

Immune Globulin

Implementation Date: August 1, 2019

Rationale for Update:

- Updated NACI recommendations for measles post-exposure prophylaxis for susceptible contacts who are pregnant or immunocompromised weighing 30 kg or more.
- Susceptible contacts who are pregnant or immunocompromised and 30 kg or more will not receive measles antibody concentrations that are considered to be fully protective from IMIG (maximum dose 15 mL).
- Susceptible-individuals excluding infants, pregnant or immunocompromised are no longer routinely recommended to receive IG following measles exposure.

Please consult the Product Monograph^{1,2} for further information about this product.

	IMIG GamaSTAN® S/D	IVIG Canada has a number of IVIG preparations available ³
Manufacturers	Grifols Therapeutics Inc. – distributed by Grifols Canada Ltd. ¹	<ul style="list-style-type: none"> • Grifols Therapeutics Inc. – distributed by Grifols Canada Ltd. (Gamunex®)² • Shire Pharma Canada ULC (Gammagard®) • Grifols Therapeutics Inc. (IGIVnex®) • CSL Behring Canada Inc. (Privigen®) • Octapharma (Panzyga®) <p>Access: IVIG stocked at hospitals and available through CBS.</p>
Off-license use	None	<p>IVIG – measles PEP for susceptible contacts who are pregnant or immunocompromised and weighing 30 kg or more.</p> <p><u>Note:</u> Although IVIG preparations are not currently indicated for measles PEP in Canada, NACI determined that it is an important strategy to prevent post-exposure measles disease in susceptible contacts who are pregnant or immunocompromised, particularly individuals weighing more than 30 kg.^{3,4}</p>
Indications for use of IG in Measles Post-Exposure	<p>Measles: Post-exposure for measles-susceptible contacts as soon as possible, preferably within 72 hours but can be administered up to six days after exposure. Susceptible contacts should receive either measles-containing vaccine or Immune Globulin (IG) depending upon the time from exposure, age and health status.³</p> <p>Susceptible contacts: contacts without evidence of immunity.</p> <p>Evidence of immunity³ includes:</p> <ul style="list-style-type: none"> • Two doses of measles-containing vaccine; or • Laboratory evidence of immunity (i.e. positive IgG antibody); or • Laboratory confirmation of disease. 	

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	<p>IMIG should be considered for the following susceptible contacts:</p> <ul style="list-style-type: none"> • Immunocompromised individuals less than 30 kg for whom measles-containing vaccine is contraindicated.³ • HIV-infected individuals less than 30 kg after a known exposure to confirmed measles even with documented previous MMR immunization.³ (Infectious Diseases Physician should be consulted if any HIV-infected individual is exposed to measles.) • Infants younger than six months of age.³ <ul style="list-style-type: none"> ○ Infants younger than six months of age are generally considered to have the same susceptibility/protection as their mother due to antibody transfer.⁵ ○ Infants are considered susceptible IF their mother does not have evidence of immunity. ○ Infants born to mothers with evidence of immunity are not considered susceptible, however, IG is recommended as a precaution due to waning maternal antibodies. (<i>This may be particularly relevant for infants whose mothers who have vaccine induced immunity, infants who are preterm, and infants greater than 3 months of age.</i>) • Infants 6 -11 months of age who cannot receive MMR vaccine within 72 hours of exposure.^{3,4,7} 	<p>IVIG should be considered for the following susceptible contacts:^{3,4}</p> <ul style="list-style-type: none"> • Immunocompromised individuals 30 kg or more for whom measles-containing vaccine is contraindicated.³ • HIV-infected individuals 30 kg or more after a known exposure to confirmed measles even with documented previous MMR immunization.³ Infectious Diseases Physician should be consulted if any HIV-infected individual is exposed to measles. • Pregnant women.³ • Infants younger than six months of age when IMIG injection volume is a concern.³ <ul style="list-style-type: none"> ○ Infants younger than six months of age are generally considered to have the same susceptibility/protection as their mother due to antibody transfer.⁵ ○ Infants are considered susceptible IF their mother does not have evidence of immunity.⁴ ○ Infants born to mothers with evidence of immunity are not considered susceptible, however, IG is recommended as a precaution due to waning maternal antibodies. • Infants 6 -11 months of age who cannot receive MMR vaccine within 72 hours of exposure^{3,4,7} but IMIG injection volume is a concern.³ <p>IVIG necessitates administration in a setting where there is active patient monitoring over several hours of infusion, performed by appropriately trained staff.⁴</p>
<p>Notes:</p> <ul style="list-style-type: none"> • Individuals already receiving replacement IVIG at 400 mg/kg of body weight or higher are considered protected against measles and do not require IG if the last dose of IVIG was received within three weeks prior to measles exposure.³ • If receiving IVIG is not operationally feasible for those susceptible individuals who are pregnant or immunocompromised, IMIG can be provided understanding that those weighing 30 kg or more will not receive the measles antibody concentrations that are considered to be fully protective.³ • Individuals who receive IG should receive age-appropriate measles-containing vaccine at specified intervals after receipt of IG depending upon the dosage of IG administered unless the vaccine is contraindicated. Refer to Assessment Prior to Vaccine Administration – Guidelines for Interval between Blood Products and MMR, MMR-Var and Varicella Vaccines. See also, Canadian Immunization Guide – Blood products, human immune globulin and timing of immunization 		

	<p>Additional Note:</p> <ul style="list-style-type: none"> Susceptible-individuals excluding infants, pregnant or immunocompromised are no longer routinely recommended to receive IG following measles exposure. ⁴ <table border="1" data-bbox="422 262 1432 808"> <thead> <tr> <th colspan="3">Summary of updated measles post-exposure prophylaxis recommendations for contacts</th> </tr> <tr> <th rowspan="2">Population</th> <th colspan="2">Time since exposure to measles</th> </tr> <tr> <th>≤ 72 hours</th> <th>73 hours to 6 days</th> </tr> </thead> <tbody> <tr> <td>Infants 0-6 months of age</td> <td colspan="2">IMIG</td> </tr> <tr> <td>Susceptible immunocompetent infants 6 -12 months of age</td> <td>MMR vaccine</td> <td>IMIG</td> </tr> <tr> <td>Susceptible immunocompetent infants 12 months of age and older</td> <td>MMR vaccine</td> <td>N/A</td> </tr> <tr> <td>Susceptible pregnant individuals</td> <td colspan="2">IVIG or IMIG (limited protection if 30 kg or more)</td> </tr> <tr> <td>Immunocompromised individuals six months of age and older</td> <td colspan="2">IVIG (30 kg or more) or IMIG (less than 30 kg)</td> </tr> </tbody> </table> <p>Adapted from: Updated NACI recommendations for measles post-exposure prophylaxis (2018).⁴</p> <p>For disease investigation, contact assessment and reporting requirements refer to <i>Public Health Notifiable Disease Management Guidelines – Measles</i>.⁷</p>	Summary of updated measles post-exposure prophylaxis recommendations for contacts			Population	Time since exposure to measles		≤ 72 hours	73 hours to 6 days	Infants 0-6 months of age	IMIG		Susceptible immunocompetent infants 6 -12 months of age	MMR vaccine	IMIG	Susceptible immunocompetent infants 12 months of age and older	MMR vaccine	N/A	Susceptible pregnant individuals	IVIG or IMIG (limited protection if 30 kg or more)		Immunocompromised individuals six months of age and older	IVIG (30 kg or more) or IMIG (less than 30 kg)	
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<p>Indications for use of IG in Hepatitis A Post-Exposure</p>	<p>IMIG</p> <p>Hepatitis A: Post-exposure prophylaxis for hepatitis A susceptible contacts should be administered as soon as possible within 14 days of the last exposure to the case (when the exposure occurred while the case was in the infectious period) and may include hepatitis A vaccine, immune globulin or both. See specific recommendations below.</p> <ul style="list-style-type: none"> Contacts at risk of developing severe complications (i.e. those with chronic liver disease; hepatitis B carriers; hepatitis C infection (anti-HCV positive); candidates and recipients of liver transplant) and individuals who are immunocompromised (congenital and acquired immunodeficiency; immunosuppressive therapy and HIV infection)³ should receive both IG and hepatitis A vaccine (two-dose series). See Biological Products – Hepatitis A Vaccine. Contacts younger than 6 months of age and individuals in whom hepatitis A vaccine is contraindicated should receive immune globulin only.³ All other contacts should receive hepatitis A vaccine only.³ See Biological Products - Hepatitis A Vaccine. For disease investigation, contact assessment and reporting information refer to <i>Public Health Notifiable Disease Management Guidelines – Hepatitis A</i>.⁸ <p>IVIG - N/A</p>																							
<p>Dose</p>	<p>Measles post-exposure:</p> <p>IMIG - 0.5 mL/kg of body weight (maximum 15 mL)^{3,4}</p> <p>IVIG - 400 mg/kg^{3,4}</p> <p>Hepatitis A post-exposure (IMIG):</p> <ul style="list-style-type: none"> 0.1 mL/kg of body weight^{9,10} 																							

Route	IMIG - Intramuscular injection	IVIG - Intravenous infusion ²
Schedule	<p>Measles contacts:</p> <p>IG should be administered as soon as possible but can be administered up to six days after exposure to prevent or modify measles.^{3,4}</p> <p>Notes:</p> <ul style="list-style-type: none"> • The recommended interval between IMIG and subsequent immunization with MMR, MMR-Var or Varicella vaccines is six months. • The recommended interval between IVIG and subsequent immunization with MMR, MMR-Var or Varicella vaccine is 8 months.³ • When it is necessary for IG to be administered less than 14 days after receiving MMR, MMR-Var or Varicella vaccine, the immunization should be repeated as per the intervals outlined in the <i>Guidelines for Interval between Blood Products and MMR, MMR-Var, and Varicella Vaccines</i>. If IG is administered more than 14 days post MMR containing or varicella containing immunization, the dose does not need to be repeated.³ <p>Refer to Assessment Prior to Vaccine Administration – Guidelines for Interval between Blood Products and MMR, MMR-Var and Varicella Vaccines. See also Canadian Immunization Guide³ – Blood products, human immune globulin and timing of immunization</p> <p>Hepatitis A contacts:</p> <p>IG should be administered as soon as possible after a known exposure for individuals who are eligible. It should be administered within 14 days of the last exposure. Efficacy of IG is unknown if more than 14 days after exposure.³</p> <p>Notes:</p> <ul style="list-style-type: none"> • The recommended interval between IMIG and subsequent immunization with MMR, MMR-Var or Varicella vaccines is 3 months. • When it is necessary for IG to be administered less than 14 days after receiving MMR, MMR-Var or Varicella vaccine, the immunization should be repeated 3 months after the administration of IG.¹⁰ If IG is administered more than 14 days post MMR containing or varicella containing immunization, the dose does not need to be repeated.³ 	
Contraindications	<p>IMIG</p> <ul style="list-style-type: none"> • Known severe hypersensitivity to any component of GamaSTAN® S/D or its container.¹ • Should not be given to individuals with isolated IgA deficiency.^{1,11} Such persons have the potential for developing antibodies to IgA and could develop anaphylactic reactions to subsequent administration of blood products that contain IgA.¹ 	<p>IVIG</p> <ul style="list-style-type: none"> • Individuals with known anaphylactic or severe response to IG.² • Refer to specific product monograph for contraindications.²
Precautions	<ul style="list-style-type: none"> • Use with caution for individuals with a history of prior systemic allergic reactions following administration of human immunoglobulin preparations.⁸ • Human IG preparations are among the safest blood-derived products available.³ 	

	<ul style="list-style-type: none"> IG is made from human plasma. Products made from human plasma may contain infectious agents, such as viruses, and theoretically, the Creutzfeldt-Jakob (CJD) agent that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, testing for the presence of certain current viral infections and inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit disease.^{1,2} 	
Possible reactions following IG administration	<p>IMIG</p> <p>Common:</p> <ul style="list-style-type: none"> Local pain, tenderness, and erythema at the injection site^{1,3} Stiffness of local muscles³ Mild fever and malaise³ <p>Uncommon:</p> <ul style="list-style-type: none"> Flushing, headache, chills or nausea³ <p>Rare:</p> <ul style="list-style-type: none"> Anaphylactic reactions.^{1,3} Urticaria and angioedema^{1,3} There is clinical evidence of an association between the administration of all immunoglobulins and thromboembolic events such as myocardial infarction, stroke, pulmonary embolism and deep vein thrombosis.¹ 	<p>IVIG</p> <p>Refer to specific product monographs prior to administering IVIG products for information on possible reactions.</p>
Pregnancy	Should be administered if indicated. ^{1,2,3,11} Intact IgG crosses the placenta from the maternal circulation increasingly after 30 weeks gestation. ¹¹	
Lactation	Should be administered if indicated. It is not known if IG antibodies are excreted in breast milk. ¹¹	

References

- ¹ Grifols Therapeutics Inc. (2018, February 6). GamaSTAN® S/D: Immune globulin (human). *Product Monograph*. https://pdf.hres.ca/dpd_pm/00043801.PDF
- ² Grifols Therapeutics Inc. (2016, January 26). Gamunex®: Immune globulin intravenous (human), 10%. *Product Monograph*. This is the product monograph that was referenced for this biological page. Refer to specific product monograph for preparation being administered.

Shire Pharma Canada ULC (2018, May 4) Gammagard®. Immune globulin intravenous (human), 10%. *Product Monograph* <https://www.shirecanada.com/-/media/shire/shireglobal/shirecanada/pdf/files/product%20information/gammagard-liquid-pm-en.pdf>
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- CSL Behring Canada Inc. (2019, April 15). Privigen®: Immune globulin intravenous (human), 10%. *Product Monograph*. <http://labeling.cslbehring.ca/PM/CA/Privigen/EN/Privigen-Product-Monograph.pdf>
- Octapharma (2018, August 29). Panzyga®: Immune globulin intravenous (human), 10%. *Product Monograph*. https://www.octapharma.ca/fileadmin/user_upload/octapharma.ca/Product_Monographs/PANZYGA-PM-EN.pdf
- ³ National Advisory Committee on Immunization. (2018). *Canadian Immunization Guide* (Evergreen ed.). Ottawa, ON: Public Health Agency of Canada. www.canada.ca/en/public-health/services/canadian-immunization-guide.html
- ⁴ Public Health Agency of Canada. (2018) *Canada Communicable Disease Report (CCDR)*. Updated NACI recommendations for measles post-exposure prophylaxis. <https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2018-44/issue-9-september-6-2018/article-7-naci-recommendation-pep.html>
- ⁵ Public Health Agency of Canada. (2013) *Canada Communicable Disease Report (CCDR)*. Guidelines for the prevention and control of measles outbreaks in Canada. <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/13vol39/acs-dcc-3/assets/pdf/meas-roug-eng.pdf>
- ⁶ Centers for Disease Control and Prevention. (2013) Prevention of Measles, Rubella, Congenital Rubella Syndrome, and Mumps: Summary Recommendations of the Advisory Committee on Immunization Practices (ACIP) *Morbidity and Mortality Weekly Report (MMWR)*, 67(No.4):1-34. <https://www.cdc.gov/mmwr/pdf/rr/rr6204.pdf>
- ⁷ Alberta Health. Measles. In *Public Health Notifiable Disease Management Guidelines*. www.health.alberta.ca/professionals/notifiable-diseases-guide.html
- ⁸ Alberta Health. Hepatitis A. In *Public Health Notifiable Disease Management Guidelines*. www.health.alberta.ca/professionals/notifiable-diseases-guide.html
- ⁹ Grifols Therapeutics Inc. (2017, July 7). *Important Change in prescribing Information – Immune Globulin (Human): GamaSTAN®S/D*. Retrieved October 16, 2017 from: <https://www.hypermunes.com/documents/31474919/31475115/Healthcare+Provider+Letter+GamaSTAN+SD+Revised+Dosage+July+7+2017+with+LIT+CODE.pdf/b831e517-9d0b-472c-b5b5-719f5bb5e47c>
- ¹⁰ Centers for Disease Control and Prevention. (2017) *Morbidity and Mortality Weekly Report (MMWR)*. Updated Dosing Instructions for Immune Globulin (Human) GamaSTAN S/D for Hepatitis A Virus Prophylaxis. <https://www.cdc.gov/mmwr/volumes/66/wr/mm6636a5.htm>
- ¹¹ Grabenstein, J. D. (2012). *ImmunoFacts: Vaccines and Immunologic Drugs - 2013*. St. Louis, MO: Wolters Kluwer Health.