Stiff person syndrome

Condition for which Ig has an established therapeutic role.

Specific Conditions	• Stiff person syndrome
Indication for Ig Use	• Stiff person syndrome or variants with significant disability
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	Patients with stiff person syndrome present with symptoms related to muscular rigidity and superimposed episodic spasms. The rigidity insidiously spreads involving axial muscles, primarily abdominal and thoracolumbar, as well as proximal limb muscles. Typically, co-contraction of truncal agonist and antagonistic muscles leads to a board-like appearance with hyperlordosis. Less frequently, respiratory muscle involvement leads to breathing difficulty and facial muscle involvement to a mask-like face. Investigations that may be useful for diagnosis include auto-antibodies to GAD-65 or GAD-67, electromyography recordings from stiff muscles that may show continuous discharges of motor unit, and cerebrospinal fluid oligoclonal bands.
Justification for Evidence Category	The Biotext (2004) review included one randomised, double blind, placebo-controlled trial with a crossover design of 16 patients with stiff person syndrome and anti-GAD-65 antibodies. A significant treatment effect with intravenous immunoglobulin (IVIg) was seen, resulting in patients' decreased stiffness and heightened sensitivity scores. According to expert consensus, considering the disabling progressive course of stiff person syndrome, intravenous immunoglobulin (IVIg) should be offered as the first-line treatment if there is inadequate response to benzodiazepines, baclofen and gabapentin. Although periodic infusions would be required in the majority, further studies are needed to determine optimal dosage and duration.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.
Qualifying Criteria for Ig Therapy	• Significant disability as measured by the Modified Rankin Scale (MRS) score of at least three points and the Distribution of Stiffness (DOS) index of at least one point IVIg should be used for six months before determining whether the patient has responded. If there is no benefit after six months, IVIg therapy should be abandoned. Review by a neurologist is required after six months and at least annually thereafter. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy.
Review Criteria for Assessing the Effectiveness of Ig Use	IVIg should be used for six months before determining whether the patient has responded. If there is no benefit after six months, IVIg therapy should be abandoned. Review by a neurologist is required after six months and at least annually thereafter. Documentation of clinical effectiveness is necessary for continuation of IVIg therapy. **Clinical effectiveness of Ig therapy may be assessedby:** **On review of the initial authorisation period** • Improvement in the degree of disability and relief of symptoms of stiffness compared to the qualifying assessment as demonstrated by the Modified Rankin Scale (MRS) score and the Distribution of Stiffness (DOS) index **On review of a continuing authorisation period** • Improvement in or stabilisation of the degree of disability and symptoms of stiffness as demonstrated by the Modified Rankin Scale (MRS) score, which is less than or equal to the score at previous review assessment

Dose	

- **Induction Dose (IVIg)** - Up to 2 g/kg in 2 to 5 divided doses.
- **Maintenance Dose (IVIg)** - 0.4–1g/kg, 2–6 weekly. A maximum dose of 2g/kg may be given in any 4 week period. This might be by smaller doses more frequently than monthly. A reduced dose may be appropriate when patients are stable.

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.

Bibliography

Biotext 2004, 'Summary data on conditions and papers', in *A systematic literature review and report on the efficacy of intravenous immunoglobulin therapy and its risks*, commissioned by the National Blood Authority on behalf of all Australian Governments, pp. 190–1. Available from: https://catalogue.nla.gov.au/Record/3808068

Bonita, R & Beaglehole, R 1988, 'Modification of Rankin Scale: Recovery of motor function after stroke.', *Stroke;* vol. 19, no. 12, pp. 1497-1500.

Dalakas, MC 2005, 'The role of IVIg in the treatment of patients with stiff person syndrome and other neurological diseases associated with anti-GAD antibodies', *Journal of Neurology*, vol. 252, suppl. 1, pp. 119–25. https://www.ncbi.nlm.nih.gov/pubmed/15959668

Dalakas, MC, Fujii, M, Li, M, et al 2001, 'High-dose intravenous immune globulin for stiff-person syndrome' , *New England Journal of Medicine*, vol. 345, no. 26, pp. 1870–6. https://www.ncbi.nlm.nih.gov/pubmed/11756577

Dalakas, MC, Rakocevic, G, Dambrosia, JM, et al 2017, 'A double-blind, placebo-controlled study of rituximab in patients with stiff person syndrome', vol. 82, no. 2, pp. 271-277. https://www.ncbi.nlm.nih.gov/pubmed/28749549

Dalakas, MC, Fujii, M, Li, M, et al 2000, 'The clinical spectrum of anti-GAD antibody-positive patients with stiff-person syndrome', *Neurology,* vol. 55, no. 10, pp. 1531-5. http://n.neurology.org/content/55/10/1531.long

Rowland, LP & Layzer, RB, 2005, 'Stiff man syndrome (Moersch– Woltman syndrome), in LP, Rowland (ed.), *Merritt's Neurology*, 11th edn, Lippincott Williams & Wilkins, Philadelphia, p. 927.

Rankin, J 1957, 'Cerebral vascular accidents in patients over the age of 60', *Scottish Medical Journa,l May* 1957, vol. 2, no. 5, pp. 200-15. http://journals.sagepub.com/doi/abs/10.1177/003693305700200504?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed

Stroke Engine Canada, 'The Modified Rankin Scale'. Available from Modified Rankin Scale (MRS) – Strokengine

Van Swieten, JC, Koudstaal, PJ, Visser, MC, et al 1988, 'Interobserver agreement for the assessment of handicap in stroke patients', *Stroke* 1987, vol. 19, no. 5. pp. 604-607. https://www.ncbi.nlm.nih.gov/pubmed/3363593

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