Immune Globulin – Site of Care

Guideline Number: MMG145.M
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Instructions for Use

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- Skilled Care and Custodial Care Services

Coverage Rationale

This guideline addresses the criteria for consideration of allowing hospital outpatient facility infusion service for intravenous Immune Globulin (IVIG) and subcutaneous Immune Globulin (SCIG) therapy. This includes hospital based services with the following CMS/AMA Place of Service (POS) codes:

- 19 (Off Campus-Outpatient hospital); and
- 22 (On Campus-Outpatient Hospital)

Alternative Sites of Care, such as non-hospital outpatient infusion, physician office, ambulatory infusion suites, or home infusion services are well accepted POS for medication infusion therapy. If a member does not meet criteria for outpatient hospital facility infusion, alternative Sites of Care may be used.

Clinical use of Immune Globulin is proven and medically necessary, in certain circumstances.

Outpatient hospital facility-based Immune Globulin infusion is medically necessary for members who meet at least one of the following criteria (submission of medical records is required):

- Documentation that the member is medically unstable for administration of Immune Globulin at the alternative Sites of Care as determined by any of the following:
  - The member's complex medical status or therapy requires enhanced monitoring and potential intervention above and beyond the capabilities of the office or home infusion setting; or
  - The member's documented history of a significant comorbidity (e.g., cardiopulmonary disorder) or fluid overload status that precludes treatment at an alternative Site of Care; or
  - Outpatient treatment in the home or office setting presents a health risk due to a clinically significant physical or cognitive impairment; or
  - Difficulty establishing and maintaining patent vascular access; or
  - To initiate, re-initiate, or change Immune Globulin products for a short duration (e.g., 4 weeks);

  or
- Documentation (e.g., infusion records, medical records) of episodes of severe or potentially life-threatening adverse events (e.g., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure) that have not been responsive to acetaminophen, steroids, diphenhydramine, fluids, infusion rate reductions, or other pre-medications, thereby increasing risk to the member when administration is in the home or office setting

or

- Initial infusion, change of Immune Globulin product, or re-initiation of therapy after more than 6 months
  or
- Member has immunoglobulin A (IgA) deficiency with anti-IgA antibodies
  or
- Homecare or infusion provider has deemed that the member, home caregiver, or home environment is not suitable for home infusion therapy (if the prescriber cannot infuse in the office setting).

Ongoing outpatient hospital facility-based infusion duration of therapy will be no more than 6 months to allow for reassessment of the member's ability to receive therapy at an alternative Site of Care.

Note: If more than one of the above criteria are met, then the greatest of the applicable approval time periods will be allowed.

Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

Medication	Required Clinical Information
Asceniv™ (IV)	Refer to Protocol titled Medical Record Requirements for Pre-Service Reviews for documentation requirements. Note: Once in the Medical Record Requirements for Pre-Service Reviews document, search for the medication name or applicable HCPCS code.
Bivigam® (IV)	
Carimune® NF (IV)	
Cutaquig® (SC)	
Cuvitru® (SC)	
Flebogamma® DIF (IV)	
Gammagard® Liquid (IV, SC)	
Gammagard® S/D (IV)	
Gammaked™ (IV, SC)	
Gammaplex® (IV)	
Gamunex®-C (IV, SC)	
Hizentra® (SC)	
HyQvia® (SC)	
Octagam® (IV)	
Panzyga® (IV)	
Privigen® (IV)	
Xembify® (SC)	

Definitions

Immune Globulin: Immune Globulins are components of the immune system. There are several types of Immune Globulin produced by the body (e.g., IgA, IgD, IgE, IgG, IgM). This policy addresses therapeutic use Immune Globulin G (IgG) an antibody produced by the B lymphocytes. References to Immune Globulin within this guideline refer to IgG. IgG products have been referred to in multiple ways, some of which are: Immune Globulin (IG), immunoglobulin, gamma globulin, and also by its route of administration – intravenous immune globulin (IVIG), Immune Globulin intravenous (IGIV), Subcutaneous Immune Globulin (SCIG), Immune Globulin subcutaneous (IGSC).

Site of Care: Choice for physical location of infusion administration. Sites of care include hospital inpatient, hospital outpatient, community office, ambulatory infusion suite, or home-based setting.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1459	Injection, immune globulin (Privigen), intravenous, nonlyophilized (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
J1558	Injection, immune globulin (Xembify), 100 mg
J1559	Injection, immune globulin (Hizentra), 100 mg
J1561	Injection, immune globulin, (Gamunex, Gamunex-C/Gammaked), nonlyophilized (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, nonlyophilized (e.g., liquid), 500 mg
J1569	Injection, immune globulin, (Gammagard liquid), nonlyophilized, (e.g., liquid), 500 mg
J1572	Injection, immune globulin, (Flebogamma/Flebogamma DIF), intravenous, nonlyophilized (e.g., liquid), 500 mg
J1575	Injection, immune globulin/hyaluronidase, 100 mg immunoglobulin
J1599	Injection, immune globulin, intravenous, nonlyophilized (e.g., liquid), not otherwise specified, 500 mg
J3590	Unclassified biologics

Clinical Evidence

In a retrospective data analysis of over one thousand patients (n=1,076) with primary immunodeficiency diseases (PIDD), Wasserman et al. (2017), examined the infection rates for these patients who received IVIG in a home or hospital outpatient infusion center (HOIC). Patients were eligible for analysis if they had at least 1 inpatient or emergency room claim or at least 2 outpatient claims with a PIDD diagnosis from January 2002 and March 2013, 12 months of continuous health plan enrollment prior to index date (i.e., first IGIV infusion date), and 6 months of continuous IGIV at the same site of care after the index date. Incidences of pneumonia (bacterial or viral) and bronchitis (all types) within 7 days of IGIV infusion were retrospectively determined and compared between sites of care. Of the patients included in the analysis, 51% received IVIG in the home whereas 49% at an HOIC. The event/patient year of pneumonia was significantly lower in patients receiving IVIG at home compared to an outpatient hospital (0.102 vs. 0.216, $p = 0.0071$). The event/patient year of bronchitis was also significantly lower among patients infusing at home compared to an outpatient hospital (0.150 vs. 0.288, $p < 0.0001$). The authors concluded that PIDD patients receiving IVIG in the home experienced significantly lower rates of pneumonia and bronchitis than those who received outpatient hospital based IVIG treatment. The lower infection rates in the home setting suggest that infection risk may be an important factor in site of care selection.

Immune globulin infusion is administered in various sites of care. The Immune Deficiency Foundation surveyed 1,030 patients on where they were treated with immune globulin. Twenty-six percent usually received infusions at a hospital outpatient department (21%) or at a hospital clinic (5%). Other sites reported included a doctor's private office (9%) or an infusion suite (16%). The most common site was in the home (42%), most commonly administered by a nursing professional (2008).

Infusion in the home (POS 12) is well established and accepted by physicians. A survey of home infusion providers by the National Home Infusion Association reported 1.24 million therapies had been provided to approximately 829,000 patients, including 129,071 infusion therapies of specialty medications including immune globulin (Chowdary et al., 2010).

Professional Societies

American Academy of Allergy Asthma and Immunology (AAAAI)

AAAAI treatment guidelines provide several site of care options for administering immune globulin, with the appropriate option being based on the patient's clinical condition (2011):

- Hospital inpatient physician/nurse supervised infusion
- Hospital outpatient physician/nurse supervised infusion
- Physician office based physician/nurse supervised infusion
- Home based infusion with nurse supervision
- Home based infusion without nurse supervision

References

American Academy of Allergy Asthma and Immunology (AAAAI). Guidelines for the site of care for administration of IGIV therapy; December 2011.

American Academy of Allergy Asthma and Immunology (AAAAI); Eight Guiding Principles for Effective Use of IGIV for Patients with Primary Immunodeficiency; December 2011.

Centers for Medicare & Medicaid Services: Place of Service Code Set. http://www.cms.gov/Medicare/Coding/place-of-service-codes/Place_of_Service_Code_Set.html.

Chowdary P, Nair D, Davies N, et al.; Anaphylactic reaction with prothrombin complex concentrate in a patient with IgA deficiency and anti-IgA antibodies; Blood Coagul Fibrinolysis; 2010; 21 (8): 764.

Phase I: 2010 NHIA Provider Survey Comprehensive Aggregate Analysis Report; National Home Infusion Association; 2011.

Treatment Experiences and Preferences Among Patients with Primary Immunodeficiency Disease; National Survey of Patients: 2008; Immune Deficiency Foundation; May 6, 2009.

Wasserman RL, Ito D, Xiong Y, et al. Impact of site of care on infection rates among patients with primary immunodeficiency diseases receiving intravenous immunoglobulin therapy. J Clin Immunol. 2017; 37(2): 180–186.

Guideline History/Revision Information

Date	Summary of Changes
01/01/2021	Template Update • Reformatted policy; transferred content to new template
07/01/2020	Template Update • Added *Documentation Requirements* section Applicable Codes • Added list of applicable HCPCS codes: J1459, J1555, J1556, J1557, J1558, J1559, J1561, J1566, J1568, J1569, J1572, J1575, J1599, and J3590 Supporting Information • Archived previous policy version MMG145.L

Instructions for Use

This Medical Management Guideline provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this guideline, please check the member specific benefit plan document and any applicable federal or state

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