Texas Vendor Drug Program

Drug Use Criteria: Immune Globulins

Publication History

1. Developed June 2018.
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Medications listed in the tables and non-FDA approved indications included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.

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1 Dosage

1.1 Adults

Immune globulins, solutions comprised primarily of human immunoglobulin (Ig) G with minute concentrations of IgA and IgM, are obtained from pooled plasma from a variety of donors to guarantee a diverse antibody collection with variable antigen-binding sites. Immune globulins work by providing adequate antibody concentrations against an extensive selection of different pathogens.[1,2] Immune globulins are FDA-approved to manage primary and secondary immunodeficiencies, prevent infectious diseases, and treat other inflammatory and autoimmune disorders.[1-16] Hyperimmune globulins like cytomegalovirus immune globulin are prepared from pooled donor serum with high antibody titers to specific infectious organisms and are used to prevent or mitigate the targeted infection.[1-3] Immune globulins are administered by the intravenous or subcutaneous routes.[1-16] Maximum recommended dosage regimens in adult patients for available immune globulins and hyperimmune globulins are summarized in **Tables 1 & 2.**

Table 1. Adult Immune Globulin Recommended Dosages: Intravenous Products [1-11]

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
cytomegalovirus immune globulin, human (Cytogam®)	50 mg/mL single-use vial (50 mL)	Prevention of cytomegalovirus disease in heart, kidney, lung, liver and pancreas transplant recipients	*kidney allograft recipients:* 150 mg/kg as IV infusion given within 72 hours after transplant, followed by 100 mg/kg as single IV dose at 2, 4, 6 and 8 weeks posttransplant; 50 mg/kg at weeks 12 and 16 after transplant *heart, liver, lung, pancreas allograft recipients:* 150 mg/kg as IV infusion given within 72 hours after transplant, followed by 150 mg/kg as single IV dose at 2, 4, 6 and 8 weeks posttransplant; 100 mg/kg at weeks 12 and 16 after transplant
immune globulin, human (Flebogamma® 5% DIF)	0.5 g, 2.5 g, 5 g, 10 g, 20 g single-use vials	Primary Humoral immunodeficiency (PI)	300 to 600 mg/kg as IV infusion every 3 to 4 weeks (maximum 5 mg/kg/min)
immune globulin, human (Flebogamma® 10% DIF)	**5 g, 10 g, 20 g single-use vials**	PI	300 to 600 mg/kg as IV infusion every 3 to 4 weeks (maximum 8 mg/kg/min)
		Chronic primary immune thrombocytopenia	**1 g/kg as IV daily for 2 consecutive days (maximum 8 mg/ kg/ min)**
immune globulin, human (Gammagard Liquid®)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 30 g protein (100 mg/mL) as single-use bottles	multifocal motor neuropathy	0.5 to 2.4 g/kg/month as IV infusion based on clinical response **(maximum 9 mg/kg/min)**

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
		PI	300 to 600 mg/kg as IV infusion every 3 to 4 weeks **based on clinical response** (maximum 8 mg/kg/min)
immune globulin, human [Gammaked® 10% (sucrose-free)]	1 g protein, 5 g protein, 10 g protein, 20 g protein, single-use vials	idiopathic thrombocytopenic purpura (ITP)	2 g/kg in two divided doses (1 g/kg) over two consecutive days, or five divided doses (0.4 g/kg) over five consecutive days^ (maximum 8 mg/kg/min)
		chronic inflammatory demyelinating polyneuropathy (CIDP)	2 g/kg as IV loading dose in divided doses over 2-4 consecutive days followed by 1 g/kg IV maintenance dose as single dose or two divided doses (0.5 g/kg) over two consecutive days every 3 weeks **(maximum 8 mg/kg/min)**
		PI	300 to 600 mg/kg as IV infusion every 3 to 4 weeks (maximum 8 mg/kg/min)
immune globulin, human (Gamunex®-C)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 40 g protein single use vials	CIDP	2 g/kg as IV loading dose in divided doses over 2-4 consecutive days followed by 1 g/kg IV maintenance dose as single dose or two divided doses (0.5 g/kg) over two consecutive days every 3 weeks **(maximum 8 mg/kg/min)**
		ITP	2 g/kg in two divided doses (1 g/kg) over two consecutive days, or five divided doses (0.4 g/kg) over five consecutive days^ (maximum 8 mg/kg/min)

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
		PI	300 mg/kg to 600 mg/kg every 3-4 weeks (maximum 8 mg/kg/min)
immune globulin, human (Octagam® 5%)	1 g, 2.5 g, 5 g, 10 g, 25 g single use vials	PI	300 to 600 mg/kg as IV infusion every 3 to 4 weeks **(maximum 3.3 mg/kg/min)**
immune globulin, human (Octagam® 10%)	2 g, 5 g, 10 g, 20 g, 30 g single use vials	chronic ITP	2 g/kg IV as total dose, given as two 1 g/kg IV doses on 2 consecutive days (maximum 12 mg/kg/min)
		dermatomyositis	**2 g/kg IV divided in equal doses given over 2-5 consecutive days every 4 weeks (maximum 4 mg/kg/min)**
immune globulin, human (Privigen®)	**5 g, 10 g, 20 g, 40 g single use vials**	CIDP	2 g/kg as loading dose in divided doses over 2-5 consecutive days followed by 1 g/kg maintenance dose as single dose or two divided doses (0.5 g/kg) over two consecutive days every 3 weeks **(maximum 8 mg/kg/min)**
		chronic ITP	1 g/kg IV daily for two consecutive days (maximum 4 mg/kg/min)
		PI	200 to 800 mg/kg IV every 3 to 4 weeks; adjust dose based on clinical response and serum IgG trough levels (maximum 8 mg/kg/min)

^if platelet counts return to normal after first 1 g/kg dose, the second 1g/kg dose does not need to be administered

Table 2. Adult Immune Globulin Recommended Dosages: Subcutaneous Products[1,2,6-8,12-16]

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human (Cutaquig®)	165 mg/1 mL	Primary humoral immunodeficiency (PI)	for patients receiving IVIG for at least 3 months, dose based off previous IVIG dose in grams divided by the number of weeks between IVIG doses, then multiply by **1.3;** begin one week after last IVIG dose[##] **for patients receiving subcutaneous immune globulin (SCIG) for at least 3 months, maintain the previous SCIG dose[##]**
immune globulin, human (Cuvitru®)	**1 g, 2 g, 4 g, 8 g, 10 g single use vials**	PI	dose based on previous IVIG or Hyqvia® dose in grams divided by weeks treated with previous immune globulin x 1.3 and administered weekly or every two weeks; based on clinical response and serum IgG trough levels[+] **for patients receiving SCIG, weekly dose should be the same as previous SCIG therapy[+]**
immune globulin, human (Gammagard Liquid®)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 30 g protein (100 mg/mL) as single-use bottles	PI	*begin one week after last IVIG infusion*; dose based on previous IVIG dose in grams x 1.37 divided by number of weeks between doses; dosages based on clinical response and serum IgG trough levels[^^]

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human [Gammaked® 10% (sucrose-free)]	1 g protein, 5 g protein, 10 g protein, 20 g protein, single-use vials	PI	*begin one week after last IVIG infusion*; dose based on previous IVIG dose in grams x 1.37 divided by number of weeks between doses; dosages based on clinical response and serum IgG trough levels++
immune globulin, human (Gamunex®-C)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 40 g protein single use vial	PI	SC dose based on previous IVIG dose in grams x 1.37 divided by number of weeks between doses; based on clinical response and serum IgG trough levels#
immune globulin, human (Hizentra®)	**1 g, 2 g, 4 g, 10 g single use vials; 1 g, 2 g, 4 g, 10 g prefilled syringe**	chronic inflammatory demyelinating polyneuropathy (CIDP)	begin 1 week after last IVIG infusion; 0.4 g/kg/week SC given in 1 or 2 sessions over 1 to 2 consecutive days
		PI	may be given after patient has received IVIG for at least 3 months; SC dose based on previous IVIG dose in grams divided by number of weeks between doses x 1.37 and administered weekly or every two weeks; based on clinical response and serum IgG trough levels@

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human with recombinant human hyaluronidase (Hyqvia®)	**2.5 g, 5 g, 10 g, 20 g, 30 g single use vials**	PI	*patients switching from previous IVIG treatment:* administer same dose and frequency as previous IVIG treatment as SC doses, after initial SC dose ramp-up** *treatment-naïve patients:* 300 to 600 mg/kg every 3 to 4 weeks SC, after initial SC dose ramp-up**
immune globulin, human (Xembify®)	**1 g, 2 g, 4 g, 10 g single use vials**	PI	*patients switching from previous IVIG treatment:* divide the previous monthly IVIG dose in grams by the number of weeks between IVIG doses, then multiply by 1.37@@

##consult Cutaquig® package insert for specific SC dosage requirements
+consult Cuvitru® package insert for specific SC dosage requirements
#consult Gamunex® - C package insert for specific SC dosage requirements
@consult Hizentra® package insert for specific SC dosage requirements
***Hyqvia® dose ramp-up requires graduated dose increase over 3 to 4 weeks to targeted dose*
++consult Gammaked® package insert for specific SC dosage requirements
^^ consult Gammagard Liquid® package insert for specific SC dosage requirements
@@ consult Xembify® package insert for specific SC dosage requirements

Pediatrics

Select immune globulins are FDA-approved for use in pediatric patients to manage immune thrombocytopenic purpura and primary immunodeficiencies.[1-16] Pediatric safety and efficacy have not yet been established for Hyqvia®.[1,2,15] ~~Varicella zoster immune globulin is indicated for use in pediatric patients at high risk for adverse outcomes following exposure to chickenpox or herpes zoster.~~[9] Maximum recommended dosages for pediatric patients are summarized in **Tables 3 & 4.**

Table 3. Pediatric Immune Globulin Recommended Dosages: Intravenous Products[1,2,4-9,11]

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human (Flebogamma® 5% DIF)	0.5 g, 2.5 g, 5 g, 10 g, 20 g single-use vials	PI	*2 years to < 18 years:* 300 to 600 mg/kg as IV infusion every 3 to 4 weeks (maximum 5 mg/kg/min)
immune globulin, human (Flebogamma® 10% DIF)	**5 g, 10 g, 20 g single-use vials**	**chronic primary immune thrombocytopenia**	***2 years to < 18 years:* 1 g/kg as IV daily for 2 consecutive days (maximum 8 mg/ kg/ min)**
immune globulin, human (Gammagard Liquid®)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 30 g protein (100 mg/mL) as single-use bottles	PI	*2 years to < 18 years:* 300 to 600 mg/kg as IV infusion every 3 to 4 weeks (maximum 8 mg/kg/min)
immune globulin, human [Gammaked® 10% (sucrose-free)]	1 g protein, 5 g protein, 10 g protein, 20 g protein, single-use vials	ITP	2 g/kg in two divided doses (1 g/kg) over two consecutive days, or five divided doses (0.4 g/kg) over five consecutive days^ (maximum 8 mg/kg/min)

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
		PI	*2 years to < 18 years:* 300 to 600 mg/kg as IV infusion every 3 to 4 weeks. (maximum 8 mg/kg/min)
immune globulin, human (Gamunex®-C)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 40 g protein single-use vials	ITP	2 g/kg in two divided doses (1 g/kg) over two consecutive days, or five divided doses (0.4 g/kg) over five consecutive days^ (maximum 8 mg/kg/min)
		PI	*2 years to < 18 years:* 300 mg/kg to 600 mg/kg every 3-4 weeks (maximum 8 mg/kg/min)
immune globulin, human (Octagam® 5%)	1 g, 2.5 g, 5 g, 10 g, 25 g single use vials	PI	*6 years to < 18 years:* 300 to 600 mg/kg as IV infusion every 3 to 4 weeks
immune globulin, human (Privigen®)	**5 g, 10 g, 20 g, 40 g single use vials**	chronic ITP	*15 years to < 18 years:* 1 g/kg IV daily for two consecutive days (maximum 4 mg/kg/min)
		PI	*3 years to < 18 years:* 200 to 800 mg/kg IV every 3 to 4 weeks; adjust dose based on clinical response and serum IgG trough levels (maximum 8 mg/kg/min)

^*if platelet counts return to normal after first 1 g/kg dose, the second 1g/kg dose does not need to be administered*

Table 4. Pediatric Immune Globulin Recommended Dosages: Subcutaneous Products[1,2,6-8,12-14,16]

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human (Cutaquig®)	**1 g, 2 g, 4 g, 8 g single use vials**	**PI**	***2 years to 16 years of age*: for patients receiving IVIG for at least 3 months, dose based off previous IVIG dose in grams divided by the number of weeks between IVIG doses, then multiply by 1.3; begin one week after last IVIG dose[##]** **for patients receiving subcutaneous immune globulin (SCIG) for at least 3 months, maintain the previous SCIG dose[##]**
immune globulin, human (Cuvitru®)	**1 g, 2 g, 4 g, 8 g, 10 g single use vials**	PI	*2 years to < 18 years:* dose based on previous IVIG or Hyqvia® dose in grams divided by weeks treated with previous immune globulin x 1.3 and administered weekly or every two weeks; based on clinical response and serum IgG trough levels[+] **for patients receiving SCIG, weekly dose should be the same as previous SCIG therapy[+]**

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human (Gammagard Liquid®)	1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 30 g protein (100 mg/mL) as single-use bottles	PI	*2 years to < 18 years:* SC dose based on previous IVIG dose x 1.37 divided by number of weeks between doses; dosage adjustments based on clinical response and serum IgG trough levels^
immune globulin, human [Gammaked® 10% (sucrose-free)]	**1 g protein, 5 g protein, 10 g protein, 20 g protein, single-use vials**	**PI**	***2 years to < 18 years:* begin one week after last IVIG infusion; dose based on previous IVIG dose in grams x 1.37 divided by number of weeks between doses; dosages based on clinical response and serum IgG trough levels++**
immune globulin, human (Gamunex®-C)	**1 g protein, 2.5 g protein, 5 g protein, 10 g protein, 20 g protein, 40 g protein single-use vials**	**PI**	***2 years to < 18 years:* SC dose based on previous IVIG dose in grams x 1.37 divided by number of weeks between doses; based on clinical response and serum IgG trough levels#**
immune globulin, human (Hizentra®)	**1 g, 2 g, 4 g, 10 g single use vials; 1 g, 2 g, 4 g, 10 g prefilled syringe**	PI	*2 years to < 18 years:* may be given after patient has received IVIG for at least 3 months; dose based on previous IVIG dose in grams divided by number of weeks between doses x 1.37 and administered weekly or every two weeks; based on clinical response and serum IgG trough levels@

Drug Name	Dosage Form/ Strength	Treatment Indication	Maximum Recommended Dosage
immune globulin, human (Xembify®)	**1 g, 2 g, 4 g, 10 g single use vials**	PI	*2 years to < 18 years:* for patients already receiving IVIG. Divide previous monthly IVIG dose in grams by the number of weeks between IVIG doses, then multiply by 1.37@@

##consult Cutaquig® package insert for specific SC dosage requirements
+ consult Cuvitru® package insert for specific SC dosage requirements
^consult Gammagard Liquid® package insert for specific SC dosage requirements
++consult Gammaked® package insert for specific SC dosage requirements
#consult Gamunex® - C package insert for specific SC dosage requirements
@consult Hizentra® package insert for specific SC dosage requirements
@@consult Xembify® package insert for specific SC dosage requirement

Duration of Therapy

Immune globulins, when used to manage primary immunodeficiency, may be continued indefinitely as primary immunodeficiency is a chronic, lifelong disease.[1,2,4-9,11-16] Patients diagnosed with idiopathic thrombocytopenic purpura, an autoimmune disorder characterized by platelet destruction, may require immune globulin therapy to increase platelet counts. Immune globulin therapy is typically required for only 24-48 hours to stabilize platelet counts, but patients may require repeat courses of immune globulin therapy as ITP can be a chronic, lifelong condition.[1,2,5,7,8,10,11] Cytomegalovirus immune globulin (Cytogam®) is administered at an every 2- or 4-week dosing interval through week 16 following organ transplant.[1-3]

Duplicative Therapy

Concurrent administration of multiple immune globulins does not provide additional therapeutic benefit and is not recommended. However, adjunctive administration of an immune globulin and a hyperimmune globulin could potentially be necessary in

certain circumstances. Patient profiles containing concomitant prescriptions for two or more immune globulin products will be reviewed.

Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. The following drug-drug interactions are considered clinically relevant for immune globulins. Only those drug-drug interactions classified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

Live/Live Attenuated Virus Vaccines[1,2]

(e.g., measles, mumps, rubella, varicella) [clinical significance level- major (DrugReax); 2-major (CP)]

Adjunctive administration of immune globulins with live/live attenuated virus vaccines may inhibit the immune response to the vaccination by passively transferring antibodies and diminishing the desired vaccine effect. Antibodies present in immune globulins may diminish the response to mumps, rubella, and varicella vaccines for up to 6 months, while the measles vaccine response may be compromised for up to one year or more. Do not administer live vaccines for at least three months after immune globulin administration. Immune globulin and the hyperimmune globulin, varicella zoster immune globulin, should not be administered concurrently with the live varicella zoster vaccine. There should be at least a five-month interval between immune globulin (including varicella zoster immune globulin) administration and live varicella vaccination. Immune globulin should not be administered for two months after live varicella vaccine administration unless the benefits of immune globulin administration outweigh the potential for reduced vaccine effects.

References

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13. Immune globulin subcutaneous – human (Cuvitru®) package insert. **Baxalta US Inc., October 2021.**
14. Immune globulin subcutaneous – human (Hizentra®) package insert. CSL Behring LLC, **April 2022.**
15. Immune globulin infusion 10% - human, with recombinant human hyaluronidase (Hyqvia®) package insert. Baxalta US Inc., **March 2021.**

16. Immune globulin subcutaneous- human-klhw (Xembify®) package insert. Grifols Therapeutics Inc., **February 2022.**