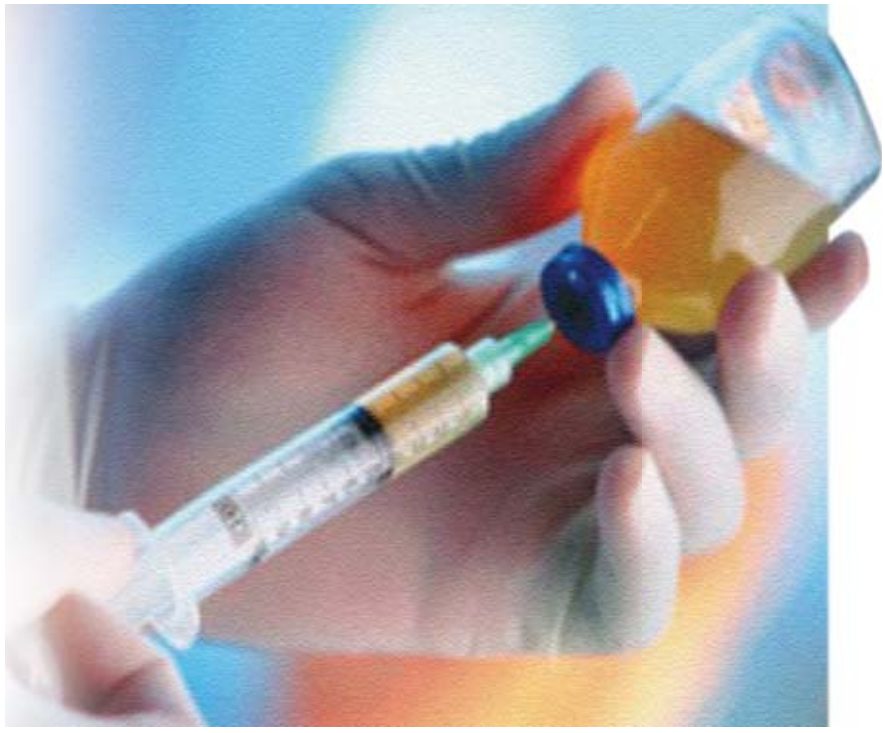
Immune Globulins:

Therapeutic, Pharmaceutical, Cost, and Administration Considerations

JERRY SIEGEL, PHARMD, FASHP

Clinical Associate Professor
The Ohio State University College of Pharmacy
Columbus, Ohio



Having so many immune globulin (Ig) products on the market makes product selection more challenging, and providers frequently have questions about the best approach to product selection. The charts in this review should help pharmacists guide that decision.

What is the best approach to Ig product selection? Should all the available Ig products be considered equivalent and price be the only consideration? Are there special considerations that may be important for individual patients based on their comorbidities? Does the clinical condition of the patient change the selection criteria for the Ig? All of these factors need to be weighed along with the product formulation to match the best product to the patient. Not all Ig products are the same, nor are all patients the same. The information in the following charts will help clinicians understand the differences in Ig products so they can make the best selection.

New products have become available, providing more treatment options. There are 6 Ig products indicated for subcutaneous (SQ) use in patients with primary immunodeficiency (PID): Hyqvia (Shire) in a 10% concentration is only for SQ administration; Gammagard Liquid (Shire), Gammaked (Kedrion), and Gamunex-C (Grifols) come in 10% concentrations for IV or SQ administration; and Cuvitru 20% (Shire) and Hizentra (CSL Behring), come in 20% concentrations and are indicated for SQ administration. It should be noted that dosing adjustments are required for all SQ agents when converting from IV.

Cuvitru 20%, which was approved in 2016, is the newest SQ Ig product. It is the only SQ 20% option in the United States to treat adult and pediatric patients with PID that uses glycine as the stabilizer.

Although the IgG portion of Hyqvia is identical to Gammagard Liquid 10%, it should be used in combination with recombinant human hyaluronidase (HY). This combination product allows for SQ administration of a large amount of Ig to one site, in a monthly dose that is equivalent to that of IVIG products based on a 1:1 conversion ratio. It is FDA approved for PID in adults. This is the first product of its type. In the chart, it looks identical to Gammagard Liquid 10%, but it is distributed as a dual package with the 5-mL vial of HY. Instructions for administration are unique and specific to this product.

Two products, Gammaked and Gamunex-C, are approved for use in patients with chronic inflammatory demyelinating polyneuropathy (IV only). Gammagard Liquid is approved to treat multifocal motor neuropathy.

The reasons for switching products may be clinical in nature and related to tolerability, they may be fiscal and based on contracting issues, or they may be due to product availability. It is best to consider product changes as if the patient is naive to Ig use, with increased monitoring and conservative infusion times.

Whereas Tables 1 to 5 may help facilitate these decisions, it is important to understand the clinical effect of changing products. Although all of the products contain primarily IgG, trace amounts of other Igs—IgA and IgM—as well as widely different stabilizing agents, may affect tolerability.

Text continues on page 6

Table 1. Therapeutic Considerations

Product[a]	Manufacturer	FDA-Approved Indications	IgA Content	pH (after reconstitution)	Plasma Source	Half-life, d[b]	Pathogen Inactivation/Removal
Carimune NF	CSL Behring Customer service: (800) 683-1288 Medical info: (800) 504-5434 www.cslbehring.com	ITP, PID	1,000-2,000 mcg/mL (6%)	6.4-6.8	Plasmapheresis, US donors (>16,000)	23	pH 4.0/pepsin, nanofiltration, TSE removal
Cuvitru 20%	Shire Customer service: (800) 423-2090 Medical info: (866) 424-6724 www.shire.com	PID	80 mcg/mL (average)	4.6-5.1	Plasma from FDA-registered sites	NA	SD, low pH, nanofiltration
Flebogamma 5% DIF **Flebogamma 10% DIF**	Instituto Grifols SA Barcelona, Spain Grifols Biologicals Inc. Los Angeles, CA 90032 Customer service: (888) GRIFOLS www.grifols.com	PID ITP (10%)	<3.1 mcg/mL[c,d]	5.6±0.1 (5%)[c,d] 5.5±0.1 (10%)[c,d]	US source IQPP-certified plasma from FDA-registered sites	4-week dosing: 32±5 (5%) 37±13 (10%)	Pasteurization (60°C, 10 h), SD, 20 nm nanofiltration, fraction I precipitation, fraction II+III incubation, PEG precipitation, acid treatment, TSE removal
Gammagard Liquid 10%	Shire Customer service: (800) 423-2090 Medical info: (866) 424-6724 www.shire.com	MMN, PID	37 mcg/mL	4.9-5.2	Plasma from FDA-registered sites	35	SD, low pH, nanofiltration
Gammagard S/D 5%	Shire Customer service: (800) 423-2090 Medical info: (866) 424-6724 www.shire.com	CLL, ITP, KD, PID	<1 mcg/mL[e]	6.4-7.2	Plasmapheresis, 10,000 donors from FDA-registered sites	37.7±15	SD
Gammaked 10%	Manufactured by Grifols Therapeutics Inc for Kedrion Biopharma Customer service/medical info: (855) 353-7466; www.gammaked.com; www.kedrion.com	CIDP, ITP, PID[f]	46 mcg/mL[c,d]	4.0-4.5[c,d]	US source IQPP-certified plasma from FDA-registered sites	35	Caprylate precipitation/depth filtration, caprylate incubation, depth filtration, column chromatography, low pH incubation, TSE removal
Gammaplex 5%	Bio Products Laboratory Ltd Customer service: 844-4BPLUSA medInfo@BPL-US.com www.gammaplex.com	ITP, PID	<10 mcg/mL	4.8-5.1	U.S. source plasma from FDA-registered sites	4-week dosing: 41±14	SD, nanofiltration, terminal low pH incubation
Gammaplex 10%	Bio Products Laboratory Ltd Customer service: 844-4BPLUSA medInfo@BPL-US.com www.gammaplex.com	ITP, PID	<20 mcg/mL	4.9-5.2	U.S. source plasma from FDA-registered sites	4-week dosing: 34.8	SD, nanofiltration, terminal low pH incubation
Gamunex-C 10%	Grifols Therapeutics Inc Research Triangle Park, NC 27709 Customer service: (800) 243-4153 Medical info: (800) 520-2807 www.gamunex-c.com	CIDP, ITP, PID[f]	46 mcg/mL[c,d]	4.0-4.5[c,d]	US source IQPP-certified plasma from FDA-registered sites	35	Caprylate precipitation/depth filtration, caprylate incubation, depth filtration, column chromatography, low pH incubation, TSE removal
Hizentra 20%[g]	CSL Behring Customer service: (800) 683-1288 Medical info: (800) 504-5434 www.cslbehring.com www.hizentra.com	PID SQ only	≤50 mcg/mL	4.6-5.2	Plasmapheresis, US donors	NA	pH 4.0 incubation, nanofiltration, depth filtration, virus filtration, TSE reduction
Hyqvia (IgG 10% + HY 5%)	Shire Customer service: (800) 423-2090 Medical info: (866) 424-6724 www.shire.com	PID SQ only	37 mcg/mL	4.6-5.1	Plasma from FDA-registered sites	35	SD, low pH, nanofiltration
Octagam 5%	Octapharma USA Customer service: (866) 766-4860 www.octapharma.com	PID	<200 mcg/mL[h]	5.1-6.0	US source and recovered plasma from FDA-registered sites	40	Cold ethanol, pH 4.0 incubation, SD
Octagam 10%	Octapharma USA Customer service: (866) 766-4860 www.octapharma.com	Chronic ITP	106 mcg/m	4.5-5.0	US source and recovered plasma from FDA-registered sites	36-40	Cold ethanol, pH 4.0 incubation, SD
Privigen 10%	CSL Behring Customer service: (800) 683-1288 Medical info: (800) 504-5434 www.cslbehring.com www.privigen.com	CIDP, ITP, PID	≤25 mcg/mL	4.6-5.0	Plasmapheresis, US donors (≥60,000)	36.6	pH 4.0 incubation, 20 nm virus filtration, depth filtration, TSE removal

Footnotes and Key on page 8.

IgG Subclass,[c] %				Diphtheria Toxin[c]	*Streptococcus pneumoniae*[c]		*Haemophilus influenzae* Type B[c]	Streptolysin O[c]	CMV[c]	HAV[c]	HBV (surface antibody)[c]	Herpes Simplex Type 1[c]	Polio Type 2[c]
IgG1	IgG2	IgG3	IgG4		Type 1	Type 3							
60.5	30.2	6.6	2.8	3.6 IU/mL (NT)	313 (EIA)	180 (EIA)	1:60 (CF)	300 IU/mL (HAI)	1:512 (IFA); 1:2,560 (EIA)	1:348 (RIA)	1:64 (RIA)	1:128 (CF)	1:64 (NT)
57.6-64.6	28.4-34.7	3.9-7.0	1.8-3.1	≥2.4 U/mL	NA	NA	NA	NA	NA	≥7.0 IU/mL	≥0.4 IU/mL	**NA**	**NA**
66.6	28.5 (5%) 27.9 (10%)	2.7 (5%) 3.0 (10%)	2.2 (5%) 2.5 (10%)	7.0±1.0 IU/mL (5%); 13.7±1.4 IU/mL (10%)	NA	NA	15±1 mg/L (5%)	NA	30±6 PEI U/mL (5%); 36±7 IU/mL (10%)	21±4 IU/mL (5%)	88.0±41.8 IU/g Ig (5%); 80.7±23.0 IU/g Ig (10%)	NA	NA
60.9	32.1	5	2.1	4.0 U/mL (NT)	NA	21.2 mcg/mL (EIA)	1:2,320 (EIA)	NA	68 PEI U/mL (EIA)	16.4 IU/mL (RIA)	≥0.20 IU/mL (EIA)	VZV: 32 U/mL (NT)	Type 1: 1:190 mIU/mL (NT)
67	25	5	3	2-5 IU/mL (NT); J5 lipid A 1:273	17.5 mcgAbN/mL (EIA)	8.5 mcg/mL (EIA)	11 mcg/mL (EIA)	1,150 IU (HH)	37 PEI mcg/mL (EIA), 1:2,480 (NT)	1:267 (RIA)	820 mIU/mL (RIA)	1:1,000 (EIA)	1:305 (NT)
62.8	29.7	4.8	2.7	7±2 AU/mL	87.4±22.2 mcg/mL	26.1±7.7 mcg/mL	13.0±2.4 mcg/mL	16,846± 13,648 Todd U/mL	57 PEI U/mL	1:139	65±19 IU/g Ig	NA	1:22±0.35
64	30	5	1	2.2 IU/mL	NA	NA	613 U/mL	NA	365 U/mL	199 IU/g IgG	77 IU/g IgG	NA	NA
63.6	30.6	4.8	1	16.8 IU/mL	NA	NA	1,039 U/mL	NA	759 U/mL	239 IU/g IgG	89 IU/g IgG	NA	NA
62.8	29.7	4.8	2.7	7±2 AU/mL	87.4±22.2 mcg/mL	26.1±7.7 mcg/mL	13.0±2.4 mcg/mL	16,846± 13,648 Todd U/mL	57 PEI U/mL	1:139	65±19 IU/g Ig	NA	1:22±0.35
68.7	26.6	2.7	2	≥2.5 IU/mL	NA	NA	NA	≥1,000 IU/mL	NA	NA	≥0.4 IU/mL	NA	NA
60.9	32.1	5	2.1	4.0 U/mL (NT)	NA	21.2 mcg/mL (EIA)	1:2,320 (EIA)	NA	68 PEI U/mL (EIA)	16.4 IU/mL (RIA)	≥0.20 IU/mL (EIA)	VZV: 32 U/mL (NT)	Type 1: 1:190 mIU/mL (NT)
65	30	3	2	5-30 IU/mL	NA	NA	NA	600-800 IU/mL	33-40 IU/mL	21-25 IU/mL	51 IU/g	1:8,192	1:160-1:320 (NT)
65	30	3	2										
67.8	28.7	2.3	1.2	4.9 (3.8-7.3) IU/mL	NA	NA	36.1 (26.4-45.0) IU/mL	1,746 (1,310-2,010) IU/mL	76.4 (51.2-116.8) IU/mL	NA	5.3 (3.0-10.1) IU/mL	NA	NA

Table 2. Pharmaceutical Considerations

Product[a]	Method of Preparation	Available Dosing Forms	Form	Gamma Globulin, %	Monomers, %
Carimune NF	Kistler-Nitschmann,[i] pH 4.0 + trace pepsin, nanofiltration	IV	Lyophilized	≥96	92
Cuvitru 20%	Cohn-Oncley,[i] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	SQ	Liquid	≥98	≥90 monomers + dimers
Flebogamma 5% DIF **Flebogamma 10% DIF**	Cohn-Oncley,[i] ion-exchange chromatography, acid pH treatment, PEG precipitation, SD, pasteurization, dual nanofiltration (35+20 nm)	IV	Liquid	≥99[c,d]	>99.96 monomers 5%[c,d] >99.87 monomers 10%[c,d]
Gammagard Liquid 10%	Cohn-Oncley,[i] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	IV, SQ (SQ for PID only)	Liquid	≥98	≥95 monomers + dimers
Gammagard S/D 5%	Cohn-Oncley,[i] ultrafiltration, anion-exchange chromatography, SD	IV	Lyophilized	≥90	96.4
Gammaked 10%	Cold ethanol fractionation, anion-exchange chromatography, caprylate chromatography purified, low pH incubation	IV, SQ (SQ for PID only)	Liquid	100	100 monomers + dimers[c,d]
Gammaplex 5%	Cold ethanol fractionation, ion-exchange chromatography, SD, nanofiltration (20 nm), ultrafiltration/diafiltration, terminal low pH incubation	IV	Liquid	>99	≥99 monomers + dimers
Gammaplex 10%	Cold ethanol fractionation, ion-exchange chromatography, SD, nanofiltration (20 nm), ultrafiltration/diafiltration, terminal low pH incubation	IV	Liquid	>99	99.7-100 monomers + dimers
Gamunex-C 10%	Cold ethanol fractionation, anion-exchange chromatography, caprylate chromatography purified, low pH incubation	IV, SQ (SQ for PID only)	Liquid	100	100 monomers + dimers[c,d]
Hizentra 20%[g]	Cold ethanol fractionation, anion-exchange chromatography, octanoic acid fractionation, pH 4.0 incubation, depth filtration, nanofiltration (20 nm)	SQ	Liquid	≥98	≥90 monomers + dimers
Hyqvia (IgG 10% + HY 5%)	Cohn-Oncley,[i] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	SQ	Liquid	≥98	≥95 monomers + dimers
Octagam 5%	Cold ethanol fractionation, ultrafiltration, chromatography, SD, pH 4.0 incubation	IV	Liquid	≥96	≥90 monomers + dimers
Octagam 10%	Cold ethanol fractionation, ultrafiltration, chromatography, SD, pH 4.0 incubation	IV	Liquid	≥96	≥94 monomers + dimers
Privigen 10%	Cold ethanol fractionation, octanoic acid fractionation, anion-exchange chromatography, pH 4.0 incubation, depth filtration, nanofiltration (20 nm)	IV	Liquid	≥98	≥98 monomers + dimers

Footnotes and Key on page 8.

	IgM Content	Albumin	PEG	Sodium Content	Stabilizer	Osmolality/Osmolarity
	Trace	0	0	0% water, 0.9% NS	5% sucrose	In sterile water: 3%, 192 mOsm/kg; 6%, 384 mOsm/kg; 12%, 768 mOsm/kg In NS: 3%, 498 mOsm/kg; 6%, 690 mOsm/kg; 12%, 1,074 mOsm/kg
	NA	NA	Not detectable	No sodium added	Glycine	280-292 mOsm/kg
	Trace	<2 mcg/mL (5%)[c,d] <5 mcg/mL (10%)[c,d]	Not detectable	Trace (<3.2 mEq/L)[c,d]	5% sorbitol (polyol)	325±4.8 mOsm/kg (5%)[c,d] 343±6.4 mOsm/kg (10%)[c,d]
	Trace	NA	Not detectable	No sodium added	Glycine	240-300 mOsm/kg
	Trace	<3 mg/mL	<2 mg/mL	0.85%	2% glucose, glycine	636 mOsm/L (5%), 1,250 mOsm/L (10%)[j]
	Trace	<2 mcg/mL[c,d]	0	Trace (<7 mEq/L)[c,d]	Glycine	258 mOsm/kg[c,d]
	<0.1 mg/mL[k]	0[k]	0[k]	30-50 mM	Sorbitol and glycine	420-500 mOsm/kg, but not <240 mOsm/kg
	<0.1 mg/mL	0	0	≤5 mM	Glycine	280-288 mOsm/kg, but not <240 mOsm/kg
	Trace	<2 mcg/mL[c,d]	0	Trace (<7 mEq/L)[c,d]	Glycine	258 mOsm/kg[c,d]
	Trace	≤2 mcg/mL	NA	Trace	Proline	380 mOsm/kg
	Trace	NA	Not detectable	No sodium added	Glycine	240-300 mOsm/kg
	≤0.1 mg/mL	0	0	≤30 mmol/L	10% Maltose[l]	310-380 mOsm/kg
	<106 mcg/mL	0	0	≤30 mmol/L	Maltose[l] (90 mg/mL)	310-380 mOsm/kg
	3 mg/L	Trace	0	Trace	Proline	240-440 mOsm/kg

Table 3. IVIG Infusion Rates[m]

IVIG[a]	Initial Infusion Rate	Maintenance Infusion Rate	Maximum Infusion Rate[n]	Comments[o]
Carimune NF 3%-12%	0.48 mL/kg/h	1-2 mL/kg/h	3 mL/kg/h	Reconstitution time is several minutes; no filter required; compatible with NaCl, D5W; increased risk for renal and thrombotic adverse effects[p]
Cuvitru 20%	10-20 mL/h per site		≤60 mL/h per site	Infusion rate and volume depends on patient size: patients <40 kg; patients ≥40 kg
Flebogamma 5% DIF Flebogamma 10% DIF	0.6 mL/kg/h	Increase gradually as tolerated to 6 mL/kg/h (5%), 4.8 mL/kg/h (10%)	6 mL/kg/h (5%), 4.8 mL/kg/h (10%)	No filter required; administer at the minimum infusion rate practical to patients >65 and those at risk for renal failure or thrombotic events[p]
Gammagard Liquid 10%	0.5 mL/kg/h for 30 min (PID)	Increase every 30 min if tolerated, up to 5 mL/kg/h (PID)	5 mL/kg/h (PID)	No filter required; patients at risk for renal dysfunction or thrombotic events should be gradually titrated up to a more conservative maximum rate <2 mL/kg/h[p]
Gammagard S/D 5%	0.5 mL/kg/h for 30 min	Increase gradually as tolerated to 4 mL/kg/h	4 mL/kg/h (5%)	Reconstitution time is <5 min at RT and >20 min if cold; 15-micron filter required and supplied with administration set; compatible with sterile water
Gammaked 10%	0.6 mL/kg/h, 1.2 mL/kg/h (CIDP)	Increase gradually as tolerated to 4.8 mL/kg/h	4.8 mL/kg/h	No filter required; do not dilute with NaCl, but NaCl flush is fine; incompatible with heparin (refer to full PI for details); administer at minimum infusion rate practical to patients aged >65 y or at risk for renal or thrombotic events[p]
Gammaplex 5%	0.6 mL/kg/h for 15 min	Increase gradually as tolerated every 15 min to 4.8 mL/kg/h	4.8 mL/kg/h	No filter required; ensure that patients with pre-existing renal insufficiency are not volume depleted; discontinue if renal function deteriorates; for patients at risk for renal dysfunction, thrombotic events or volume overload, administer at the minimum infusion rate practicable[p]
Gammaplex 10%	0.3 mL/kg/h for 15 min	Increase gradually as tolerated every 15 min to 4.8 mL/kg/h	4.8 mL/kg/h	No filter required; ensure that patients with pre-existing renal insufficiency are not volume depleted; discontinue if renal function deteriorates; for patients at risk for renal dysfunction, thrombotic events or volume overload, administer at the minimum infusion rate practicable[p]
Gamunex-C 10%	0.6 mL/kg/h, 1.2 mL/kg/h (CIDP)	Increase gradually as tolerated to 4.8 mL/kg/h	4.8 mL/kg/h	No filter required; do not dilute with NaCl, but NaCl flush is fine; incompatible with heparin (refer to full PI for details); administer at minimum infusion rate practical to patients aged >65 y or at risk for renal or thrombotic events[p]
Octagam 5%	0.6 mL/kg/h for 30 min	1.2 mL/kg/h for 30 min, then 2.4 mL/kg/h for 30 min, then as tolerated, up to maximum rate	<4.2 mL/kg/h	No filter required or supplied; if in-line filter used, pore size should be 0.2-200 microns; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion rate practical, not to exceed 0.07 mL/kg/min[p]
Octagam 10%	0.6 mL/kg/h for 30 min	Increase gradually as tolerated every 30 min to 7.2 mL/kg/h	7.2 mL/kg/h	No filter required or supplied; if an in-line filter is used, the pore size should be 0.2-200 microns; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion rate practical, not to exceed 0.03 mL/kg/min[p]
Privigen 10%	0.3 mL/kg/h (CIDP requires loading dose)	As tolerated, up to maximum recommended rate	2.4 mL/kg/h (ITP) 4.8 mL/kg/h (CIDP, PID)	No filter required; administer at minimum infusion rate practical to patients at risk for renal dysfunction or thrombotic events[p]

Footnotes and Key on page 8.

Text continued from page 1

The differences in salt, sugar, and overall osmolarity of these products are particularly important when patients have various comorbidities, such as renal dysfunction, diabetes mellitus, vascular disease, or heart failure. Differences between lyophilized and liquid products may result in changes in product concentration and infusion rate, as well as tolerability.

The tables in this review may be helpful for providing optimal care for patients receiving Ig products. They should be used as a general guide to help determine the product that is best suited for a particular patient population. Because there is variation from batch to batch, the exact numbers represent averages of selected batches; any one batch of any Ig product may have ranges outside these average numbers. When comparing administration rates, clinicians need to keep in mind that each patient has a maximum tolerated rate. This rate may be different for each Ig product. Ig must be administered slowly initially and titrated as tolerated. The rate also should be adjusted based on comorbidities. The infusion should be slowed or stopped if adverse events (AEs) become evident during the infusion.

(See the prescribing information for each agent for more information about AEs.)

Table 4. Cost Consideration Criteria

Product[a]	Supply	Storage[q]	Distribution	Return Policy Warranty	Packaging or Labeling Enhancements
Carimune NF	3, 6, 12 g	≤30°C, 24 mo	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident seal, RSS barcode, peel-off label with lot number, expiration date
Cuvitru 20%	1, 2, 4, 8 g	2°C-8°C, 36 mo; ≤25°C, 12 mo; do not freeze	Direct	Shire shipping error; defective or damaged product; no out-of-date products	Latex-free packaging, tamper-evident cap, RSS barcode, peel-off label with lot number, expiration date
Flebogamma 5% DIF Flebogamma 10% DIF	2.5, 5, 10, 20 g (5%); 5, 10, 20 g (10%)	2°C-25°C, 24 mo; do not freeze	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident seal with hologram, prior handling recognition, integral suspension band, laser-etched vials with UIN, barcode, peel-off label with product lot number
Gammagard Liquid 10%	1, 2.5, 5, 10, 20, 30 g	2°C-8°C, 36 mo; ≤25°C, 24 mo; do not freeze	Wholesaler or direct	Shire shipping error; defective or damaged product; no out-of-date products	Latex-free packaging, tamper-evident cap, RSS barcode, peel-off label with lot number, expiration date
Gammagard S/D 5%	2.5, 5, 10 g	≤25°C, 24 mo; do not freeze	Wholesaler or direct	Shire shipping error; defective or damaged product; no out-of-date products	Tamper-evident cap, peel-off label with lot number, expiration date
Gammaked 10%	1, 2.5, 5, 10, 20 g	2°C-8°C, 36 mo; ≤25°C, 6 mo; do not freeze	Wholesaler	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident cap, laser-etched vials with UIN, NDC barcode, integral suspension band on larger vial sizes, peel-off label with product lot number, vial stopper not made with natural rubber latex
Gammaplex 5%	5, 10, 20 g	2°C-25°C, 36 mo; do not freeze	Wholesaler	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident cap, peel-off label with lot number, expiration date
Gammaplex 10%	5, 10, 20 g	2°C-25°C, 36 mo; do not freeze	Wholesaler	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident cap, peel-off label with lot number, expiration date
Gamunex-C 10%	1, 2.5, 5, 10, 20, 40 g	2°C-8°C, 36 mo; ≤25°C, 6 mo; do not freeze	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident cap, laser-etched vials with UIN, NDC barcode, integral suspension band on larger vial sizes, peel-off label with product lot number, vial stopper not made with natural rubber latex
Hizentra 20%[g]	1, 2, 4, 10 g	≤25°C, 30 mo	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Latex-free packaging, single-use tamper-evident vials, peel-off label with lot number, expiration date
Hyqvia (IgG 10% + HY 5%)	2.5, 5, 10, 20, 30 g	2°C-8°C, 36 mo; do not freeze[r]	Wholesaler or direct	Shire shipping error; defective or damaged product; no out-of-date products	Latex-free packaging, tamper-evident cap, RSS barcode, peel-off label with lot number, expiration date
Octagam 5%	1, 2.5, 5, 10, 25 g	2°C-25°C, 24 mo; do not freeze	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident, latex-free packaging, peel-off label with lot number, expiration date
Octagam 10%	2, 5, 10, 20 g	2°C-8°C, 24 mo; ≤25°C, 9 mo; after storage at ≤25°C, product must be used or discarded	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident, latex-free packaging, peel-off label with lot number, expiration date
Privigen 10%	5, 10, 20, 40 g	≤25°C, 36 mo	Wholesaler or direct	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident seal, RSS barcode, peel-off label with lot number, expiration date

Footnotes and Key on page 8.

Table 5. Log Reduction Factor Comparisons[s]

Product[a]	Enveloped Viruses					Nonenveloped Virus	TSE (prion)
	HIV	Models for HCV		Model For Large DNA			
		SBV	BVDV	PRV	B19		
Carimune NF	≥26	≥19	≥9	≥25		≥19 (BEV)	NA
Cuvitru 20%	>21.0		>17.4	≥21.6		>12.3 (HAV), >12.3 (EMCV), 10.3 (MMV)	≥3.2
Flebogamma 5% DIF, 10% DIF	≥25.11	≥6.49	≥21.28	≥27.78		≥15.04 (PPV), ≥19.25 (EMCV)	≥11.64
Gammagard Liquid 10%	>14.8	NA	>16.8	>16.9		>5.7 (HAV), >7.7 (EMCV), >5.1 (MMV)	NA
Gammagard S/D 5%	>15 (HIV-1)	NA	>7.5	>9.3		>5.2 (HAV), >5.0 (EMCV), >5.3 (MMV)	NA
Gammaked 10%	≥14	NA	≥16.3	≥12.2		≥5.0 (HAV), 8.2 (PPV)	≥6.6
Gammaplex 5%	>12.9	>20.2	>11.7	>6.2	6.0	>5.9 (HAV), >7.5 (EMCV), 4.6 (CPV)	>9.4
Gammaplex 10%	>12.8	>18.3	>9.6	>6.2	6.0	>6.3 (HAV), >8.2 (EMCV), 4.2 (CPV)	>9.4
Gamunex-C 10%	≥14	NA	≥16.3	≥12.2		≥5.0 (HAV)	≥6.6
Hizentra 20%[g]	≥16.0	NA	≥11.8	≥17.7		≥9.6 (EMCV), ≥7.8 (MMV)	≥14.8
Hyqvia	>14.8	NA	≥16.8	>16.9		5.7 (HAV), >7.7 (EMCV), 5.1 (MMV)	NA
Octagam 5%	≥14.6	≥16.7	NA	≥16.1		≥9.5 (MEV), ≥7.7 (PPV)	≥6.7[t]
Octagam 10%	≥14.7	≥20.61	NA	≥18.22		≥20.20 (MEV), ≥6.53 (PPV)	NA
Privigen 10%	≥16.0	NA	≥11.8	≥17.7		≥9.6 (EMCV), ≥7.8 (MMV)	≥14.8

FOOTNOTES

a All agents are contraindicated for IgA deficiency with antibodies to IgA.

b Varies with disease state, immune status, and age of the patient.

c Average of sample lots.

d Data on file at Grifols.

e As of Dec. 2012, Baxter (now Shire) has discontinued Gammagard S/D 5%; the low IgA product will remain available for patients with known reactions to IgA or IgA deficiency with antibodies; all Gammagard S/D will be manufactured with IgA <1; special request only.

f DO NOT USE Gammaked or Gamunex-C subcutaneously for ITP or CIDP.

g Provided the total weekly dose is maintained, any dosing interval from daily to biweekly can be used and will result in systemic serum IgG exposure that is comparable to the previous IVIG or weekly Hizentra treatment. For biweekly dosing, multiply the calculated Hizentra weekly dose by 2.

h With additional purification steps added in 2010, current release lots contain <100 mcg/mL. Data on file at Octapharma.

i Cohn-Oncley is the original method of cold ethanol fractionation; Kistler-Nitschmann is the specific cold ethanol fractionation method used by the manufacturer (CSL Behring).

j Limit infusion rate to <3.3 mg IgG/kg per minute (2 mL/kg/h) for 10% solutions.

k Data on file at Bio Products Laboratory.

l Maltose does not significantly affect serum glucose or insulin levels and can be safely administered to diabetic patients. Certain BGMS falsely interpret maltose, icodextrin, galactose, and xylose as glucose and can provide falsely elevated glucose readings. If insulin is administered as a result of these readings, hypoglycemia can occur. The BGMS that use test strips containing GDH-PQQ and GDO can provide these false readings. See PI for full details.

m Some infusion rates were converted from those listed in the PI for consistency and reader convenience.

n Certain severe adverse drug reactions may be related to the rate of infusion. Slowing or stopping the infusion usually allows the symptoms to disappear promptly.

o Unless specific compatibility information is available, do not mix with other drugs or solutions.

p Patients at high risk for thromboembolic events include patients who are elderly, overweight, or immobilized; patients with a history of hypertension, cardiovascular disease, or thrombotic disorders; and those who are >65 y or dehydrated.

q Under appropriate storage conditions.

r Must be used within 3 mo after removal from refrigerator to RT or less if expiration date is shorter.

s Log reduction factor values obtained from those listed in the PI; most are available on respective websites.

t Data on file at Octapharma.

KEY

AU automic unit
B19 human parvovirus B19
BEV bovine enterovirus (RNA model)
BGMS blood glucose monitoring systems
BVDV bovine viral diarrhea virus
CF complement fixation
CIDP chronic inflammatory demyelinating polyneuropathy
CLL chronic lymphocytic leukemia
CMV cytomegalovirus
CPV canine parvovirus
D5W dextrose 5% in water
EIA enzyme immunoassay
EMCV encephalomyocarditis virus (RNA model)
FDA Food and Drug Administration
GDH-PQQ glucose dehydrogenase-pyrroloquinolone quinone
GDO glucose-dye-oxidoreductase
HAI heterologous anti-immunoglobulin
HAV hepatitis A virus
HBV hepatitis B virus
HCV hepatitis C virus
HH inhibition of hemolysis
HIV human immunodeficiency virus
IFA immunofluorescence assay
IgA immune globulin A
IgG immune globulin G
IgM immune globulin M
IQPP International Quality Plasma Program
ITP idiopathic thrombocytopenic purpura
IU international unit
IVIG intravenous immune globulin
KD Kawasaki disease
MEV mouse encephalomyelitis virus
MMN multifocal motor neuropathy
MMV mouse minute virus (model for nonlipid DNA virus)
NA information not available
NaCl sodium chloride
NDC National Drug Code (cost considerations online)
NS normal saline
NT neutralization test
PEG polyethylene glycol
PEI Paul Ehrlich Institute International Units
PI prescribing information
PID primary immunodeficiency
PRV pseudorabies virus
RIA radioimmunoassay
RSS reduced space symbology
RT room temperature
SBV Sindbis virus
SD solvent detergent
SQ subcutaneous
TSE transmissible spongiform encephalopathies
UIN unique identifier number (cost considerations online)
VZV varicella zoster virus