POST EXPOSURE PROPHYLAXIS FOR MEASLES

REASON FOR ISSUE: Update to add intravenous immunoglobulin dosage guidance for Gamunex 10% – refer CCP715. Implement DCR38651 & DCR38889.

1. INTRODUCTION

Previous outbreaks of measles at several sites in New Zealand have prompted a review of the optimal approach for prophylaxis following exposure to the virus.

The Datasheet for Normal Immunoglobulin-VF (NIG), 160S013 Datasheet - Normal Immunoglobulin-VF, identifies an indication for use in post-exposure prophylaxis. Measles antibody levels will have declined with the routine use of measles vaccination. Measles antibody will continue to be present in the product but at lower levels than when the current recommendations in the datasheet were developed.

NZBS has worked with the Ministry of Health to update recommendations for post-exposure prophylaxis and these recommendations are identified below. These are based on recommendations produced by the United Kingdom Health Protection Agency.

Furthermore, Gamunex 10% solution (160S032) can be considered where intravenous immunoglobulin is indicated for prophylaxis. Dose guidance for intravenous immunoglobulin has been based on the recommendations of the Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidelines.

This document is provided for information purposes only. New Zealand Blood Service recommends that all requests for access to Normal Immunoglobulin-VF or Gamunex 10% relating to Measles prophylaxis are directed to an NZBS Transfusion Medicine Specialist or Medical Officer.

2. SUMMARY

- Confirmed measles cases continue to occur.
- Administering Measles, Mumps and Rubella (MMR) vaccine should be considered from 6 months onwards (or earlier on a case-by-case basis) among susceptible contacts.
- Changes to the dosages of NIG are recommended.
- Intravenous Immunoglobulin (IVIG) Gamunex 10% can be considered for immune suppressed and deficient measles contacts or in those where large doses are required.

3. MMR POST-EXPOSURE VACCINATION

For infants and other healthy individuals where post-exposure vaccination is indicated, MMR can be given within 72 hours of last exposure. Administering MMR should be considered from 6 months onwards among susceptible contacts. MMR can be considered on a case-by-case basis for those under 6 months of age, particularly if the child's mother has vaccine-induced immunity.

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4. NORMAL IMMUNOGLOBULIN- VF PROPHYLAXIS FOR CONTACTS – INTRAMUSCULAR ADMINISTRATION

In measles-susceptible individuals in whom the vaccine is contraindicated, susceptible pregnant contacts and others where indicated (vide infra), NIG is given to attenuate disease and can be considered up to 6 days from last exposure.

NIG should be given to the following contacts of measles cases as soon as possible after exposure:

- immunocompromised or immune-deficient people.
- susceptible pregnant women (if no evidence of two measles-containing vaccine doses, give NIG or check serology).
- immune-competent infants aged under 6 months: because maternal antibody wanes in the first six months of life, evidence of maternal vaccination status or serology tests may not predict protection for these infants. Maternal serology may be helpful for neonates. The role of an infant measles IgG test is unclear but may be helpful if available rapidly. Discuss use of NHIG for these infants with a paediatrician.
- immune-competent children aged between 6 and 12 months, who are outside the 72-hour exposure window for MMR vaccination.
- infants born prematurely <28 weeks' gestation are considered non-immune irrespective of maternal immune status.
- infants aged under 12 months born to mothers who received immunomodulatory biologic agents in pregnancy, unable to receive MMR.

The level of measles-specific antibody in Normal Human Immunoglobulin is believed to be in the order of 14-16 IU/mL. This is significantly lower than the minimum potency of 50 IU/mL identified in the British Pharmacopoeia. The current Medsafe approved datasheet for NIG indicates a dose of 0.2mL/Kg for measles post exposure prophylaxis. Based on the antibody levels identified above this is likely to be sub-optimal for effective post-exposure prophylaxis.

The new recommended doses of NIG are:
a) Immunocompetent infants (under 12 months) should receive 0.6mL/kg with a maximum volume of 5mL.
b) Pregnant women, immunocompetent adults and immune compromised or deficient children should receive 0.6mL/kg with a maximum dose of 15mL (recommended in three 5mL injections).
c) Immunocompetent children aged 12 months and over who have not received MMR within 72 hrs should receive 0.6mL/kg with a maximum volume of 15mL.

5. PROPHYLAXIS WITH INTRAVENOUS IMMUNOGLOBULIN

Intravenous administration of Gamunex 10% Solution can be considered for immune suppressed and deficient measles contacts (who may for example have a central venous catheter) or in those where large doses are required.

Post-exposure prophylaxis doses can be calculated based on the FDA and EMA IVIg recommendations for measles (400mg/kg) and minimum allowable potency (0.36 x CBER standard lot #176). Potency of each batch will vary, and the dose must be adjusted accordingly. Potency data for each Gamunex 10% batch are available on the CoA.

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Table 1: Measles Post-Exposure Prophylaxis using 10% Gamunex Solution

NOTE: Gamunex 10% dose[#] listed in this table is based on the minimum allowable potency (10% Protein (w/v) @ 0.36 CBER potency). A further calculation **must** be applied to adjust the dose for the potency of the batch to be administered. Refer to Section 5.1.

Body weight	Post-Exposure Prophylaxis Dose in mg (400mg/kg)	Post-Exposure Prophylaxis Dose in IU (theoretical)	Gamunex 10% dose[#], Volume (mL) Based on 10% Protein (w/v) @ 0.36 CBER potency
5 kg	2000	183	20.0[#]
10 kg	4000	367	40.0[#]
15 kg	6000	550	60.0[#]
20 kg	8000	733	80.0[#]
25 kg	10000	916	100.0[#]
30 kg	12000	1100	120.0[#]
35 kg	14000	1283	140.0[#]
40 kg	16000	1466	160.0[#]
45 kg	18000	1649	180.0[#]
50 kg	20000	1833	200.0[#]
55 kg	22000	2016	220.0[#]
60 kg	24000	2199	240.0[#]
65 kg	26000	2383	260.0[#]
70 kg	28000	2566	280.0[#]
75 kg	30000	2749	300.0[#]
80 kg	32000	2932	320.0[#]
85 kg	34000	3116	340.0[#]
90 kg	36000	3299	360.0[#]
95 kg	38000	3482	380.0[#]
100 kg	40000	3665	400.0[#]
105 kg	42000	3849	420.0[#]
110 kg	44000	4032	440.0[#]

 # Based on 10% Protein (w/v) @ 0.36 CBER potency. To be adjusted for Batch Potency.

5.1. Adjustment of Dose for Batch Potency

5.1.1. Locate the batch Certificate of Analysis of the specific batch of Gamunex 10% Solution in Q-Pulse. To do this, search 'COA-008' (Gamunex 10%) in Q-Pulse then select the specific batch (Lot) number from the list of Gamunex 10% solution batches received at NZBS e.g. B03H002603.

5.1.2. Open the file and record the 'Measles Antibody Potency' from the COA e.g. 1.07 x CBER#176 (Note CBER#176 is the international standard that batches of products are referenced against for Measles Antibody Potency)

5.1.3. Calculate Potency Correction Factor:

The doses stated in the Measles Post-Exposure Prophylaxis Table are based on a Measles Antibody Potency of 0.36 x CBER#176. A potency conversion factor is determined by dividing the potency used in the table (0.36 x CBER) by the batch specific potency of the Gamunex 10% batch (e.g.1.07 x CBER).

$$e.g., \frac{0.36 \times CBER}{1.07 \times CBER} = \text{Potency Correction Factor of } 0.336$$

5.1.4. Calculate the batch specific dose:

Select the appropriate Gamunex 10% dose [#] from Table 1, based on the patient body weight and exposure risk (400mg/kg). This dose is then multiplied by the calculated Potency Correction Factor.

e.g., For a 30 Kg patient requiring Post-Exposure Prophylaxis (400mg/kg):

Dose from Table 1 (120mL) x Potency Correction Factor (0.336) = 40.3mL batch specific dose

5.1.5. Round the dose:

For body weight >50kg – round up to the nearest whole 100mL vial.
For body weight < 50kg – give the calculated dose without rounding.

6. REFERENCES

1. *Public Health England:* Guidelines on Post-Exposure Prophylaxis for measles June 2019 (publishing.service.gov.uk)
2. FDA: *Letter to Immune Globulin (Human) Licensed Manufacturers: Option to Lower Lot Release Specification for Required Measles Antibody Potency Testing* (Dated 05 November 2018).
   https://www.fda.gov/media/118428/download
3. European Medicines Agency (EMA) Guideline on Core SmPC for Normal Immunoglobulin for Intravenous Administration (IVIg) Revision 6 (Effective 01 Jan 2022)
4. Measles. In *Immunisation Handbook 2020*. Ministry of Health.
   https://www.health.govt.nz/our-work/immunisation-handbook-2020/12-measles