications:
    - Acquired Immune Deficiency secondary to Acute Lymphoblastic Leukemia (ALL) and ALL of the following:
      - Disease response as evidenced by one or more of the following:
        - Decrease in the frequency of infection
        - Decrease in the severity of infection
      - Individual continues to be at an increased risk of infection necessitating continued therapy
      - Renewals will be approved for a year
    - Acquired Immune Deficiency secondary to Chronic lymphocytic leukemia or Multiple Myeloma with ALL of the following:
      - Disease response as evidenced by one or more of the following:
        - Decrease in the frequency of infection
        - Decrease in the severity of infection
      - Individual continues to be at an increased risk of infection necessitating continued therapy
      - Renewals will be approved for a year
    - Allogeneic Bone Marrow or Stem Cell Transplant if ALL of the following:
      - Individuals IgG is less than 400mg/dL
      - Renewal authorizations are provided for 3 months
    - Autoimmune mucocutaneous blistering diseases with ALL of the following:
      - Documented improvement over baseline per physical exam
      - Renewals will be approved for 6 months
    - Chronic Immune Thrombocytopenia/ITP with ALL of the following:
      - Disease response as indicated by the achievement and maintenance of a platelet count of at least 50 X 10^9/L as necessary to reduce the risk for bleeding
      - Renewals will be approved for a year
    - Chronic Inflammatory Demyelinating Polyneuropathy with ALL of the following:
      - Individual has demonstrated a clinical response to therapy based on an objective clinical measuring tool (e.g. INCAT, Medical Research Council (MRC) muscle strength, 6 MWT, Rankin, Modified Rankin)

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• Renewals will be approved for a year
  ▪ Complications of transplanted solid organ (kidney, liver, lung, heart, pancreas) and bone marrow transplant if ALL of the following:
    • Disease response as evidenced by ANY ONE of the following:
      o Decrease in the frequency of infection
      o Decrease in the severity of infection
    • Individual continues to be at an increased risk of infection necessitating continued therapy
    • Renewals will be approved for a year
  ▪ Dermatomyositis/Polymyositis with ALL of the following:
    • Improvement above baseline per physical exam
    • Renewals will be approved for 6 months
  ▪ Management of Immune Checkpoint Inhibitor related Toxicity may not be renewed.
  ▪ Multifocal Motor Neuropathy with ALL of the following:
    • Individual has demonstrated a clinical response to therapy based on an objective clinical measuring tool (e.g. INCAT, Medical Research Council (MRC) muscle strength, 6 MWT, Rankin, Modified Rankin)
    • Renewals will be approved for a year
  ▪ Pediatric HIV for bacterial control or prevention if ALL of the following:
    • Disease response as evidenced by one or more of the following:
      o Decrease in the frequency of infection
      o Decrease in the severity of infection
    • Individual continues to be at an increased risk of infection necessitating continued therapy
    • Renewals will be approved for a year
  ▪ Primary immunodeficiency (PID) if ALL of the following:
    • Disease response as evidenced by one or more of the following:
      o Decrease in the frequency of infection
      o Decrease in the severity of infection
    • Renewals will be approved for a year
  ▪ Stiff Person Disease if ALL of the following:
    • Documented improvement over baseline per physical exam
    • Renewals will be approved for a year
    • Renewal authorizations are provided for 6 months

**Dosing Recommendations:**

- Patient’s dose should be reduced to the lowest necessary to maintain benefit for their condition. Patients who are stable, or who have reached the maximum therapeutic response, should have a trial of dose reduction (e.g., 25-50% reduction in dose every 3 months).
- Patients who have tolerated dose reduction and continue to show sustained improvement should have had a trial of treatment discontinuation; with the following exceptions:
  o PID would be excluded from a trial of discontinuation
  o HIV-infected children should show satisfactory control of the underlying disease [e.g., undetectable viral load, CD4 counts elevated above 200 or >15% (ages 9 months – 5 years) on antiretroviral therapy, etc.]
  o Solid organ transplant, CLL, and MM patients should not be at an increased risk of infection

Dosing should be calculated using adjusted body weight if one or more of the following criteria are met:
- Patient’s body mass index (BMI) is 30 kg/m2 or more; OR
- Patient’s actual body weight is 20% higher than his or her ideal body weight (IBW)
- Use the following dosing formulas to calculate the adjusted body weight (round dose to nearest 5 gram increment in adult patients):
  o BMI = 703 x (weight in pounds/height in inches^2)
  o IBW(kg) for males = 50 + [2.3 (height in inches – 60)]

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- IBW(kg) for females = 45.5 + [2.3 x (height in inches – 60)]
- Adjusted body weight = IBW + 0.5 (actual body weight – IBW)

This information is not meant to replace clinical decision making when initiating or modifying medication therapy and should only be used as a guide. Patient-specific variables should be taken into account.

<table>
<thead>
<tr>
<th>INDICATION(S)</th>
<th>DOSAGE &amp; ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PID</td>
<td>200 to 800 mg/kg every 21 to 28 days</td>
</tr>
<tr>
<td>CIDP</td>
<td>2 g/kg divided over 2-5 days initially, then 1 g/kg administered in 1-2 infusions every 21 days</td>
</tr>
<tr>
<td>ITP</td>
<td>2 g/kg divided over 5 days or 1 g/kg once daily for 2 consecutive days in a 28-day cycle</td>
</tr>
<tr>
<td>FAIT</td>
<td>1 g/kg/week until delivery</td>
</tr>
<tr>
<td>Kawasaki’s Disease (Pediatric Patients)</td>
<td>1 g/kg to 2 g/kg x 1 course</td>
</tr>
<tr>
<td>Multifocal Motor Neuropathy</td>
<td>Up to 2 g/kg divided over 5 days in a 28-day cycle</td>
</tr>
<tr>
<td>Acquired immune deficiency: CLL, MM and ALL</td>
<td>400 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Pediatric HIV</td>
<td>400 mg/kg every 2 to 4 weeks</td>
</tr>
<tr>
<td>Guillain-Barre</td>
<td>2 g/kg divided over 5 days x 1 course</td>
</tr>
<tr>
<td>Myasthenia Gravis</td>
<td>1-2 g/kg divided as either 0.5 g/kg daily x 2 days or 0.4 g/kg daily x 5 days x 1 course</td>
</tr>
<tr>
<td>Auto-immune blistering diseases</td>
<td>Up to 2 g/kg divided over 5 days in a 28-day cycle</td>
</tr>
<tr>
<td>Dermatomyositis/Polymyositis</td>
<td>2 g/kg divided over 2 to 5 days in a 28-day cycle</td>
</tr>
<tr>
<td>Bone Marrow or Stem Cell Transplant</td>
<td>500 mg/kg once weekly x 90 days, then 500 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Complications of transplanted solid organ:</td>
<td>2 g/kg divided over 5 days in a 28-day cycle</td>
</tr>
<tr>
<td>(kidney, liver, lung, heart, pancreas)</td>
<td></td>
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<tr>
<td>Transplant</td>
<td></td>
</tr>
<tr>
<td>Stiff Person</td>
<td>2 g/kg divided over 5 days in a 28-day cycle</td>
</tr>
<tr>
<td>Toxic shock syndrome</td>
<td>2 g/kg divided over 5 days x 1 course</td>
</tr>
<tr>
<td>Neonatal Alloimmune Thrombocytopenia</td>
<td>1 g/kg x 1 dose, may be repeated once if needed</td>
</tr>
<tr>
<td>Management of Immune Checkpoint Inhibitor</td>
<td>2 g/kg divided over 5 days x 1 course</td>
</tr>
<tr>
<td>Related Toxicity</td>
<td></td>
</tr>
</tbody>
</table>

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

LENGTH OF AUTHORIZATION

Initial and renewal authorization periods vary by specific covered indication. Unless otherwise specified, the initial authorization will be provided for 6 months and may be renewed.

Click here to view DOSAGE LIMITS

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

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BlueCross BlueShield of Tennessee’s Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member’s health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

<table>
<thead>
<tr>
<th>Brand Name/ Formulation</th>
<th>FDA Indication</th>
<th>Contraindications</th>
<th>Product Specs</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>Bivigam (liquid)</td>
<td>PID (peds ≥6)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>IgA: ≤200 mcg/mL  Osmolality: 510 mOsm/kg  Stabilizer: glycine</td>
<td></td>
</tr>
<tr>
<td>Carimune NF (lyophilized)</td>
<td>PID (peds/adults) a/cITP (peds/adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>IgA: 1000-2000 mcg/mL (6% soln)  Osmolality: 192 to 1074 mOsm/kg (depends on diluent and final conc)  Stabilizer: sucrose</td>
<td>1.67 gm of sugar per gm of protein</td>
</tr>
<tr>
<td>Flebogamma 5% (liquid)</td>
<td>PID (peds ≥2)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>IgA: &lt;50 mcg/mL  Osmolality: 240 to 370 mOsm/kg  Stabilizer: sorbitol</td>
<td></td>
</tr>
<tr>
<td>Flebogamma 10% (liquid)</td>
<td>PID (peds ≥2)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>IgA: &lt;32 mcg/mL  Osmolality: 240 to 370 mOsm/L  Stabilizer: sorbitol</td>
<td></td>
</tr>
<tr>
<td>Gammagard (liquid)</td>
<td>PID (peds ≥2)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>IgA: 37 mcg/mL  Osmolality: 240 to 300 mOsm/kg  Stabilizer: glycine</td>
<td>May be used SC (see policy for criteria</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Product</th>
<th>Indications</th>
<th>History of anaphylaxis</th>
<th>IgA:</th>
<th>Osmolality:</th>
<th>Stabilizer:</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gammagard S/D</td>
<td>PID ITP, CLL, Kawasaki (adults/peds for all indx)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>&lt;1 mcg/mL (5% solution)</td>
<td>636 mOsm/L (5% soln)</td>
<td>Glycine</td>
<td>Contains some sugar (20mg/mL when prepared)</td>
</tr>
<tr>
<td>Gammaked (liquid)</td>
<td>PID (peds ≥2), ITP (peds/adults), CIDP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>46 mcg/mL</td>
<td>258 mOsm/kg</td>
<td>Glycine</td>
<td>May be used SC (see policy for criteria)</td>
</tr>
<tr>
<td>Gammaplex 5%</td>
<td>PID (peds ≥2), cITP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies Fructose intolerance</td>
<td>&lt;10 mcg/mL</td>
<td>420 to 500 mOsm/kg</td>
<td>Glycine</td>
<td>Other stabilizer used is Polysorbate 80</td>
</tr>
<tr>
<td>Gammaplex 10%</td>
<td>PID (adults), cITP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>&lt;20 mcg/mL</td>
<td>280 mOsm/kg</td>
<td>Glycine</td>
<td>Other stabilizer used is Polysorbate 80</td>
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<tr>
<td>Gamunex-C</td>
<td>PID (peds ≥2), ITP (peds/adults), CIDP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>46 mcg/mL</td>
<td>258 mOsm/kg</td>
<td>Glycine</td>
<td>May be used SC (see policy for criteria)</td>
</tr>
<tr>
<td>Octagam 5%</td>
<td>PID (peds≥6)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies Corn allergy</td>
<td>≤200 mcg/mL</td>
<td>310 to 380 mOsm/kg</td>
<td>Maltose</td>
<td></td>
</tr>
<tr>
<td>Octagam 10%</td>
<td>ITP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>106 mcg/mL</td>
<td>310 to 390 mOsm/kg</td>
<td>Maltose</td>
<td></td>
</tr>
<tr>
<td>Privigen</td>
<td>PID cITP (peds ≥15), CIDP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies Hyperprolinemia</td>
<td>≤25 mcg/mL</td>
<td>320 mOsm/kg</td>
<td>L-proline</td>
<td></td>
</tr>
<tr>
<td>Panzyga</td>
<td>PID (peds ≥2), cITP (adults)</td>
<td>History of anaphylaxis to IgG IgA-deficient with IgA antibodies</td>
<td>≤100 mcg/mL</td>
<td>240-310 mOsm/kg</td>
<td>Glycine</td>
<td></td>
</tr>
</tbody>
</table>

- All intravenous immunoglobulins are derived from human plasma.
- Products with higher IgA content pose a greater risk for anaphylactic reactions, especially in patients with IgA deficiencies.
- All products may predispose patients to nephrotoxicity especially those with sugar-based or proline-based stabilizers. To lower risks, lower concentration products and infusions rates should be used as well as using products with osmolality/osmolarity that is near physiologic range (around 300 mOsm/kg or mOsm/L).
- Premedications (e.g., acetaminophen, antihistamine, etc) are recommended to reduce the risk of infusion related reactions.
SOURCES


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