Guillain–Barré syndrome including variants (GBS)

Condition for which Ig has an established therapeutic role.

Specific Conditions	• Guillain–Barré syndrome (GBS) • Guillain–Barré syndrome (GBS) variants
Indication for Ig Use	• Initial therapy for GBS with significant disability and progression • Relapse in GBS - treatment related fluctuation with initial improvement and subsequent deterioration post IVIg treatment
Level of Evidence	Clear evidence of benefit (Category 1)
Description and Diagnostic Criteria	Guillain–Barré syndrome (GBS) is the commonest cause of acute flaccid paralysis in the West. The syndrome typically presents with rapidly progressive, relatively symmetrical ascending limb weakness consistent with a polyradiculoneuropathy and often with associated cranial nerve involvement. Motor signs and symptoms usually predominate over sensory signs and symptoms. Loss of tendon reflexes occurs in most cases. Major complications include respiratory failure and autonomic dysfunction. The disease is monophasic, usually reaching its nadir within two weeks, although arbitrary definition accepts a limit of four weeks. A plateau phase of variable duration follows the nadir before gradual recovery. Although recovery is generally good or complete in the majority of patients, persistent disability has been reported to occur in about 20 percent and death in 4-15 percent of patients. Treatment related fluctuations within 8 weeks of treatment occur in about 10% of patients and typically exhibit as improvement or stabilisation of the patient after completing treatment followed by deterioration. Improvement/stabilisation and subsequent deterioration is evident using GBS disability score or Medical Research Council (MRC) sum score assessment. Chronic inflammatory demyelinating polyneuropathy (CIDP) may present acutely (acute-CIDP) after initially being diagnosed as GBS. Acute-CIDP is defined by worsening clinical features such as weakness more than 4 weeks after onset. The CIDP criteria should be considered in that context, but should not be applied in the context of GBS where recovery is slow or incomplete (Walgaard et al, 2021). Intravenous immunoglobulin (IVIg) has been shown to have the same efficacy as plasma exchange. While the Asia-Pacific IVIg Advisory Group suggests that the choice between Ig and plasma exchange is based on availability, practicality, convenience, cost, and ease or safety of administration, Australia's National Ig Governance program has a policy to preference alternative therapies where available and appropriate. **Investigations** There is no biological marker for GBS. It is diagnosed by clinical recognition of rapidly evolving paralysis with areflexia. Investigations include the following: • Cerebrospinal fluid (CSF) protein elevation, although the level may be normal in the first two weeks of illness. The CSF white cell count may rise transiently, but a sustained pleocytosis suggests an alternative diagnosis or association with an underlying illness (e.g. HIV). • Electrophysiological studies may show changes after the first or second week of the illness, including conduction block, conduction slowing or abnormalities in F waves.
Justification for Evidence Category	One systematic review of nine randomised controlled trials (RCTs) of moderate quality found IVIg hastened recovery in adults with GBS to the same degree as plasma exchange (Biotext, 2004). This conclusion was confirmed in a 2014 Cochrane review (Hughes et al). In severe disease, IVIg started within two weeks of onset hastens recovery as much as plasma exchange. Three studies, including a total of 75 children, suggested that IVIg significantly hastens recovery compared with supportive care. One low-quality RCT with 21 mildly affected children showed earlier signs of improvement and lower disability grades after four weeks with IVIg than supportive treatment alone (Frommer and Madronio, 2006). Persistent weakness or failure to recover with persistent weakness does not qualify for a second dose of IVIg. An RCT investigating the effectiveness of a second dose of IVIg (Walgaard et al, 2021) showed no benefit and increased adverse events associated with the administration of a second dose.
Diagnosis Requirements	A diagnosis must be made by a Neurologist, Paediatrician, General Medicine Physician or an Intensivist.

Qualifying Criteria for Ig Therapy

Initial therapy for GBS with significant disability and progression

This indication must be used for initial GBS therapy only.

The failure to improve from GBS with persistent weakness or failure to recover with persistent weakness does not qualify for a second IVIg dose, except where treatment-related fluctuations occur within 8 weeks of treatment and there is evidence of initial improvement followed by deterioration. A second dose is available under Indication 2: **Relapse in GBS - treatment related fluctuation with initial improvement and subsequent deterioration post IVIg treatment** but must only be on the advice of, and after assessment by, a neurologist.

- Weakness is progressive and indicates a trajectory to significant disability

AND

- Significant disability as objectively measured by the Guillain–Barré syndrome (GBS) disability score of greater than one point

  OR

- The patient has bulbar or autonomic features of GBS variant with significant disability

Relapse in GBS (treatment-related fluctuation - TRF) within 8 weeks with recurrent weakness after initial improvement may require a second treatment with IVIg. A second dose is available under Indication 2 (GBS TRF), but must only be on the advice of, and after assessment by, a neurologist.

Treatment-related fluctuations (TRFs) are defined as:

1. improvement in GBS disability score of at least 1 grade or improvement in MRC sum score of more than 5 points after completion of therapy, followed by a worsening in GBS disability score of at least 1 grade or a decrease in MRC sum score of more than 5 points within the first months after onset of disease, OR
2. stabilisation of the clinical course for more than 1 week after completion of therapy, followed by a worsening of at least 1 grade of the GBS disability score or more than 5 points on the MRC sum score.

Note: an application can be made for either a second course under Indication 2 (GBS TRF) or a switch to acute-CIDP in the 4-8 week window after onset.

	Relapse in GBS - treatment related fluctuation with initial improvement and subsequent deterioration post IVIg treatment Relapse in GBS (treatment related fluctuation) within 8 weeks with recurrent weakness after initial improvement may require a second treatment with IVIg. After qualifying for initial treatment under Indication 1: **Initial therapy for GBS with significant disability and progression,** a second dose is available under this indication but must only be on the advice of, and after assessment by, a neurologist. Treatment-related fluctuations (TRFs) are defined as: 1. improvement in GBS disability score of at least 1 grade or improvement in MRC sum score of more than 5 points after completion of therapy, followed by a worsening in GBS disability score of at least 1 grade or a decrease in MRC sum score of more than 5 points within the first months after onset of disease, OR 2. stabilisation of the clinical course for more than 1 week after completion of therapy, followed by a worsening of at least 1 grade of the GBS disability score or more than 5 points on the MRC sum score. Note: an application can be made for either a second course under Indication 2 (GBS TRF) or a switch to acute-CIDP in the 4-8 week window after onset. • Initial response to Ig therapy was followed by recurrent weakness within 8 weeks with no alternative explanation and deterioration in a recent Medical Research Council (MRC) sum score OR • Initial response to Ig therapy was followed by recurrent weakness within 8 weeks with no alternative explanation and deterioration in a recent GBS outcome score
Exclusion Criteria	Chronic inflammatory demyelinating polyneuropathy (CIDP) - see Chronic inflammatory demyelinating polyneuropathy (CIDP) Acute-chronic inflammatory demyelinating polyneuropathy (CIDP) - see Chronic inflammatory demyelinating polyneuropathy (CIDP)

Review Criteria for Assessing the Effectiveness of Ig Use

Initial therapy for GBS with significant disability and progression

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

- Improvement in disability at 4 weeks after Ig treatment as assessed by the Guillain–Barré syndrome (GBS) disability score

  OR

- Improvement in bulbar or autonomic symptoms in patients with Guillain–Barré syndrome variant

AND

- Patient survival and symptom improvement

Relapse in GBS TRF with recurrent weakness after initial improvement may require a second treatment with IVIg. A second dose is available under Indication 2 (GBS TRF) but must only be on the advice of, and after assessment by, a neurologist.

Relapse in GBS - treatment related fluctuation with initial improvement and subsequent deterioration post IVIg treatment

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

- Improvement in disability at 4 weeks after Ig treatment as assessed by the MRC sum score

  OR

- Improvement in disability at four weeks after Ig treatment as assessed by the Guillain–Barré syndrome (GBS) disability score

AND

- Patient survival and symptom improvement

Dose

Initial therapy for GBS with significant disability and progression

- **Initial Dose (IVIg)** - 2 g/kg in 2 to 5 divided doses.

Relapse in GBS TRF within 8 weeks with recurrent weakness after initial improvement may require a second treatment with IVIg. A second dose is available under Indication 2 (GBS TRF), but must only be on the advice of, and after assessment by, a neurologist.

Treatment-related fluctuations (TRFs) are defined as:

1. improvement in GBS disability score of at least 1 grade or improvement in MRC sum score of more than 5 points after completion of therapy, followed by a worsening in GBS disability score of at least 1 grade or a decrease in MRC sum score of more than 5 points within the first months after onset of disease, OR
2. stabilisation of the clinical course for more than 1 week after completion of therapy, followed by a worsening of at least 1 grade of the GBS disability score or more than 5 points on the MRC sum score.

Note: an application can be made for either a second course under Indication 2 (GBS TRF) or a switch to acute-CIDP in the 4-8 week window after onset.

Refer to the current product information sheet for further information on dose, administration and contraindications.

Relapse in GBS - treatment related fluctuation with initial improvement and subsequent deterioration post IVIg treatment

- **Second dose (IVIg)** - 2 g/kg in 2 to 5 divided doses.

Refer to the current product information sheet for further information on dose, administration and contraindications.

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