

INTRAGAM P AND PRIVIGEN NZ DOSES FOR ZOSTER, TETANUS AND CMV ANTIBODY

REASON FOR ISSUE: Update to add dosage guidance for PRIVIGEN NZ – refer CCP715.

- BACKGROUND** Intravenously administered Intragam P has historically been used, on occasion, as an alternative to intramuscular injection of specific antibody for Herpes zoster (Zoster Immunoglobulin-VF) or tetanus (Tetanus Immunoglobulin-VF). Intragam P is also used in CMV prophylaxis or treatment.

Intragam P will no longer be manufactured by CSL Behring and in July 2023, NZBS commenced the phased transition of intravenous immunoglobulin from Intragam P to Privigen NZ. Current NZBS inventory of Intragam P will be depleted, with stock expected to be available until November 2023.

These guidelines provide generic dosing for Intragam P or Privigen NZ that will provide sufficient antibody content to cover the pathogens of interest. **QUICK GUIDE TO DOSING** Chickenpox prophylaxis (Herpes zoster)

Body weight	Intragam P dose, chickenpox prophylaxis (IU)	Dose in grams	Dose Volume Intragam P (mL) Based on 10.0 IU/ml	Dose Volume Privigen NZ (mL) Based on 16.67 IU/ml
Up to 10 kg	125 IU	0.75 g	13 mL	8 mL
Up to 20 kg	250 IU	1.50 g	25 mL	15 mL
Up to 30 kg	375 IU	2.25 g	38 mL	23 mL
Up to 40 kg	500 IU	3.00 g	50 mL	30 mL
Up to 50 kg	625 IU	3.75 g	63 mL	38 mL
Up to 60 kg	750 IU	4.50 g	75 mL	45 mL
Up to 70 kg	875 IU	5.25 g	88 mL	53 mL
Up to 80 kg	1000 IU	6.00 g	100 mL	60 mL
Up to 90 kg	1125 IU	6.75 g	113 mL	68 mL
Up to 100 kg	1250 IU	7.50 g	125 mL	75 mL
Up to 110 kg	1375 IU	8.25 g	138 mL	83 mL

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2.2 Tetanus treatment

Body weight	Dose	Intragam P dose, tetanus treatment (g)	Intragam P dose, Volume (mL) Based on 0.3 g/kg & 6% Protein	Privigen NZ dose, Volume (mL) Based on 0.3 g/kg & 10% Protein
5 kg	0.3 g/kg	1.5 g	34 mL	15 mL
10 kg	0.3 g/kg	3.0 g	50 mL	30 mL
15 kg	0.3 g/kg	4.5 g	84 mL	45 mL
20 kg	0.3 g/kg	6.0 g	100 mL	60 mL
25 kg	0.3 g/kg	7.5 g	134 mL	75 mL
30 kg	0.3 g/kg	9.0 g	150 mL	90 mL
35 kg	0.3 g/kg	10.5 g	184 mL	105 mL
40 kg	0.3g/kg	12.0 g	200 mL	120 mL
45 kg	0.3 g/kg	13.5 g	234 mL	135 mL
50 kg	0.3 g/kg	15.0 g	250 mL	150 mL
55 kg	0.3 g/kg	16.5 g	284 mL	165 mL
60 kg	0.3 g/kg	18.0 g	300 mL	180 mL
65 kg	0.3 g/kg	19.5 g	334 mL	195 mL
70 kg	0.3 g/kg	21.0 g	350 mL	210 mL
75 kg	0.3 g/kg	22.5 g	384 mL	225 mL
80 kg	0.3 g/kg	24.0 g	400 mL	240 mL
85 kg	0.3 g/kg	25.5 g	434 mL	255 mL
90 kg	0.3 g/kg	27.0 g	450 mL	270 mL
95 kg	0.3 g/kg	28.5 g	484 mL	285 mL
100 kg	0.3 g/kg	30.0 g	500 mL	300 mL
105 kg	0.3 g/kg	31.5 g	534 mL	315 mL
110 kg	0.3 g/kg	33.0 g	550 mL	330 mL

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2.3 CMV Prophylaxis

Body weight	Dose in Units (25000 U/kg)	CMV prophylaxis (g)	Dose Volume Intragam P (mL)	Dose Volume Privigen NZ (mL)
5 kg	125000	1.83 g	31 mL	19 mL
10 kg	250000	3.67 g	62 mL	37 mL
15 kg	375000	5.50 g	92 mL	55 mL
20 kg	500000	7.33 g	123 mL	74 mL
25 kg	625000	9.17 g	153 mL	92 mL
30 kg	750000	11.00 g	184 mL	110 mL
35 kg	875000	12.83 g	214 mL	129 mL
40 kg	1000000	14.66 g	245 mL	147 mL
45 kg	1125000	16.50 g	275 mL	165 mL
50 kg	1250000	18.33 g	306 mL	184 mL
55 kg	1375000	20.16 g	337 mL	202 mL
60 kg	1500000	22.0 g	367 mL	220 mL
65 kg	1625000	23.83 g	398 mL	239 mL
70 kg	1750000	25.66 g	428 mL	257 mL
75 kg	1875000	27.50 g	459 mL	275 mL
80 kg	2000000	29.33 g	489 mL	294 mL
85 kg	2125000	31.16 g	520 mL	312 mL
90 kg	2250000	32.99 g	550 mL	330 mL
95 kg	2375000	34.83 g	581 mL	349 mL
100 kg	2500000	36.66 g	611 mL	367 mL
105 kg	2625000	38.49 g	642 mL	385 mL
110 kg	2750000	40.33 g	673 mL	404 mL

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2.4 CMV Treatment

Body weight	Dose in Units (50000 U/kg)	CMV treatment (g)	Dose Volume Intragam P (mL)	Dose Volume Privigen NZ (mL)
5 kg	250000	3.66 g	62 mL	37 mL
10 kg	500000	7.34 g	123 mL	74 mL
15 kg	750000	11.00 g	184 mL	110 mL
20 kg	1000000	14.66 g	245 mL	147 mL
25 kg	1250000	18.34 g	306 mL	184 mL
30 kg	1500000	22.00 g	367 mL	220 mL
35 kg	1750000	25.66 g	428 mL	257 mL
40 kg	2000000	29.32 g	489 mL	294 mL
45 kg	2250000	33.00 g	550 mL	330 mL
50 kg	2500000	36.66 g	611 mL	367 mL
55 kg	2750000	40.32 g	673 mL	404 mL
60 kg	3000000	44.00 g	734 mL	440 mL
65 kg	3250000	47.66 g	795 mL	477 mL
70 kg	3500000	51.32 g	856 mL	514 mL
75 kg	3750000	55.00 g	917 mL	550 mL
80 kg	4000000	58.66 g	978 mL	587 mL
85 kg	4250000	62.32 g	1039 mL	624 mL
90 kg	4500000	65.98 g	1100 mL	660 mL
95 kg	4750000	69.66 g	1161 mL	697 mL
100 kg	5000000	73.32 g	1222 mL	734 mL
105 kg	5250000	76.98 g	1284 mL	770 mL
110 kg	5500000	80.66 g	1345 mL	807 mL

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2.5 METHODS

Dose volume is calculated from historical levels of antibodies in the NZ donor pool adjusted for the relative proportion of human protein in each product:

Intragam P – 6 g of human protein in each 100mL

Privigen NZ – 10 g of human protein in each 100mL

The Certificate of Analysis (COA) for each batch of IVIg received are available in Q-Pulse. This COA contains quality information from the manufacturer which contains potency values for selected antibodies. The COA's from the manufacturer no longer include potency values for Zoster, CMV or Tetanus so historical data gathered from the NZ donor pool is used. This historical data was used to generate the following dosing information:

Prophylaxis for chicken pox:

The required dose is 125 IU per 10 kg bodyweight. For the intramuscular product, this is rounded up to the nearest 200 IU to a maximum of 600 IU (based on Zoster Immunoglobulin-VF datasheet).

Treatment of clinical tetanus:

The required dose of IV tetanus immunoglobulin for treating clinical tetanus is 4000IU (in this document the weight-based dosing recommended by the CDC will be used instead).

Prophylaxis / treatment for CMV infection:

Use of intravenous immunoglobulin to provide CMV prophylaxis should only be undertaken by a physician who has experience in this treatment. The usual recommended dose for CMV prophylaxis is 25000 U/kg. The usual recommended dose for treatment of CMV infection in appropriate patients is 50000 U/kg.

2.6 Calculation of dose for chickenpox (Herpes zoster) prophylaxis

For zoster antibody levels in Intragam P all batches have been assigned 10 IU/mL. This was related to a change in the assay used by CSL that led to a relative overestimation of the level compared to the previous assay.

2.7 Calculation of dose for tetanus treatment

The dose of intravenous immunoglobulin for tetanus treatment suggested by the Centers for Disease Control and Prevention is 200-400mg/kg (see <https://www.cdc.gov/tetanus/clinicians.html#symptoms>). A value of 300mg/kg will be used to calculate the dose rather than a standard dose of 4000 IU.

2.8 Calculation of dose for CMV prophylaxis and treatment

For 53 batches of Intragam P the CMV antibody levels are shown in the table:

Statistic	CMV Antibody conc. U/mL
Mean	5354.60
Median	5381.00
Standard deviation	420.30
95% confidence interval	5241.44 - 5467.76

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To maintain a safety margin (given that there is variability of antibody levels) the level of antibody used for dose calculation will be: *mean – 3 standard deviations*, i.e., $5354.60 - 3 \times 420.30 = 4093.70$ U/mL.

Intragam P is a 6% solution (6 g/ 100 mL). Each mL contains 0.06 g of immunoglobulin.

Privigen NZ is a 10% solution (10 g/ 100mL). Each mL contains 0.1 g of immunoglobulin.

Extrapolating the Intragam P data, the level of antibody used for dose calculation for Privigen NZ will be 6822.83 U/mL ($4093.70 / 0.06 \times 0.1$).

The usual recommended dose for CMV **prophylaxis** is 25000 U/kg. Therefore:

Intragam P will be needed at 6.11 mL/kg body weight ($25000 / 4093.70$) or 0.37 g/kg body weight (0.06×6.11).

Privigen NZ will be needed at 3.67 mL/kg body weight ($25000 / 6822.83$) or 0.13 g/kg body weight (0.01×3.67).

The usual recommended dose for **treatment** of CMV infection in appropriate patients is 50000 U/kg. Therefore:

Intragam P will be needed at 12.22 mL/kg body weight ($50000 / 4093.70$) or 0.73 g/kg body weight (0.06×12.22).

Privigen NZ will be needed at 7.34 mL/kg body weight ($50000 / 6822.83$) or 0.26 g/kg body weight (0.01×7.34).