Title of policy or policy statement:	Commissioning Criteria Policy for the use of therapeutic immunoglobulin (Ig) England, 2021
Programme of Care:	Blood and Infection

Background

The clinical commissioning policy proposition for the use of therapeutic Immunoglobulin in England was supported by Clinical Panel on 16th June 2021. Clinical Panel recommended that this proposition is returned to a future meeting once the proposition had been through a stakeholder testing and PPVG for comment with any suggested changes addressed, before the final sign off.

Stakeholder Testing

The policy proposition was sent for stakeholder testing for 2 weeks from 2nd to 16th July 2021. There were 34 responses received with 76% of them supporting the proposition (59% fully supported the proposition a further 18% supported the proposition with suggested changes). There were 20% of respondents who did not support the proposition.

As a result of stakeholder testing, the following changes were made to the clinical commissioning policy:

Stakeholder Comment	Amendment
Cochrane is only any good if there are enough patients for a study to be meaningful. I suggest where the logic looks sensible, based on our understanding of the mechanism of a rare condition, the same approach as NICE has with new TAs in a similar situation- give it a go and review until it's obvious Are conditions in Grey disproportionately common in certain ethnic groups?	Action: MDSAS data will be reviewed and findings reported to the Ig Clinical expert working group and CRG with any recommendations on changes in policy will be updated in line with recommendations. MDSAS data will be analysed for ethnic groups to ensure any possible inequality in access is identified.
For CIDP, please consider using the latest revision of the diagnostic criteria for CIDP which is just about to be published simultaneously in both the European Journal of Neurology and the Journal of the peripheral nervous system European Academy of Neurology/Peripheral Nerve Society Guideline on diagnosis and	Action: The CRG will review the document as per NHSEI policy review process or when there is a significant change in evidence.

treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force - Second Revision - PubMed (nih.gov) The 'probable CIDP' category no longer exists so IVIG commissioning should require a diagnosis of 'CIDP' according to these revised criteria "	
The policy states that 'in patients with refractory disease associated with myositis-specific antibodies, rituximab has been approved as a second line treatment by NHS England'. That is only true for adults; children do not meet the criteria to access rituximab, leaving no second-line treatment available if IVIG is not approved.	The NHS England policy for rituximab is for adults; however, it is available Action: In adult patients (and post-pubescent children through the NHSE Medicines for Children policy) with refractory disease associated with myositis-specific antibodies, rituximab (or biosimilar) has been approved as a second…" NHS England » Commissioning Medicines for Children in Specialised Services
Use of PLEX in Guillain Barre syndrome (GBS). GBS is a common indication for Ig but there is evidence to support PLEX as equivalent first line treatment. Where PLEX is easily available and where there are no contra-indications, PLEX should be considered	PLEX is equally efficacious as IVIg in GBS and should be preferentially considered where it is clinically appropriate and easily accessible. The policy proposition has been amended to include: 'Position of Ig ……..' in the CCP and IMP; PLEX is equally efficacious as IVIg in GBS and should be preferentially considered where it is clinically appropriate and easily accessible.
The wording regarding 2nd dosing in GBS should be more emphatic re lack of efficacy.	Agreed – amend guidance to 2nd doses of IVIg are not effective in the treatment of GBS and may be associated with real potential harm (Lunn MP. Preventing expensive harms in GBS. Lancet Neurology 2021;20:249-251). The policy proposition has been amended to: "Second doses of g are not effective in the treatment of GBS and may be associated with real potential harm (Lunn MP. Preventing expensive harms in GBS. Lancet Neurology 2021;20:249-251)".
Secondary antibody deficiency outcomes measures should included treatment	Agreed. The policy proposition secondary antibody deficiency

courses of antibiotics (similar to PID indications).	outcomes measures have been amended to include: Treatment courses of antibiotics
As a general principle, where conditions apply to children, relevant paediatric assessment tools should be applied.	Agreed. The policy proposition has been amended to include: For Dermatomyositis (juvenile – JDM); • MMT-8 • CMAS score • CK for baseline and asses how a patient has improved after each infusion or at least after 3 infusions. • PGALs is used to assess how many inflamed or swollen joints a patient has.
For myositis: Concern as to why CDASI chosen as the only skin score and would advise (since no proven validated benefit of this score above others) to state "skin assessment score such as CDASI, CAT or DAS' HAQ should be changed to HAQ or CHAQ to include the childhood score.	Agreed. The policy proposition has been amended to include: CDASI, CAT or DAS' HAQ should be changed to HAQ or CHAQ to include the childhood score
ANCA-associated systemic vasculitides (AAV): Suggest BVAS changed to BVAS/PVAS to capture paediatric assessment tool	Agreed. The policy proposition has been amended to: BVAS changed to BVAS/PVAS to capture paediatric assessment tool.
The advice to use IVIg in paediatrics is based on small numbers of cases given the rarity in this condition. There are very small number of cases and not all are children nor in paediatric services. As PIMS-TS occurs in adults please include these adults in this section. If an upper age limit in adults is to be considered this should be stated. As these diagnoses are difficult wording could be "clinical diagnosis of PIMS-TS by a paediatrician, paediatric infectious disease consultant or paediatric immunologist " and for adults " clinical diagnosis of PIMS-TS in an adult (also known as MIS-A or AIMS-TS) by an infectious diseases consultant or immunologist or appropriate specialist MDT	Agreed. The policy proposition has been amended to: clinical diagnosis of PIMS-TS by a paediatrician, paediatric consultant in infection or paediatric immunologist " and for adults " clinical diagnosis of PIMS-TS in an adult (also known as MIS-A or AIMS-TS) by consultant in infection or immunologist or appropriate specialist MDT".
There is no mention of infection specialists (infectious diseases or microbiologists) in the eligibility criteria except paediatric infectious diseases in PIMS-TS. We presume this is an inadvertent oversight and please add this to the final version.	Infectious Disease expertise is rarely required for the diagnosis and management of VITT. There is clear guidance on all aspects of VITT from the Expert Haematology panel under the auspices of the BSH. The

Consultants in infection (this term could be used broadly to cover consultants in microbiology, infectious diseases, virology and paediatric infectious diseases) would be expected to be involved in the eligibility discussions for all infections listed in the section 'Use of Immunoglobulin in Infectious Diseases' and this should be specifically stated to ensure access is not arranged without local clinician engagement and appropriate discussions and accurate diagnosis. Infectious diseases consultants may diagnose Haemophagocytic syndrome and we suggest for this section 'consultant rheumatologist or haematologist or infectious diseases consultant' (the expectation is 2-3 of these should be involved in an MDM decision) and VITT (the expectation would be haematologist with infection input).	policy proposition has been changed to: consultant rheumatologist or haematologist or consultant in infection (the expectation is 2-3 of these should be involved in an MDT decision). For VITT (the expectation would be a haematologist following expert panel guidelines).
Indications that are approved by PHE only require retrospective panel approval (as long as PHE have approved first).	Prior panel approval is not required if usage has been discussed with PHE. The policy proposition has been amended to: prior approval is NOT required.
For AIE in paediatrics on PICU we do not use prednisolone as stated as 1st line but rather IV methylpre	Agreed. The policy proposition has been amended to: prednisolone/Methylprednisolone
The criteria for starting PID patients is inadequate. More specific eligibility criteria is required (as per haematology/neurology criteria).	In newly diagnosed patients with PID with no significant burden of infection, the decision to start Ig replacement should be based on an MDT discussion. The table in the policy proposition has been amended to: In newly diagnosed patients with PID with no significant burden of infection, the decision to start Ig replacement should be based on a MDT discussion.
Lower threshold for IVIg use in ITP " "Haemoglobin values should be in g/l not g/dl (e.g. p14 6g/dL should be 60g/L - this changed in 2013)	Agreed. The haemoglobin values in the policy proposition has been amended to be in g/l not g/dl (e.g. p14 6g/dL should be 60g/L)
Reviewed Immunology indications only Sec ondary antibody deficiency outcomes measures should included treatment courses of antibiotics (similar to PID indications).	Action: To include: "Treatment courses of antibiotics" to secondary antibody deficiency outcomes measures

We would wish for viral pneumonitis post-transplantation to be included within the list of indications that can be given without prior SR-IAP approval	When this is not possible in a timely manner treatment should proceed and approval obtained. The introduction of the policy proposition has been amended to include: 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 also be able to advise on dose optimisation and trials of treatment withdrawal
Page 15 Acute idiopathic/autoimmune dysautonomia/ganglionopathy. “Acute onset autonomic failure with presence of nicotinic pre-ganglionic acetylcholine (muscarinic) antibodies”. This is a bit muddled. I think this should instead say “ganglionic (alpha3) acetylcholine receptor antibodies” and delete pre-ganglionic and delete muscarinic.	Agreed. The policy proposition has been amended to: Acute onset autonomic failure with presence of nicotinic pre-ganglionic acetylcholine (muscarinic) antibodies” to “ganglionic (alpha3) acetylcholine receptor antibodies”
Delayed haemolytic infusion reaction-position of IVIg- Rituximab is now commissioned for this indication-is this to be included in the commissioning criteria as not clear from guidelines that Rituximab could be given before IVIg.	Agree. The policy proposition has been amended to align to the NHS England policy for treatment and prophylaxis: https://www.england.nhs.uk/publication/rituximab-and-eculizumab-for-the-prevention-and-management-of-delayed-haemolytic-transfusion-reactions-and-hyperhaemolysis-in-patients-with-haemoglobinopathies/
Haemolytic disease of the foetus and newborn - disparity between NHSE commissioning criteria for Ig and NICE guidelines. NHSE criteria is broader than NICE guidelines which state “ use IVIG as an adjunct to continuous intensified phototherapy in cases of rhesus haemolytic disease or ABO haemolytic disease when the serum bilirubin continues to rise by more than 8.5 micromol/litre per hour” versus NHSE guidelines which just states rising bilirubin, are there any plans to align with NICE on this?	Agree. The policy proposition has been amended to align to the NICE guideline.(CG98)