Neuromyelitis optica spectrum disorders (NMOSD)

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Condition for which IVIg use is in exceptional circumstances only

Specific Conditions	• NMOSD–AQP4 ab positive • NMOSD–MOG ab positive • NMOSD–seronegative • LETMs
Indication for IVIg Use	• Acute relapse of NMOSD with significant disability and corticosteroids and/or plasmapheresis have failed, are contraindicated or unavailable (one month treatment only) • Further significant relapse of NMOSD post Ig therapy with significant disability and resistant to corticosteroids and other immunosuppressant agents
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	Neuromyelitis optica spectrum disorders (NMOSD) is an idiopathic, antibody mediated astrocytopathy of the central nervous system, characterised by recurrent bouts of optic neuritis and myelitis. It is distinct from multiple sclerosis and evidence of B-cell autoimmunity has been found. A circulatory antibody to aquaporin-4 is found in many patients providing further evidence of B-cell autoimmunity in its pathogenesis and suggestive of a role for intravenous immunoglobulin (IVIg) therapy. Single case reports of various therapies, including IVIg, have shown variable benefit in this otherwise devastating disorder. Diagnostic criteria have been published in 2015 by the International panel for NMO diagnosis (Wingerchuk et al, 2015). There are only small retrospective case series of IVIg for this condition, with no randomised controlled trials (RCTs). Recent work has clearly defined that plasma exchange and intravenous corticosteroids are the treatment of choice for acute attacks (Kleiter et al, 2016). Chronic immune suppression is required for most patients with AQP4 ab NMOSD, and immune suppressant agents such as azathioprine, mycophenolatemofetil, methotreaxate, rituximab and cyclophosphamide reduce annualised relapse rates in uncontrolled retrospective and prospective studies. IVIg does not generally have a role in chronic immune modulation of AQP4 ab NMOSD. A newer antigenic target, myelin oligodendrocyte glycoprotein (MOG) has been identified which accounts for 20 percent of previously sero-negative patients and is more commonly detected in paediatric populations. The disease course is slightly different and literature is still emerging, however, a relapsing course with steroid dependence will require more than a single course of Ig, and/or immunosuppressant therapy (Sato et al, 2014).
Justification for Evidence Category	There is significant anecdotal evidence to support the use of intravenous immunoglobulin (IVIg) in the treatment of acute attacks of neuromyelitis optica spectrum disorders (NMOSD) if plasma exchange and/or intravenous corticosteroids are contraindicated or have failed. There is no evidence for the use of IVIg as long-term therapy or prophylaxis. Two very small studies (Viswanathan et al, 2015 and Elsone et al, 2014), show that IVIg may be effective in reducing relapse risk although both are of limited significance.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.

Qualifying Criteria for IVIg Therapy	Acute relapse of NMOSD with significant disability and corticosteroids and/or plasmapheresis have failed, are contraindicated or unavailable (one month treatment only) This indication should be used for patients with NMOSD who have not previously been treated with Ig therapy. For patients who have been treated with Ig, and have had further subsequent relapse please use the indication: **Further significant relapse of NMOSD post Ig therapy with significant disability and resistant to corticosteroids and other immunosuppressant agents.** • Diagnosis of NMOSD consistent with criteria of the International Panel for NMO Diagnosis and significant disability as measured by an Expanded Disability Status Scale (EDSS) score of at least two points. AND • Presence of AQP4-IgG or MOG-IgG antibodies OR • Diagnosis of sero-negative NMOSD or testing unavailable and multiple sclerosis has been excluded or is considered unlikely AND • No clinical response has been achieved following standard steroid therapy (at least three days) OR • Steroid therapy is contraindicated AND • Plasmapheresis therapy is ineffective or contraindicated OR • Plasmapheresis treatment is unavailable

Further significant relapse of NMOSD post Ig therapy with significant disability and resistant to corticosteroids and other immunosuppressant agents

This indication should be used for patients who have relapsed following a previous treatment with Ig. For patients who have not yet been treated with Ig please use the indication: **Acute relapse of neuromyelitis optica spectrum disorders (NMOSD) with significant disability and corticosteroids and/or plasmapheresis have failed, are contraindicated or unavailable.**

- Diagnosis is consistent with criteria of the International Panel for NMO Diagnosis and further relapse with significant disability as measured by an Expanded Disability Status Scale (EDSS) score of at least two points.

AND

- Moderate improvement was demonstrated in the severity of symptoms and degree of disability in response to Ig therapy as measured by EDSS score compared to the pre-treatment assessment

AND

- No clinical response has been achieved following standard steroid therapy in the treatment of this relapse.

  OR

- Steroid therapy is contraindicated

AND

- No clinical response following treatment with prolonged plasma exchange (at least five cycles) and/or at least two Immunosuppressant agents

Ig therapy for steroid resistant NMOSD is recommended to be used as combination therapy.

Review by a neurologist is required within six months of treatment and six monthly thereafter. Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Review Criteria for Assessing the Effectiveness of IVIg Use

Acute relapse of NMOSD with significant disability and corticosteroids and/or plasmapheresis have failed, are contraindicated or unavailable (one month treatment only)

Review is not mandated for this condition, however clinical effectiveness of Ig therapy can be assessed by:

- Post Ig treatment improvement in the severity of symptoms and degree of disability as assessed by Expanded Disability Status Scale (EDSS) compared to the qualifying assessment

Further significant relapse of NMOSD post Ig therapy with significant disability and resistant to corticosteroids and other immunosuppressant agents

Review by a neurologist is required within six months of treatment and six monthly thereafter. Documentation of clinical effectiveness is necessary for continuation of Ig therapy.

Clinical effectiveness of Ig therapy can be demonstrated by:

On review of the initial authorisation period

- Moderate improvement in the severity of symptoms and degree of disability as assessed by a reduction of the Expanded Disability Status Scale (EDSS) score of at least one point compared to qualifying assessment for this relapse indication

On review of a continuing authorisation period

- Improvement in the severity of symptoms and degree of disability as assessed by the Expanded Disability Status Scale (EDSS) score compared to the previous review

  AND

- A trial of Ig weaning towards cessation of Ig therapy is planned for patients who are clinically stable to identify those in remission or a reason provided as to why a trial is not planned

A trial of Ig weaning should be considered annually in stable patients on maintenance therapy to identify patiuents who are in remission.

Dose	Acute relapse of NMOSD with significant disability and corticosteroids and/or plasmapheresis have failed, are contraindicated or unavailable (one month treatment only) • **Induction Dose** - 2 g/kg in divided doses over 2 to 5 days The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient. Refer to the current product information sheet for further information on dose, administration and contraindications. Further significant relapse of NMOSD post Ig therapy with significant disability and resistant to corticosteroids and other immunosuppressant agents • **Induction Dose** - 2 g/kg in divided doses over 2 to 5 days • **Maintenance Dose** - 1 g/kg in single or divided doses over 2 to 5 days, four to six weekly. Ig therapy is intended to be used in combination with an immunosuppressant agent The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient. Refer to the current product information sheet for further information on dose, administration and contraindications.

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