Anti-neutrophil cytoplasmic antibody (ANCA) [Proteinase 3 (PR3) or myeloperoxidase (MPO)] - positive systemic necrotising vasculitis

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Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• PR3 or MPO ANCA-positive idiopathic rapidly progressive glomerulonephritis • Microscopic polyangiitis • Wegener granulomatosis • Churg-Strauss syndrome
Indication for IVIg Use	• Control of vasculitic activity in rare cases of ANCA-positive systemic necrotising vasculitis failing to respond to corticosteroids and cytotoxic immunosuppression.
Level of Evidence	Evidence of probable benefit – more research needed (Category 2a)
Description and Diagnostic Criteria	ANCA-associated systemic necrotising vasculitides are life-threatening immune-mediated inflammatory diseases comprising one of four clinical syndromes: 1. Granulomatosis with polyangiitis (Wegener's granulomatosis) 2. Microscopic polyangiitis 3. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome) 4. PR3 or MPO ANCA-positive idiopathic rapidly progressive glomerulonephritis. In these cases, the ANCA specificity is directed against the neutrophil cytoplasmic antigens PR3 (proteinase 3) and MPO (myeloperoxidase). ANCA that lack MPO or PR3 specificity tend to be non-specific. Biopsy of affected tissue is required to establish the diagnosis. Standard combinations of corticosteroids and cytotoxic immunosuppression are generally effective at controlling disease, but relapses are common. Intravenous immunoglobulin (IVIg) has a limited role as one of several therapeutic options in relapsing disease.
Justification for Evidence Category	The Biotext (2004) review found one randomised trial of 34 patients and one case series of seven patients with ANCA-associated systemic vasculitis (AASV). Different AASVs were represented in the studies. The Biotext (2004) review concluded that there is possible benefit in the treatment of AASV with IVIg if disease activity persists after standard therapy.

Qualifying Criteria for IVIg Therapy	• Evidence of MPO or PR3 ANCA-positive systemic necrotising vasculitis. AND • Persistent active disease as assessed by at least one of: Birmingham Vasculitis Activity Score (BVAS version 3), erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) AND • Persistent disease despite standard corticosteroid therapy within the last six months. OR • Corticosteroid therapy is contraindicated. AND • Persistent disease despite immunosuppressant therapy within the last six months. OR • Immunosuppressant therapy is contraindicated.
Exclusion Criteria	First-line or initial treatment for ANCA.
Review Criteria for Assessing the Effectiveness of IVIg Use	A review by the Treating Medical Specialist is required each six months to assess evidence of clinical benefit. A trial off therapy should be considered at each review. **On review of the initial authorisation period** Clinical effectiveness of Ig therapy may be demonstrated by: • Improvement, as measured by a reduction in at least one indicator of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, ANCA level or Birmingham Vasculitis Activity Score (BVAS) compared to the original qualifying value. **On review of a continuing authorisation period** Clinical effectiveness of Ig therapy may be demonstrated by: • Stabilisation of disease, as measured by at least one indicator of erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, ANCA level or Birmingham Vasculitis Activity Score (BVAS) compared to the previous review score.

Dose	
	• **Maintenance Dose** - 2 g/kg in single or divided doses. **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.** **Dosing above 1 g/kg per day is contraindicated for some IVIg products.** **Refer to the current product information sheet for further information.**

Bibliography

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