Characteristics of Immunoglobulin Products Used to Treat Primary Immunodeficiency Diseases Licensed for Use in the United States

PRODUCT NAME	Bivigam	Cuvitru	Flebogamma DIF	Gammagard Liquid	Gammagard S/D	Gammaked	Gammaplex	Gamunex - C	Hizentra	HYQVIA[3]	Octagam	Privigen
MANUFACTURER	Biotest Pharmaceuticals Corporation[2]	Shire	Grifols	Shire	Shire	Kedrion	Bio Products Laboratory	Grifols	CSL Behring	Shire	Octapharma	CSL Behring
METHOD OF PRODUCTION (Including Viral Inactivation)	Cohn-Oncley fractionation, Anion exchange chromatography; Precipitation and removal of fraction III of the cold ethanol process, solvent/detergent treatment, 35 nm nanofiltration.	Cohn-Oncley fractionation, ion-exhange chromatograph solvent/detergent treatment, 35nm nanofiltration, low pH/elevated temperature incubation.	Cold alcohol fractionation, polyethylene glycol precipitation, ion exchange chromatography, pH 4 treatment, pasteurization, solvent detergent treatment, and double sequential nanofiltration through 35 and 20 nm filters.	Cohn-Oncley fractionation, ion-exhange chromatography solvent/ detergent treatment, 35nm nanofiltration, low pH/elevated temperature incubation.	Cohn-Oncley fractionation, ion-exchange chromatography, solvent detergent treatment.	Cohn-Oncley fractionation, caprylate/chromatography purification, cloth and depth filtration, final container low pH incubation.	Kistler & Nitschmann fractionation, DEAE-Sephadex chromatography, Solvent/detergent, CM-Sepharose chromatography, Virus Filration (20 nm) Terminal low pH incubation.	Cohn-Oncley fractionation, caprylate/chromatography purification, cloth and depth filtration, final container low pH incubation.	Cold alcohol fractionation, octanoic acid fractionation, anion exchange chromatography; pH 4 incubation, depth filtration, nanofiltration; TSE reduction steps include octanoic acid fractionation, depth filtration, and virus filtration.	IG 10% (Human) of HYQVIA: Cohn-Oncley fractionation, ion-exhange chromatography solvent/detergent treatment, 35nm nanofiltration, low pH/elevated temperature incubation recombinant human hyaluronidase: produced from genetically engineered Chinese Hamster Ovary (CHO) cells containing a DNA plasmid encoding for a soluble fragment of human hyaluronidase PH20.	Cohn-Oncley cold ethanol fractionation, ultra-filtration, chromatography, solvent detergent treatment.	Octanoic Acid Fractionation, CH9 Filtration, pH 4.0 incubation, Depth filtration, Chromatography, Nanofiltration, TSE Reduction Steps.
FORM	Liquid	Liquid	Liquid	Liquid	Lyophilized	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid	Liquid
SHELF-LIFE/STORAGE REQUIREMENT	24 Months (refrigerated)	12 Months (room temperature storage not to exceed 25°C or 77°F)	24 Months (room temperature storage)	36 Months (refrigerated) 24 Months (room temperature storage not to exceed 25°C or 77°F)	24 Months (room temperature storage)	36 Months	36 months (room temperature storage)	36 Months	30 Months (room temperature storage)	36 Months (refrigerated) 3 Months[4] (room temperature storage not to exceed 25°C or 77°F)	24 Months	36 Months (room temperature storage)
RECONSTITUTION TIME	N/A	None (Liquid solution)	None (Liquid solution)	None (Liquid solution)	N/A	None (Liquid solution)	None (Liquid solution)	None (Liquid solution)	None (Ready-to-use liquid solution)	None (Liquid solution)	None (Liquid solution)	None (Liquid solution)
AVAILABLE CONCENTRATIONS	10%	20%	5% | 10%	10%	5% | 10%	10%	5% | 10%	10%	20% (200 mg/mL)	10%	5% | 10%	10%
MAXIMUM RECOMMENDED INFUSION RATE	3.5 mL/kg/hour	First 2 Infusions: 10 - 20 mL/hr/site Subsequent Infusions: ≤60 mL/hr/site	6.0 mL/kg/ hour | 4.8 mL/kg/ hour	5 mL/kg/hr (IV) | ≥40 kg BW: 30 mL/site at 20-30mL/hour site <40 kg BW: 20 mL/site at 15-20 mL/ hour/site (SC)	4 mL/ kg/hour | 8 mL/ kg/hour	4.8 mL/kg/ hour (IV) | 20 mL per hour (SC)	4.8 mL/kg/hour	4.8 mL/kg/ hour (IV) | 20 mL per hour (SC)	Up to 25 mL/hr/injection site (50 mL/hr for all sites combined)	< 40kg BW: maximum 160 mL/site > 40kg BW: maximum 300 mL/site	<4.2 mL/kg/ hour | <7.2 mL/kg/ hour	4.8mL/kg/hour
TIME TO INFUSE 35 gms[1]	Time will vary based upon patient tolerability; 146.5 min based on recommended infusion rates.	Time will vary based upon patient tolerability.	1.6 hours | 1 hour	Time will vary based on tolerability and route of administration.	Time will vary based on concentration and tolerability.	Time will vary depending on route of administration.	35 grams for 70kg person, 2 hrs 40 minutes if infused according to PI recommended schedule | For 70 kg person, 1 hr 53 minutes if infused according to PI recommended schedule; time will vary based on patient tolerability	Time will vary depending on route of administration.	Time will vary depending upon volume and tolerability.	Time will vary based on patient tolerability.	2.5 hours Time can vary based on patient tolerability. | 1.44 hours Time can vary based on patient tolerability.	Variable based on patient tolerability.
SUGAR CONTENT	No added sugars	No added sugars	None	No added sugars	20 mg/ml glucose | 40 mg/ml glucose	None	5% D-sorbitol (polyol) | None	None	None	No added sugars	100 mg/ml. maltose | 90 mg/ml. maltose	None
SODIUM CONTENT	0.100-0.140 M sodium chloride	No added sodium	Trace amounts	No added sodium	8.5 mg/mL sodium chloride | 17 mg mL sodium chloride	Trace amounts	30 - 50 mmol/L | < 30 mM	Trace amounts	Trace amounts (≤10 mmol/L)	8.5 mg/mL sodium chloride in recombinant human hyaluronidase, no added sodium in IG 10%	≤30 mmol/L	Trace amounts
OSMOLARITY/ OSMOLALITY	≤ 510 mOsm/kg	280-292 mOsm/kg	240-370 mOsm/kg	240 - 300 mOsm/kg	636 mOsm/kg | 1250 mOsm/L	258 mOsm/kg	460 - 500 mOsm/kg | Typically, 280 mOsmol/ kg	258 mOsm/kg	380 mOsmol/kg	240 - 300 mOsm/kg	310 - 380 mOsm/kg	Isotonic (320 mOsmol/kg)
PH	4.0 - 4.6	4.6 - 5.1	5.0 – 6.0	4.6 – 5.1	6.8 ± 0.4	4.0 – 4.5	4.6 – 5.1 | 4.9 – 5.2	4.0 – 4.5	4.6 – 5.2	4.6 - 5.1	5.1 – 6.0 | 4.5 – 5.0	4.8
IgA CONTENT	≤ 200 µg/mL	80 µg/mL	Average: < 3 mcg/mL (Specification value: < 50 mcg/mL) | Average: < 3 mcg/mL (Specification value: < 100 mcg/mL)	37 µg/mL	≤ 1 µg/mL ≤ 2.2 µg/mL | N/A	46 µg/mL	Average: <4 mcg/mL | Specification value: < 20 mcg/ml	46 µg/mL	≤50 mcg/mL	37 µg/mL	<100 µg/mL | Average of 106 µg/mL of IgA	< or = 25mcg/mL
APPROVED METHOD OF ADMINISTRATION	Intravenous	Subcutaneous	Intravenous	Intravenous | Subcutaneous	Intravenous	Intravenous | Subcutaneous	Intravenous	Intravenous | Subcutaneous	Subcutaneous	Subcutaneous	Intravenous	Intravenous

[1] 0.5 gm/kg for a 70 kg adult = 35 gms; 5% Concentrations: 1g = 20 mL; 10% Concentrations: 1g = 10 mL.
[2] Distributed by Kedrion Pharmaceuticals.
[3] HYQVIA is a dual vial unit containing 10% IgG (100 mg/mL) and 160 U/mL recombinant human hyaluronidase.
[4] Shorter room temperature shelf life of HYQVIA (3 months) compared to Gammagard Liquid (24 months) is due to the recombinant human hyaluronidase component of HYQVIA.

The time to infuse is based on the maximal infusion rate. Check product label for storage temperatures, which vary among immunoglobulin products. Check package insert for detailed prescribing information. Information for each of the products listed above has been provided directly to IDF by the manufacturer of that product.

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Download this chart at: www.primaryimmune.org/ig-products

Table updated April 2018