PI

PRIMARY HUMORAL IMMUNODEFICIENCY

PROVEN TO PREVENT INFECTIONS IN PEOPLE WITH PI[5]

> As demonstrated in a 9 month study

> Indicated for the treatment of PI* in patients 2 years of age and older[1]

*Includes, but is not limited to, congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies[1]

GAMMAKED CAN BE ADMINISTERED SUBCUTANEOUSLY (SC) IN ADULTS AND CHILDREN WITH PI[1]

ROUTE OF ADMINISTRATION	INITIAL DOSE	INITIAL INFUSION RATE	MAINTENANCE INFUSION RATE (IF TOLERATED)
Intravenous (IV)	300-600 mg/kg (may be adjusted over time to achieve desired trough levels and clinical responses)	1 mg/kg/min	8 mg/kg/min Every 3-4 weeks
Subcutaneous (SC)	1.37 x current IV dose in grams/ IV dose interval in weeks (should be individualized based on clinical response and serum IgG trough levels)	**Adult:*** 20 mL/hr/site **Pediatric:*** 10 mL/hr/site (< 25 kg) 15 mL/hr/site (≥ 25 kg)	**Adult:*** 20 mL/hr/site **Pediatric:*** 10 mL/hr/site (< 25 kg) 15 mL/hr/site (≥ 25 kg) Weekly

*Adults: use up to 8 infusion sites simultaneously; pediatric: use up to 6 infusion sites simultaneously; for all ages, ensure infusion sites are at least 2 inches (5 cm) apart.

In PI clinical studies, the most common adverse reactions with GAMMAKED (≥5% of subjects) were cough increased, rhinitis, pharyngitis, headache, asthma, nausea, fever, diarrhea, and sinusitis with intravenous use; and local infusion site reactions, fatigue, headache, upper respiratory tract infection, arthralgia, diarrhea, nausea, sinusitis, bronchitis, depression, allergic dermatitis, erythema, migraine, myalgia, viral infection, and pyrexia with subcutaneous use.

ITP

IDIOPATHIC THROMBOCYTOPENIC PURPURA

GAMMAKED IS PROVEN TO RAISE PLATELET COUNTS IN PATIENTS WITH ITP[6]

> Indicated for the treatment of adults and children with ITP to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery[1]

GAMMAKED IS ADMINISTERED ONLY INTRAVENOUSLY FOR PATIENTS WITH ITP[1]

DOSE	INITIAL INFUSION RATE	MAINTENANCE INFUSION RATE (IF TOLERATED)
2 g/kg	1 mg/kg/min (0.01 mL/kg/min)	8 mg/kg/min (0.08 mL/kg/min)

In ITP clinical studies, the most common adverse reactions (≥ 5% of subjects) with GAMMAKED were headache, ecchymosis, vomiting, fever, nausea, rash, abdominal pain, back pain, and dyspepsia.

Please see the Full Important Safety Information on page 5 and the accompanying Full Prescribing Information, located in the back pocket, for complete prescribing details including Boxed Warning, contraindications and dosing and administration information.

STORAGE & HANDLING[1]

> Ready-to-infuse, 10% IG solution
> Built-in hanger on 5, 10, and 20 g vials
> 3-year refrigerated shelf life; up to 6-month room temperature storage (within total shelf life)*
> No components of vial made with natural rubber latex
> 5 color-coded package sizes with barcoding
> Peel-off labels to help simplify recordkeeping

*Up to 6 months at any time during 36-month shelf life, after which the product should be used immediately or discarded

gammaked™
immune globulin injection (human), 10% caprylate/chromatography purified

GAMMAKED PROPERTIES[1]

> Sucrose-free
> Glycine stabilized
> Near physiologic osmolality
> pH of solution: 4.0-4.5
> Trace amounts of IgA (average 46 mcg/mL)

APPROVED IN 5 SIZES: 1 g (10 mL) · 2.5 g (25 mL) · 5 g (50 mL) · 10 g (100 mL) · 20 g (200 mL)

IMPORTANT SAFETY INFORMATION

Boxed Warning: Thrombosis, Renal Dysfunction and Acute Renal Failure

> **Thrombosis may occur with immune globulin products, including GAMMAKED. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors.**
> **For patients at risk of thrombosis, administer GAMMAKED 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 with immune globulin intravenous (IGIV) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of pre-existing 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. GAMMAKED does not contain sucrose.**
> **For patients at risk of renal dysfunction or failure, administer GAMMAKED at the minimum concentration available and the minimum infusion rate practicable.**

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References: 1. GAMMAKED [prescribing information]. Fort Lee, NJ: Kedrion Biopharma Inc.; 2018. **2.** Hughes RAC, Donofrio P, Bril V, et al, on behalf of the ICE Study Group. Intravenous immune globulin (10% caprylate-chromatography purified) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (ICE study); a randomized placebo-controlled trial. *Lancet Neurol.* 2008;7:136-44. **3.** Merkies ISJ, Bril V, Dalakas MC, et al. Health-related quality-of-life improvements in CIDP with immune globulin IV 10%: The ICE study. *Neurology.* 2009;72:1337-44. **4.** Latov N, Deng C, Dalakas MC, et al, on behalf of the ICE Study Group. Timing and course of clinical response to intravenous immunoglobulin in chronic inflammatory demyelinating polyradiculoneuropathy. *Arch Neurol.* 2010;67(7):802-807. **5.** Roifman CM, Schroeder H, Berger M, et al. Comparison of the efficacy of IGIV-C, 10% (caprylate/chromatography) and IGIV-SD, 10% as replacement therapy in primary immune deficiency: a randomized double-blind trial. *Int Immunopharmacol.* 2003;3:1325-33. **6.** Bussel JB, Eldor A, Kelton JG, et al. IGIV-C, a novel intravenous immunoglobulin: evaluation of safety, efficacy, mechanisms of action and impact on quality of life. *Thromb Haemost.* 2004;91:771-8.

KEDRION BIOPHARMA

gammaked™
immune globulin injection (human), 10% caprylate/chromatography purified

GAMMAKED KEY FEATURES

> 10% IG LIQUID SOLUTION, READY TO INFUSE
> SUCROSE-FREE
> 3-YEAR REFRIGERATED SHELF LIFE

INDICATED FOR THE TREATMENT OF:

CIDP chronic inflammatory demyelinating polyneuropathy in adults:
1. to improve neuromuscular disability and impairment
2. for maintenance therapy to prevent relapse

PI primary humoral immunodeficiency disease in patients 2 years of age and older, including but not limited to congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies

ITP idiopathic thrombocytopenic purpura in adults and children to raise platelet counts to prevent bleeding or to allow a patient with ITP to undergo surgery

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> **For patients at risk of thrombosis, administer GAMMAKED 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.**
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> **Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMMAKED does not contain sucrose.**
> **For patients at risk of renal dysfunction or failure, administer GAMMAKED at the minimum concentration available and the minimum infusion rate practicable.**

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KEDRION BIOPHARMA

CUSTOMER SERVICE CONTACT INFORMATION

Kedrion Biopharma has established one convenient phone number to answer your medical inquiries and/or customer service questions.

PHONE (855) 353-7466 **CUSTOMER SERVICE EMAIL** US_CustomerService@kedrion.com

FAX (855) 751-7951 **MEDICAL INFORMATION EMAIL** US_Medicalinfo@kedrion.com

Customer service hours are
MONDAY-FRIDAY
8:00am - 6:00pm CT

ORDERING GAMMAKED

Order GAMMAKED from any of the following authorized distributors:

ASD Healthcare® | BioCare | Cardinal Health™ Specialty Distribution
FFF Enterprises | McKesson | McKesson Plasma and Biologics LLC

NDC Number	Size	Grams Protein
76125-900-01	10 mL	1
76125-900-50	50 mL	5
76125-900-10	100 mL	10
76125-900-20	200 mL	20

THE ICE STUDY (IGIV-C CIDP EFFICACY)

CIDP

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY

The ICE* Study: 48-week study for the long-term efficacy of GAMMAKED for the treatment of CIDP[1]

*IGIV-C for CIDP Efficacy

24-WEEK EFFICACY PERIOD + 24-WEEK EXTENSION PHASE = 48-WEEK STUDY

Patients receiving GAMMAKED experienced:

1. Improved physical functioning through week 24[1-3]
   - > Including the ability to walk or climb stairs, and activities of daily living, including work
2. Continued improvement over 24 weeks of therapy[4]
   - > The number of patients reaching their maximal improvement continued to increase over the full 24 weeks of the Efficacy Period (weeks 0 to 24)
   - > Discontinuing treatment before maximal improvement is achieved may deprive patients the full therapeutic benefit
3. Lower probability of relapse with treatment beyond 24 weeks[1,2]
   - > Patients re-randomized to GAMMAKED in the 24-week Extension Phase (weeks 24 to 48) had a lower probability of relapse (13% vs. 45% for those receiving placebo)

GAMMAKED IS ADMINISTERED ONLY INTRAVENOUSLY (IV) FOR PATIENTS WITH CIDP[1]

DOSE	INITIAL INFUSION RATE	MAINTENANCE INFUSION RATE (IF TOLERATED)
Loading dose: 2 g/kg Maintenance dose: 1 g/kg	2 mg/kg/min (0.02 mL/kg/min)	8 mg/kg/min (0.08 mL/kg/min) Every 3 weeks

In CIDP clinical studies, the most common adverse reactions with GAMMAKED (≥ 5% of subjects) were headache, pyrexia, hypertension, chills, rash, nausea, arthralgia, and asthenia.

IMPORTANT SAFETY INFORMATION (continued)

GAMMAKED is contraindicated in patients who have had an anaphylactic or severe systemic reaction to human immunoglobulin. It is also contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity. Have epinephrine available immediately to treat any acute severe hypersensitivity reactions.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy, including GAMMAKED.

Aseptic Meningitis Syndrome (AMS) may occur infrequently, especially with high doses or rapid infusion.

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- > **For patients at risk of thrombosis, administer GAMMAKED 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 with immune globulin intravenous (IGIV) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs.**
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- > Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy, including GAMMAKED.
- > Aseptic Meningitis Syndrome (AMS) may occur infrequently, especially with high doses or rapid infusion.
- > Hemolysis, either intravascular or due to enhanced red blood cell (RBC) sequestration, can develop subsequent to GAMMAKED treatment. Risk factors include high doses and non-O blood group. Closely monitor patients for hemolysis and hemolytic anemia, especially in patients with pre-existing anemia and/or cardiovascular or pulmonary compromise.
- > Noncardiogenic pulmonary edema may occur in patients following treatment with IGIV products, including GAMMAKED. Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
- > The high dose regimen (1g/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.
- > GAMMAKED is made from human plasma. Because this product is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.
- > GAMMAKED is not approved for subcutaneous use in patients with ITP. Due to the potential risk of hematoma formation, GAMMAKED should not be administered subcutaneously in patients with ITP.
- > After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.
- > In clinical studies, the most common adverse reactions with GAMMAKED (≥5% of subjects) were: (in PI intravenous) cough increased, rhinitis, pharyngitis, headache, asthma, nausea, fever, diarrhea, and sinusitis; (in PI subcutaneous) local infusion site reactions, fatigue, headache, upper respiratory tract infection, arthralgia, diarrhea, nausea, sinusitis, bronchitis, depression, allergic dermatitis, erythema, migraine, myalgia, viral infection, and pyrexia; (in ITP) headache, ecchymosis, vomiting, fever, nausea, rash, abdominal pain, back pain, and dyspepsia; (in CIDP) headache, pyrexia, hypertension, chills, rash, nausea, arthralgia, and asthenia.

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