Chronic inflammatory demyelinating polyneuropathy (CIDP), (including IgG and IgA paraproteinaemic demyelinating neuropathies)

Condition for which Ig has an established therapeutic role.

Specific Conditions	• Chronic inflammatory demyelinating polyneuropathy (CIDP) • IgA paraproteinaemic demyelinating neuropathy • IgG paraproteinaemic demyelinating neuropathy
Indication for Ig Use	• Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) for patients in whom walking is compromised or there is significant disability • Relapse of chronic inflammatory demyelinating polyneuropathy (CIDP) patients within six months of commencement of trial off Ig therapy
Level of Evidence	Clear evidence of benefit (Category 1)
Description and Diagnostic Criteria	Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired sensorimotor polyneuropathy characterised by a progressive or relapsing/remitting course developing over at least two months with evidence of demyelination on electrophysiological or pathological studies and response to immunomodulating therapies. There is no specific diagnostic test, but characteristic clinical and laboratory findings help distinguish this disorder from other immune mediated neuropathic syndromes. Serum protein electrophoresis with immunofixation may be indicated to search for monoclonal gammopathy and associated conditions.
Justification for Evidence Category	The Biotext (2004) review found one Cochrane review (2002) of six randomised controlled trials (RCTs) with a total sample size of 170. The quality of the studies was low–moderate, found intravenous immunoglobulin (IVIg) improved disability in the short-term, and had comparable results to treatment with plasma exchange or prednisolone. This review was updated in 2013, with two additional RCTs increasing participants to 332. A significantly higher proportion of patients had short term improvement in disability after IVIg compared with placebo RR2.4, NNT3 (high quality evidence). One study confirmed long term improvement over 24 and 48 weeks. IVIg had similar efficacy to plasma exchange, oral prednisolone and intravenous methyl prednisolone in the short term.
Diagnosis Requirements	A diagnosis must be made by a Neurologist.
Qualifying Criteria for Ig Therapy	Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) for patients in whom walking is compromised or there is significant disability This indication should be used to cover first line (prior to trial off) treatment of CIDP patients. For patients who have trialled off Ig therapy and subsequently relapse within six months, please use the indication **Relapse of chronic inflammatory demyelinating polyneuropathy (CIDP) patients within six months of commencement of trial off Ig therapy** In adults or children 10 years or older • Significant disability or compromised walking in an adult or child 10 years or older as objectively measured by an Overall Neuropathy Limitations Scale (ONLS) score of at least two points and the Medical Research Council (MRC) sum score OR In children less than 10 years • Significant disability or compromised walking in a child less than 10 years as measured by the Six Minute Walk Test (6MWT) and/or a Modified Rankin Scale (MRS) score of at least two points Review by a neurologist is required after four months of Ig therapy to determine whether the patient has responded. If there is no benefit after this period of treatment, IVIg therapy should be abandoned. Where treatment is continued, a review by a neurologist or general physician is required each 12 months. A trial of cessation should be considered each 12 months in patients in remission on maintenance therapy. Once a patient has relapsed in the first six months of a trial off therapy, a further trial might be considered after at least two years. Documentation of clinical efficacy is necessary for continuation of IVIg therapy.

Relapse of chronic inflammatory demyelinating polyneuropathy (CIDP) patients within six months of commencement of trial off Ig therapy

This indication should be used for patients who have previously trialled off Ig therapy and subsequently relapsed within six months. For patients requiring first line therapy (i.e. prior to trial off please use the indication: **Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) for patients in whom walking is compromised or there is significant disability**

- In a previously stable adult or child (10 years or older), deterioration in disability as measured by an increase of at least one point in the Adjusted Overall Neuropathy Limitations Scale (ONLS) or a reduction in the Medical Research Council (MRC) sum score of at least three points, when compared to the review score before stopping previous treatment

  OR

- In a previously stable child (less than 10 years), deterioration in disability as measured by a reduction in the Six Minute Walk Test (6MWT) or an increase of at least one point in the Modified Rankin Scale (MRS) compared to the review score before stopping previous treatment

AND

- Relapse has occurred within six months of the last immunoglobulin dose

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 treatment, IVIg therapy should be abandoned.

Review by a neurologist is required within four months and annually thereafter (neurologist or general physician).

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

Once a patient has relapsed when trialled off Ig treatment, a second line immunomodulatory agent should be strongly considered as additional therapy.

Review Criteria for Assessing the Effectiveness of Ig Use

Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) for patients in whom walking is compromised or there is significant disability

Review by a neurologist is required after four months of Ig therapy to determine whether the patient has responded. If there is no benefit after this period of treatment, IVIg therapy should be abandoned.

Where treatment is continued, a review by a neurologist or general physician is required each 12 months.

A trial of cessation should be considered each 12 months in patients in remission on maintenance therapy.

Once a patient has relapsed in the first six months of a trial off therapy, a further trial might be considered after at least two years.

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

Clinical effectiveness of Ig therapy may be demonstrated by:

On review of the initial authorisation period

For adults or children 10 years or older

- Improvement in disability as measured by a reduction in the Adjusted Overall Neuropathy Limitations Scale (ONLS) by at least one point; or by an increase in the Medical Research Council (MRC) sum score by at least three points, as compared to the qualifying assessment

OR

For children less than 10 years

- Improvement in disability as measured by the Six Minute Walk Test (6MWT) and/or the Modified Rankin Scale (MRS) as compared to the qualifying assessment

On review of a continuing authorisation period

- In an adult or child 10 years or older, stabilisation or continued improvement in disease as measured by the adjusted Overall Neuropathy Limitations Scale (ONLS) or the Medical Research Council (MRC) sum score compared to the previous review score

  OR

- Adult patient with severe disease continues to report post infusion improvement that is better or comparable to the level reported at the previous review, with end-of-cycle deterioration and additional immunosuppressant agents have been commenced.

  OR

- In a child under 10, stabilisation or continued improvement in disease after previous evidence of deterioration in the Six Minute Walk Test (6MWT) or the Modified Rankin Scale (MRS) compared to the previous review scores

AND

- A trial of weaning towards cessation of Ig therapy is planned for clinically stable patients to identify those in remission, or a valid reason provided as to why a trial is not planned or is contraindicated at this time is provided

A trial of Ig weaning should be considered annually in stable patients on maintenance therapy to identify patients who are in remission.

Relapse of chronic inflammatory demyelinating polyneuropathy (CIDP) patients within six months of commencement of trial off Ig therapy

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 treatment, IVIg therapy should be abandoned.

Review by a neurologist is required within four months and annually thereafter (neurologist or general physician).

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

Once a patient has relapsed when trialled off Ig treatment, a second line immunomodulatory agent should be strongly considered as additional therapy.

Clinical effectiveness of Ig therapy may be demonstrated by:

On review of the initial authorisation period

- In an adult or child (10 years or older), improvement in disability as measured by a decrease of at least one point in the Adjusted Overall Neuropathy Limitations Scale (ONLS) score or an increase of at least three points in the Medical Research Council (MRC) sum score

  OR

- In a child (less than 10 years), improvement in disability as measured by improvement in the Six Minute Walk Test (6MWT) or a reduction of at least one point in the Modified Rankin Scale (MRS) score

AND

- A trial of weaning towards cessation of Ig therapy is planned 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

On review of a continuing authorisation period

- In an adult or child (10 years or older), stabilisation or continued improvement in disease as measured by the Overall Neuropathy Limitations Scale (ONLS) score, or the MRC score, as compared to the previous assessment

  OR

- Adult patient with severe disease continues to report post infusion improvement that is better or comparable to the level reported at the previous assessment, with end-of-cycle deterioration and additional immunosuppressant agents have been commenced

  OR

- In a child (less than 10 years), stabilisation or continued improvement in disease after previous evidence of deterioration as measured by the Six Minute Walk Test (6MWT) or the Modified Rankin Scale (MRS) score

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 valid reason provided as to why a trial is not being planned or is contraindicated at this time

Once a patient has relapsed in the first six months of a trial off therapy, a further trial might be considered after at least two years.

Dose	Treatment of chronic inflammatory demyelinating polyneuropathy (CIDP) for patients in whom walking is compromised or there is significant disability • **Loading Dose (IVIg)** - One loading dose of 2 g/kg in 2 to 5 divided doses in the first month of therapy (in addition to the maintenance dose) is permitted. This dose is only available as intravenous immunoglobulin • **Maintenance Dose (IVIg)** - 0.4–1g/kg, is permitted every 2 to 6 weeks. The amount per dose should be titrated to the individual's response, and may be reduced while weaning. A maximum dose of 2g/kg may be given in any 4 week period. This might be by smaller doses more frequently than fortnightly. Subcutaneous administration of immunoglobulin can be considered as an alternative to intravenous immunoglobulin following stabilisation with intravenous immunoglobulin. • **Supplementary Dose (IVIg)** - One additional dose of up to 2 g/kg, administered in divided doses where appropriate, may be given where there is acute deterioration/relapse in the context of a severe infection, surgery or other acute illness. Deterioration of a patient on Ig therapy may be an indication for alternative or additional immunosuppressant agents. Access to an additional dose should be a rare occurrence. This dose is also available as subcutaneous immunoglobulin. • **Maintenance Dose (SCIg)** - 0.2–0.5g/kg, is permitted every 1 week. The amount per dose should be titrated to the individual's response, and may be reduced while weaning. A maximum dose of 2g/kg may be given in any 4 week period. This might be by smaller doses more frequently than weekly. This dose is also available as intravenous immunoglobulin. • **Supplementary Dose (SCIg)** - One additional dose of up to 2 g/kg, administered in divided doses where appropriate, may be given where there is acute deterioration/relapse in the context of a severe infection, surgery or other acute illness. Deterioration of a patient on Ig therapy may be an indication for alternative or additional immunosuppressant agents. Access to an additional dose should be a rare occurrence. This dose is also available as intravenous immunoglobulin. 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 chronic inflammatory demyelinating polyneuropathy (CIDP) patients within six months of commencement of trial off Ig therapy

- **Loading Dose (IVIg)** - One loading dose of 2 g/kg in 2 to 5 divided doses in the first month of therapy (in addition to the maintenance dose) is permitted.

  This dose is only available as intravenous immunoglobulin
- **Maintenance Dose (IVIg)** - 0.4–1g/kg, is permitted every 2 to 6 weeks. The amount per dose should be titrated to the individual's response, and may be reduced while weaning. A maximum dose of 2g/kg may be given in any 4 week period. This might be by smaller doses more frequently than fortnightly.

  Subcutaneous administration of immunoglobulin can be considered as an alternative to intravenous immunoglobulin following stabilisation with intravenous immunoglobulin.
- **Supplementary Dose (IVIg)** - One additional dose of up to 2 g/kg, administered in divided doses where appropriate, may be given where there is acute deterioration/relapse in the context of a severe infection, surgery or other acute illness. Deterioration of a patient on Ig therapy may be an indication for alternative or additional immunosuppressant agents.

  Access to an additional dose should be a rare occurrence.

  This dose is also available as subcutaneous immunoglobulin.
- **Maintenance Dose (SCIg)** - 0.2–0.5g/kg, is permitted every 1 week. The amount per dose should be titrated to the individual's response, and may be reduced while weaning. A maximum dose of 2g/kg may be given in any 4 week period. This might be by smaller doses more frequently than weekly.

  This dose is also available as intravenous immunoglobulin.
- **Supplementary Dose (SCIg)** - One additional dose of up to 2 g/kg, administered in divided doses where appropriate, may be given where there is acute deterioration/relapse in the context of a severe infection, surgery or other acute illness. Deterioration of a patient on Ig therapy may be an indication for alternative or additional immunosuppressant agents.

  Access to an additional dose should be a rare occurrence.

  This dose is also available as intravenous immunoglobulin.

Once a patient has relapsed when trialled off Ig treatment, a second line immunomodulatory agent should be strongly considered as additional therapy.

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

ATS Statement 2002, 'Guidelines for the Six-Minute Walk Test', *American journal of respiratory and critical care medicine*, vol. 166, no. 1, pp. 111-7. https://www.atsjournals.org/doi/full/10.1164/ajrccm.166.1.at1102

ATS Statement: Guidelines for the Six-Minute Walk Test. 2002, *American Thoracic Society*, THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY WAS APPROVED BY THE ATS BOARD OF DIRECTORS. Available from: https://www.thoracic.org/statements/resources/pfet/sixminute.pdf

Asia–Pacific IVIg Advisory Board 2004, 'Bringing consensus to the use of IVIg in neurology. Expert consensus statements on the use of IVIg in neurology', 1st edn, Asia–Pacific IVIg Advisory Board Inc., pp. 21–29.

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. 132–3. Available from: https://catalogue.nla.gov.au/Record/3808068

Bonita, R & Beaglehole, R 1988, 'Recovery of motor function after stroke', *Stroke*, vol 19, no. 12, pp. 1497-1500. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.1027.3989&rep=rep1&type=pdf

Dunaway, S, Montes, J, Garber CE, et al 2014, 'Performance of the timed 'Up and Go' test in spinal muscular atrophy', *Muscle & Nerve*, vol. 50, no. 2, pp. 273–277. https://www.ncbi.nlm.nih.gov/pubmed/24375426

Frommer M & Madronio C 2006, 'The use of intravenous immunoglobulin in Australia. A report for the National Blood Authority', '*Part B, systematic literature review'* Sydney Health Projects Group, University of Sydney, Sydney, pp. 29–31.

Geiger, R, Strasak, A, Treml, B, et al 2007, 'Six-minute walk test in children and adolescents', *The Journal of pediatrics*, vol. 150, no. 4, pp. 395-9. https://www.ncbi.nlm.nih.gov/pubmed/17382117

Goemans, N, Klingels, K, van den Hauwe, M, et al 2013, 'Six-minute walk test: reference values and prediction equation in healthy boys aged 5 to 12 years', *Public Library of Sciene One*, vol. 8, no. 12, pp. 1-9. https://lirias.kuleuven.be/bitstream/123456789/432666/3/Six+Minute+Walk+Test+Reference+Values+and+Prediction+Equation+in+Healthy+Boys+Aged.pdf

Bibliography

Graham, RC & Hughes, RA 2006, 'A Modified Peripheral Neuropathy Scale: The Overall Neuropathy Limitations Scale', *Journal of neurology, neurosurgery, and psychiatry*, vol. 77, no. 8, pp. 973–976. https://www.ncbi.nlm.nih.gov/pubmed/16574730

Hughes, RAC, Bensa, S, Willison, HJ, et al 2001, 'Randomized controlled trial of intravenous immunoglobulin versus oral prednisolone in chronic inflammatory demyelinating polyradiculoneuropathy', *Annals of Neurology*, vol. 50, no. 2, pp. 195–201. https://www.ncbi.nlm.nih.gov/pubmed/11506402

Hughes, RAC, Bouche, P, Cornblath, DR, et al 2006, 'European Federation of Neurological Societies/Peripheral Nerve Society guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society', *European Journal of Neurology*, vol. 13, no. 4, pp. 326–32. https://www.ncbi.nlm.nih.gov/pubmed/16643309

Kleyweg, RP, van der Meché, FGA & Schmitz PIM 1991, 'Interobserver agreement in the assessment of muscle strength and functional abilities in Guillain-Barré syndrome', *Muscle Nerve*, vol. 14, no. 11, pp. 1103–1109. https://www.ncbi.nlm.nih.gov/pubmed/1745285

Lammers, AE, Hislop, AA, Flynn, Y, et al 2008, 'The 6-minute walk test: normal values for children of 4-11 years of age', *Archives of disease in childhood*, vol. 93, no. 6, pp. 464-8. https://www.ncbi.nlm.nih.gov/pubmed/17675356

Medical Research Council. Aids to the examination of the peripheral nervous system, Memorandum no. 45, Her Majesty's Stationery Office, London, 1981.

MRC Muscle Scale. 1976, 'Aids to the Examination of the Peripheral Nervous System -Memorandum No. 45', , *Medical Research Council.* Available from: https://mrc.ukri.org/research/facilities-and-resources-for-researchers/mrc-scales/mrc-muscle-scale/

Rankin J. 1957, 'Cerebral vascular accidents in patients over the age of 60', *Scottish Medical Journal*, vol. 2, pp. 200-15.

Stroke Society of Australia, 'The Modified Rankin Scale'. Available from: http://www.strokesociety.com.au/index.php?option=com_content&view=article&id=292:modified-rankin-scale-astn&catid=40:astn

Van Schaik, IN, Winer JB, de Haan, R, et al 2002, 'Intravenous immunoglobulin for chronic inflammatory demyelinating polyradiculoneuropathy', *Review,* vol.1, no. 8, pp. 491-498. https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(02)00222-3/abstract

Van Swieten, JC, Koudstaal, PJ, Visser MC, et al 1988, 'Interobserver agreement for the assessment of handicap in stroke patients', *Stroke* Vol. 19, no. 5, Pp. 604-607. https://pdfs.semanticscholar.org/215e/00b285abdb1679d4ae7063cff9eb68153184.pdf

Zinman, LH, Sutton, D, Ng, E, et al 2005, 'A pilot study to compare the use of the Excorim staphylococcal protein immunoadsorption system and IVIG in chronic inflammatory demyelinating polyneuropathy', *Transfusion and Apheresis Science*, vol. 33, no. 3, pp. 317–24. https://www.ncbi.nlm.nih.gov/pubmed/16239123

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