Acute disseminated encephalomyelitis (ADEM)

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Acute disseminated encephalomyelitis
Indication for IVIg Use	• Monophasic ADEM unresponsive to corticosteroid therapy or where corticosteroids are contraindicated (e.g. suspicion of central nervous system infection). • Recurrent or multiphasic ADEM unresponsive to corticosteroid therapy or where corticosteroid therapy has become intolerable or is contraindicated.
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Acute disseminated encephalomyelitis (ADEM) is a monophasic inflammatory condition of the central nervous system that usually presents in children and young adults. It typically occurs following a viral prodrome with multifocal neurological disturbance and altered conscious state. ADEM usually follows a monophasic course, but patients may experience recurrence of the initial symptom complex (recurrent ADEM) or a second episode of ADEM (multiphasic ADEM). The majority make a full recovery. ADEM is thought to have an autoimmune basis. Pathologic similarities to experimental allergic encephalomyelitis (EAE), an animal model of inflammatory demyelination, support this theory. It is postulated that a common antigen shared by an infectious agent and a myelin epitope results in an autoimmune response. Patients show multiple demyelinating lesions on magnetic resonance imaging (MRI) in the deep and subcortical white matter. The differential diagnosis includes other inflammatory demyelinating disorders, such as multiple sclerosis, optic neuritis and transverse myelitis. High-dose corticosteroids are first-line treatment of ADEM. Intravenous immunoglobulin (IVIg) has been used for patients who fail to respond to corticosteroid therapy or in patients where corticosteroids are contraindicated. Most patients with ADEM recover completely over a period of six weeks from onset. There is no biological marker for ADEM. Diagnosis is by clinical recognition of the multifocal neurological disturbance and altered conscious state, with the typical magnetic resonance imaging (MRI) findings of demyelination.
Justification for Evidence Category	Review of multiple case series of IVIg use for paediatric ADEM found that children with monophasic ADEM completely recovered after administration of IVIg or IVIg plus corticosteroids. In recurrent ADEM, children either completely recovered after IVIg, or showed improvement. Adults with monophasic or recurrent ADEM recovered after treatment with IVIg.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.

Qualifying Criteria for IVIg Therapy	Monophasic ADEM unresponsive to corticosteroid therapy or where corticosteroids are contraindicated (e.g. suspicion of central nervous system infection). • Symptomatic ADEM AND • Unresponsive to corticosteroid therapy. OR • Corticosteroid therapy is contraindicated.
	Recurrent or multiphasic ADEM unresponsive to corticosteroid therapy or where corticosteroid therapy has become intolerable or is contraindicated. • Symptomatic ADEM AND • Unresponsive to corticosteroid therapy. OR • Corticosteroid therapy has become intolerable or is contraindicated.

Review Criteria for Assessing the Effectiveness of IVIg Use

Monophasic ADEM unresponsive to corticosteroid therapy or where corticosteroids are contraindicated (e.g. suspicion of central nervous system infection).

Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy.

- Improvement in symptoms in comparison to previous assessment.

Recurrent or multiphasic ADEM unresponsive to corticosteroid therapy or where corticosteroid therapy has become intolerable or is contraindicated.

Six-monthly review by a neurologist is required for recurrent or multiphasic ADEM. Cessation of treatment should be considered at each review.

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

On review of the initial authorisation period

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement in relapse rate in comparison to pre-treatment levels.

On review of a continuing authorisation period

Clinical effectiveness of Ig therapy may be demonstrated by:

- Improvement in symptoms and clinical course in comparison to the previous review assessment.

Dose	
	Monophasic ADEM unresponsive to corticosteroid therapy or where corticosteroids are contraindicated (e.g. suspicion of central nervous system infection). • **Dose** - up to 2 g/kg in 2 to 5 divided doses. Up to three doses may be used for extended monophasic ADEM. After three months, if symptoms persist, an alternative diagnosis should be considered. **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.** **Dosing above 1 g/kg per day is contraindicated for some IVIg products.** **Refer to the current product information sheet for further information.**
	Recurrent or multiphasic ADEM unresponsive to corticosteroid therapy or where corticosteroid therapy has become intolerable or is contraindicated. • **Induction Dose** - up to 2 g/kg in 2 to 5 divided doses. • **Maintenance Dose** - 0.4–2 g/kg, 4–6 weekly. Aim for the minimum dose to maintain optimal functional status and prevent relapses. **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.** **Dosing above 1 g/kg per day is contraindicated for some IVIg products.** **Refer to the current product information sheet for further information.**

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