Lambert–Eaton myasthenic syndrome (LEMS)

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Condition for which IVIg has an established therapeutic role.

Specific Conditions	• Lambert–Eaton myasthenic syndrome
Indication for IVIg Use	• Additional therapy for LEMS patients with disability where symptomatic therapy is insufficient
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Lambert–Eaton myasthenic syndrome (LEMS) is a disorder of neuromuscular transmission first recognised clinically in association with lung cancer and subsequently in cases in which no neoplasm was detected. Patients with LEMS have a presynaptic neuromuscular junction defect. The clinical picture is characterised by proximal muscle weakness with augmentation of strength after exercise, mild oculomotor signs, depressed deep tendon reflexes and autonomic dysfunction (dry mouth, constipation, erectile failure). Diagnosis should be confirmed by the presence of antibodies to Voltage gated calcium channels, electrophysiology consistent with LEMS, or both.
Justification for Evidence Category	In the Biotext (2004) review, one systematic review (containing one randomised control trial [RCT] with nine patients) and one case series of seven patients with a crossover design were included. Intravenous immunoglobulin (IVIg) appeared to provide some benefit to patients with LEMS. However, both studies only included a small number of patients. Expert consensus states that IVIg produces temporary improvement in patients with LEMS. It therefore has a role as second line therapy (Asia–Pacific IVIg Advisory Board 2004). Treatment of LEMS with 3,4DAP and pyridostigmine has been shown to be efficacious in an RCT (Wirtz 2009) and should be regarded as combined first line therapy. 3,4DAP is not a licensed medication in Australia but can be sourced as an import and used under the Special Access (SASB) scheme. One submission to the National Blood Authority reported on a RCT that showed significant improvement in strength associated with a decline in the level of pathogenic antibodies (NSW IVIg User Group). IVIG may provide additional benefit. Immunosuppression with prednisone, azathioprine or cyclosporine has been reported in cases to be beneficial in non-paraneoplastic LEMS however has not been subject to an RCT. Treatment of paraneoplastic LEMS including with 3,4DAP, pyridostigmine or with IVIG will not treat the underlying neoplasia but may be necessary for symptomatic reasons. Treatment of the underlying neoplasia often helps the LEMS (Newsom-Davis Semin Neurol 2003). Patients with paraneoplastic LEMS due to small cell lung cancer have been associated with a significantly longer mean survival than patients with small cell lung cancer suggesting an immune vs tumour effect. Accordingly immunosuppression (as opposed to IVIg) has not generally been applied in paraneoplastic LEMS.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.

Qualifying Criteria for IVIg Therapy	• Severe LEMS with motor impairment as demonstrated by Medical Research Council (MRC) sum score of 58 or less OR • Severe LEMS with significant autonomic involvement AND • Alternative therapies have failed or an insufficient response has been achieved Intravenous immunoglobulin (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 period, IVIg therapy should be abandoned. Review by a neurologist is required within four months of treatment and annually thereafter. Consideration should be given to a trial of weaning at each review. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.

Review Criteria for Assessing the Effectiveness of IVIg Use	Intravenous immunoglobulin (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 period, IVIg therapy should be abandoned. Review by a neurologist is required within four months of treatment and annually thereafter. Consideration should be given to a trial of weaning at each review. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy. **Clinical effectiveness of Ig therapy may be assessed by:** **On review of the initial authorisation period** • Clinically significant improvement in muscle weakness as measured by an increase of at least one point in the Medical Research Council (MRC) sum score compared to the qualifying score OR • Clinically significant improvement in the severity of autonomic symptoms compared to the severity of symptoms at the qualifying assessment OR • Patient with severe disease continues to report post infusion improvement with end-of-cycle deterioration and additional immunosuppressant agents have been commenced **On review of a continuing authorisation period** • Stabilised disease as assessed by the Medical Research Council (MRC) sum score that is greater than or equal to the previous review score and greater than the qualifying score OR • Patient with severe disease continues to report post infusion improvement with end-of-cycle deterioration and additional immunosuppressant agents have been commenced OR • Stability in autonomic symptoms compared to the previous review and sustained improvement compared to symptoms at qualifying 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
Dose	• **Induction Dose** - 2 g/kg in 2 to 5 divided doses. • **Maintenance Dose** - 0.4–1g/kg, 2–6 weekly. A maximum dose of 2 g/kg may be given in any four week period. This might be by smaller doses more frequently. 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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