GAMMAKED Important Safety Information for Patients/Consumers

IMPORTANT SAFETY INFORMATION

What is GAMMAKED?
GAMMAKED™ [Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified] is an immune globulin injection that is used to treat primary humoral immunodeficiency (PI) in patients 2 years of age and older, idiopathic thrombocytopenic purpura (ITP) in adults and children, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults.

What is the most important information I should know about GAMMAKED?
If you have primary humoral immunodeficiency (PI), you may take GAMMAKED™ under the skin (subcutaneously) or in a vein (intravenously). When used to treat and self-administer for primary humoral immunodeficiency (PI) subcutaneously, GAMMAKED should be infused under your skin (in the subcutaneous tissue). DO NOT inject GAMMAKED into a blood vessel or directly into a muscle. When you are being treated for ITP or CIDP, a healthcare professional will insert an IV and you will receive GAMMAKED by intravenous infusion.

GAMMAKED May Cause

1. **Blood Clots (Thrombosis). Blood clots may occur in patients taking immune globulin intravenous (IGIV) products, including GAMMAKED. You may be at greater risk for blood clots if you are of advanced age, sit or lie for long periods, have a clotting condition or a history of blood clots, take estrogen hormones, have a central catheter, have thick blood, and/or if you have other conditions that put you at risk for cardiovascular disease. Blood clots may occur even if you do not have any of these known risk factors.**
2. **Impaired kidney function or kidney failure. IGIV products, particularly those that contain sugar (sucrose), have been reported to be associated with kidney dysfunction and damage, kidney failure, and death. Kidney damage and kidney failure happen more often in patients receiving IGIV products containing sucrose. GAMMAKED does not contain sucrose. You may be at greater risk for kidney**

failure if you have kidney disease, diabetes, are over age 65, are seriously dehydrated, have a blood infection (sepsis), have a blood condition called paraproteinemia, or take drugs that can damage your kidneys.

CONTRAINDICATIONS

- **Do not use GAMMAKED if:**
    - You have a history of severe allergic reactions to human immune globulin. Tell your healthcare provider if you have had a serious reaction to other medicines that contain human immune globulin. Ask if you are not sure.
    - You have an immunoglobulin A (IgA) deficiency and have antibodies to IgA and have a history of allergic reactions. Tell your healthcare provider if you have an IgA deficiency or ask if you are not sure.

WARNINGS AND PRECAUTIONS

- Severe allergic reactions may occur with IGIV products, including GAMMAKED. IgA deficient patients who have antibodies against IgA are at greater risk of developing severe allergic reactions. Your healthcare provider should have medications, such as epinephrine, to immediately treat any sudden severe allergic reactions.
- If you are receiving GAMMAKED, you could experience higher than normal levels of protein in your blood, thick blood, or low sodium (salt) in your blood. This may prevent your blood from flowing easily and possibly lead to blood clots.
- Brain inflammation or brain swelling called Aseptic Meningitis Syndrome (AMS) may occur infrequently with IGIV products, including GAMMAKED, especially if you receive a high dose or a rapid infusion.
- Blood damage called hemolysis and hemolytic anemia can develop after treatment with GAMMAKED. Your healthcare provider will closely monitor you for signs and symptoms of hemolysis and hemolytic anemia.

- Swelling of the lungs may occur in patients following IGIV treatment, including GAMMAKED. Your healthcare provider will monitor you for signs of lung damage (also known as transfusion-related acute lung injury [TRALI]).
- GAMMAKED is made from human blood and, therefore, carries a risk of transmitting infectious agents, such as viruses, the agent of the variant Creutzfeldt-Jakob disease (vCJD), or unknown infectious agents. You should consult with your healthcare provider if you have any questions or concerns.
- Be sure to tell your healthcare provider about your recent history of vaccinations. Live vaccines for diseases like measles, mumps, rubella and varicella may not work as well for you while you are receiving GAMMAKED. Tell your healthcare provider that you are taking GAMMAKED before you receive any vaccination.

ADVERSE REACTIONS

- In clinical studies, the most common side effects of GAMMAKED were:
    - Increased cough, stuffy nose, sore throat, headache, asthma, nausea, fever, diarrhea, and sinus infection, when administered intravenously to patients with PI.
    - Swelling and itching at the injection site, fatigue, headache, upper respiratory infection, joint pain, diarrhea, nausea, sinus infection, bronchitis, depression, allergic skin reactions, redness of the skin, migraine, muscle pain, viral infection, and fever, when administered subcutaneously to patients with PI.
    - Headache, bruising, vomiting, fever, nausea, rash, abdominal pain, back pain, and indigestion in patients with ITP.
    - Headache, fever, increased blood pressure, chills, rash, nausea, joint pain, and weakness in patients with CIDP.
- During treatment with GAMMAKED, be sure to tell your healthcare provider about any unusual symptoms you experience as they may indicate a possible side effect.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/MedWatch, or call 1-800-FDA-1088.

Please see [or "Click here for..."] accompanying Full Prescribing Information statement.

GAMMAKED Important Safety Information for HCPs

INDICATIONS AND USAGE

GAMMAKED™ [Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified] is an immune globulin injection that is indicated to treat primary humoral immunodeficiency (PI) in patients 2 years of age and older, idiopathic thrombocytopenic purpura (ITP) in adults and children, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults.

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.**

CONTRAINDICATIONS

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.

WARNINGS AND PRECAUTIONS

Hypersensitivity: Severe hypersensitivity reactions may occur with IGIV products, including GAMMAKED. In case of hypersensitivity, discontinue GAMMAKED infusion immediately and institute appropriate treatment. GAMMAKED contains trace amounts of IgA (average 46 micrograms/mL). Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. It is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity reaction.

GAMMAKED Important Safety Information for HCPs

Renal Failure: Acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis and death may occur upon use of IGIV products, especially those containing sucrose.[7, 8] GAMMAKED does not contain sucrose. Ensure that patients are not volume depleted prior to the initiation of the infusion of GAMMAKED. Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk for developing acute renal failure. Assess renal function, including measurement of blood urea nitrogen (BUN)/serum creatinine, prior to the initial infusion of GAMMAKED and again at appropriate intervals thereafter. If renal function deteriorates, consider discontinuation of GAMMAKED. For patients judged to be at risk for developing renal dysfunction, including patients with any degree of pre-existing renal insufficiency or risk factors for renal insufficiency, administer GAMMAKED at the minimum infusion rate practicable [less than 8 mg/kg/min (0.08 mL/kg/min)].

Hyperproteinemia, Increased Serum Viscosity, and Hyponatremia: Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy, including GAMMAKED. It is clinically critical to distinguish true hyponatremia from a pseudohyponatremia that is associated with concomitant decreased calculated serum osmolality or elevated osmolar gap, because treatment aimed at decreasing serum free water in patients with pseudohyponatremia may lead to volume depletion, a further increase in serum viscosity and a possible predisposition to thrombosis.

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

Hemolysis: 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.

Transfusion-related Acute Lung Injury (TRALI): 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]).

Volume Overload: 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.

Transmission of Infectious Agents: 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.

Hematoma Formation: 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.

Interference with Laboratory Tests: 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.

ADVERSE REACTIONS

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.

["Please see accompanying Full Prescribing Information" statement]