Coverage and Reimbursement Guide

Disclaimer: This reimbursement and coverage guide is for informational purposes only. Codes and coverage are subject to payer discretion and should always be verified by the payer. Clinicians make the determination as to when to use a specific product, based on clinical appropriateness. This reimbursement and coverage guide is not intended to provide specific guidance on how to utilize, code, bill, or charge for any product. Biotest Pharmaceuticals Corporation cannot guarantee success in obtaining payment for products and services.

Please refer to important safety information about BIVIGAM® on page 3 or Full Prescribing Information on page 24.
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Biotest Pharmaceuticals Corporation has created this Coverage and Reimbursement Guide to help physicians and other providers understand payers’ coverage and reimbursement for BIVIGAM® and, if necessary, to help address reimbursement issues.

Specifically, this guide presents general information on coverage, coding, reimbursement, and claims submission for BIVIGAM. It also provides guidance on how to manage denied claims.

In addition, Biotest Pharmaceuticals has established the BIVIGAM CareLine (1-855-BIVIGAM) to assist providers with the following activities:

- Conduct patient-specific reimbursement research with insurers to help verify coverage for BIVIGAM and its administration
- Help verify prior authorization requirements and facilitate submission
- Investigate the cause of denied or underpaid BIVIGAM claims and facilitate submission of appeals
- Assist with coding and reimbursement inquiries related to BIVIGAM, such as HCPCS codes, CPT codes, and ICD-9-CM diagnosis codes

As information and forms may change quicker than this booklet can get updated, please visit: www.BIVIGAM.com in order to check that the most updated information and forms are used.
Important Safety Information for BIVIGAM®

Important Safety Information for BIVIGAM® [Immune Globulin Intravenous (Human), 10% Liquid]

BIVIGAM® (Immune Globulin Intravenous (Human), 10% Liquid) is indicated for the treatment of 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.

**Warning:** 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, the use of estrogens, indwelling vascular catheters, hyperviscosity and cardiovascular risk factors. Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with the administration of Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. BIVIGAM does not contain sucrose. For patients the risk of thrombosis, renal dysfunction, or renal failure, administer BIVIGAM at the minimum dose recommended and infusion rate practicable. Ensure adequate hydration in patients before administrations. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for viscosity.

See full Prescribing Information for complete boxed warning.

BIVIGAM is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin and in IgA-deficient patients with antibodies to IgA and history of hypersensitivity.

Hyperproteinemia, increased serum viscosity, and hyponatremia or pseudohyponatremia can occur in patients receiving IGIV therapy.

Aseptic meningitis syndrome (AMS) has been reported with IGIV treatments; AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IGIV.

As hemolysis can develop subsequent to treatment with IGIV products, monitor patients for hemolysis and hemolytic anemia.

Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]). If TRALI is suspected, test the product and patient for antineutrophil antibodies.

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.
Serious adverse reactions observed in clinical trial subjects receiving BIVIGAM were vomiting and dehydration in one subject. The most common adverse reactions to BIVIGAM (reported in ≥5% of clinical study subjects) were headache, fatigue, infusion site reaction, nausea, sinusitis, blood pressure increase, diarrhea, dizziness, and lethargy.

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.

For more information about BIVIGAM please see full Prescribing Information for complete details on page 24.
Coverage

Coverage refers to the decision by an insurer to provide program benefits for a specific product or medical service. Coverage policies, which vary by payer, specify whether a proposed course of treatment is medically necessary and eligible for reimbursement under a patient's healthcare plan. Most private and public payers cover IVIG products for labeled indications and should cover BIVIGAM® as well.

If you have questions about a patient’s coverage for BIVIGAM, please contact the BIVIGAM CareLine at 1-855-BIVIGAM.

PRIVATE PAYERS
The majority of private or commercial insurers cover FDA-approved drugs and biologics that are infused under the medical benefit when determined to be medically necessary and appropriate. However, benefits vary by payer and also depend on the specific contract terms that a provider negotiates with a given plan. Some private insurers have medical criteria for coverage similar to those used by Medicare, while others develop their own policies. In some cases, BIVIGAM may be covered as part of a bundled payment for multiple healthcare services (such as a per diem payment) and may not be paid for separately.

As a condition of coverage, some managed care plans may require the following:
• a referral from the patient’s primary care provider (PCP) to a specialist,
• prior authorization before using BIVIGAM, and
• statement of medical necessity.

MEDICARE PART B
Medicare should cover BIVIGAM when used for its FDA-approved indication under medically necessary and appropriate conditions. Medicare Part B does not use a prior authorization process, so Medicare’s coverage policy should be understood before treatment is initiated.

Coverage of BIVIGAM will be subject to local coverage determinations (LCDs) issued by regional Medicare Part B carriers and Medicare Administrative Contractors (MACs). Carriers and MACs are companies under contract with the federal government to handle LCDs and process claims for Medicare services.
MEDICARE MANAGED CARE (MEDICARE PART C)

Medicare Managed Care, or Medicare Advantage (also called Medicare Part C), plans are required to provide all of the benefits covered under Medicare Part B and frequently cover additional services to those in Part B. Therefore, if the Medicare Part B requirements for coverage of BIVIGAM® are met, it is likely that a patient with Medicare Advantage will be covered as well. However, you should determine coverage prior to ordering BIVIGAM. Medicare Part C works like a commercial managed care plan and may require prior authorization.

MEDICAID

Medicaid coverage policies are determined on a state-by-state basis. FDA approval of BIVIGAM will not necessarily trigger automatic coverage and payment under each state’s Medicaid program. Some programs have established review criteria for inclusion of a product as an approved drug or service, and may require a certain amount of time post-launch to conduct reviews. While some states’ Medicaid programs may utilize coverage guidelines for BIVIGAM that are based on Medicare’s policies, other programs may provide more limited benefits. In some cases, depending on the setting, BIVIGAM may be covered within a bundled payment for multiple healthcare services and not paid for separately.

In addition, some Medicaid programs may require:

- Prior authorization before using BIVIGAM
- Statement of medical necessity

Confirm the patient’s eligibility for the state Medicaid program before ordering BIVIGAM as states’ Medicaid policies are updated frequently.

If you have questions about a specific Medicaid program’s coverage of BIVIGAM, please contact the BIVIGAM CareLine at 1-855-BIVIGAM.

Please refer to the accompanying full Prescribing Information for complete details.
Proper coding is crucial to obtain appropriate reimbursement for BIVIGAM® and its administration. The following codes could be applicable within the physician office setting or the hospital outpatient department.

**HCPCS CODE**

HCPCS codes are used to describe most drugs and biologics. The following HCPCS code should be used to bill for BIVIGAM.

<table>
<thead>
<tr>
<th>SETTING</th>
<th>HCPCS CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHYSICIAN OFFICE/ HOSPITAL OUTPATIENT DEPARTMENT</td>
<td>J1556</td>
<td>Injection, Immune Globulin (BIVIGAM) Intravenous, Non-Lyophilized (e.g. Liquid), 500 mg</td>
</tr>
</tbody>
</table>

**CPT CODES**

CPT codes are generally used to report specific professional medical services. The following CPT codes can be used for the administration of BIVIGAM.

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>96365</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour</td>
</tr>
<tr>
<td>96366</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour</td>
</tr>
</tbody>
</table>

If you also provide Evaluation and Management Services (E&M) on the day of the infusion you may be able to bill for these services using CPT codes 99212-99215. CPT modifier “25” may be used to specify separate and distinct E&M services on the same day as an infusion of BIVIGAM. Please consult your local payer for specific policies or call the BIVIGAM CareLine for assistance at 1-855-BIVIGAM.

**NDC**

National Drug Codes (NDC) are unique identifiers issued to each drug approved by the FDA. BIVIGAM has been assigned the following NDCs.

<table>
<thead>
<tr>
<th>VIAL SIZE</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 ML VIAL (5 G IGG)</td>
<td>59730-6502-1</td>
</tr>
<tr>
<td>100 ML VIAL (10 G IGG)</td>
<td>59730-6503-1</td>
</tr>
</tbody>
</table>

**CPT five digit codes, nomenclature, and other data are ©2012 American Medical Association. All rights reserved. No fee schedules, basic units, relative values, or related listings are included in CPT. The AMA assumes no liability for the data included herein.**
ICD-9-CM DIAGNOSIS CODES

ICD-9-CM diagnosis codes are used to report a patient’s diagnosis and should be noted in Item 21 on the CMS-1500 claim form then referenced in Item 24E, next to the relevant service or drug codes. When administering BIVIGAM in the physician’s office, providers must submit a properly coded CMS-1500 claim form for the drug and associated services rendered. Please see Appendix A for current CMS-1500 claim form.

Hospital outpatient departments must submit a properly coded claim form to obtain reimbursement for facility costs. The UB-04 form is a standard claim form required by Medicare and other payers for billing hospital outpatient services. ICD-9-CM diagnosis codes should be entered in Locator Box 66 of the UB-04 claim form. The following ICD-9-CM diagnosis codes may be used when billing for BIVIGAM and are covered by Medicare Part B.

<table>
<thead>
<tr>
<th>ICD-9-CM CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>279.00</td>
<td>Hypogammaglobulinemia, unspecified</td>
</tr>
<tr>
<td>279.03</td>
<td>Other selective immunoglobulin deficiencies</td>
</tr>
<tr>
<td>279.04</td>
<td>Congenital hypogammaglobulinemia</td>
</tr>
<tr>
<td>279.05</td>
<td>Immunodeficiency with increased IgM</td>
</tr>
<tr>
<td>279.06</td>
<td>Common variable immunodeficiency</td>
</tr>
<tr>
<td>279.09</td>
<td>Other deficiency of humoral immunity</td>
</tr>
<tr>
<td>279.12</td>
<td>Wiskott-Aldrich syndrome</td>
</tr>
<tr>
<td>279.2</td>
<td>Combined immunity deficiency</td>
</tr>
</tbody>
</table>

The following ICD-9 codes also may be used for patients treated with BIVIGAM, and may be covered by other payers.

<table>
<thead>
<tr>
<th>ICD-9-CM CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>279.01</td>
<td>Selective IgA immunodeficiency</td>
</tr>
<tr>
<td>279.02</td>
<td>Selective IgM immunodeficiency</td>
</tr>
<tr>
<td>279.10</td>
<td>Immunodeficiency with predominant T-cell defect, unspecified</td>
</tr>
<tr>
<td>279.11</td>
<td>DiGeorge's syndrome</td>
</tr>
<tr>
<td>279.13</td>
<td>Nezelof's syndrome</td>
</tr>
</tbody>
</table>

Please refer to the accompanying full Prescribing Information for complete details.
Reimbursement

PHYSICIAN OFFICE SETTING

PRIVATE PAYERS
Private insurers use a variety of reimbursement methodologies for provider administered drugs and biologics, which are separately reimbursed. Reimbursement for physician-administered drugs is often based on Average Wholesale Price (AWP) or Average Sales Price (ASP). Reimbursement for services varies, depending on the negotiated rate between the provider and insurance company or the insurance company’s fee schedule.

MEDICARE
Medicare reimburses physicians’ services based on the resource-based relative value scale (RBRVS) Medicare Physician Fee Schedule (MPFS). This payment system also applies to physicians’ professional services furnished in other settings of care. Payment levels under the physician fee schedule are calculated separately for each covered CPT code.

The Medicare allowable amount for provider-administered drugs is ASP plus 6%. Rates are updated quarterly. Medicare covers 80% of the allowable amount, and the beneficiary or their supplemental policy is responsible for the remaining 20%.

MEDICAID
Medicaid programs may pay for BIVIGAM based on AWP, ASP, a percentage of charges, or state-specific fee schedules. There is significant variation in Medicaid payment amounts among states. Please check with the specific state Medicaid program to determine its coding policies for BIVIGAM or call the BIVIGAM CareLine for assistance.

HOSPITAL OUTPATIENT SETTING

PRIVATE PAYERS
Private insurers use a variety of reimbursement methodologies for drugs and biologics administered in the hospital outpatient setting, including AWP, ASP, invoice, or percentage of charges. Private payer reimbursement mechanisms for the administration procedure may include fee schedules, per-visit/per diem rates, or percentage of charges.

MEDICARE
Under the Hospital Outpatient Prospective Payment System (OPPS), hospitals will receive Medicare reimbursement on a per service basis. Under this payment system, hospital services fall under specific ambulatory payment classifications (APCs), which bundles additional services or items used in association with the primary service. Each APC is then included into a calculation which also accounts for the facility’s type and geographic location, the complexity of the treatment, and any applicable outlier payments.
The Outpatient Prospective Payment System does not include physician services, which are reimbursed separately under Medicare’s physician fee schedule. Additionally, many drugs are paid for separately, if the costs to administer the product are over a certain threshold. In 2014, the threshold allows for drugs and biologics to be paid for separately if they cost more than $90, and will be paid based on ASP + 6%. Medicare beneficiaries generally pay 20%, after their plan has paid a majority of the costs calculated under the Outpatient Prospective Payment System.

**MEDICAID**

Like reimbursement in the physician’s office setting, Medicaid programs may pay for BIVIGAM based on a variety of payment methods, including fee schedules. Providers should consult the specific state Medicaid program to determine its coding policies for BIVIGAM.

**HOME HEALTH SETTING**

**MEDICARE**

Medicare pays for home healthcare using a prospective payment system based on an episode of care for a 60-day period. Currently, except under very limited circumstances, traditional Medicare Part B does not cover injectable drugs administered in the home. However, infusion drugs administered in the home that do not qualify for Part B coverage may be covered under Part D. Although they must comply with certain statutory and regulatory standards, Part D plans may develop and maintain their own formularies. Therefore, coverage may vary from plan to plan and prior authorization may be required.

**MEDICAID**

Most Medicaid programs provide coverage for care provided in the home setting. While many Medicaid programs cover care in the home setting, some do not provide separate reimbursement for drugs. Where separate payment for drugs is provided, payment is typically based on a percentage of AWP, WAC, or ASP.

**PRIVATE PAYERS**

Most private payers provide coverage for care provided in the home setting. Many private payers have contracts with home care agencies that provide comprehensive home health services to their insured members. Plans may assign case managers to complex cases. These case managers are primarily responsible for supervising the coordination of care from setting to setting. A wide variety of methods are used by private payers to pay for services provided in the home setting, including per diems, case rates, and reasonable costs. Separate payment for drugs is usually provided and this payment may be based on a percentage of AWP, WAC, or ASP.

Please refer to the accompanying full Prescribing Information for complete details.
BIVIGAM will likely be covered when considered medically necessary and appropriate for a patient’s diagnosis. However, some insurers may be less familiar with BIVIGAM and may require additional documentation. These documents will serve to strengthen the establishment of the Medical Necessity requirements as insurers have set forth. As such, you may wish to include the following items with your claim:

- Letter of medical necessity from the attending physician to the insurer
- BIVIGAM’s package insert
- Documentation of BIVIGAM’s FDA approval
- Documentation of clinical evidence supporting BIVIGAM’s safety and efficacy
- Specific details of the patient’s case history and clinical course
Instructions for Appealing Denied Claims

Some of the most common reasons for denials or underpaid claims include:

- Lack of specific details of the patient’s case history and clinical course
- Use of incorrect billing codes
- Lack of documentation supporting choice of codes and/or medical necessity of services
- Omission of an accurate description of services
- Omission of special coding requirements, such as the use of a modifier

Insurers may deny coverage and claims for a variety of reasons, including variations in policies, confusion or lack of knowledge about the services provided, or technical billing errors, such as code omissions, misspellings, or transposed numbers. Therefore, it is important to include appropriate supporting documentation when requesting coverage for a patient, and to carefully review claims that have been denied to identify technical errors. When coverage or claims are denied physicians, pharmacists, patients, and patients’ families often can appeal successfully if the treatment is medically necessary and given for the appropriate indication.

If a patient is denied coverage for BIVIGAM, you should consider the patient’s and the family’s rights in the appeal process. For example, patients insured through an employer can begin their advocacy at their personnel office. Patients insured by traditional Medicare can contact their local Medicare claims processor to inquire about their appeal rights. Patients enrolled in a Medicare managed care plan should contact the consumer affairs hotline at their plan to ask for reconsideration. Patients insured by Medicaid can contact their state Medicaid program office to obtain information on appeals. The following steps may serve as a guide for appealing coverage or claims denials.

**Step One.** Review the claim for submission errors. An insurer could deny coverage because a claim form could be missing billable codes, identification numbers, patient names, or signatures.

**Step Two.** Review the insurer’s rationale for the denial. Discuss the denial reason with the insurer. Often, claims are denied because the insurer is not familiar with the product or procedure. They may need additional information about the product and its safety and efficacy profile. Additionally, peer-reviewed articles may help inform the insurer about the positive outcomes that a patient could experience with appropriate treatment.

Please refer to the accompanying full Prescribing Information for complete details.
Step Three. If you rule out claims submission errors, or if you determine that the insurer denied coverage because it was not convinced the therapy was necessary, you will need to submit documentation to justify the medical necessity of the drug. You will need to submit your appeal within the specified time limits of the corresponding payer. Submit a letter of medical necessity with your appeal. A sample letter of medical necessity is attached as Appendix C. Make sure the letter highlights the following information where relevant and applicable:

- Resubmission of claim with correct coding information (if applicable)
- Patient’s medical history
- Other therapies that have been tried unsuccessfully
- Reasons the drug was recommended for this particular patient
- Risks of forgoing the recommended drug therapy

In addition, include the following information with the resubmitted claim:

- Package insert
- Peer-reviewed publications (which can be downloaded using the following links)

- FDA approval letter

Step Four. If you receive a second denial, please advise the patient to call the insurer’s medical director or claims manager to request another review or a hearing. You may be asked for a copy of all the paperwork, so be prepared to resubmit already prepared material or additional information. Note that this step is not applicable under Medicare.

It is important to encourage patients to contact their benefits office when coverage is denied and talk to the benefits manager if necessary. Although the process may be lengthy, remember that many efforts to pursue coverage and payment are successful, and that efforts for one patient may ensure that the next patient will not experience similar problems with the insurer.
Appendix A: Sample CMS-1500 Claim Form

Please refer to the accompanying full Prescribing Information for complete details.
Appendix B: Sample CMS UB-04 Claim Form

Please refer to the accompanying full Prescribing Information for complete details.
Appendix C: Sample Letter of Medical Necessity

Please visit www.BIVIGAM.com to download this form.

The following can be used as a template that providers may consider using to help document the medical necessity of administering BIVIGAM [Immune Globulin Intravenous (Human), 10% Liquid] for your patient. If you choose a different format for the letters of medical necessity, the letters should be tailored to the particular patient.

[Provider Letterhead]
[Insert Date]

[Insert Payer’s Name]
[Insert Payer’s Address]
[Insert City, State, Zip Code]

R.e: BIVIGAM Therapy for [Insert Patient’s Name]
[Insert Patient Identification Number]
[Insert Insurance Policy Group Number (If Applicable)]
[Insert Date of Birth]

Dear Sir or Madam:

I am writing on behalf of my patient, [Insert Patient’s Name], to document the medical necessity of BIVIGAM™ [Immune Globulin Intravenous (Human), 10% Liquid]. BIVIGAM™ has been approved by the U.S. Food and Drug Administration (FDA) for primary immune deficiency. For additional information, see the attached BIVIGAM Prescribing Information.

[Provide a detailed overview of the patient’s medical history, diagnostic testing, and course of treatment. Also, describe the anticipated clinical outcome for the patient once BIVIGAM is initiated as well as the anticipated clinical outcome without the treatment.]

In summary, BIVIGAM is medically necessary and reasonable for this patient’s medical condition and [Insert Payer’s Name] should cover this product for my patient without delay. Please contact me at [Insert Provider’s Contact Information] if any additional information is required to ensure the prompt approval of this course of treatment.

Sincerely,
### Appendix D: Sample Insurance Verification Request Form

Please visit www.BIVIGAM.com to download this form.

**BIVIGAM Careline**

**Insurance Verification Request Form**

Please Fax the Completed Form to: 855-330-5477

You may contact the BIVIGAM Careline by calling 855-BIVIGAM (855-248-4426)

Monday through Friday between the hours of 9:00am and 6:00pm Eastern Time (ET)

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#### PROVIDER INFORMATION

<table>
<thead>
<tr>
<th>Provider Name:</th>
<th>Specialty:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office Contact Name:</td>
<td></td>
</tr>
<tr>
<td>Facility Name:</td>
<td></td>
</tr>
<tr>
<td>Street Address:</td>
<td></td>
</tr>
<tr>
<td>City:</td>
<td>State:</td>
</tr>
<tr>
<td>Phone #: (include ext.):</td>
<td>Fax #:</td>
</tr>
</tbody>
</table>

**Place of Service (check all to be verified):**

- [ ] Physician Office (11)
- [ ] Hospital Outpatient Department (22)
- [ ] Other: Please specify: ________________________________

How do you intend to supply the medication?

- [ ] Specialty Pharmacy Name ________________________________
- [ ] Buy and Bill

**Place of Service Name and Address (if different than Facility Name listed above):**

<table>
<thead>
<tr>
<th>Provider NPI #:</th>
<th>Provider Tax ID #:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facility NPI #:</td>
<td>Facility Tax ID #:</td>
</tr>
<tr>
<td>Medicare PTAN #:</td>
<td>Medicaid Provider #:</td>
</tr>
<tr>
<td>State License #:</td>
<td></td>
</tr>
</tbody>
</table>

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#### PATIENT INFORMATION

Please attach an enlarged copy of the front and back of the patient’s insurance card along with this form.

<table>
<thead>
<tr>
<th>Patient First Name:</th>
<th>Patient Last Name:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Security #:</td>
<td>Date of Birth (mm/dd/yyyy):</td>
</tr>
<tr>
<td></td>
<td>Gender: F ☐ M ☐</td>
</tr>
<tr>
<td>Street Address:</td>
<td>City:</td>
</tr>
<tr>
<td>Home Phone #:</td>
<td>Work Phone #:</td>
</tr>
<tr>
<td></td>
<td>( )</td>
</tr>
<tr>
<td>Primary Insurance Name:</td>
<td>Phone #:</td>
</tr>
<tr>
<td>Secondary Insurance Name:</td>
<td>Phone #:</td>
</tr>
<tr>
<td>Subscriber Name:</td>
<td>Subscriber ID #:</td>
</tr>
<tr>
<td>Subscriber Date of Birth (mm/dd/yyyy):</td>
<td>Subscriber Social Security #:</td>
</tr>
<tr>
<td>Employer Name:</td>
<td></td>
</tr>
<tr>
<td>Subscriber Date of Birth (mm/dd/yyyy):</td>
<td>Subscriber Social Security #:</td>
</tr>
<tr>
<td>Subscriber ID #:</td>
<td>Group ID #:</td>
</tr>
</tbody>
</table>

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#### TREATMENT INFORMATION

to be completed by provider

Diagnosis Code 1 (ICD-9): ______________

Diagnosis Code 2 (ICD-9): ______________

Diagnosis Code 3 (ICD-9): ______________

Estimated Date of Treatment with BIVIGAM®:

If the patient’s insurer requires a prior authorization, would you like assistance with pursuing the prior authorization? ☐ Yes ☐ No

---

**IMPORTANT NOTICE:** This is not a guarantee of insurance benefits. All benefits are subject to the insured’s plan. Under no circumstances shall the BIVIGAM® CareLine be held responsible or liable for payment of any claims, benefits or costs.

**IMPORTANT WARNING:** This message is intended for the use of the person or entity to which it is addressed and may contain information that is privileged and confidential, the disclosure of which is governed by applicable law. If the reader of this message is not the intended recipient, or is the employee or agent responsible for delivering it to the intended recipient, you are hereby notified that any dissemination, distribution or copying of this information is STRICTLY PROHIBITED. If you received this documentation in error, please notify us immediately and destroy the related documentation. This is not a guarantee of insurance benefits.

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Please refer to the accompanying full Prescribing Information for complete details.

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Appendix E: Glossary

<table>
<thead>
<tr>
<th>APC SYSTEM</th>
<th>Ambulatory Payment Classification. The Medicare prospective payment system (PPS) for hospital outpatient services.</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASP</td>
<td>Average Sales Price. A reference point defined by statute for pricing drugs and biologics. The manufacturer’s total sales—excluding sales that are exempt from the Medicare best price calculation and sales to an entity that are nominal in amount, including prompt pay discounts, cash discounts, free goods, and rebates—to all purchasers in the U.S. for a NDC for a quarter divided by the total number of units of that NDC sold by the manufacturer within that same quarter.</td>
</tr>
<tr>
<td>AWP</td>
<td>Average Wholesale Price. A price point often used to facilitate electronic processing of reimbursement claims. The AWP for a drug typically is published in drug pricing compendia, like First DataBank, Inc. or Red Book®.</td>
</tr>
<tr>
<td>CMS</td>
<td>Centers for Medicare and Medicaid Services. U.S. federal agency that administers the Medicare and Medicaid programs.</td>
</tr>
<tr>
<td>CMS-1500</td>
<td>A standard claim form required by Medicare and other payers for billing services provided in freestanding facilities (for example, IV infusion centers) and physician offices as well as physicians’ professional services in other settings of care; used to bill durable medical equipment.</td>
</tr>
<tr>
<td>CPT</td>
<td>Current Procedural Terminology. Uniform listing of descriptive terms and codes used throughout the industry for reporting professional medical services.</td>
</tr>
<tr>
<td>FEE SCHEDULE</td>
<td>Listing of the maximum fees that an insurer will pay for certain services; physician fee schedules usually are based on CPT codes.</td>
</tr>
<tr>
<td>HCPCS</td>
<td>Health Care Common Procedure Coding System. Describes drugs and biologics, some supplies and devices, and certain services/procedures not described by CPT codes; used in the physician office and hospital outpatient settings.</td>
</tr>
<tr>
<td>ICD-9-CM</td>
<td>International Classification of Diseases, 9th Revision, Clinical Modification. Statistical classification system consisting of a listing of diagnosis and identifying codes for reporting diagnosis of health plan enrollees identified by physicians; coding and terminology to accurately describe primary and secondary diagnosis and provide for consistent documentation for claims.</td>
</tr>
<tr>
<td>LCD</td>
<td>Local Coverage Determination. Local policy established by a Medicare fiscal intermediary or carrier to review medical claims for appropriateness of treatment based on factors such as type of provider or patient diagnosis; the policies can vary based on local interpretation of national policies, local practice patterns, or both; available to the public.</td>
</tr>
<tr>
<td>MAC</td>
<td>Medicare Administrative Contractor. A company under contract with the federal government to handle claims processing for Medicare services.</td>
</tr>
<tr>
<td>NDC</td>
<td>National Drug Code. Serves as a universal product identifier for human drugs; NDC directory consists of all prescriptions and selected over-the-counter drugs, domestic, and foreign products that are in commercial distribution in the U.S.; each drug product listed under section 520 of the Federal Food, Drug, and Cosmetic Act is assigned a unique 11-digit, 3-segment number.</td>
</tr>
<tr>
<td>OPPS</td>
<td>Outpatient Prospective Payment System. Medicare payment system that went into effect on August 1, 2000, and is based on predetermined rates or fees related to Ambulatory Patient Classifications (APCs).</td>
</tr>
</tbody>
</table>

Please refer to the accompanying full Prescribing Information for complete details.
## Appendix E: Glossary

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PDP</strong></td>
<td>Prescription Drug Plan. Medicare Prescription Drug Plans, or Medicare Advantage Prescription Drug (MA-PD), are Medicare Part D plans which add coverage to the original Medicare Plan and often offered by private companies approved by Medicare.</td>
</tr>
<tr>
<td><strong>RBRVS</strong></td>
<td>Resource-Based Relative Value Scale. Medicare fee schedule that is the basis for Medicare and Medicaid fee-for-service payment.</td>
</tr>
<tr>
<td><strong>REVENUE CODES</strong></td>
<td>Four-digit codes required on all hospital claims which allow facilities to attribute supplies and services to specific cost centers within the hospital; maintained by the National Uniform Billing Committee.</td>
</tr>
<tr>
<td><strong>SEPARATE PAYMENT</strong></td>
<td>Drugs and biologics that are eligible for separate payment are reimbursed by the payer individually rather than as a bundled payment with other healthcare services.</td>
</tr>
<tr>
<td><strong>UB-04 CLAIM FORM</strong></td>
<td>A standard claim form required by Medicare and other payers for billing institutional (for example, hospital) services.</td>
</tr>
</tbody>
</table>
## Appendix F: Quick Coding Reference Sheet

### HCPCS CODE

<table>
<thead>
<tr>
<th>SETTING</th>
<th>HCPCS CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHYSICIAN OFFICE/ HOSPITAL OUTPATIENT DEPARTMENT</td>
<td>J1556</td>
<td>Injection, Immune Globulin (BIVIGAM) Intravenous, Non-Lyophilized (e.g. Liquid), 500 mg</td>
</tr>
</tbody>
</table>

### CPT CODES

<table>
<thead>
<tr>
<th>CPT CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>96365</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour</td>
</tr>
<tr>
<td>96366</td>
<td>Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour</td>
</tr>
</tbody>
</table>

### NDCs

<table>
<thead>
<tr>
<th>VIAL SIZE</th>
<th>NDC</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 ML VIAL (5 G IGG)</td>
<td>59730-6502-1</td>
</tr>
<tr>
<td>100 ML VIAL (10 G IGG)</td>
<td>59730-6503-1</td>
</tr>
</tbody>
</table>

### ICD-9-CM DIAGNOSIS CODES

<table>
<thead>
<tr>
<th>ICD-9-CM CODE</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>279.00</td>
<td>Hypogammaglobulinemia, unspecified</td>
</tr>
<tr>
<td>279.03</td>
<td>Other selective immunoglobulin deficiencies</td>
</tr>
<tr>
<td>279.04</td>
<td>Congenital hypogammaglobulinemia</td>
</tr>
<tr>
<td>279.05</td>
<td>Immunodeficiency with increased IgM</td>
</tr>
<tr>
<td>279.06</td>
<td>Common variable immunodeficiency</td>
</tr>
<tr>
<td>279.09</td>
<td>Other deficiency of humoral immunity</td>
</tr>
<tr>
<td>279.12</td>
<td>Wiskott-Aldrich syndrome</td>
</tr>
<tr>
<td>279.2</td>
<td>Combined immunity deficiency</td>
</tr>
</tbody>
</table>
For Questions About Coding and Billing, Call the BIVIGAM CARELINE at:

1 (855) BIVIGAM
1 (855) 248-4426

BIVIGam
Immune Globulin Intravenous (Human), 10% Liquid
HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use BIVIGAM® safely and effectively. See full prescribing information for BIVIGAM.

Immune Globulin Intravenous (Human), 10% Liquid
BIVIGAM
Initial U.S. Approval: 2012

WARNING: THROMBOSIS, RENAL DYSFUNCTION, AND ACUTE RENAL FAILURE
See full Prescribing Information for complete boxed warning.
- 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, the use of estrogen, indwelling vascular catheters, hyperviscosity and cardiovascular risk factors.
- Renal dysfunction, acute renal failure, azotemia, and death may occur with the administration of Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients. [5,3]
- 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. [2,3,5,3]

INDICATIONS AND USAGE
BIVIGAM is an Immune Globulin Intravenous (Human), 10% Liquid, indicated for the treatment of primary humoral immunodeficiency (PI). [1]

DOSEAGE AND ADMINISTRATION

Intravenous Use Only

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Initial Infusion Rate</th>
<th>Maintenance Infusion Rate (if tolerated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>300-800 mg/kg every 3-4 weeks</td>
<td>0.5 mg/kg/min for the first 10 minutes</td>
<td>Increase every 20 minutes (if tolerated) by 0.8 mg/kg/min up to 6 mg/kg/min</td>
</tr>
</tbody>
</table>

- Ensure that patients with pre-existing renal insufficiency are not volume depleted; discontinue BIVIGAM if renal function deteriorates. [5,3]
- For patients at risk of renal dysfunction or thrombotic events, administer BIVIGAM at the minimum infusion rate practicable. [5,1,5,3]

DOSEAGE FORMS AND STRENGTHS
BIVIGAM is a liquid solution containing 10% IgG (100mg/mL) for intravenous infusion; (5g in 50mL solution, 10g in 100mL solution). [3]

CONTRAINDICATIONS
- History of anaphylactic or severe systemic reactions to human immunoglobulin. [4]

FULL PRESCRIBING INFORMATION: CONTENTS
WARNING – THROMBOSIS, RENAL DYSFUNCTION AND ACUTE RENAL FAILURE

1 INDICATIONS AND USAGE
1.1 Primary Humoral Immunodeficiency

2 DOSAGE AND ADMINISTRATION
2.1 Preparation and Handling
2.2 Recommended Dose
2.3 Administration

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS
5.1 Thrombosis
5.2 Hypersensitivity
5.3 Acute Renal Dysfunction and Acute Renal Failure
5.4 Hyperproteinemia, Increased Serum Viscosity, and Hyperviscosity
5.5 Aseptic Meningitis Syndrome (AMS)
5.6 Hemolytic
5.7 Transfusion-Related Acute Lung Injury (TRALI)
5.8 Transmissible Infectious Agents
5.9 Monitoring Laboratory Tests
5.10 Interference with Laboratory Tests

6 ADVERSE REACTIONS
6.1 Clinical Trials Experience
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7 DRUG INTERACTIONS
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8 USE IN SPECIFIC POPULATIONS
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11 DESCRIPTION

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology

Issued: June 2013
FULL PRESCRIBING INFORMATION

WARNING: THROMBOSIS, RENAL DYSFUNCTION, AND ACUTE RENAL FAILURE

- Thrombosis may occur with immune globulin (IGIV) products, including BIVIGAM. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, a history of venous or arterial thrombosis, the use of estrogens, indwelling central vascular catheters, hyperviscosity and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. (see Warnings and Precautions [5.1], Patient Counseling Information [17.2])
- 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 (see Warnings and Precautions [5.3]).
- 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 (see Dosage and Administration [2.2, 2.3], Warnings and Precautions [5.3]).

1 INDICATIONS AND USAGE

1.1 Primary Humoral Immunodeficiency

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.

2 DOSAGE AND ADMINISTRATION

For Intravenous Use Only

2.1 Preparation and Handling

- BIVIGAM is a clear or slightly opalescent, colorless to pale yellow solution. Inspect BIVIGAM visually for particulate matter and discoloration prior to administration. Do not use if the solution is cloudy or turbid, or contains particulate matter.
- Allow refrigerated product to come to room temperature before use.
- Do not freeze or heat. Do not use any solution that has been frozen or heated.
- DO NOT SHAKE.
- Do not mix BIVIGAM with other IGIV products or other intravenous medications. If large doses of BIVIGAM are to be administered, several vials may be pooled using aseptic technique into sterile infusion bags and infused.
- Do not dilute BIVIGAM.
- BIVIGAM contains no preservatives. BIVIGAM vial is for single use only. Any vial of BIVIGAM that has been entered should be used promptly and any unused portion should be discarded immediately. Do not re-use or save for further use.
- Maintain BIVIGAM at room temperature during administration.
- Do not use after expiration date.

2.2 Recommended Dose

As there are significant differences in the half-life of IgG among patients with primary humoral immunodeficiency, the frequency and amount of immunoglobulin therapy may vary from patient to patient. The proper amount can be determined by monitoring clinical response.

The recommended dose of BIVIGAM for replacement therapy in primary humoral immunodeficiency (PI) is 300 to 800 mg/kg body weight administered every 3 to 4 weeks. The dosage may be adjusted over time to achieve the desired trough levels and clinical response.

BIVIGAM dose adjustments may be required in patients who fail to maintain trough total IgG concentrations of at least 500 mg/dL with a target of 600 mg/dL. Starting with the second infusion, the dose will be adjusted proportionally, targeting a trough of ≥ 600 mg/dL, based on the previous trough and the associated dose.

2.3 Administration

It has been reported that the frequency of adverse drug reactions to IGIV increases with the infusion rate. Initial infusion rates should be slow. If there are no adverse drug 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.

Table 1: Recommended Infusion Rates for BIVIGAM

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial Infusion Rate (for first 10 minutes)</th>
<th>Maintenance Infusion Rate (if tolerated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>0.5 mg/kg/min (0.005 mL/kg/min)</td>
<td>Increase every 20 minutes (if tolerated) by 0.8 mg/kg/min up to 6 mg/kg/min.</td>
</tr>
</tbody>
</table>

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 lower rate that is comfortable for the patient.
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 (see Boxed Warning, Warnings and Precautions [5.1, 5.3]).

3 DOSAGE FORMS AND STRENGTHS

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

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Thrombosis

Thrombosis may occur following treatment with immune globulin products (IGIV), including BIVIGAM.4,5,6 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.

Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients at risk of thrombosis, 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 (see Boxed Warning, Dosage and Administration [2.3], Patient Counseling Information [17.2]).

5.2 Hypersensitivity

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 may be available for immediate treatment of acute hypersensitivity reactions.

BIVIGAM contains trace amounts of IgA (≤ 200 micrograms per milliliter) (see Description [11]). Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. BIVIGAM is contraindicated in IgA deficient patients with antibodies against IgA and a history of hypersensitivity reaction (see Contraindications [4]).

5.3 Acute Renal Dysfunction and Acute Renal Failure

Acute renal dysfunction/failure, osmotic nephrosis, and death1-2 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.3 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 (see Patient Counseling Information [17.1f]). In patients who are at risk of developing renal dysfunction, because of pre-existing renal insufficiency or predisposition to acute renal failure (such as diabetes mellitus, hypovolemia, overweight, use of concomitant nephrotoxic medicinal products or age of >65 years), administer BIVIGAM at the minimum infusion rate practicable (see Dosage and Administration [2.3]).

5.4 Hyperproteinaemia, Increased Serum Viscosity, and Hyponatraemia

Hyperproteinaemia, increased serum viscosity, and hyponatraemia may occur in patients receiving IGIV therapy, including BIVIGAM. It is critical to clinically distinguish true hyponatraemia from a pseudohyponatraemia that is associated with or causally related to hyperproteinaemia with concomitant decreased calculated serum osmolality or elevated osmolar gap, because treatment aimed at decreasing serum free water in patients with pseudohyponatraemia may lead to volume depletion, a further increase in serum viscosity, and a possible predisposition to thrombotic events.3

5.5 Aseptic Meningitis Syndrome (AMS)

AMS may occur infrequently with IGIV treatments including BIVIGAM. AMS usually begins within several hours to 2 days following IGIV treatment. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.7,8,9

AMS is characterized by the following signs and symptoms: severe headache, neck rigidity, drowsiness, fever, photophobia, painful eye movements, nausea, and vomiting (see Patient Counseling Information [17.3f]). Cerebrospinal fluid (CSF) studies frequently reveal pleocytosis up to several thousand cells per cubic millimeter, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dL, but negative culture results. Conduct a thorough neurological examination on patients exhibiting such signs and symptoms, including CSF studies, to rule out other causes of meningitis.

AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IGIV.

5.6 Hemolysis

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.10,11,12 Delayed hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration,11 and acute hemolysis, consistent with intravascular hemolysis, has been reported.

Monitor patients for clinical signs and symptoms of hemolysis (see Patient Counseling Information [17.4f]). If these are present after BIVIGAM infusion, perform appropriate confirmatory laboratory testing. If transfusion is indicated for patients who develop hemolysis with clinically compromising anemia after receiving IGIV, perform adequate cross-matching to avoid exacerbating on-going hemolysis.

5.7 Transfusion-Related Acute Lung Injury (TRALI)

Noncardiogenic pulmonary edema may occur in patients following IGIV treatment13 including BIVIGAM. 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 (see Patient Counseling Information [17.5f]).

TRALI may be managed using oxygen therapy with adequate ventilatory support.
5.8 Transmissible Infectious Agents
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.

No cases of transmission of viral diseases or CJD have been associated with the use of BIVIGAM. All infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Biotest Pharmaceuticals Corporation at 1-800-488-4244. Before prescribing BIVIGAM, the physician should discuss the risks and benefits of its use with the patient (see Patient Counseling Information [176]).

5.9 Monitoring Laboratory Tests
- 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.
- Because of the potentially increased risk of thrombosis with IGIV treatment, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammapathies.
- If signs and/or symptoms of hemolysis are present after an infusion of BIVIGAM, perform appropriate laboratory testing for confirmation.
- If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient’s serum.

5.10 Interference with Laboratory Tests
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.

6 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 (reported in ≥5% of clinical study subjects) were headache, fatigue, infusion site reaction, nausea, sinusitis, blood pressure increased, diarrhea, dizziness, and lethargy.

6.1 Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in clinical trials cannot be directly compared to rates in the clinical trials of another product and may not reflect the rates observed in clinical practice.

In a multicenter, open-label, non-randomized clinical trial, 63 subjects with PI, on regular IGIV replacement therapy, received doses of BIVIGAM ranging from 254 to 1029 mg/kg (median dose 462.8 mg/kg) every 3 weeks or 4 weeks for up to 12 months (mean 313.3 days; range 66 – 386 days) (see Clinical Studies [14]). The use of pre-medication was discouraged; however, if subjects required pre-medication (antipyretic, antihistamine, or antiemetic agent) for recurrent reactions to immune globulins, they were allowed to continue those medications for this trial. Of the 746 infusions administered, 41 (65%) subjects received premedication prior to 415 (56%) infusions.

Fifty-nine subjects (94%) had an adverse reaction at some time during the study. The proportion of subjects who had at least one adverse reaction was the same for both the 3- and 4-week cycles. The most common adverse reactions observed in this clinical trial were headache (32 subjects, 51%), sinusitis (24 subjects, 38%), fatigue (18 subjects, 29%), upper respiratory tract infection (16 subjects, 25%), diarrhea (13 subjects, 21%), cough (14 subjects, 22%), bronchitis (12 subjects, 19%), pyrexia (12 subjects, 19%), and nausea (9 subjects, 14%).

Adverse reactions (ARs) are those occurring during or within 72 hours after the end of an infusion. In this study, the upper bound of the 1-sided 95% confidence interval for the proportion of BIVIGAM infusions with one or more temporally associated adverse reactions was 31%. The total number of adverse reactions was 431 (a rate of 0.58 ARs per infusion).

<table>
<thead>
<tr>
<th>ARs</th>
<th>No. Subjects Reporting ARs (% of Subjects) [n=63]</th>
<th>No. Infusions With ARs (% of Infusions) [n=746]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>27 (43%)</td>
<td>115 (15.4%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>15 (24%)</td>
<td>59 (7.9%)</td>
</tr>
<tr>
<td>Infusion Site Reaction</td>
<td>5 (8%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (8%)</td>
<td>8 (1.1%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>5 (8%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Blood Pressure Increased</td>
<td>4 (6%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (6%)</td>
<td>4 (0.5%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4 (6%)</td>
<td>4 (0.5%)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>4 (6%)</td>
<td>4 (0.5%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>3 (5%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Blood Pressure Diastolic Decreased</td>
<td>3 (5%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Fibromyalgia*</td>
<td>3 (5%)</td>
<td>17 (2.3%)</td>
</tr>
<tr>
<td>Migraine</td>
<td>3 (5%)</td>
<td>8 (1.1%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>3 (5%)</td>
<td>4 (0.5%)</td>
</tr>
<tr>
<td>Pharyngolaryngeal Pain</td>
<td>3 (5%)</td>
<td>3 (0.4%)</td>
</tr>
</tbody>
</table>

*Symptoms occurring under pre-existing fibromyalgia

Seven subjects (11.1%) experienced 11 serious ARs. Two of these were related serious ARs (vomiting and dehydration) that occurred in one subject.

One subject withdrew from the study due to ARs related to BIVIGAM (lethargy, headache, tachycardia and pruritus).
All 63 subjects enrolled in this study had a negative direct antiglobulin (Coombs') test at baseline. During the study, no subjects showed clinical evidence of hemolytic anemia.

No cases of transmission of viral diseases or CJD have been associated with the use of BIVIGAM. During the clinical trial, no subjects tested positive for infection due to human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV). There was a single positive finding for parvovirus (B19 virus) during the study. This subject came in contact with acute B19 virus from working at a school greeting children where a child was reported to have symptomatic Fifth's disease. There was no cluster (no other cases in other subjects) of B19 virus transmission with the IGIV batch concerned.

6.2 Postmarketing Experience
Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions or establish a causal relationship to product exposure. The following adverse reactions have been identified and reported during the post-approval use of IGIV products:

- Respiratory: Apnea, Acute Respiratory Distress Syndrome (ARDS), Transfusion Associated Lung Injury (TRALI), cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm.
- Cardiovascular: Cardiac arrest, thromboembolism, vascular collapse, hypotension.
- Neurological: Coma, loss of consciousness, seizures, tremor.
- Integumentary: Stevens-Johnson syndrome, epidermolysis, erythema multiforme, bullous dermatitis.
- Hematologic: Pancreatitis, leukopenia, hemolysis, positive direct antiglobulin (Coombs') test.
- General/Body as a Whole: Pyrexia, rigors.
- Musculoskeletal: Back pain.
- Gastrointestinal: Hepatic dysfunction, abdominal pain.

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines
Immunoglobulin administration may transiently impair the efficacy of live attenuated virus vaccines such as measles, mumps, rubella, and varicella because the continued presence of high levels of passively acquired antibody may interfere with an active antibody response.10,16 The immunizing physician should be informed of recent therapy with BIVIGAM so that appropriate measures may be taken (see Patient Counseling Information [17,17]).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Pregnancy Category C. Animal reproduction studies have not been conducted with BIVIGAM. It is not known whether BIVIGAM can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. BIVIGAM should be given to pregnant women only if clearly needed.17,18

8.3 Nursing Mothers
Use of BIVIGAM in nursing mothers has not been evaluated. BIVIGAM should be given to nursing mothers only if clearly needed.

8.4 Pediatric Use
BIVIGAM was evaluated in 9 pediatric patients (4 children ages 6–11 years and 5 adolescents ages 12–16 years) with PL. This number of pediatric patients was too small for safety or efficacy. The safety and effectiveness of BIVIGAM has not been established in pediatric patients with PL who are under the age of 6 (see Clinical Studies [14]).

8.5 Geriatric Use
BIVIGAM should be used with caution in patients age 65 and over who are judged to be at increased risk of developing renal insufficiency or thrombotic events (see Boxed Warning, Warnings and Precautions [5.1, 5.2]). Do not exceed recommended doses and administer BIVIGAM at the minimum infusion rate practicable.

BIVIGAM was evaluated in 9 patients age 65 and older with PL. This number of geriatric patients is not being sufficient to determine whether they respond differently from younger patients (see Clinical Studies [14]).

11 DESCRIPTION

BIVIGAM is a purified, sterile, ready-to-use preparation of concentrated human immunoglobulin G (IgG) antibodies. The distribution of IgG subclasses is similar to that of normal plasma.19,20 The active ingredient is human immunoglobulin purified from source human plasma and processed using a modified classical Cohn Method 6 / Onley Method 9 fractionation procedure. BIVIGAM contains 100 ± 10 mg/mL protein, of which not less than 96% is human immunoglobulin obtained from source human plasma. It is formulated in water for injection containing 0.100-0.140 M sodium chloride, 0.20-0.29 M glycine, 0.15-0.25% polysorbate 80, and pH 4.0-4.6. BIVIGAM contains ≤ 200 μg/mL of IgA.

Each plasma donation used for the manufacture of BIVIGAM is collected from FDA licensed facilities and undergoes rigorous testing. Plasma donations must test negative for hepatitis B virus (HBV) surface antigen (HBsAg), antibodies to human immunodeficiency virus (HIV) strains 1 and 2 (anti-HIV-1/2), and antibodies to the hepatitis C virus (anti-HCV) as determined by enzyme immuno assay (EIA). In addition, each plasma unit must test negative and/or non-reactive for HIV RNA, HCV RNA, HBV DNA, Hepatitis A Virus (HAV) RNA, and Parvovirus B19 (B19 virus) DNA as determined by Nucleic Acid Amplification Testing (NAT) of plasma minipools. NAT for B19 virus DNA is also performed on the sample of the manufacturing pool and the limit for B19 virus DNA in a manufacturing pool is set not to exceed 10^4 IU/mL.

The manufacturing process of BIVIGAM employs three steps to remove/inactivate adventitious viruses to minimize the risk of virus transmission. The steps are "Precipitation and removal of fraction III" during cold ethanol fractionation, classical "Solvent/detergent treatment" and "35 nm virus filtration". In compliance with current guidelines, the steps have been separately validated in a series of in vitro experiments for their capacity to inactivate or remove both enveloped and non-enveloped viruses.

Precipitation and removal of fraction III removes both enveloped and non-enveloped viruses, solvent/detergent treatment represents a virus inactivation step for enveloped viruses, and 35 nm virus filtration removes both enveloped and non-enveloped viruses by size exclusion. In addition to the steps above, low pH during several steps of the production process contributes to virus inactivation. The results of virus validation studies for BIVIGAM are shown in Table 3, expressed as log_{10} reduction factors.
Table 3: Virus Validation Data for BIVIGAM

<table>
<thead>
<tr>
<th>Virus Type/Family</th>
<th>Enveloped viruses</th>
<th>Non-enveloped viruses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Retrovirus</td>
<td>Flavi</td>
</tr>
<tr>
<td>Step/Virus</td>
<td>HIV</td>
<td>BVDV</td>
</tr>
<tr>
<td>Precipitation and Removal of Fraction III and Depth Filtration</td>
<td>--</td>
<td>1.87*</td>
</tr>
<tr>
<td>TNBF/Trition X-100 Treatment</td>
<td>&gt; 4.43</td>
<td>&gt; 8.04</td>
</tr>
<tr>
<td>30 mm Virus Filtration</td>
<td>&gt; 5.19</td>
<td>&gt; 4.88</td>
</tr>
<tr>
<td>Total Clearance</td>
<td>&gt; 9.62</td>
<td>&gt; 11.79</td>
</tr>
</tbody>
</table>

* without depth filtration -- not done values below 1 log_{10} are considered as insignificant and are not used for total clearance; HIV: human immunodeficiency virus; BVDV: Bovine viral diarrhea virus; model virus for HCV; SindV: Sindbis virus, model virus for HCV; WNV: West Nile virus; PRV: Pseudorabies virus, model virus for herpes viruses and Hepatitis B virus; MEV: Murine encephalomyelitis virus, model virus for hepatitis A virus; BPV: Bovine parvovirus, model virus for human B19 virus; PPV, Porcine parovirus, model virus for human B19 virus; SV40, Simian virus 40, model virus for highly resistant non-enveloped viruses.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

BIVIGAM is a replacement therapy in patients with primary humoral immunodeficiency (PI) (e.g. agammaglobulinemia, hypogammaglobulinemia, CVID, SCID).

The broad spectrum of neutralizing IgG antibodies against bacterial and viral pathogens and their toxins helps to avoid recurrent serious opportunistic infections. IgG antibodies are opsonins that increase phagocytosis and elimination of pathogens from the circulation. The mechanism of action has not been fully elucidated in PI.

12.3 Pharmacokinetics

In the clinical study assessing the efficacy and safety of BIVIGAM in 63 subjects with PI (see Clinical Studies [114.1]), serum concentrations of total IgG and IgG subclasses were measured in 21 subjects (ages 18 to 75) following the 4th infusion for the 5 subjects on the 3-week dosing interval and following the 5th infusion for the 16 subjects on the 4-week dosing interval. The dose of BIVIGAM used in these subjects ranged from 300 mg/kg to 800 mg/kg. After the infusion, blood samples were taken until Day 21 and Day 28 for the 3-week and 4-week dosing intervals, respectively. Table 4 summarizes the total IgG Pharmacokinetic Parameters of BIVIGAM, based on serum concentrations of total IgG. Trough concentrations were maintained throughout the study for both treatment cycles and mean trough concentrations were well above the target trough concentration of 500 mg/L for both treatment cycles in pediatric (≥ 6 years old) as well as adult subjects at all time points.

Table 4: Total IgG Pharmacokinetic Parameter Estimates (PK Population) in Adults

<table>
<thead>
<tr>
<th>Statistic</th>
<th>3-week cycle (n = 5)</th>
<th>4-week cycle (n = 16)</th>
<th>Total (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C_{max} (mg/dL)</td>
<td>2184 (293)</td>
<td>2122 (425)</td>
<td>2137 (392)</td>
</tr>
<tr>
<td>C_{min} (mg/dL)</td>
<td>996 (176)</td>
<td>1106 (396)</td>
<td>1080 (355)</td>
</tr>
<tr>
<td>T_{max} (h)</td>
<td>4.05 (2.67 – 2.61)</td>
<td>3.47 (2.58 – 78.6)</td>
<td>3.50 (2.58 – 78.6)</td>
</tr>
<tr>
<td>AUC_{inf} (day*mg/dL)</td>
<td>27841 (4925)</td>
<td>35509 (6472)</td>
<td>33592 (6898)</td>
</tr>
<tr>
<td>t_{1/2} (d)</td>
<td>19.6 (4.1)</td>
<td>33.5 (10.7)</td>
<td>30.0 (11.2)</td>
</tr>
<tr>
<td>CL (dL/kg/d)</td>
<td>0.0197 (0.002234)</td>
<td>0.0141 (0.00463)</td>
<td>0.0155 (0.00480)</td>
</tr>
<tr>
<td>V_{d} (dL/kg)</td>
<td>0.584 (0.132)</td>
<td>0.640 (0.141)</td>
<td>0.626 (0.138)</td>
</tr>
<tr>
<td>MRT (day)</td>
<td>29.5 (5.1)</td>
<td>48.3 (14.6)</td>
<td>43.6 (15.2)</td>
</tr>
</tbody>
</table>

AUC_{inf} = steady-state area under the plasma concentration versus time curve with t_{1/2} = dosing interval; CL = total body clearance; C_{max} = maximum concentration; C_{min} = minimum concentration; CV = coefficient of variation; n = number of subjects; NA = not applicable; SD = standard deviation; T_{max} = time of maximum concentration; t_{1/2} = terminal half-life; V_{d} = Volume of distribution steady-state; MRT = mean residence time; * Median and Range.

The median terminal half-life of BIVIGAM was 30 days for the 21 subjects. Mean trough IgG subclass levels were consistent with physiological values.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No animal studies were conducted to evaluate the carcinogenic or mutagenic effects of BIVIGAM or its effects on fertility.

13.2 Animal Toxicology and/or Pharmacology

No animal studies were conducted to evaluate possible toxicity of BIVIGAM in animals.

BIVIGAM contains Polysorbate 80 at a concentration of up to 2.5 mg/mL. Intravenous administrations of Polysorbate 80 in multiple species have been linked with a decrease in blood pressure. In rats, single doses of Polysorbate 80 that were up to 25 times higher than the amount from 800 mg/kg BIVIGAM resulted in an increase of liver enzymes and total bilirubin.
14.1 Treatment of Primary Humoral Immunodeficiency

A prospective, open-labeled, single-arm, multicenter trial assessed the efficacy, safety, and pharmacokinetics of BIVIGAM in adult and pediatric subjects with PI. Study subjects were receiving regular IgIV replacement therapy, with a stable dose between 300 and 800 mg/kg for at least 3 months prior to participation. Subjects received a BIVIGAM infusion administered every 3 or 4 weeks (both the dose and schedule depending on their prior therapy) for approximately 1 year.

A total of 63 subjects were enrolled in the trial, 31 men and 32 women with a mean age of 41 years. Forty-four subjects were adults (70%) between 18 and 64 years of age. There were 9 pediatric subjects (see Pediatric Use [8.4]), and 9 elderly subjects (14%, ≥65 years of age). The oldest subject was 75 years of age.

There were 17 subjects with a 3-week cycle and 46 subjects with a 4-week cycle. There were 51 subjects (81%) with common variable immunodeficiency as their primary diagnosis, followed by X-linked agammaglobulinemia and ‘Other’ (9.5% each). The intent to treat (ITT) population included 58 subjects and was used for efficacy analysis.

The primary endpoint of the study was to assess the efficacy of BIVIGAM in preventing serious bacterial infections (SBIs) defined as rates of <1.0 cases of bacterial pneumonia, bacteremia/septicaemia, osteomyelitis/septic arthritis, visceral abscess, and bacterial meningitis per person-year. Secondary efficacy parameters included time to first SBI and time to first infection of any kind/severity, days on antibiotics (excluding prophylaxis), days off school/work due to infections, all confirmed infections of any kind or seriousness, and hospitalizations due to infection.

During the 12-month study period, two serious acute bacterial infections occurred in two subjects with an onset date between the first infusion of BIVIGAM and the first follow-up visit, inclusive. Thus, the mean event rate of serious, acute, bacterial infections per year was 0.037 (with an upper 1-sided 99% confidence interval of 0.101, which met the study’s primary efficacy endpoint).

The two SBIs were cases of bacterial pneumonia. Thirty-three percent of subjects had days off work or school due to an infection. Of the 197 infections reported, 2 resulted in hospitalization. Results for the pediatric subjects were similar to those for the adult subjects. (see Table 5).

<table>
<thead>
<tr>
<th>Table 5: Summary of Efficacy Results in Subjects with PI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Subjects (ITT Population)</strong></td>
</tr>
<tr>
<td>Total Number of person-years$^a$</td>
</tr>
<tr>
<td><strong>Infections</strong></td>
</tr>
<tr>
<td>Number of confirmed serious acute bacterial infections$^b$</td>
</tr>
<tr>
<td>Rate of SBIs (SBIs/total person-years)</td>
</tr>
<tr>
<td>Total infections</td>
</tr>
<tr>
<td>Infections per subject per year</td>
</tr>
<tr>
<td><strong>Antibiotic use$^c$</strong></td>
</tr>
<tr>
<td>Number of subjects (%)</td>
</tr>
<tr>
<td>Days per subject per year</td>
</tr>
<tr>
<td><strong>Days off school/work due to Infections</strong></td>
</tr>
<tr>
<td>Number of persons with days off of school or work due to infections (%)</td>
</tr>
<tr>
<td>Total days (%)</td>
</tr>
<tr>
<td>Days per subject per year</td>
</tr>
<tr>
<td><strong>Hospitalization</strong></td>
</tr>
<tr>
<td>Number of subjects (%)</td>
</tr>
<tr>
<td>Number of Days</td>
</tr>
<tr>
<td>Days per subject per year</td>
</tr>
</tbody>
</table>

$^a$Person-years: Person-time in years with 2 decimals = (the Final Clinical Visit Date - the Day 0 date +1)/365.25, where the final clinical visit date is defined as the specimen collection date of the final clinical visit for urinalysis, or the specimen collection date for the clinical laboratory tests at the final clinical visit and Day 0 date is the start date of the first BIVIGAM infusion.

$^b$Defined as bacterial pneumonia, bacterial meningitis, bacteremia/septicaemia, osteomyelitis/septic arthritis, and visceral abscess.

$^c$The calculation of antibiotic use excludes 8 subjects who were on antibiotics throughout the study either prophylactically or for ongoing or recurrent conditions.

15 REFERENCES


16 HOW SUPPLIED/STORAGE AND HANDLING

BIVIGAM is supplied in a single-use, tamper-evident vial. The components used in the packaging for BIVIGAM are not made with natural rubber latex.

BIVIGAM is supplied in the following sizes:

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Size</th>
<th>Grams Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>59730-6530-1</td>
<td>50mL</td>
<td>5</td>
</tr>
<tr>
<td>59730-6530-1</td>
<td>100mL</td>
<td>10</td>
</tr>
</tbody>
</table>

Storage
Refrigerate between 2 to 8°C (36 to 46°F).

Special Precautions for Storage
Do not freeze or heat. Do not use any solutions that have been frozen or heated.
Allow refrigerated product to come to room temperature before use.

Do not use after expiration date.

Shelf Life
BIVIGAM may be stored until expiration date on vial packaging at 2 to 8°C (36 to 46°F).

Incompatibilities
Do not dilute.
BIVIGAM should be infused using a separate line by itself, without mixing with other intravenous fluids or medications the patient may be receiving.

17 PATIENT COUNSELING INFORMATION

17.1 Acute Renal Dysfunction and Acute Renal Failure
Instruct patients to immediately report symptoms of decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath. Such symptoms suggest kidney damage (see Boxed Warning, Warnings and Precautions [5.3]).

17.2 Thrombosis
Instruct patients to immediately report symptoms of thrombosis. These symptoms may include: pain and/or swelling of an arm or leg/feet with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, acute chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body, (see Warnings and Precautions [5.7]).

17.3 Aseptic Meningitis Syndrome (AMS)
Instruct patients to immediately report signs and symptoms of AMS. These symptoms include severe headache, neck stiffness, drowsiness, fever, sensitivity to light, painful eye movements, nausea and vomiting (see Warnings and Precautions [5.5]).

17.4 Hemolysis
Instruct patients to immediately report signs and symptoms of hemolysis. These symptoms include fatigue, increased heart rate, yellowing of skin or eyes, dark-colored urine (see Warnings and Precautions [5.6]).

17.5 Transfusion-Related Acute Lung Injury (TRALI)
Instruct patients to immediately report signs and symptoms of TRALI. These symptoms include trouble breathing, chest pain, blue lips or extremities, fever (see Warnings and Precautions [5.7]).

17.6 Transmissible Infectious Agents
Inform patients that BIVIGAM is made from human plasma and may contain infectious agents that can cause disease. While the risk that BIVIGAM can transmit an infection has been reduced by screening plasma donors for prior exposure, testing donated plasma, and inactivating or removing certain viruses during manufacture, patients should report any symptoms that concern them (see Description [11] and Warnings and Precautions [5.8]).

17.7 Live Virus Vaccines
Inform patients that BIVIGAM can interfere with their immune response to live viral vaccines (e.g., measles, mumps, rubella, and varicella), and instruct patients to notify their healthcare professional of this potential interaction when they are receiving vaccinations (see Drug Interactions [7]).

Manufacturer: Biotest Pharmaceuticals Corporation, Boca Raton, FL 33487. USA
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