

Draft document (2004). Not approved for use in ADHB institutions.

Accepted Indications for the Use of Intravenous Immunoglobulin Within Auckland District Health Board Institutions

The following are accepted indications for the use of intravenous immunoglobulin (IVIG) according to the recommendations of the IVIG committee. The indications have been established to ensure the appropriate use of a valuable and limited resource. The indications will be enforced by the blood bank when ordering the product. The IVIG dose and frequency should be appropriate as recommended in current medical literature.

Recommendations are evidence-based where possible. In some conditions, e.g. immune deficiency, therapeutic trials are not ethical and consequently the level of evidence is low. Rare conditions are not addressed here but will be considered on a case-by-case basis. In addition some conditions are indications only after other treatments have failed or where particular disease markers are present. The criteria in such conditions are listed within the appendices. Some conditions are only indications at the recommendation of a named individual e.g. for solid organ transplants.

Any use of IVIG outside these indications should be reviewed with two members of the IVIG Committee in the acute situation. The recommendations will be reviewed annually and any request for consideration of an indication should be placed in writing to the committee accompanied by the relevant literature.

These indications only apply to the use of the currently recommended product from CSL, Intragam P. Any request for alternative agents such as Sandoglobulin will need to be addressed to the Committee with clear reasons provided for the alternative.

IVIG Committee

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Indications

1. Immune deficiency
 - a. Antibody deficiency (see appendix 1 & 2)
 - b. Other immune deficiency (see appendix 1 & 2)

2. Neurological disorders
 - a. Guillain-Barre syndrome (see appendix 3)
 - b. Multifocal motor neuropathy (see appendix 3)
 - c. Chronic inflammatory demyelinating polyradiculoneuropathy
Unresponsive to corticosteroids or corticosteroids
contraindicated (see appendix 3)
 - d. Dermatomyositis
Unresponsive to corticosteroids or corticosteroids
contraindicated (see appendix 3)
 - e. Myasthenia gravis
Myasthenic crisis (see appendix 3)

3. Haematological disorders
 - a. Immune thrombocytopenia
 1. ITP
Unresponsive to corticosteroids, corticosteroids contraindicated or potentially life-threatening haemorrhage
 2. Post-transfusion purpura
 3. Antenatal alloimmune thrombocytopenia
 - b. HIV associated thrombocytopenia
 - c. Chronic lymphocytic leukaemia with hypogammaglobulinaemia
IgG<6g/L and recurrent severe bacterial infections (more than 2 in 12 months)
 - d. Multiple myeloma
IgG<6g/L (except IgG myeloma) and recurrent severe bacterial infections (more than 2 in 6-12 months)
 - e. Acute leukaemia in childhood
 - f. Autoimmune haemolytic anaemia
Unresponsive to corticosteroids, corticosteroids contraindicated or severe anaemia
 - g. Red cell aplasia with proven parvovirus B19 infection

4. Transplantation
 - a. Solid organ (if recommended by Transplant Team)
 - b. Allogeneic stem cell or bone marrow transplantation

5. HIV / AIDS
Thrombocytopenia (see ITP under haematology).

6. Kawasaki's disease
One to two doses at diagnosis.

7. Sepsis
Toxic shock syndrome (if recommended by infectious disease specialists).

Appendix 1

A+ accepted indications for IVIG replacement therapy in immune deficiency

1. Antibody deficiency

The following are accepted indications for IVIG:

1. In adults IgG repeatedly <3 g/L without any explanation
2. In children IgG levels are age dependent, therefore the Paediatric Immunology Service should always be involved in the assessment of abnormality
3. Recurrent / chronic infections and evidence of impaired vaccination responses (to at least two vaccines)

The following are not accepted indications for IVIG. Use of IVIG in these circumstances will require review and approval by the IVIG committee:

1. Selective IgA deficiency
2. Selective IgA deficiency with IgG subclass deficiency unless evidence of impaired vaccination responses (to at least two vaccinations)
3. IgG subclass deficiency unless evidence of impaired vaccination responses (to at least two vaccinations)

All cases should be discussed / reviewed at the immunology meeting before commencing replacement therapy irrespective of whether they fulfil these criteria and should be under the care or shared care of an immunologist due to the complexity of these patients.

2. Other immune deficiency

The use of IVIG is accepted in other primary immune deficiencies including:

1. Severe Combined Immune Deficiency
2. Hyper IgM Syndrome
3. Wiskott Aldrich Syndrome

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Appendix 2

The immunology guidelines have been separately published and can be found here:
<http://www.nzma.org.nz/journal/117-1195/914/>

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Appendix 3

Guidelines for the use of high-dose intravenous immunoglobulin [IVIg] in neurological disorders

Category 1: Conditions for which IVIg is the preferred or only effective treatment:-

- Guillain-Barre syndrome (GBS)
- Multifocal motor neuropathy (MMN)

IVIg is considered the primary therapeutic option in category 1 conditions.

Category 2: Conditions for which the efficacy of IVIg has been established but for which effective and less expensive alternatives exist:-

- Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
- Dermatomyositis
- Myasthenia gravis

In category 2 conditions, IVIg should be used only if primary therapeutic options have failed, are poorly tolerated or are contraindicated.

Category 3: Conditions for which IVIg may be beneficial in selected cases but its efficacy is not definitely established:-

- Polymyositis
- Paraproteinemic neuropathy
- Lambert-Eaton myasthenic syndrome
- Diabetic amyotrophy
- Multiple sclerosis (MS)
- Acute disseminated encephalomyelitis (ADEM)
- Rasmussen's encephalitis

In category 3 conditions, IVIg would not usually be considered a therapeutic option; use of IVIg in these conditions would be considered on a case by case basis. Use of IVIg in category 3 conditions should be considered a therapeutic trial with clearly defined outcome measures and a strategy for withdrawing treatment if those measures are not met.

The use of IVIg has been reported in a very large number of other neurological conditions including, but not limited to, motor neurone diseases, paraneoplastic syndromes, critical illness polyneuropathy, opsoclonus-myoclonus syndrome, intractable status epilepticus and stiff-man syndrome. There is insufficient data to allow recommendations to be made for IVIg use in these situations. Individual cases will be discussed with the IVIG committee as needed.

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Guidelines for the treatment of GBS with IVIg

Diagnosis of GBS

AND

Unable to ambulate 10 paces independently

OR

Unable to protect airway because of bulbar palsy

OR

Significant compromise of respiratory function

OR

Bulbar palsy + mild-moderate respiratory compromise.

Patients with mild GBS or with restricted forms such as the Miller Fisher syndrome do not usually need to be treated.

Rare patients may have prognostic factors that indicate a high likelihood of progression to severe disease and it therefore may be expedient to begin treatment before they meet the criteria listed above. These prognostic indicators include short interval between antecedent event and onset of neurological symptoms (<8 days), post-surgical GBS, post-diarrhoeal GBS and documented rapid progression of weakness.

Protocol for IVIg administration in GBS

0.4gm/kg/day for 5 consecutive days.

Infuse over 2-4 hours.

If treatment is started within 3 days of symptom onset consider giving the IVIg on days 1,2,4,6,8 to minimize risk of post-treatment relapse.

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Guidelines for the treatment of MMN with IVIg

Diagnosis of MMN

AND

Sufficient weakness to interfere with important activities.

Protocol for IVIg administration in MMN

0.5gm/kg/day for 4 consecutive days. Repeat as necessary.

N.B. It is important to document objective improvement in strength following treatment and an objective decline before repeating treatment.

If a consistent pattern of relapse can be established a regular treatment schedule may be instituted to anticipate relapses. There should be repeated attempts to reduce the administered dose or increase the inter-treatment intervals.

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Guidelines for the treatment of CIDP with IVIg

Diagnosis of CIDP

AND

Sufficient weakness to interfere with important activities

AND

Contra-indication to corticosteroid use*

OR

Intolerant of corticosteroid use

OR

Failed trial of corticosteroids.

*Contra-indications to corticosteroid use may include previous serious adverse reactions to corticosteroids, age, diabetes and HIV infection, Tb, active peptic ulcer disease, osteoporosis, others.

Protocol for IVIg administration in CIDP

0.5gm/kg/day for 4 consecutive days. Repeat as necessary.

N.B. It is important to document objective improvement in strength following treatment and an objective decline before repeating treatment. Predominantly sensory features would not ordinarily be considered an indication for IVIg treatment.

If a consistent pattern of relapse can be established a regular treatment schedule may be instituted to anticipate relapses. There should be repeated attempts to reduce the administered dose or increase the inter-treatment intervals.

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Guidelines for the treatment of dermatomyositis with IVIg

Diagnosis of dermatomyositis.

AND

Sufficient weakness to interfere with important activities

AND

Contra-indication to corticosteroid use*

OR

Intolerant of corticosteroid use

OR

Failed trial of corticosteroids.

*Contra-indications to corticosteroid use may include previous serious adverse reactions to corticosteroids, age, diabetes and HIV infection.

Protocol for IVIg administration in dermatomyositis

0.5gm/kg/day for 4 consecutive days. Repeat as necessary.

N.B. It is important to document objective improvement in strength following treatment and an objective decline before repeating treatment.

If a consistent pattern of relapse can be established a regular treatment schedule may be instituted to anticipate relapses. There should be repeated attempts to reduce the administered dose or increase the inter-treatment intervals.

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Guidelines for the treatment of myasthenia gravis with IVIg

Treatment of myasthenia gravis with IVIg should be restricted to those patients in myasthenic crisis where it may be used as an alternative to plasma exchange.

Diagnosis of myasthenia gravis

AND

Severe bulbar or respiratory muscle weakness.

Protocol for IVIg administration in myasthenic crisis

0.5gm/kg/day for 4 consecutive days.