When treating primary immunodeficiency disease...

Switch to Privigen.

Privigen delivers IVIg therapy that is:

**Simple.**
- Ready-to-use 10% liquid IVIg
- Room temperature storage up to 36 months

**Sophisticated.**
- First and only IVIg stabilized with proline
- Sucrose-free
- IgA ≤ 25 mcg/mL

**Safe.**
- In clinical trials, 97% of related adverse events were non-serious; 95% of 1038 infusions were administered without premedication. The most common adverse reactions were headache, pain, nausea, pyrexia/hyperthermia, fatigue, and chills
- 3-step virus inactivation/removal process, including nanofiltration to 20 nanometers, reduces the risk of pathogen transmission

For more information about Privigen, visit [www.Privigen.com](http://www.Privigen.com).

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**Important Safety Information**

Privigen is indicated for the treatment of patients with primary immunodeficiency (PI) associated with defects in humoral immunity, including but not limited to common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

**WARNING:** Renal dysfunction, acute renal failure, osmotic nephrosis, and death may be associated with the administration of Immune Globulin Intravenous (Human) (IVIg) products in predisposed patients. Administer IVIg products at the minimum infusion rate possible. Renal dysfunction and acute renal failure occur more commonly in patients receiving IVIg products containing sucrose. Privigen does not contain sucrose. See full Prescribing Information for complete Boxed Warning.

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

In patients at risk for developing renal failure, monitor urine output and renal function, including blood urea nitrogen and serum creatinine. Thrombotic events have been reported with Privigen and other IVIg treatments. Monitor patients with risk factors for thrombotic events, including a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and/or known or suspected hyperviscosity.

Aseptic meningitis syndrome (AMS) may occur infrequently with Privigen and other IVIg treatments; AMS may occur more frequently with high doses and/or rapid infusion of IVIg. Hemolysis, hemolytic anemia, and pulmonary adverse events have also been reported. There have been reports of noncardiogenic pulmonary edema in patients administered IVIg. If transfusion-related acute lung injury is suspected, test product and patient for antineutrophil antibodies.

Privigen is derived from human plasma. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

In clinical studies, the most common adverse reactions with Privigen were headache, pain, nausea, pyrexia/hyperthermia, fatigue, and chills.

Please see brief summary of full Prescribing Information on following pages.
Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

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

2.3 DOSAGE FORMS AND STRENGTHS
Privigen is a liquid solution containing 10% IgG (0.1 g/mL) for intravenous infusion.

4 CONTRAINDICATIONS
Privigen contains trace amounts of IgA (25 mcg/mL).

5.1 Hypersensitivity
Privigen contains trace amounts of IgA.

5.3 Hyperproteinemia
Hyperproteinemia may increase serum viscosity, and hypoproteinaemia may occur in patients receiving Privigen and other IGIV product treatments.

5.5 Aseptic Meningitis Syndrome (AMS)
AMS may occur in patients with Privigen or other IGIV product treatments. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.

6 ADVERSE REACTIONS
The most serious adverse reaction observed in clinical study subjects receiving Privigen for PI was hypersensitivity in one subject. The most common adverse reactions observed in >10% of clinical study subjects with PI were headache, pain, nausea, fatigue, and chills.

6.1 Clinical Trials Experience

6.4 Thrombotic Events
Thrombotic events may occur following treatment with Privigen and other IGIV products.

6.5 Transfusion-Related Acute Lung Injury (TRALI)

6.6 Hemolysis
Privigen 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. Hemolytic anemia can develop subsequent to Privigen infusion due to enhanced RBC sequestration and/or intravascular RBC destruction. Hemolysis, possibly intravascular, occurred in two subjects treated with Privigen in the ITP study (see Adverse Reactions [6.6.1]). These cases resolved eventually. Six other subjects experienced hemolysis in the ITP study as documented from clinical laboratory data. MONITOR patients for clinical signs and symptoms of hemolysis (see Patient Counseling Information [17]). If hemolysis is suspected, perform appropriate tests for the presence of anti-erythrocyte antibodies in both the product and the patient's serum. Treatment may be managed using oxygen therapy with adequate ventilatory support.

6.7 Transfusion-Related Acute Lung Injury (TRALI)

6.8 Volume Overload
The high-volume regimen (1 g/kg/day for 2 days) used to treat patients with chronic ITP is not recommended for individuals with expanded fluid volumes or where fluid volume may be of concern (see Dosage and Administration [2.2]).

6.9 Transmissible Infectious Agents
Privigen is made from human plasma. Based on effective donor screening and product processing (see Description [11]), Privigen contains a significantly remote risk of transmission of viral diseases. A theoretical risk for transmission of Creutzfeldt-Jakob disease (CJD) is also considered to be extremely remote. No cases of transmission of viral disease (e.g., HIV) have been associated with the use of Privigen. All infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare professional to CSL Behring Pharmacoepidemiology at 1-888-915-6958.

7 DOSAGE AND ADMINISTRATION

7.1 Primary Humoral Immunodeficiency
Privigen is indicated as replacement therapy for primary humoral immunodeficiency (PI).

7.2 Chronic Immune Thrombocytopenic Purpura
Privigen is indicated for the treatment of patients with chronic immune thrombocytopenic purpura (ITP) to raise platelet counts.

7.3 Dose
Privigen contains trace amounts of IgA (25 mcg/mL) for intravenous infusion.

7.4 Administration

7.5 Monitoring of Patients

7.6 Place of Administration

7.7 Storage

7.8 Handling and Storage

8 DOSAGE FORMS AND STRENGTHS
Privigen is available in 500 mg vials.

9 CONTRAINDICATIONS

9.1 Hypersensitivity

9.2 Renal Failure

9.3 Hyperproteinemia

9.4 Thrombotic Events

9.5 Transfusion-Related Acute Lung Injury (TRALI)

9.6 Hemolysis

9.7 Volume Overload

9.8 Transmissible Infectious Agents

9.9 Transmissible Infectious Agents

9.10 Monitoring: Laboratory Tests

9.11 Interventions With Laboratory Tests

9.12 Reactions With Other Drugs

9.13 Precautions

10 Adverse Reactions

11 Interactions

12 Use In Specific Populations

13 Nonclinical Laboratory Studies

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34 Monitoring of Patients

of total 1038 infusions of Privigen were administered, 272 in the 3-week schedule and 766 in the 4-week schedule. Of the 1038 infusions, 435 were administered to females and 603 to males.

Routine predmedication was not allowed. However, subjects who experienced two consecutive infusion-related adverse events (AEs) that were likely to be prevented by predmedication were permitted to receive antipyretics, antihistamines, NSAIDs, or antiemetic agents. During the study, 8 (10%) subjects received predmedication prior to 51 (4.9%) of the 1038 infusions administered.

Temporally associated AEs are those occurring during or within 72 hours after the end of an infusion, irrespective of causality. In this study, the upper bound of the 1-sided 95% confidence interval for the proportion of Privigen infusions temporally associated with one or more AEs was 23.8% (actual proportion: 20.8%). This is below the target of 40% for this safety endpoint. The total number of temporally associated AEs was 397 (a rate of 0.38 AEs per infusion), reflecting that some subjects experienced more than one AE during the observation period.

Table 2 lists the temporally associated AEs that occurred in more than 5% of subjects during a Privigen infusion or within 72 hours after the end of an infusion, irrespective of causality.

### Table 2: Adverse Events* Occurring in >5% of Subjects With PI During a Privigen Infusion or Within 72 Hours After the End of an Infusion, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
<th>Infusions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>35 (43.8)</td>
<td>87 (8.9)</td>
</tr>
<tr>
<td>Pain</td>
<td>27 (33.0)</td>
<td>44 (4.2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>13 (16.3)</td>
<td>27 (2.6)</td>
</tr>
<tr>
<td>Nausea</td>
<td>10 (12.5)</td>
<td>19 (1.8)</td>
</tr>
<tr>
<td>Chills</td>
<td>9 (11.3)</td>
<td>15 (1.4)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (8.8)</td>
<td>13 (1.3)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>6 (7.5)</td>
<td>10 (1.0)</td>
</tr>
<tr>
<td>Cough</td>
<td>5 (6.3)</td>
<td>5 (0.5)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>5 (6.3)</td>
<td>5 (0.5)</td>
</tr>
<tr>
<td>Stomach discomfort</td>
<td>5 (6.3)</td>
<td>5 (0.5)</td>
</tr>
</tbody>
</table>

*Excluding infections.

Of the 397 temporally associated AEs reported for the 80 subjects with PI, the investigators judged 192 to be related to the infusion of Privigen (including 5 serious, severe AEs described below). Of the 187 non-serious AEs related to the infusion of Privigen, 91 were mild, 81 were moderate, 14 were severe, and 1 was of unknown severity. The most common temporally associated AEs judged by the investigators to be "at least possibly" related to the infusion were headache (29% of subjects), pain (14% of subjects), nausea (11% of subjects), fatigue (11% of subjects), and chills (11% of subjects). Sixteen subjects (20%) experienced 41 serious AEs. Five of these were related severe AEs that were considered by the investigator to be at least possibly related to the infusion of Privigen. Of the 149 non-serious AEs related to the infusion ofPrivigen, 103 were mild, 37 were moderate, and 9 were severe. The most common temporally associated AEs judged by the investigators to be "at least possibly" related to the infusion were headache (65% of subjects) and pyrexia/hyperpyresis (35% of subjects).

Three subjects experienced three serious AEs, one of which (aseptic meningitis) was related to the infusion of Privigen. One subject withdrew from the study due to gingival bleeding, which was not related to Privigen.

Eight subjects, all of whom had a positive DAT, experienced transient drug-related hemolytic reactions, which were associated with elevated bilirubin, elevated lactate dehydrogenase, and a decrease in hemoglobin level within two days after the infusion of Privigen. Two of the eight subjects were clinically anemic but did not require clinical intervention.

Four other subjects with active bleeding were reported to have developed anemia without evidence of hemolysis. In this study, there was a decrease in hemoglobin after the first Privigen infusion (median decrease of 1.2 g/dL by Day 8) followed by a return to near baseline by Day 29. Fifty-six of the 57 subjects in this study had a negative DAT at baseline. Of these 56 subjects, 12 (21.4%) developed a positive DAT during the 29-day study period.

### 6.2 Postmarketing Experience

Because postmarketing reporting of adverse events is voluntary and from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. Evaluation and interpretation of these postmarketing reactions is confounded by underlying diagnosis, concomitant medications, pre-existing conditions, and inherent limitations of passive surveillance.

### Privenig Postmarketing Experience

Adverse reactions reported during worldwide postmarketing use of Privigen do not differ from what has been observed in clinical studies with Privigen and from what is known for IGIV products.

#### General

The following mild to moderate reactions may occur with the administration of IGIV products: headache, dizziness, tachycardia, fever, fatigue, dizziness, malaise, chills, flushing, skin reactions, wheezing or chest tightness, nausea, vomiting, rigor, back pain, chest pain, myalgia, arthralgia, and changes in blood pressure. Immediate hypersensitivity and anaphylactic reactions are also a possibility.

The following adverse reactions have been identified and reported during the post-approval use of IGIV products:

- **Respiratory:** Anaphylaxis, respiratory distress, syndrome (ARDS), ARDS, cytokins, hypoxemia, pulmonary edema, dyspnea, bronchospasm
- **Cardiovascular:** Cardiac arrest, thromboembolism, vascular collapse, hypertension
- **Neurological:** Coma, loss of consciousness, seizures, tremor, asptic meningitis syndrome
- **Integumentary:** Stevens-Johnson syndrome, epidemicidosis, erythema multiforme, bullous dermatitis
- **Hematologic:** Panocytopenia, leukopenia, hemorrhage, direct positive antiglobulin (Coombs) test
- **Musculoskeletal:** Back pain
- **Gastrointestinal:** Hepatic dysfunction, abdominal pain
- **General/Body as a Whole:** Pyrexia, rigors

### 7. DRUG INTERACTIONS

Passive transfer of antibodies may transiently interfere with the immune response to live virus vaccines such as measles, mumps, and rubella. The immunizing physician should be informed of recent therapy with Privigen so that appropriate measures may be taken (see Patient Counseling Information [17]).

### 8. USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

#### Pregnancy Category C.

Animal reproduction studies have not been conducted with Privigen. It is not known whether Privigen can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Privigen should be given to pregnant women only if clearly needed. Immuneglobulins cross the placenta from maternal circulation increasingly after 30 weeks of gestation.

#### 8.3 Nursing Mothers

Use of Privigen in nursing mothers has not been evaluated.

#### 8.4 Pediatric Use

#### Treatment of Primary Humoral Immunodeficiency

Privigen was evaluated in 31 pediatric subjects (19 children and 12 adolescents) with PI. There were no apparent differences in the safety and efficacy profiles as compared to those in adult subjects. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels. The safety and effectiveness of Privigen have not been established in pediatric patients with PI who are under the age of 3.

#### Treatment of Chronic Immune Thrombocytopenic Purpura

Safety and effectiveness of Privigen have not been established in pediatric patients with chronic ITP who are under the age of 15.

#### 8.5 Geriatric Use

Clinical studies of Privigen did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects.

Use caution when administering Privigen to patients age 65 and over who are judged to be at increased risk of developing renal insufficiency (see Boxed Warning, Warnings and Precautions [5.2]). Do not exceed recommended doses, and administer Privigen at the minimum infusion rate practicable.

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Bern, Switzerland

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Produced in barley, these proteins are animal, bacterial, and viral free, and are ultra pure, with extremely low endotoxin.

Cell Sciences offers innovative, unique growth factors and hard-to-produce recombinant proteins, bypassing the use of bacterial or animal cell systems. These ultra pure proteins contain no contamination from other growth factors and negligible amounts of endotoxin.

Background: barley endosperm

The host organism, barley, with its specialized endosperm storage tissue, provides many unique features including proficient protein machinery, with eukaryotic folding, and a distinct route for long-term protein protection and storage. A biochemically inert environment, void of endotoxins, low protease activity and secondary metabolite content, and a simple protein profile, aid in downstream processing. Barley has also a G.R.A.S. (generally recognized as safe) status from the FDA.

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- for use in all in vivo animal studies

Ultra pure cytokines & growth factors

- FGF1, human
- FGF2, human
- FLT3 ligand, human
- GCSF, human
- IFNA2, human
- IFN gamma, human
- IGF1, human
- IL1-alpha, human
- IL2, human
- IL3, human
- IL4, human
- IL5, human
- IL6, human
- IL7, human
- IL9, human
- IL16, human
- IL22, human
- KGF, human
- M-CSF, human
- NRG1/HRG beta 2, human
- SCF, mouse
- SF20/IL25, human
- TNF-alpha, human
- TNF-beta, human
- VEGF121, human
- VEGF165, human