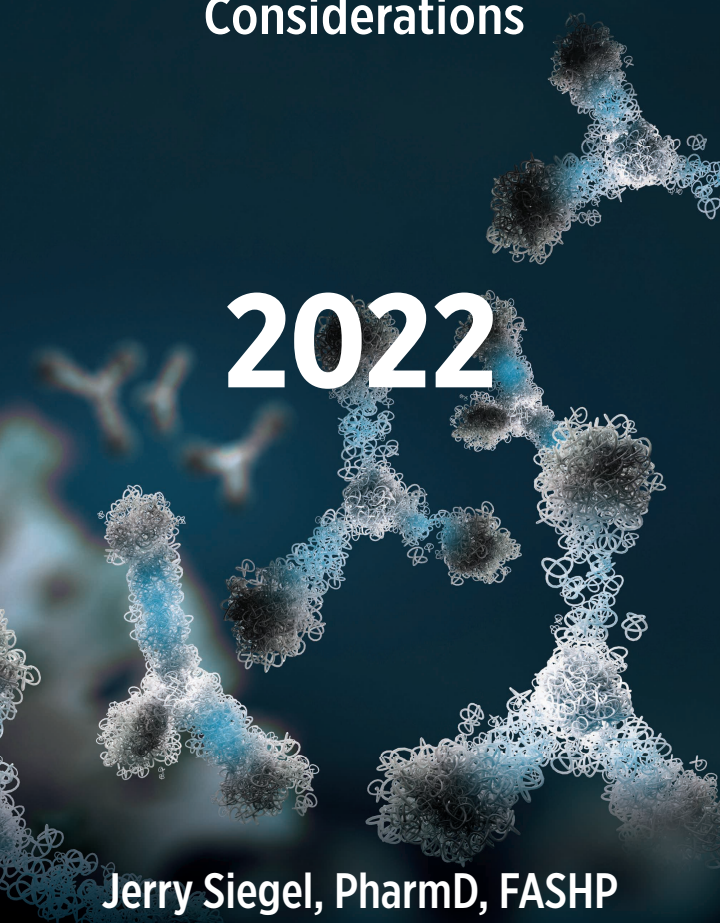
Immune Globulins:

Therapeutic, Pharmaceutical, Cost, and Administration Considerations



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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 8 IG products indicated for subcutaneous (SQ) use in patients with primary immunodeficiency (PID): Hyqvia (Takeda) in a 10% concentration is only for SQ administration; Gammagard Liquid (Takeda), Gammaked (Kedrion), and Gamunex-C (Grifols) come in 10% concentrations for IV or SQ administration; Cutaquig (Octapharma) comes in a 16.5% concentration for SQ administration; and Cuvitru 20% (Takeda), Hizentra (CSL Behring), and Xembify (Grifols) 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% and Xembify 20% are the only SQ 20% options 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.

Five products, Gammaked, Gamunex-C, Hizentra, Panzyga, and Privigen (CSL Behring), are approved for use in patients with chronic inflammatory demyelinating polyneuropathy. Gammagard Liquid is approved to treat multifocal motor neuropathy. Panzyga is approved to treat chronic immune thrombocytopenia in adults. Asceniv 10% is a new IV product from ADMA Biologics for primary immunodeficiency in adults over 12 years of age. It is derived from a highly selected population of donors with high titers of respiratory syncytial virus (RSV) even though it is not marketed for RSV-specific patient populations only.

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. 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.

The SARS-CoV-2 coronavirus that causes COVID-19 is a large lipid-coated virus that is easily removed in plasma product fractionation by SD or caprylate utilization, as well as nanofiltration and pasteurization viral inactivation and removal steps. Strict screening of donors for and qualification processes over a 6-month period also serve to protect the plasma supply. Additional information can be found at pptaglobal.org.

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

Dr Siegel reported financial relationships with ADMA Biologics, Kedrion Biopharma, and Takeda.

Table 1. Therapeutic Considerations

Product[a]	Manufacturer	FDA-Approved Indications	IgA Content	pH (After Reconstitution)	Plasma Source	Pathogen Inactivation/Removal	Half-life, d[b]	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							
Asceniv 10%	ADMA Biologics www.admabiologics.com; www.asceniv.com (800) 458-4244	PID	≤200 mcg/mL (72 mcg/mL average)[d]	4.0-4.6	Normal sourced plasma pooled with plasma from donors with sufficient RSV neutralizing antibody titers from a total of not less than 1,000 donors	Precipitation and removal of fraction III during the cold ethanol process, SD, 35-nm nanofiltration, low pH	3-wk dosing: 28.5±4.4; 4-wk dosing: 39.7±11.6	60	31	7	1.7	10.94 U/mL	NA	NA	NA	NA	NA	NA	9.7 IU/mL	NA	Type 1: 1.10 × Ref (176)
Bivigam 10%	ADMA Biologics www.admabiologics.com; www.bivigam.com (800) 458-4244	PID	≤200 mcg/mL (72 mcg/mL average)[d]	4.0-4.6	Pooled plasma from not less than 1,000 donors	Precipitation and removal of fraction III during the cold ethanol process, SD, 35-nm nanofiltration, low pH	3-wk dosing: 19.6±4.1; 4-wk dosing: 33.5±10.7	61	31	7	1.7	8.57 U/mL	NA	NA	NA	NA	NA	NA	7.2 IU/mL	NA	Type 1: 1.12 × Ref (176)
Cutaquig 16.5%	Octapharma USA CS: (866) 766-4860; www.octapharma.com	PID	206 mcg/mL (average)	5.0-5.5	Pooled plasma from not less than 1,000 donors	Cold ethanol, pH 4.0 incubation, SD	49.3 (1.8-98.3)	70	25	3	2										
Cuvitru 20%	Takeda CS: (800) 423-2090; MI: (866) 424-6724 www.takeda.com	PID	80 mcg/mL (average)	4.6-5.1	Plasma from FDA-registered sites	SD, low pH, nanofiltration	105 (71-119)	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
Flebogamma 5% DIF **Flebogamma 10% DIF**	Instituto Grifols SA: Barcelona, Spain Grifols Biologicals Inc, Los Angeles, CA CS: (888) GRIFOLS; www.grifols.com	PID ITP (10%)	<3.1 mcg/mL[c,e]	5.6±0.1 (5%)[c,e] 5.5±0.1 (10%)[c,e]	US source IQPP-certified plasma from FDA-registered sites	Pasteurization (60°C, 10 h), SD, 20-nm nanofiltration, fraction I precipitation, fraction II+III incubation, PEG precipitation, acid treatment, TSE removal	4-wk dosing: 32±5 (5%) 37±13 (10%)	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
Gammagard Liquid 10%	Takeda CS: (800) 423-2090; MI: (866) 424-6724 www.takeda.com	MMN, PID	37 mcg/mL	4.6-5.1	Plasma from FDA-registered sites	SD, low pH, nanofiltration	35	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)
Gammagard S/D 5%	Takeda CS: (800) 423-2090; MI: (866) 424-6724 www.takeda.com	CLL, ITP, KD, PID	<1 mcg/mL[f]	6.4-7.2	Plasmapheresis, 10,000 donors from FDA-registered sites	SD	37.7±15	67	25	5	3	2-5 IU/mL (NT); J5 lipid A 1:273	17.5 mcg/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)
Gammaked 10%	Manufactured by Grifols Therapeutics Inc for Kedrion Biopharma; CS/MI: (855) 353-7466 www.gammaked.com; www.kedrion.com	CIDP, ITP, PID[g]	46 mcg/mL[c,e]	4.0-4.5[c,e]	US source IQPP-certified plasma from FDA-registered sites	Caprylate precipitation/depth filtration, caprylate incubation, depth filtration, column chromatography, low pH incubation, TSE removal	35	62.8	29.7	4.8	2.7	7.4±1.4 AU/mL	NA	NA	NA	NA	NA	20±6 IU/mL	52±15 IU/g IgG	NA	Type 1: 0.88±0.34 (ratio to CBER ref)
Gammaplex 5%	Bio Products Laboratory Ltd CS: (844) 4BPLUSA; medInfo@BPL-US.com www.gammaplex.com	ITP, PID	<10 mcg/mL	4.8-5.1	US source plasma from FDA-registered sites	SD, nanofiltration, terminal low pH incubation	4-wk dosing: 41±14	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
Gammaplex 10%	Bio Products Laboratory Ltd CS: (844) 4BPLUSA; medInfo@BPL-US.com www.gammaplex.com	ITP, PID	<20 mcg/mL	4.9-5.3	US source plasma from FDA-registered sites	SD, nanofiltration, terminal low pH incubation	4-wk dosing: 34.8	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
Gamunex-C 10%	Grifols Therapeutics Inc, Research Triangle Park, NC CS: (800) 243-4153; MI: (800) 520-2807 www.gamunex-c.com	CIDP, ITP, PID[g]	46 mcg/mL[c,e]	4.0-4.5[c,e]	US source IQPP-certified plasma from FDA-registered sites	Caprylate precipitation/depth filtration, caprylate incubation, depth filtration, column chromatography, low pH incubation, TSE removal	35	62.8	29.7	4.8	2.7	7.4±1.4 AU/mL	NA	NA	NA	NA	NA	20±6 IU/mL	52±15 IU/g IgG	NA	Type 1: 0.88±0.34 (ratio to CBER ref)
Hizentra 20%[h]	CSL Behring CS: (800) 683-1288; MI: (800) 504-5434 www.cslbehring.com; www.hizentra.com	CIDP, PID SQ only	≤50 mcg/mL	4.6-5.2	Plasmapheresis, US donors	Cold ethanol, octanoic acid fractionation, anion exchange chromatography, pH 4.0 incubation, 20-nm virus filtration, depth filtration, TSE reduction	NA	68.8 (62.2-73.8)	26.5 (22.4-33.7)	2.7 (1.7-5.2)	2.0 (1.0-2.8)	13.5±3.4 (7.2-16.5) IU/mL	NA	NA	NA	3,337±561 (2,330-4,190) IU/mL	NA	NA	9.4±2.7 (5.5-16.6) IU/mL	NA	NA
Hyqvia (IgG 10% + HY 5%)	Takeda CS: (800) 423-2090; MI: (866) 424-6724 www.takeda.com	PID SQ only	37 mcg/mL	4.6-5.1	Plasma from FDA-registered sites	SD, low pH, nanofiltration	59.3	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)
Octagam 5%	Octapharma USA CS: (866) 766-4860; www.octapharma.com	PID	<200 mcg/mL[i]	5.1-6.0	US source and recovered plasma from FDA-registered sites	Cold ethanol, pH 4.0 incubation, SD	40	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)
Octagam 10%	Octapharma USA CS: (866) 766-4860; www.octapharma.com	Chronic ITP, Dermatomyositis	106 mcg/mL	4.5-5.0	US source and recovered plasma from FDA-registered sites	Cold ethanol, pH 4.0 incubation, SD	36-40	65	30	3	2										
Panzyga 10%	Octapharma USA CS: (866) 766-4860; www.octapharma.com	Chronic ITP, CIDP, PID	100 mcg/mL	4.5-5.0	Plasma from FDA-approved sites, pooled plasma from not less than 1,000 donors	Cold ethanol, SD, nanofiltration, ion exchange chromatography after octanoic acid fractionation	4-wk dosing: 36.1	65	28	3	4										
Privigen 10%	CSL Behring CS: (800) 683-1288; MI: (800) 504-5434 www.cslbehring.com; www.privigen.com	Chronic ITP, CIDP, PID	≤25 mcg/mL	4.6-5.0	Plasmapheresis, US donors (up to 60,000)	Cold ethanol, octanoic acid fractionation, anion exchange chromatography, pH 4.0 incubation, 20-nm virus filtration, depth filtration, TSE reduction	4-wk dosing: 45.4±18.5 in patients with PID	67.8	28.7	2.3	1.2	6.8 (2.5-14.4) IU/mL	NA	NA	NA	1,832 (1,050-2,260) IU/mL	NA	NA	6.2 (2.5-10.9) IU/mL	NA	NA
Xembify 20%	Grifols Therapeutics Inc, Research Triangle Park, NC CS: (800) 243-4153; MI: (800) 520-2807 www.xembify.com	PID	≤70 mcg/mL	4.1-4.8	US source IQPP-certified plasma from FDA-registered sites	Cold ethanol fractionation, caprylate precipitation and filtration, anion-exchange chromatography	NA	62	30	4.3	3.2	14±4.9 AU/mL	NA	NA	NA	NA	NA	40±16 IU/mL	52±16 IU/g IgG	NA	Type 1: 0.93 ±0.18 (ratio to CBER ref)

Table 2. Cost Consideration Criteria

Product[a]	Supply	Distribution	Storage[j]	Return Policy Warranty	Packaging or Labeling Enhancements
Asceniv 10%	5 g	Wholesaler or direct	Refrigerate between 2°C to 8°C (36°F to 46°F) until expiration date; do not freeze or heat	Shipping error; defective or damaged product; no out-of-date products	Single-use, tamper-evident vial. The components used in the packaging for Asceniv are latex free
Bivigam 10%	5, 10 g	Wholesaler or direct	Refrigerate between 2°C to 8°C (36°F to 46°F) until expiration date; do not freeze or heat	Shipping error; defective or damaged product; no out-of-date products	Single-use, tamper-evident vial. The components used in the packaging for Bivigam are latex free
Cutaquig 16.5%	1, 1.65, 2, 3.3, 4, 8 g	Wholesaler or direct	2°C-8°C, 36 mo; ≤25°C, 9 mo; do not freeze	Shipping error; defective or damaged product; no out-of-date products	Latex-free packaging, expiration date
Cuvitru 20%	1, 2, 4, 8, 10 g	Direct	2°C-8°C, 36 mo; ≤25°C, 12 mo; do not freeze	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**	0.5, 2.5, 5, 10, 20 g (5%); 5, 10, 20 g (10%)	Wholesaler or direct	2°C-25°C, 24 mo; do not freeze	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	Wholesaler or direct	2°C-8°C, 36 mo; ≤25°C, 24 mo; do not freeze	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%	5, 10 g	Wholesaler or direct	≤25°C, 24 mo; do not freeze	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	Wholesaler	2°C-8°C, 36 mo; <25°C, 6 mo; do not freeze	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	Wholesaler	2°C-25°C, 36 mo; do not freeze	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident cap, peel-off label with product name and lot number
Gammaplex 10%	5, 10, 20 g	Wholesaler	2°C-25°C, 36 mo; do not freeze	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident cap, peel-off label with product name and lot number
Gamunex-C 10%	1, 2.5, 5, 10, 20, 40 g	Wholesaler or direct	2°C-8°C, 36 mo; ≤25°C, 6 mo; do not freeze	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%[h]	Vials: 1, 2, 4, 10 g; PFS: 1, 2, 4 g	Wholesaler or direct	≤25°C, 30 mo; do not freeze	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	Wholesaler or direct	2°C-8°C, 36 mo; do not freeze[k]	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	Wholesaler or direct	2°C-25°C, 24 mo; do not freeze	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, 30 g	Wholesaler or direct	2°C-8°C, 36 mo; ≤25°C, 9 mo within shelf life; after storage at ≤25°C, use or discard product	Shipping error; defective or damaged product; no out-of-date products	Tamper-evident, latex-free packaging, peel-off label with lot number, expiration date
Panzyga 10%	1, 2.5, 5, 10, 20, 30 g	Wholesaler or direct	2°C-8°C, 36 mo; ≤25°C, 12 mo; after storage at ≤25°C, product must be used or discarded	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	Wholesaler or direct	≤25°C, 36 mo; do not freeze	Shipping error; defective or damaged product; no out-of-date products	Latex-free, single-use vial, tamper-evident seal, peel-off label with lot number, expiration date
Xembify 20%	1, 2, 4, 10 g	Wholesaler or direct	2°C-8°C; ≤25°C, 6 mo; after storage at ≤25°C, product must be used or discarded	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

Table 3. Pharmaceutical Considerations

Product[a]	Available Dosing Forms	Form	Method of Preparation	Gamma Globulin, %	Monomers, %	IgM Content	Albumin	PEG	Sodium Content	Stabilizer	Osmolality/Osmolarity
Asceniv 10%	IV	Liquid	Modified classic Cohn Method 6/Oncley Method 9 fractionation procedure.[l] Precipitation and removal of fraction III of the cold ethanol process, SD, 35-nm nanofiltration, low pH	≥96	>95% monomers + dimers	≤80 mcg/mL	≤2%	NA	0.100-0.140 M	Glycine	370-510 mOsm/kg
Bivigam 10%	IV	Liquid	Modified classic Cohn Method 6/Oncley Method 9 fractionation procedure.[l] Precipitation and removal of fraction III of the cold ethanol process, SD, 35-nm nanofiltration, low pH	≥96	>95% monomers + dimers	≤80 mcg/mL	≤2%	NA	0.100-0.140 M	Glycine	370-510 mOsm/kg
Cutaquig 16.5%	SQ	Liquid	Cold ethanol fractionation, ultrafiltration, chromatography, SD, pH 4.0 incubation	≥96	≥94 monomers + dimers	Trace	0	0	≤30 mmol/L	Maltose	310-380 mOsm/kg
Cuvitru 20%	SQ	Liquid	Cohn-Oncley,[l] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	≥98	≥90 monomers + dimers	NA	NA	Not detectable	No sodium added	Glycine	280-292 mOsm/kg
Flebogamma 5% DIF **Flebogamma 10% DIF**	IV	Liquid	Cohn-Oncley,[l] ion-exchange chromatography, acid pH treatment, PEG precipitation, SD, pasteurization, dual nanofiltration (35+20 nm)	≥99[c,e]	>99.96 monomers 5%[c,e] >99.87 monomers 10%[c,e]	Trace	<2 mcg/mL (5%)[c,e] <5 mcg/mL (10%)[c,e]	≤3 mg/mL (5%) ≤6 mg/mL (10%)	Trace (<3.2 mEq/L)[c,e]	5% sorbitol (polyol)	240-370 mOsm/kg[c,e]
Gammagard Liquid 10%	IV, SQ (SQ for PID only)	Liquid	Cohn-Oncley,[l] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	≥98	≥95 monomers + dimers	Trace	NA	Not detectable	No sodium added	Glycine	240-300 mOsm/kg
Gammagard S/D 5%	IV	Lyophilized	Cohn-Oncley,[l] ultrafiltration, SD, anion-exchange chromatography	≥90	96.4	Trace	<3 mg/mL	<2 mg/mL	0.85%	2% glucose, glycine	636 mOsm/L (5%), 1,250 mOsm/L (10%)[m]
Gammaked 10%	IV, SQ (SQ for PID only)	Liquid	Cold ethanol fractionation, anion-exchange chromatography, caprylate chromatography purified, low pH incubation	≥98	100 monomers + dimers[c,e]	Trace	<2 mcg/mL[c,e]	0	Trace (<7 mEq/L)[c,e]	Glycine	258 mOsm/kg[c,e]
Gammaplex 5%	IV	Liquid	Cold ethanol fractionation, ion-exchange chromatography, SD, nanofiltration (20 nm), ultrafiltration/diafiltration, terminal low pH incubation	>95	≥99 monomers + dimers	<0.1 mg/mL[n]	0[n]	0[n]	30-50 mM	Sorbitol and glycine	420-500 mOsm/kg, but not <240 mOsm/kg
Gammaplex 10%	IV	Liquid	Cold ethanol fractionation, ion-exchange chromatography, SD, nanofiltration (20 nm), ultrafiltration/diafiltration, terminal low pH incubation	≥98	99.7-100 monomers + dimers	<0.1 mg/mL	0	0	≤5 mM	Glycine	280-288 mOsm/kg, but not <240 mOsm/kg
Gamunex-C 10%	IV, SQ (SQ for PID only)	Liquid	Cold ethanol fractionation, anion-exchange chromatography, caprylate chromatography purified, low pH incubation	≥98	100 monomers + dimers[c,e]	Trace	<2 mcg/mL[c,e]	0	Trace (<7 mEq/L)[c,e]	Glycine	258 mOsm/kg[c,e]
Hizentra 20%[h]	SQ	Liquid	Cold ethanol fractionation, anion-exchange chromatography, octanoic acid fractionation, pH 4.0 incubation, depth filtration, virus filtration, nanofiltration (20 nm)	≥98	≥90 monomers + dimers	NA	NA	NA	Trace	Proline	380 mOsm/kg
Hyqvia (IgG 10% + HY 5%)	SQ	Liquid	Cohn-Oncley,[l] anion-exchange chromatography, SD, nanofiltration, ultrafiltration, low pH incubation	≥98	≥95 monomers + dimers	Trace	1 mg/mL	Not detectable	No sodium added	Glycine	240-300 mOsmol/kg (physiologic range, 285-295 mOsmol/kg)
Octagam 5%	IV	Liquid	Cold ethanol fractionation, ultrafiltration, chromatography, SD, pH 4.0 incubation	≥96	≥90 monomers + dimers	≤0.1 mg/mL	0	0	≤30 mmol/L	Maltose[o] (100 mg/mL)	310-380 mOsm/kg
Octagam 10%	IV	Liquid	Cold ethanol fractionation, ultrafiltration, chromatography, SD, pH 4.0 incubation	≥96	≥94 monomers + dimers	<106 mcg/mL	0	0	≤30 mmol/L	Maltose[o] (90 mg/mL)	310-380 mOsm/kg
Panzyga 10%	IV	Liquid	Cold ethanol fractionation, ultrafiltration, SD, nanofiltration (20 nm), ion-exchange chromatography	≥96	≥90 monomers + dimers	<0.1 mg/mL	0	0	Trace	Glycine	240-310 mOsm/kg
Privigen 10%	IV	Liquid	Cold ethanol fractionation, octanoic acid fractionation, anion-exchange chromatography, pH 4.0 incubation, depth filtration, virus filtration, nanofiltration (20 nm)	≥98	≥98 monomers + dimers	NA	NA	NA	Trace	Proline	320 mOsmol/kg (range: 240-440 mOsmol/kg)
Xembify 20%	SQ	Liquid	Cold ethanol fractionation, caprylate precipitation, depth filtration, low pH incubation, anion-exchange chromatography, nanofiltration	≥98	98-100 monomers + dimers	<0.004 mg/mL	NA	NA	Trace	Glycine and polysorbate 80	280-404 mOsm/kg

Table 4. Log Reduction Factor Comparisons[p]

Product[a]	Enveloped Viruses					Nonenveloped Virus	TSE (Prion)
	HIV	Models for HCV		Model for Large DNA	B19		
		SBV	BVDV	PRV			
Asceniv 10%	>9.62	>7.11	>11.79	>8.65	6.18	5.29 (MEV), 6.18 (BPV), 4.0 (PPV), >7.02 (SV40)	NA
Bivigam 10%	>9.62	>7.11	>11.79	>8.65	6.18	5.29 (MEV), 6.18 (BPV), 4.0 (PPV), >7.02 (SV40)	NA
Cutaquig 16.5%	≥14.07	≥20.61		≥18.22		≥12.20 (MEV), ≥6.53 (PPV)	
Cuvitru 20%	>19.9		>18.1	>21.8		9.6 (HAV), >11.9 (EMCV), 10.1 (MMV)	≥3.2
Flebogamma 5% DIF Flebogamma 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%	>16.8 (HIV-1)	NA	>8.8	>10.1		>5.2 (HAV), 5.0 (EMCV), >5.3 (MMV)	NA
Gammaked 10%	≥17.7	NA	≥20.4	≥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%	≥17.7	NA	≥20.4	≥12.2		≥5.0 (HAV)	≥6.6
Hizentra 20%[h]	≥16.0	NA	≥11.8	≥17.7	≥5.3	≥9.6 (EMCV), ≥7.8 (MMV)	Octanoic acid fractionation (≥6.4), depth filtration (2.6), virus filtration (≥5.8)
Hyqvia	>14.8	NA	≥16.8	>16.9	4.8	5.7 (HAV), >7.7 (EMCV), 5.1 (MMV)	NA
Octagam 5%	>14.07	>20.61	NA	>18.22		>12.20 (MEV), >6.53 (PPV)	≥6.7[q]
Octagam 10%	≥14.07	≥20.61	NA	≥18.22		≥12.20 (MEV), ≥6.53 (PPV)	NA
Panzyga 10%	≥9.37		≥8.16	≥13.16		≥11.66 (MEV), 11.61 (PPV)	≥10.4
Privigen 10%	≥16.0	NA	≥11.8	≥17.7	≥5.3	≥9.6 (EMCV), ≥7.8 (MMV)	Octanoic acid fractionation (≥6.4), depth filtration (2.6), virus filtration (≥5.8)
Xembify 20%	≥16.5	≥6.0	≥20.2	≥13.0		≥5.0 (HAV), 8.2 (PPV)	≥6.6

Table 5. IVIG Infusion Rates[r]

IVIG[a]	Initial Infusion Rate	Maintenance Infusion Rate	Maximum Infusion Rate[s]	Comments[t]
Asceniv 10%	0.3 mL/kg/h for 15 min	Increase gradually every 15 min if tolerated, up to 4.8 mL/kg/h	4.8 mL/kg/h	Ensure that patients with preexisting renal insufficiency are not volume depleted; discontinue if renal function deteriorates; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion rate practicable
Bivigam 10%	0.3 mL/kg/h for 10 min	Increase gradually every 20 min if tolerated by 0.48 mL/kg/h, up to 3.6 mL/kg/h	3.6 mL/kg/h	No filter required; for patients at risk for renal dysfunction or failure, administer at the minimum dose recommended and the minimum infusion rate practicable[r]
Cutaquig 16.5%	≥17 y: ≤20 mL/h per site; 2-16 y: ≤15 mL/h per site (first 2 infusions)	≥17 y: maximum of 52 mL/h per site; 2-16 y: maximum of 25 mL/h per site (subsequent infusions)	≥17 y: 52 mL/h per site; 2-16 y: 25 mL/h per site (subsequent infusions)	Do not dilute; in patients at risk for developing renal dysfunction because of any degree of preexisting renal insufficiency or predisposition to acute renal failure (eg, diabetes mellitus, age >65 y, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs), monitor renal function and consider lower, more frequent dosing
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 practicable to patients >65 y and those at risk for renal failure or thrombotic events[u]
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[u]
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-mcm 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 practicable to patients aged >65 y or at risk for renal or thrombotic events[u]
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 preexisting 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[u]
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 preexisting 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[u]
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[u]
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 mcm; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion rate practicable, not to exceed 0.07 mL/kg/min[u]
Octagam 10%	0.6 mL/kg/h for 30 min	Increase gradually as tolerated every 30 min to 7.2 mL/kg/h for chronic ITP and 2.4 mL/kg/h for dermatomyositis	7.2 mL/kg/h (chronic ITP); 2.4 mL/kg/h (dermatomyositis)	No filter required or supplied; if an in-line filter is used, the pore size should be 0.2-200 mcm; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion rate practicable, not to exceed 0.03 mL/kg/min[u]
Panzyga 10%	0.6 mL/kg/h	Increase gradually as tolerated every 15-30 min to 8.4 mL/kg/h (PID), 4.8 mL/kg/h (ITP), and 7.2 mL/kg/h (CIDP)	8.4 mL/kg/h (PID), 4.8 mL/kg/h (ITP), 7.2 mL/kg/h (CIDP)	Ensure that patients with preexisting renal insufficiency are not volume depleted; discontinue if renal function deteriorates; for patients at risk for renal dysfunction or thrombotic events, administer at the minimum infusion dose and rate practicable
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 practicable to patients at risk for renal dysfunction or thrombotic events[u]
Xembify 20%	Adults: maximum rate of 25 mL/h per site; up to 6 sites	Adults: maximum rate of 25 mL/h per site; up to 6 sites	≤25 mL/h per site	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[u]

Key

AU atomic unit
BGMS blood glucose monitoring systems
BVDV bovine viral diarrhea virus
B19 human parovirus B19
CBER Center for Biologics Evaluation and Research
CIDP chronic inflammatory demyelinating polyneuropathy
CLL chronic lymphocytic leukemia
CMV cytomegalovirus
CPV canine parvovirus
CS customer service
EIA enzyme immunoassay
EMCV encephalomyocarditis virus (RNA model)
GDH-PQQ glucose dehydrogenase-pyrroloquinoline quinone
GDO glucose-dye-oxidoreductase
HAV hepatitis A virus
HBV hepatitis B virus
HCV hepatitis C virus
HH inhibition of hemolysis
HIV human immunodeficiency virus
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
MI medical information
MMN multifocal motor neuropathy
MMV mouse minute virus (model for nonlipid DNA virus)
NA not available
NaCl sodium chloride
NDC National Drug Code
NT neutralization test
PEG polyethylene glycol
PEI Paul Ehrlich Institute International Units
PI prescribing information
PID primary immunodeficiency
PFS pre-filled syringes
PPV porcine parvovirus
PRV pseudorabies virus
RIA radioimmunoassay
RSS reduced space symbology
RSV respiratory syncytial virus
RT room temperature
SBV Sindbis virus
SD solvent detergent
SQ subcutaneous
SV40 simian virus 40
TSE transmissible spongiform encephalopathies
UIN unique identifier number
VZV varicella-zoster virus

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 ADMA Biologics.

e Data on file at Grifols.

f As of December 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.

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

h Provided the total weekly dose is maintained for the indication of PID, 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.

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

j Under appropriate storage conditions.

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

l 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).

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

n Data on file at Bio Products Laboratory.

o 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 the PI for full details.

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

q Data on file at Octapharma.

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

s 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.

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

u 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.