Childhood epileptic encephalopathy

Condition for which Ig use is in exceptional circumstances only

Specific Conditions	• Landau Kleffner syndrome • Lennox-Gastaut syndrome • Atypical rolandic epilepsy • West syndrome
Indication for Ig Use	• Children with epileptic encephalopathy resistant to anti-epileptic medications and steroid therapy or steroid responsive but dependent • Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Epilepsy is a clinical syndrome of recurrent epileptic seizures and has multiple causes. Immune mediated mechanisms can result in epilepsy. Patients with epilepsy due to clear cut inflammatory syndromes such as autoimmune encephalitis, Rasmussen encephalitis or post encephalitic epilepsy are considered elsewhere. It is possible that immune mechanisms have a role in some cases of epilepsy, however defining these mechanisms is challenging. A few epileptic encephalopathy syndromes in infants and young children are responsive to steroids, and for this reason, an immune mechanism is possible. Intravenous immunoglobulin (IVIg) has been trialled in these patients with mixed success. A subgroup of patients with West syndrome, Landau Kleffner syndrome and Lennox Gaustaut syndrome have been observed to respond to steroids or IVIg and there is uncontrolled case report data that supports a possible improvement of symptoms with IVIg.
Justification for Evidence Category	The literature on intravenous immunoglobulin (IVIg) in epileptic encephalopathy syndromes such as West syndrome, Landau Kleffner, Lennox Gaustaut is limited to case reports and small case series and the quality of this literature is poor. It can be concluded that a proportion of patients with these epileptic syndromes may benefit from IVIg, particularly those patients with demonstrable immune abnormalities in blood, CSF or neuroimaging.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.

Qualifying Criteria for Ig Therapy	Children with epileptic encephalopathy resistant to anti-epileptic medications and steroid therapy or steroid responsive but dependent

Please use the indication **Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response** for responding patients who have relapsed after weaning from previous Ig therapy.

- Diagnosis of Landau Kleffner syndrome, Lennox-Gastaut syndrome, West syndrome or atypical rolandic epilepsy confirmed by EEG

  AND
- Refractory epilepsy with ongoing seizures of at least weekly frequency

  AND
- Evidence of associated neurodevelopmental or neurocognitive issues

AND

- Failure of corticosteroid therapy to control seizures

  OR
- Corticosteroid responsive but patient is steroid dependent for seizure control

  OR
- Corticosteroid therapy has an *absolute* contraindication

AND

- Persistent seizures despite treatment with at least three anticonvulsant medications

AND

- Persistent seizures despite surgical intervention to control epilepsy

  OR
- Surgical intervention is inappropriate

Review by a neurologist is required after three months of treatment to determine whether the patient has responded, and annually thereafter. If there is no benefit after the first three months of treatment, IVIg therapy should be abandoned.

Documentation of clinical effectiveness (such as maintaining a seizure diary) is necessary for continuation of IVIg therapy.

Once patients are stable, a trial of weaning from Ig therapy should be considered every year to identify those in remission. Responding patients who relapse within three months of cessation of Ig therapy can reapply under the indication **Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response**.

	Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response This indication is for **responding patients who relapse within six months of cessation of Ig therapy.** For patients who have never trialled off a request must be submitted using the indication **children with epileptic encephalopathy resistant to anti-epileptic medications and steroid therapy or steroid responsive but dependent.** • Moderate deterioration in symptoms of epileptic encephalopathy within six months of ceasing Ig in a patient who had previously responded to Ig therapy AND • Increased frequency of seizures compared to when receiving Ig therapy IVIg should be used for up to three months before a review by a neurologist is required to determine whether the patient has responded. Annual review is required thereafter. If there is no improvement after the initial three month's treatment, Ig therapy should be abandoned. Documentation of clinical effectiveness (such as maintaining a seizure diary) is necessary for continuation of IVIg therapy. Once patients are stable, a trial of weaning from Ig therapy should be considered every year to identify those in remission.
Exclusion Criteria	Rasmussen encephalitis - see Rasmussen encephalitis Post encephalitic epilepsy - see Autoimmune encephalitis mediated by extracellular antibodies - see Antibody mediated autoimmune encephalitis (AMAE)

Review Criteria for Assessing the Effectiveness of Ig Use	Children with epileptic encephalopathy resistant to anti-epileptic medications and steroid therapy or steroid responsive but dependent

Review by a neurologist is required after three months of treatment to determine whether the patient has responded, and annually thereafter. If there is no benefit after the first three months of treatment, IVIg therapy should be abandoned.

Documentation of clinical effectiveness (such as maintaining a seizure diary) is necessary for continuation of IVIg therapy.

Once patients are stable, a trial of weaning from Ig therapy should be considered every year to identify those in remission. Responding patients who relapse within three months of cessation of Ig therapy can reapply under the indication **Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response**.

Clinical effectiveness of Ig therapy can be demonstrated by:

On review of the initial authorisation period

- Documented moderate improvement in the severity of symptoms (including improved cognition / behaviour / ambulation) compared to at qualifying

  AND

- Reduction in the severity and/or frequency of seizures compared to the qualifying assessment

On review of a continuing authorisation period

- Further documented improvement in or stabilisation of symptoms (cognition or behaviour or ambulation) compared to the previous review assessment

  AND

- Further documented improvement in or stabilisation of seizures compared to the previous review

  AND

- A trial of weaning from Ig therapy with a view to cessation of Ig therapy is considered annually for patients who are clinically stable to identify those in remission or a valid reason provided as to why a trial is not being planned or is contraindicated at this time

Relapse of epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response

IVIg should be used for up to three months before a review by a neurologist is required to determine whether the patient has responded. Annual review is required thereafter. If there is no improvement after the initial three month's treatment, Ig therapy should be abandoned.

Documentation of clinical effectiveness (such as maintaining a seizure diary) is necessary for continuation of IVIg therapy.

Once patients are stable, a trial of weaning from Ig therapy should be considered every year to identify those in remission.

Clinical effectiveness of Ig therapy can be assessed by:

On review of the initial authorisation period

- Moderate improvement in the severity of symptoms (improved cognition or behaviour or ambulation) compared to the severity of symptoms of relapse

  AND

- Reduction in the severity and/or frequency of seizures compared to severity and/or frequency at relapse

On review of a continuing authorisation period

- Further documented improvement in or stabilisation of symptoms (improved cognition or behaviour or ambulation) compared to the previous review assessment

  AND

- Further reduction in or stabilisation of, the severity and/or frequency of seizures compared to the most recent assessment

  AND

- A trial of weaning from Ig therapy with a view to cessation of Ig therapy is considered annually for patients who are clinically stable to identify those in remission or a valid reason provided as to why a trial is not being planned or is contraindicated at this time.

Dose	Children with epileptic encephalopathy resistant to anti-epileptic medications and steroid therapy or steroid responsive but dependent • **Induction Dose (IVIg)** - 2 g/kg as divided dose over 2 to 5 days. • **Maintenance Dose (IVIg)** - 1 g/kg as divided dose over 2 to 5 days, monthly 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 epileptic encephalopathy following a trial of weaning from Ig therapy in a patient previously demonstrating response • **Induction Dose (IVIg)** - 2 g/kg as divided dose over 2 to 5 days • **Maintenance Dose (IVIg)** - 1 g/kg as divided dose over 2 to 5 days, monthly 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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