Change form for published specifications and products developed by Clinical Reference Group (CRGs)

Product name: Clinical commissioning policy for the use of therapeutic immunoglobulin (Ig) England, 2021
Publication number:

Description of changes required

The Commissioning Criteria Policy for the use of therapeutic immunoglobulin (Ig) England, 2021 (currently published version), has been converted into a policy template with an update of the document following publication. These changes were agreed previously (v1.0 – unpublished) and do not form part of this change form.

The change form highlights further changes from the unpublished version 1.0 to version 4.0.

Describe what was stated in original document	Describe new text in the document	Section/Paragraph to which changes apply	Describe why document change required	Changes made by	Date change made
Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England, 2021	Clinical Commissioning Policy for the use of therapeutic immunoglobulin (Ig) England, 2024	Title p1,2	Update of year published		
About the use of therapeutic immunoglobulin	About the treatment	Sub-title p2	Clarity		
It is used when the immune system is either not making antibodies, not	Therapeutic immunoglobulin is used when the immune	About the treatment p2	Clarity in meaning, grammar		

making enough antibodies or the ones they are making don't work properly.	system is either not making antibodies, not making enough antibodies or the ones they are making do not work properly.				
IgG has other effects too, so it isn't just used for people with immune deficiency. You might hear about immunoglobulin being used in some people with other immune (autoimmune) problems.	IgG has other effects too, so it is not just used for people with immune deficiency.	About the treatment p2	Grammar		
About the current treatment The current use of therapeutic immunoglobulin is covered by the Commissioning Criteria Policy for the use of therapeutic immunoglobulin (Ig) England (2021) with the exception of those indications within the Department of Health and Social Care Clinical Guidelines for Immunoglobulin Use (2nd edition update; July	Deleted	About the treatment p2	Information on "not routinely commissioned" indications included in "About the new treatment" section instead for greater clarity.		

2011)1, which have not moved into routine commissioning.					
About the new treatment	New Indications	Sub-title p3	Clarity		
The following indications have been included in the policy as a result of stakeholder testing.	The following indications have been included in this version of the policy as a result of stakeholder testing and an evidence review.	New Indications p3	Clarity		
	Indications that have been considered as part of the evidence review and determined to be "not routinely commissioned" are included in Appendix B. This list is not exhaustive and therefore any indication not explicitly detailed within this policy is considered to be "not routinely commissioned".	New Indications p3	Wording added for clarity as described above. Agreement to include list of not routinely commissioned indications instead of referencing the stakeholder document.		
See the committee papers (INSERT LINK) for full details of the evidence.	deleted	Committee discussion p3			
It has been built on a	This policy was built on a	Evidence summary	Clarity		

[1] Department of Health and Social Care. *Clinical guidelines for immunoglobulin use (second edition update)*. Available from: https://www.gov.uk/government/publications/clinical-guidelines-for-immunoglobulin-use-second-edition-update

previous review of the literature including detailed scoping reviews undertaken by Cochrane Response (2020) updated with a further evidence review, expert opinion and multi-organisational input.	review of the literature including detailed scoping reviews undertaken by Cochrane Response (2020) updated with a further evidence review, expert opinion and multi-organisational input.	p4	Grammar		
The criteria have been developed by the Ig Expert Working Group following wide consultation with specialty experts, relevant scientific societies and the respective Clinical Reference Groups (CRGs) for haematology, immunology, neurology, infectious diseases and other specialities.	The commissioning criteria were developed by the Ig Expert Working Group following wide consultation with specialty experts, relevant scientific societies and the NHS England Specialised Commissioning Clinical Reference Groups (CRGs).	Evidence summary p4	Clarity		
The CRG will review the document as per NHS England policy review process or when there is a significant change in evidence. Recommendations on Ig dose and outcomes are based on a combination of available evidence and	Deleted (part moved to Implementation section)	Evidence summary p4	Clarity		

expert opinion. The colour coding scheme, which had been previously devised for demand management but was often utilised as a commissioning tool, has now been replaced by categorisation of Ig use; to routinely commissioned (see appendix A) or not routinely commissioned (NRC) categories. This is now based on the strength of clinical evidence.					
	The Immunology and Allergy CRG, in conjunction with the Ig Oversight Group, will review this document as per NHS England policy review process or when there is a significant change in evidence. Recommendations on Ig dose and outcomes are based on a combination of available evidence and expert opinion.	Implementation P4	Clarity		
These commissioning criteria are for all the indications recognised by NHS England after a	The following commissioning criteria set out all the indications recognised by NHS	Criteria p4	Clarity Removal of footnote		

systematic literature review as immunoglobulin responsive. These were previously categorised in a hierarchy of importance in a Demand Management Plan[1] as follows:	England as immunoglobulin responsive based on a systematic literature review. These were previously categorised in a hierarchy of importance in a Demand Management Plan as follows:		numbering as document will be archived upon publication of the Immunoglobulin Management Plan		
With this policy update, the colour coding system is now fully replaced, and indications are categorised as follows: • Routinely commissioned indications – see appendix A • Not routinely commissioned indications - see 'Rationale for determining the indications for which therapeutic immunoglobulin (Ig) is not routinely commissioned in England, xx 2022'	With this policy update, the colour coding system is removed and indications are instead categorised as follows: • Routinely commissioned indications – see Appendix A • Not routinely commissioned indications - see Appendix B.	Criteria p4	Clarity		
Consideration needs to be given to the requirement of panel approval and oversight. Local policy	Local policy should be followed for all applications – urgent, non-urgent and out-of-	Application process: p5	Clarity		

should be followed for the application process for all applications – urgent, non-urgent and out-of-hours. • Prior panel approval required – NO Treatment can proceed without prior panel approval. Submit a completed application form for retrospective review by the panel • Prior panel approval required – YES Treatment should not proceed without prior panel approval. If this is not possible, for example in an urgent case, retrospective approval must be sought. For urgent approvals in hours – a process will need to be in place on the agreed pathway for approval. For those cases that require out of hours approval, panels will have local processes in place, to ensure robust governance for retrospective panel approval. Where local	hours. Consideration needs to be given to the requirement of panel approval and oversight as follows: •Prior panel approval required – NO Treatment can proceed without prior panel approval. Submit a completed application form for retrospective review by the panel • Prior panel approval required – YES Treatment should not proceed without prior panel approval. For urgent approvals in hours – a process will need to be in place on the agreed pathway for approval. For those cases that require out of hours approval, panels will have local processes in place, to ensure robust governance for retrospective panel approval. Where local expertise is not available, panels will				

expertise is not available, panels will also be able to advise on dose optimisation and trials of treatment withdrawal.	also be able to advise on dose optimisation and trials of treatment withdrawal. If prior panel approval is not possible, for example in an urgent case, retrospective approval must be sought.				
Immunoglobulin data will be reviewed and findings reported to the Immunoglobulin Clinical Oversight Group and CRG to inform any recommendations on changes in policy.	Immunoglobulin data will be reviewed and findings reported to the Immunoglobulin Oversight Group and relevant CRG to inform any recommendations on changes in policy.	Application process: p5	Clarity		
Indications or clinical scenarios not listed in appendix A of this document are not routinely commissioned and require an Individual Funding Request (IFR) application subject to support by the Sub-Regional Immunoglobulin Assessment Panels (SRIAPs), to be submitted to the National IFR Panel.	Indications or clinical scenarios not listed in appendix A of this document are not routinely commissioned and require an Individual Funding Request (IFR) application to be submitted to the NHS England IFR system, should the clinician consider there is an arguable case for the IFR policy criteria to be met. If the IFR is	Application process: p5	Agreement at Ig Oversight Group to remove this step in the IFR process Clarity		

	approved, the diagnosis and locally agreed efficacy criteria are recorded on the immunoglobulin database.				
Actual body weight (ABW) should not be used.	ABW should not be used.	Dosing in paediatric patients p6	Grammar		
The recommended methods suggested by the RCPCH and NPPG to calculate IBW, include the use of the table at the back of the BNFc [Approximate Conversions and Units | About | BNFC | NICE] or methods suggested in the UKMI document . In the future, the RCPCH and NPPG aim to work on a standardised approach in conjunction with the BNFc.	The recommended methods suggested by the Royal College of Paediatrics and Child Health (RCPCH) and Neonatal and Paediatric Pharmacy Group (NPPG) to calculate IBW, include the use of the table at the back of the British National Formulary for Children (BNFC)[2] [Approximate Conversions and Units | About | BNFC | NICE] or methods suggested in the UKMI document[3]. In the future, the RCPCH	Dosing in paediatric patients p6	Clarity Grammar		

[2] MedicinesComplete. *BNF for Children*. Available from: *British National Formulary for Children | MedicinesComplete*

[3] Specialist Pharmacy Service. *UKMI NPPG - drug dosing in childhood obesity May 2021*. Available from: *How should medicines be dosed in children who are obese? – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice*

	and NPPG aim to work on a standardised approach in conjunction with the BNFC.				
Haematopoeitic stem cell transplantation (HSCT) in primary immunodeficiencies – long term use	Haematopoeitic stem cell transplantation (HSCT) in primary immunodeficiencies (PID) / inborn errors of immunity (IEI) – long term use	Appendix A - Use of Immunoglobulin in Immunology P7	Addition of alternative terminology		
Primary immunodeficiencies (PID) associated with significant antibody defects (excluding specific antibody deficiency) – long term use	Primary immunodeficiencies (PID) / Inborn errors of immunity (IEI) associated with significant antibody defects (excluding specific antibody deficiency) – long term use	Appendix A - Use of Immunoglobulin in Immunology P7	Addition of alternative terminology		
OR Hypogammaglobinaemia associated with drugs, therapeutic monoclonals targeted at B cells and plasma cells (rituximab and other anti-CD20, CD19 agents, daratumumab etc) post-	OR Hypogammaglobinaemia associated with drugs including emerging bispecifics, therapeutic monoclonals targeted at B cells and plasma cells (rituximab and other anti-CD20, CD19 agents,	Appendix A - Use of Immunoglobulin in Immunology Secondary antibody deficiency - long term use	Clarity that bispecifics (emerging drugs) are included		

HSCT*, NHL, CLL, MM or other relevant B-cell malignancy confirmed by haematologist	daratumumab etc) post-HSCT*, NHL, CLL, MM or other relevant B-cell malignancy confirmed by haematologist	Eligibility criteria p7			
[work ongoing to standardise IgG levels for paediatric patients – based on Sheffield/GOSH data)	deleted	Appendix A - Use of Immunoglobulin in Immunology Secondary antibody deficiency - long term use Eligibility criteria p8	Output not available, can be included when published		
	These eligibility criteria are also applicable for when considering the short term use of Ig in patients with chronic ITP experiencing acute bleeding or requiring invasive procedures.	Appendix A - Use of Immunoglobulin in Haematology ITP - short term use Eligibility criteria p13	Clarity		
1 g/kg (divided over 2 days if required)	1 g/kg (divided over 2 days if required)[18] [18] Misbah et al J Clin Path 2023;76:143-144	Appendix A - Use of Immunoglobulin in Haematology Covid vaccine	Insertion of reference		

		induced thrombosis and thrombocytopenia (VITT) Recommended dose p14			
No specific exclusion criteria but see general comments regarding prothrombotic risks of Ig	No specific exclusion criteria but see General notes regarding prothrombotic risks of Ig	Use of Ig in Neurology - Exclusion criteria - CIDP p17 - Inflammatory myopathies p18/19 - MMN p20 - MG p20 - Rasmussen encephalitis p23 - SPS p24	Clarity		
Inflammatory Myopathies - Dermatomyositis (DM), Juvenile dermatomyositis (JDM), Polymyositis (PM)	Inflammatory Myopathies - Dermatomyositis (DM), Juvenile dermatomyositis (JDM), Polymyositis (PM), Other inflammatory myopathies*	Use of Ig in Neurology - Indications Inflammatory myopathies, DM, JDM, PM p19	Addition of 'other inflammatory myopathies for clarity following consensus with ICOG		
• Patients with PM or	• Patients who have	Use of Ig in	Clarity to make		

DM/JDM who have significant muscle weakness;	significant muscle weakness;	Neurology - Eligibility criteria Inflammatory myopathies, DM, JDM, PM p19	inclusion criteria applicable for other inflammatory myositis		
	*Inclusion body myositis is not routinely commissioned	Use of Ig in Neurology - Exclusion criteria Inflammatory myopathies, DM, JDM, PM p19	Clarity		
PM:	PM/other inflammatory myopathies:	Use of Ig in Neurology - Outcome measures Inflammatory myopathies, DM, JDM, PM p19	Clarity to make outcome measures applicable for other inflammatory myositis		
	• Affected neonates	Use of Immunoglobulin in “Other” Indications - GALD Eligibility criteria p31	Clarity as eligibility criteria only refer to pregnant mothers and women but indication also refers to neonates (agreed by ICOG		

			based on feedback from SRIAPs)		
Ig is administered by intravenous infusion at a dose of 1 g/kg (dose capped at 60 g per week) to at risk mothers at 14 weeks, 16 weeks and then weekly from 18 weeks gestation until delivery between 37 and 38 weeks. The weight used to calculate the dose will be the mother's weight at booking.	Maternal dose: Ig is administered by intravenous infusion at a dose of 1 g/kg (dose capped at 60 g per week) to at risk mothers at 14 weeks, 16 weeks and then weekly from 18 weeks gestation until delivery between 37 and 38 weeks. The weight used to calculate the dose will be the mother's weight at booking. Neonatal dose: 1 g/kg The need for repeated doses, which may be required in exceptional cases, should be based on clinical need and locally agreed policy.	Use of Immunoglobulin in "Other" Indications - GALD Recommended dose p31	Split into maternal dose and neonatal dose - clarity		
Paediatric inflammatory multisystem syndrome temporarily associated to COVID-19 (PIMS-TS)	Paediatric inflammatory multisystem syndrome temporarily associated to COVID-19 (PIMS-TS)	PIMS-TS Indication p33	Clarity (CRG chair)		

	- short term use				
Because of the similarities between PIMS-TS and Kawasaki disease, the use of Ig is approved for any child fulfilling diagnostic criteria for PIMS https://www.rcpch.ac.uk/	Because of the similarities between PIMS-TS and Kawasaki disease, the use of Ig was approved in 2020 for any child fulfilling diagnostic criteria for PIMS https://www.rcpch.ac.uk/. More recent data suggests that steroids should be considered as first-line therapy, especially for children 6 years old and over without symptoms of Kawasaki disease – see comments under position of immunoglobulin.	PIMS-TS Eligibility criteria p33	Clarity and emerging evidence added		
	Consider steroids as first-line therapy while reserving IVIg for those cases where there is difficulty in distinguishing Kawasaki disease from MIS-C. In practice, this is particularly challenging in children under 6 years in whom IVIg may need to be considered as first-	PIMS-TS Position of immunoglobulin p33/34	Adding emerging evidence with reference		

	line therapy. IVIg was originally recommended as a first-line treatment for MIS-C based on its clinical similarities to Kawasaki disease. New data from an international observational cohort of 2009 patients with MIS-C from 39 countries randomised to receive IVIg alone (n=680), IVIg plus steroids (n= 698) and steroids alone (n=487) suggests that initial treatment with steroids was a safe and effective alternative to IVIg or combined therapy.[46] There were no significant differences between treatment arms for primary outcomes – need for ventilation, inotropic support or death. In addition, the occurrence and resolution of coronary artery aneurysms did not differ significantly				

	between treatment groups. [46]Channon-Wells et al Lancet Rheumatology 2023;5:e184-99				
Dosing optimisation in neurology for maintenance – general notes:	General notes: Dosing optimisation in neurology for maintenance	General notes p36	Clarity		
This approach is supported by recent evidence from The Oxford Programme for Immunomodulatory Immunoglobulin Therapy, which was set up to review multifocal motor neuropathy (MMN) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) treatment with immunoglobulin.	This approach is supported by evidence from The Oxford Programme for Immunomodulatory Immunoglobulin Therapy, which was set up to review multifocal motor neuropathy (MMN) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) treatment with immunoglobulin.	General notes p36	Clarity		
The demonstration of continued IVIG requirement by forced suspension on more than 2 or 3 occasions over a 5-year period probably indicates ongoing long-	The demonstration of continued IVIg requirement by forced suspension on more than 2 or 3 occasions over a 5-year period probably indicates	General notes p36	Consistency		

term dependence and further withdrawals are highly unlikely to be effective.	ongoing long-term dependence and further withdrawals are highly unlikely to be effective. Referral to a specialist neurology centre is recommended as early as possible				
	Appendix B – Not Routinely Commissioned Indications The Ig Expert Working Group (EWG) concluded that there was either insufficient evidence to support the routine commissioning of Ig to treat the following indications or that there was evidence to support a not routinely commissioned position: • Acquired red cell aplasia NOT due to parvovirus B19 • Adrenoleukodystrophy • Alzheimer's disease • Amyotrophic lateral sclerosis • Aplastic anaemia NOT due to parvovirus	p37	Clarity		

	infection • Asthma • Atopic dermatitis/eczema • Autoimmune neutropenia • Autologous BMT • Cerebral infarction with antiphospholipid antibodies • Chronic facial pain • Chronic fatigue syndrome • Chronic idiopathic urticaria • Chronic immune thrombocytopenia (ITP) • Chronic regional pain syndrome • CNS vasculitis • Critical illness neuropathy • Diabetic neuropathy • Graves' ophthalmopathy • Haemolytic uraemic syndrome • Immunodeficiency secondary to paediatric HIV infection • Inclusion body myositis • Intractable childhood				

	epilepsy • IVF failure • Multiple sclerosis • Neonatal sepsis (prevention or treatment) • Opsoclonus-myoclonus syndrome - adult carcinoma related • Paediatric myocarditis • PANS/PANDAS • Paraneoplastic syndromes not known to be T or B cell mediated • POEMS (polyneuropathy organomegaly, endocrinopathy/oedema, monoclonal protein, skin changes) • Pyoderma gangrenosum • Recurrent spontaneous pregnancy loss • Rheumatoid arthritis • Sepsis in the intensive care unit not related to specific toxins or C. difficile • SLE with secondary immunocytopenias • Systemic juvenile idiopathic arthritis				

	• Toxic epidermal necrolysis, including Steven Johnson Syndrome				