Evolent Clinical Guideline 3109 for Intravenous Immune Globulin (IG)

Guideline Number:	Applicable Codes	
Evolent_CG_3109		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date:	**Last Revised Date:**	**Implementation Date:**
September 2011	June 2025	June 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Intravenous Immune Globulin (IG) [Asceniv, Bivigam, Flebogamma DIF, Gamastan, Gammagard, Gammaked, Gammaplex, Gamunex C, Octagam, Panzyga, and Privigen] usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Idiopathic Thrombocytopenic Purpura (ITP)

- Intravenous Immune Globulin (IG) may be used in adult and pediatric members with a suspected/confirmed diagnosis of ITP and the platelet count is less than 30 x 10^9/L.

Non-Familial/Acquired/Secondary Hypogammaglobulinemia (e.g., that is associated with Chronic Lymphocytic Leukemia, Multiple Myeloma, post hematopoietic stem cell transplant, or CAR-T Cell Therapy)

- Intravenous Immune Globulin (IG) may be used in adult or pediatric members with Non- Familial/Acquired/Secondary Hypogammaglobulinemia (e.g., that is associated with B-cell CLL/SLL, multiple myeloma, post Hematopoietic Stem Cell Transplant, or CAR-T cell therapy) for any of the following requests:
  - For initial requests: The member has a documented IgG level less than 600 mg/dL within the last 4 weeks AND/OR a documented history of frequent sino-bronchial, skin, other site bacterial infections, or is clinically felt to be immunocompromised.
  - For continuation requests:

- The member has had a documented clinical benefit from IVIG therapy, e.g., reduced incidence of infections OR
- The member has a history of an increase in recurrent infections within the last 6 months.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Hypersensitivity to immune globulin or any component of the formulation; IgA deficiency (with anti-IgA antibodies and history of hypersensitivity [excluding Gammagard]); hyperprolinemia (Privigen); hypersensitivity to corn (Octagam); hereditary intolerance to fructose (Gammaplex); infants/neonates for whom sucrose or fructose tolerance has not been established (Gammaplex).
- US Boxed Warning
  - Thrombosis may occur with immune globulin products. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. For patients at risk of thrombosis, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.
  - Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur in predisposed patients with immune globulin intravenous (IGIV) products (excluding Gamastan). Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. (Note**:** The following IV products do not contain sucrose: Asceniv, Bivigam, Flebogamma DIF, Gammagard, Gammaked, Gammaplex, Gamunex C, Octagam, Panzyga, and Privigen.) For patients at risk of renal dysfunction or acute renal failure, administer IGIV products at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration.

EXCLUSION CRITERIA

- For CLL/Multiple Myeloma/Acquired Hypogammaglobulinemia the dosing exceeds 400 mg/kg for each dose and the frequency of administration is more frequent than once every 28 days.
- For ITP, the dosing exceeds 400 mg/kg daily x 5 days or 1 gm/kg x 1-2 days.
- Investigational use of Intravenous Immune Globulin (IG) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

- Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
- Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
- Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
- Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
- That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J1459 - Injection, immune globulin (privigen), intravenous, non-lyophilized (e.g., liquid), 500 mg
- J1460 - Injection, gamma globulin, intramuscular, 1 cc
- J1554 - Injection, immune globulin (asceniv), 500 mg
- J1556 - Injection, immune globulin (bivigam), 500 mg
- J1557 - Injection, immune globulin, (gammaplex), intravenous, non-lyophilized (e.g., liquid), 500 mg
- J1560 - Injection, gamma globulin, intramuscular, over 10 cc
- J1561 - Injection, immune globulin, (gamunex-c/gammaked), non-lyophilized (e.g., liquid), 500 mg
- J1568 - Injection, immune globulin, (octagam), intravenous, non-lyophilized (e.g., liquid), 500 mg
- J1569 - Injection, immune globulin, (gammagard liquid), non-lyophilized, (e.g., liquid), 500 mg
- J1572 - Injection, immune globulin, (flebogamma/flebogamma dif), intravenous, non-lyophilized (e.g., liquid), 500 mg

- J1576 - Injection, immune globulin (panzyga), intravenous, non-lyophilized (e.g., liquid), 500 mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
June 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1180 Intravenous Immune Globulin (IG) • Updated references
June 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as

required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

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