BIVIGAM® DOSING AND ADMINISTRATION

BIVIGAM is indicated for the treatment of patients with PI[1]
For intravenous use only

Dosage Forms and Strengths

BIVIGAM is a liquid solution containing 10% IgG (100 mg/mL) for intravenous infusion[1]

Recommended Dosage and Infusion Rates

Dose	Initial infusion rate (for first 10 minutes)	Maintenance infusion rate (if tolerated)
300-800 mg/kg every 3-4 weeks* *Frequency/amount of IgG therapy may vary from patient to patient. The proper amount can be determined by monitoring clinical response.	0.5 mg/kg/min (0.005 mL/kg/min)	Increase every 20 minutes by 0.8 mg/kg/min up to 6 mg/kg/min

BIVIGAM is available in single-use, non-latex, tamper-evident 5 g/50 mL and 10 g/100 mL vials.[1]

5 g/50 mL vial **10 g/100 mL vial**

IV Infusion Rates in mL (cc) per Hour

	Initial rate (first 10 min)	Maintenance rate* (mg/kg/min to mL/kg/hr)						
mg/kg/min	**0.5**	**1.3**	**2.1**	**2.9**	**3.7**	**4.5**	**5.3**	**6.0**
mL/kg/hr	**0.3**	**0.8**	**1.3**	**1.7**	**2.2**	**2.7**	**3.2**	**3.6**
Patient weight		**Infusion rate – mL (cc) per hour (rounded to the nearest whole number)**						
lb	**kg**							
13	6	2	5	8	10	13	16	19	22
22	10	3	8	13	17	22	27	32	36
44	20	6	16	26	34	44	54	64	72
66	30	9	24	39	51	66	81	96	108
88	40	12	32	52	68	88	108	128	144
110	50	15	40	65	85	110	135	160	180
132	60	18	48	78	102	132	162	192	216
154	70	21	56	91	119	154	189	224	252
176	80	24	64	104	136	176	216	256	288
198	90	27	72	117	153	198	243	288	324
220	100	30	80	130	170	220	270	320	360
242	110	33	88	143	187	242	297	352	396
264	120	36	96	156	204	264	324	384	432

*Rates are increased by 0.8 mg/kg/min every 20 minutes (if tolerated) to a maximum of 6 mg/kg/min.

Recommendations for Administering

- Monitor patient vital signs throughout the infusion. Slow or stop the infusion if adverse reactions occur. If symptoms subside promptly, the infusion may be resumed at a slower rate comfortable for the patient
- If there are no adverse reactions, the infusion rate for subsequent infusions can be slowly increased to the maximum rate. For patients experiencing adverse drug reactions, it is advisable to reduce the infusion rate in subsequent infusions
- Dose adjustments may be required in patients who fail to maintain desired trough levels. Starting with the second infusion, adjust the dose proportionally, targeting a trough of ≥600 mg/dL, based on the previous trough and the associated dose[1]
- Ensure that patients with pre-existing renal insufficiency are not volume-depleted. For patients judged to be at risk for renal dysfunction or thrombotic events, administer BIVIGAM at the minimum infusion rate practicable, and consider discontinuation of administration if renal function deteriorates

IgG=immunoglobulin class G; PI=primary humoral immunodeficiency.

Reference: 1. BIVIGAM Prescribing Information. ADMA Biologics; 2019.

BIVIGAM®
IMMUNE GLOBULIN INTRAVENOUS (HUMAN), 10% LIQUID

Indication

BIVIGAM® is an Immune Globulin Intravenous (Human), 10% Liquid, indicated for the treatment of patients with primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency (CVID), X linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (SCID).

Important Safety Information for BIVIGAM®

WARNING: THROMBOSIS, RENAL DYSFUNCTION, AND ACUTE RENAL FAILURE

Thrombosis may occur with immune globulin intravenous (IGIV) products, including BIVIGAM®. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, a 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.

Use of immune globulin intravenous (IGIV) products, particularly those containing sucrose, has been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Patients at risk of acute renal failure include those with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age (above 65 years of age), volume depletion, sepsis, paraproteinemia, or receiving known nephrotoxic drugs.

Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. BIVIGAM does not contain sucrose.

For patients at risk of thrombosis, renal dysfunction, or renal failure, administer BIVIGAM 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.

Contraindications

BIVIGAM® is contraindicated in:

- Patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin.
- IgA deficiency patients with antibodies to IgA and a history of hypersensitivity.

Warnings and Precautions

Thrombosis may occur following treatment with immune globulin (IGIV) products, including BIVIGAM. Thrombosis may occur in the absence of known risk factors. Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity and ensure adequate hydration before administration. For patients at risk of thrombosis, administer BIVIGAM at the minimum dose and infusion rate practicable. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Severe hypersensitivity reactions may occur with IGIV products, including BIVIGAM. In case of hypersensitivity, discontinue BIVIGAM infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for treatment of acute hypersensitivity reactions. Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions.

Acute renal dysfunction/failure, osmotic nephrosis, and death may occur upon use of human IGIV products. Ensure that patients are not volume depleted before administering BIVIGAM. Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, before the initial infusion of BIVIGAM and at appropriate intervals thereafter. If renal function deteriorates, consider discontinuing BIVIGAM. In at-risk patients, administer BIVIGAM at the minimum infusion rate practicable.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV treatment, including BIVIGAM. It is critical to clinically distinguish true hyponatremia from a pseudohyponatremia that is associated with or causally related to hyperproteinemia. 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 thrombotic events.

Aseptic meningitis syndrome (AMS) may occur with IGIV treatments, including BIVIGAM. AMS usually begins within several hours to 2 days following IGIV treatment. AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IGIV. Conduct a thorough neurological examination on patients exhibiting signs and symptoms of AMS, including cerebrospinal fluid (CSF) studies, to rule out other causes of meningitis.

IGIV products, including BIVIGAM, may contain blood group antibodies that can act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin reaction and, rarely, hemolysis. Monitor patients for clinical signs and symptoms of hemolysis, including appropriate confirmatory laboratory testing.

Noncardiogenic pulmonary edema may occur in patients following IGIV treatment, including BIVIGAM. Transfusion-Related Acute Lung Injury (TRALI) is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Symptoms typically appear within 1 to 6 hours following treatment. Monitor patients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and the patient's serum. TRALI may be managed using oxygen therapy with adequate ventilatory support.

Because BIVIGAM is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. All infections suspected by a physician to possibly have been transmitted by this product should be reported to ADMA Biologics at 1-800-458-4244.

After infusion of immunoglobulin, 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. Passive transmission of antibodies to erythrocyte antigens (e.g., A, B, and D) may cause a positive direct or indirect antiglobulin (Coombs') test.

Adverse Reactions

Serious adverse reactions observed in clinical trial subjects receiving BIVIGAM were vomiting and dehydration in one subject.

The most common adverse reactions to BIVIGAM (≥5% of clinical study subjects) were headache, fatigue, infusion site reaction, nausea, sinusitis, increased blood pressure, diarrhea, dizziness, and lethargy.

You are encouraged to report side effects of prescription drugs to ADMA Biologics at 1-800-458-4244 or the FDA. Visit www.fda.gov/MedWatch or call 1-800-FDA-1088.

Please see Important Safety Information for BIVIGAM® at www.bivigam.com and click here for full Prescribing Information.

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