Sjögren's syndrome associated neuropathy

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Condition for which IVIg use is in exceptional circumstances only

Specific Conditions	• Painful small fibre neuropathy • Ataxic sensory neuronopathy • Sensorimotor axonal neuropathy • Autonomic neuropathy
Indication for IVIg Use	• Severe, primary Sjögren's syndrome associated neuropathy that is unresponsive to corticosteroid and immunosuppressant therapy • Relapse of Sjögren's syndrome associated neuropathy within six months of trial off Ig therapy
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	The diagnosis of primary Sjögren's syndrome should be consistent with the criteria of the American-European Study group (Tzioufas et al, 2007). Intravenous immunoglobulin (IVIg) may be indicated in patients with some neuropathy subtypes associated with Sjögren's syndrome (excluding those caused by necrotising vasculitis) where other treatments have been ineffective.
Justification for Evidence Category	Sjögren's syndrome associated neuropathy comprises a heterogeneous group of neuropathies. There is a very low level of evidence for IVIg use in this condition, with conflicting reports of efficacy. Improvement has been reported in small case series of patients with some forms of sensory neuropathy (Pereira 2016, Rist 2011, Yamashita 2013). Conflicting reports exist for patients with ataxic sensory neuronopathy, with one study reporting benefit (Takahashi 2003) but most studies (Rist 2011, Pereira 2016) and clinical experience suggesting it is ineffective for this patient group. As there may be a subset of patients who benefit from Ig therapy for this condition the Specialist Working Groups (Immunology and Neurology) of the Immunoglobulin Governance Program have recommended to retain this condition within the *Criteria,* but only where demonstrable benefit is shown. Where no demonstrable benefit can be identified, patients will not be eligible to remain on Ig therapy under these criteria.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.

Qualifying Criteria for IVIg Therapy	Severe, primary Sjögren's syndrome associated neuropathy that is unresponsive to corticosteroid and immunosuppressant therapy

Use this indication for new patients and those that have never trialled off from Ig therapy. Please use the indication **Relapse of Sjögren's syndrome associated neuropathy within six months of trial off Ig therapy** for responding patients who have relapsed after weaning from Ig therapy.

- Primary Sjögren's syndrome associated neuropathy without necrotising vasculitis

  AND

- Significant disability due to neuropathy as measured by an adapted Modified Rankin Scale (MRS) score of at least three points

AND

- Unresponsive to an appropriate trial of corticosteroids

  OR

- Corticosteroids are contraindicated or have resulted in unacceptable side effects or significant toxicity

AND

- Unresponsive to at least one immunosuppressant agent

  OR

- Immunosuppressant medication is contraindicated

IVIg should be used for a maximum period of four months (Induction plus three maintenance cycles) before determining whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned.

Review by a neurologist is required within four months of treatment to determine whether the patient has responded. Continuing six monthly reviews may be undertaken by neurologists, rheumatologists or immunologists.

After a year of therapy a trial of Ig weaning should be attempted with a view to cessation within six months unless there is a contraindication to doing so.

Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

	Relapse of Sjögren's syndrome associated neuropathy within six months of trial off Ig therapy This indication should be used for responding Sjögren's syndrome patients who have relapsed within six months of commencement of a trial off immunoglobulin therapy. For those who have not received Ig therapy previously please use the indication **Severe, primary Sjögren's syndrome associated neuropathy that is unresponsive to corticosteroid and immunosuppressant therapy** • Deterioration of proven neuropathy and in the adapted Modified Rankin Scale (MRS) score, of at least one point, in a previously stable patient as compared to the review score prior to the trial off Ig therapy AND • Relapse occurs within six months of the last immunoglobulin dose in a previously responding patient IVIg should be used for a maximum period of four months (induction plus three maintenance cycles) before determining whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned. Review by a neurologist is required within four months of treatment to determine whether the patient has responded. Thereafter the continuing six monthly reviews may be undertaken by a neurologist, rheumatologist or immunologist. After a year of therapy a trial of Ig weaning should be attempted with a view to cessation within six months unless there is a contraindication to doing so. Documentation of clinical efficacy is necessary for continuation of IVIg therapy. **Once a patient has relapsed when trialled off Ig treatment, a second line immunomodulatory agent should be strongly considered as additional therapy.**
Exclusion Criteria	Sjögren's syndrome associated vasculitic neuropathy

Review Criteria for Assessing the Effectiveness of IVIg Use	Severe, primary Sjögren's syndrome associated neuropathy that is unresponsive to corticosteroid and immunosuppressant therapy

Review by a neurologist is required within four months (induction plus three maintenance cycles) of treatment to determine whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned. In responding patients, continuing six monthly reviews may be undertaken by neurologists, rheumatologists or immunologists.

After a year of therapy a trial of Ig weaning should be attempted with a view to cessation within six months unless there is a contraindication to doing so.

Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Clinical effectiveness of Ig therapy can be assessed by:

On review of the initial authorisation period

- Improvement of neuropathy (formally assessed) compared to the qualifying assessment

  AND

- Improvement (or no deterioration) in disability as measured by a decrease of at least one point (or no change) in the adapted Modified Rankin Scale (MRS) score compared to the qualifying assessment

On review of a continuing authorisation period

- Improvement in or stabilisation of neuropathy compared to the previous review assessment

  AND

- Improvement in or stabilisation of the degree of disability as measured by the adapted Modified Rankin Scale (MRS) score compared to the previous review assessment

AND

- After 12 months on therapy a trial of Ig weaning towards cessation of Ig therapy is planned or a reason provided as to why a trial is not planned

Relapse of Sjögren's syndrome associated neuropathy within six months of trial off Ig therapy

Review by a neurologist is required within four months (induction plus three maintenance cycles) of treatment to determine whether the patient has responded. If there is no benefit after this treatment, IVIg therapy should be abandoned. In responding patients, continuing six monthly reviews may be undertaken by neurologists, rheumatologists or immunologists.

After a year of therapy a trial of Ig weaning should be attempted with a view to cessation within six months unless there is a contraindication to doing so.

Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Once a patient has relapsed when trialled off Ig treatment, a second line immunomodulatory agent should be strongly considered as additional therapy.

Clinical effectiveness of Ig therapy may be assessed by:

On review of the initial authorisation period

- Improvement of neuropathy (formally assessed) compared to the qualifying assessment for this relapse indication

  AND

- Improvement in disability (or no further deterioration) as measured by a decrease of at least one point (or no change) in the adapted Modified Rankin Scale (MRS) score compared to the qualifying assessment

On review of a continuing authorisation period

- Improvement in or stabilisation of neuropathy compared to the previous review assessment

  AND

- Improvement in or stabilisation of the degree of disability as measured by the adapted Modified Rankin Scale (MRS) score compared to the previous review assessment

  AND

- After 12 months on therapy a trial of Ig weaning towards cessation of Ig therapy is planned or a reason provided as to why a trial is not planned

Once a patient has relapsed in the first six months of a trial off therapy, a further trial might be considered after at least one year.

Dose	
	Severe, primary Sjögren's syndrome associated neuropathy that is unresponsive to corticosteroid and immunosuppressant therapy • **Induction Dose** - 1- 2 g/kg in 2-5 divided doses • **Maintenance Dose** - 0.4-1g/kg, 4-6 weekly. The amount per dose should be titrated to the individual's response. A maximum dose of 1 g/kg may be given in any 4 week period. This might be small doses more frequently than fortnightly. 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.
	Relapse of Sjögren's syndrome associated neuropathy within six months of trial off Ig therapy • **Induction Dose** - 1- 2 g/kg in 2-5 divided doses • **Maintenance Dose** - 0.4g/kg -1 g/kg, 4-6 weekly. The amount per dose should be titrated to the individual's response. A maximum dose of 1 g/kg may be given in any 4 week period. This might be small doses more frequently than fortnightly. 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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