
Guideline

Clinical guideline for immunoglobulin treatment: East of England Immunoglobulin Assessment Panel

1 Scope

This clinical guideline outlines the following standards by indication:

- Patient selection criteria
- Exclusion criteria (when not to treat)
- Place of immunoglobulin treatment vs. alternative therapies
- Dosing recommendations
- Clinical and laboratory outcomes to be assessed for efficacy
- Actions required for clinical approval by panel

Trust-wide in all named Trusts affiliated in with the East of England Immunoglobulin Assessment Panel:

- Bedfordshire Hospitals NHS Foundation Trust
 - Excluding Luton and Dunstable University Hospital
- Cambridge University Hospitals NHS Foundation Trust
- East & North Hertfordshire NHS Trust
- East Suffolk and North East Essex NHS Foundation Trust
- James Paget University Hospitals NHS Foundation Trust
- Mid and South Essex NHS Foundation Trust
- Norfolk & Norwich University Hospitals NHS Foundation Trust
- North West Anglia NHS Foundation Trust
- Princess Alexandra Hospital NHS Trust
- Queen Elizabeth Hospital Kings Lynn NHS Trust
- Royal Papworth Hospital NHS Foundation Trust
- West Suffolk Hospital NHS Foundation Trust

2 Purpose

This guideline outlines the standards for best clinical practice with immunoglobulins. This includes ensuring standardised:

- Selection criteria for treatment per indication
- Exclusion criteria for treatment per indication
- Doses align with national commissioning and clinical advice
- Understanding for prescribers for expected monitoring outcomes per indication

This guideline reflects and adds to the [latest commissioning guidelines from NHS England and the Department of Health](#). As such all NHS prescribing of immunoglobulins within the jurisdiction of the East of England Immunoglobulin Assessment Panel should follow the advice in this guideline or by agreement with the East of England Immunoglobulin Assessment Panel. Prescribing of immunoglobulins is restricted to approved indications where clinical teams consent to record listed baseline and outcomes data for approved measures. This data facilitates the evaluation of the efficacy of immunoglobulin treatment for short-term indications and the continuing need for therapy at annual reviews, including the review of dosing regimens.

3 Definitions

ABW	actual body weight
ALK	alkaline phosphatase
CLL	chronic lymphocytic leukaemia
DDW	dose determining weight
ENRAD	Eastern Network of Rare Autoimmune Diseases
EOEIAP	East of England Immunoglobulin Assessment Panel
FBC	full blood count
fSCIG	facilitated subcutaneous immunoglobulin (with hyaluronidase)
g/Kg	grams per kilogram of body weight
Hb	haemoglobin
HSCT	haematopoietic stem cell transplant
IBW	ideal body weight
IEI	inborn errors of immunity
IgA	immunoglobulin type A
IgG	immunoglobulin type G
IgM	immunoglobulin type M
IM	intramuscular
IVIG	intravenous immunoglobulin
LFT	liver function test
MDT	multi-disciplinary team
MM	multiple myeloma
NHL	non-Hodgkin's lymphoma
NHSE	NHS England
NICE	National Institute for Health and Care Excellence
PCR	polymerase chain reaction
PID	primary immunodeficiencies
SCIG	subcutaneous immunoglobulin
TSS	toxic shock syndrome
WCC	white cell count

4 Undertaken by (staff groups)

All staff involved in any of the following aspects of immunoglobulin management:

- prescribing
- monitoring of clinical outcome(s) of therapy
- clinically checking and/or dispensing against prescriptions
- adjudication of clinical requests to the EOEIAP

To be used in conjunction with the [Immunoglobulin policy and procedure](#).

5 Inclusion

This guideline covers neonatal, paediatric and adult treatment with immunoglobulins. While most of the indications are expected to be treated with IVIg, some may be treated with SCIg or fSCIG where appropriate training and homecare infrastructure are established. Immunodeficiency (all types), long-term neurology indications and certain infectious disease indications are most suitable for treatment with SCIg.

Appropriate pre-medication (an antihistamine, paracetamol +/- corticosteroid) is expected to be given before commencing immunoglobulin therapy to correct immunodeficiency. Pre-treatment assessment for immunomodulation involves ensuring euvolaemia and assessing VTE risks. Infusion reactions are uncommon in immunocompetent individuals.

Patients with capacity should be provided the regional [Patient Information Leaflet](#) which explains immunoglobulin therapy, the role of the EOE panel and the use of patient data. This should be used to inform the patient consent process before treating.

6 Exclusion

Patients at high risk of thromboembolism (hypertension, diabetes, smoking, hypercoagulable states) should be counselled regarding the prothrombotic risks of immunoglobulin.

Test doses of SCIg are not routinely recommended. These are only indicated in isolated immunodeficiency cases and should be agreed with a consultant immunologist before prescribing.

IgA deficiency is no longer considered a contraindication to the use of immunoglobulin therapy. Measurement of anti-IgA antibodies is not warranted.

Plasmapheresis / plasma exchange, where this is part of the clinical treatment deemed necessary for the condition, should be commenced before immunoglobulin therapy, unless there is a specific agreement in place with the EOE panel. In clinical emergencies where plasmapheresis is indicated but not immediately available, IVIG may be commenced provided:

- only the minimum number of infusions are given prior to plasmapheresis
- IVIG therapy is halted on the day plasmapheresis is due to commence

It is recognised that in some cases, subsequent to plasmapheresis, further IVIG may remain a treatment option. The exposure to IVIG prior to plasmapheresis is not usually factored into post-exchange dosing regimens for IVIG.

This guideline does not provide guidance for any immunoglobulin products other than 'normal' polyvalent immunoglobulin which is predominantly IgG in content.

Specifically it does not provide guidance for:

- IgM-enriched immunoglobulin (e.g. Pentaglobin)
- Hyperimmune immunoglobulins such as:
 - Rabies IgG
 - Tetanus IgG
 - CMV IgG
 - Hepatitis B IgG (Hepatect)
 - Anti-thymocyte immunoglobulin (equine or lapine)
 - Any other specific infection (viral or bacterial) targeted immunoglobulin

7 National guidelines

In March 2025, NHS England published version 2 of the comprehensive Commissioning Guidelines including and updating version 1 (2024).

These documents in turn supersede the 2021 guideline, the 2019 Commissioning Guidance for haematology, neurology and infectious disease indications and the 2nd edition updated clinical guidelines for immunoglobulins published by the Department of Health (2011).

The East of England Immunoglobulin Assessment Panel seeks to provide comprehensive clinical guidelines which reflect best practice. At times this may be following changes to the national commissioning structure, but also before the national guidelines are updated (such as historically with Covid vaccine-induced thrombosis with thrombocytopenia or maternal treatment of alloimmune thrombocytopenia) or advice may reflect augmented good practice advice which supplements the information in the national clinical and commissioning guidance.

The information in this document aims to combine and reflect the latest commissioning and practice advice from each authority.

8 Applications to the East of England Immunoglobulin Assessment Panel (EOEIAP)

Electronic applications can be submitted to:

- add-tr.iap-eastofengland@nhs.net

Forms for application to panel are found on the EOEIAP webpage:

- <https://www.cuh.nhs.uk/health-care-professionals/east-england-immunoglobulin-assessment-panel-oe-iap/>

Application forms can also be accessed via direct URL links:

- [Immunoglobulin Clinical Application Request](#)
- [Immunodeficiency Clinical Application Form](#)

For CUH applications:

- Where single panel member approval is required (Class II only), the name of the approving consultant / panel member should be documented on the Immunoglobulin Treatment Request Form and also in Epic.
- Where a panel consensus decision is required (Class III & IV), the approval email should be printed and attached to the accompanying Immunoglobulin Treatment Request Form.

See the Policy and Procedure for Immunoglobulins for further details and responsibilities.

- [Cambridge University Hospitals Immunoglobulins Policy and Procedure](#)
- [CUH Immunoglobulins Policy and Procedure \(external website\)](#)
- Other affiliated Trusts, refer to internal intranet for local policy and procedure

9 Dosing based on weight

All immunoglobulin doses are based on weight for initial dosing.

➤ Immunoreplacement therapy (immunodeficiency)

- Use Actual Body Weight (ABW) then adjust in line with response

➤ Immunomodulation (autoimmune disease)

- In adults (for the majority of cases)
 - Use Dose Determining Weight (DDW)
 - Use ABW if <154cm, if <60kg OR if IBW > ABW
- In pregnancy, use the Booking Weight to calculate the Dose Determining Weight (DDW)
- In paediatrics, use the Actual Body Weight, unless both height >154cm and weight >60kg. Where the threshold for height and weight are reached or exceeded, use DDW.

$$\text{DDW} = \text{IBW} + 0.4(\text{ABW} - \text{IBW})$$

$$\begin{aligned} \text{IBW} &= \{\text{males}\} \quad [(\text{height}(\text{cm}) - 154) \times 0.9] + 50 \\ &= \{\text{females}\} \quad [(\text{height}(\text{cm}) - 154) \times 0.9] + 45.5 \end{aligned}$$

Total doses per treatment must use whole vials. Round calculated doses down to the nearest whole vial. For IVIg, this will mean rounding down to the nearest 5g.

Worked example for ♂ 84kg 170cm with GBS (2g/kg over 5 days)

$$\text{IBW}(\text{kg}) = (170 - 154) \times 0.9 + 50 = 64.4$$

$$\text{DDW} = 64.4 + 0.4(84 - 64.4) = 72.24$$

$$@2\text{g/kg} = 144.48 \dots \text{round down to nearest 5g} = 140\text{g}$$

Days 1-3: 30g, Days 4-5: 25g

Please note that the use of ideal body weight for all immunoglobulin indications is not implemented in the East of England.

10 Classification of indications

Historical classifications of indications into RED, BLUE, GREY and BLACK no longer exist. Treatment nationally is now either 'commissioned' or 'not commissioned', however the approval process for all indications except those which both 1) threaten life or limb and 2) demonstrate clear efficacy of IVIg over other treatment (i.e. Class I indications) require approval from the EOE Panel **prior** to treatment.

Indications in neither 'commissioned' nor 'not commissioned' categories are classified as '**not routinely commissioned**' and require 1) **clinical approval** from the EOE Panel and 2) **funding approval** from NHS England via the IFR application process **prior** to treatment.

Classifications are divided into Class I to V in order help the panel and clinicians to prioritise treatment and IVIg stocks to those who are most likely to benefit from treatment, as detailed in [Indication Classification](#).

11 Emergency treatment of conditions with high risk of mortality or morbidity; Class I

Treatment with IVIG may proceed without prior approval from the EOE Panel in the following conditions, where the [stated inclusion criteria](#) are met and;

- Alternative treatment is known to be clinically inferior, is contra-indicated or is not available.
- Failure to administer IVIG in a timely manner would risk life or limb
- The need for treatment is established by a consultant with specialist knowledge of the condition to be treated

Note: All Class I treatment must be notified retrospectively to the EOE panel. Pharmacists must ensure consultant approval and appropriate Class I indication prior to supply.

Class I indications

- Acute ITP with significant bleeding or the urgent need for emergency surgery
 - First dose only
- Autoimmune haemolytic anaemia (AHA) including Evans syndrome
- Coagulation factor inhibitors (allo- and autoantibodies)
 - Treatment may commence pending panel decision
- Haemolytic disease of the newborn

- Neonatal alloimmune thrombocytopenia (NAIT)
- Post-transfusion hyperhaemolysis
 - Treatment or prevention
- Post-transfusion purpura
- VITT (post Covid-vaccine)
 - First dose only
- Guillain-Barré syndrome
 - Respiratory and/or bulbar failure and PLEX not available
- Myasthenia Gravis
 - Myasthenic crisis (respiratory and/or bulbar failure)
- Hepatitis A
- Measles (if immunosuppressed or pregnant)
- Polio
- Staphylococcal or streptococcal toxic shock syndrome
- Tetanus prone injury or suspected Tetanus
 - See also place of tetanus Ig in therapy
- Kawasaki disease

All other indications require individual approval by the EOE panel **prior** to treatment. Failure to obtain the appropriate approval risks the ability to continue treatment and notification to NHS England who may withhold the reimbursement of costs.

12 Indication classification

Class I indications	• Short-term indications only – typically a single course with further treatment subject to panel approval (class II) • Immunoglobulin is the accepted first-line treatment (either alone or in combination with other treatments). • No alternative treatment is possible or available • Life/limb threatening or patient may incur harm if treatment is delayed. • Patients must be assessed by the treating <u>consultant</u> as meeting set clinical eligibility criteria ○ See indication specific treatment guidelines below • EOEIAP approval is not required for initial treatment providing an appropriate medical consultant specialist in the field of medicine for the indication has confirmed the minimum eligibility criteria are met. ○ EOEIAP requires <u>notification of treatment</u> for all indications including retrospectively for Class I ○ EOEIAP approval is required for re-treatment. • Out of hours treatment permitted for specified life/limb threatening indications • During shortages – to be available at all times because of risk to life or high likelihood of harm. • Response to treatment must be assessed against criteria, documented and made available to EOEIAP as required.
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Class II indications	• Acute or chronic treatment as per indication where alternative treatment may be possible, but evidence supports efficacy of immunoglobulins • Risk of harm from a short delay of access to treatment is low, or following initiation of class I treatment where further treatment is deemed necessary • Proposal to treat must originate from the treating consultant/ consultant specialist in the field of medicine for the indication. • Patients must be assessed as meeting set treatment criteria. ○ See selection criteria for indication • Clinical approval from EOEIAP is required before treatment may commence. ○ Do not consent patients for treatment with immunoglobulins until clinical approval is granted. ○ Triage to the appropriate EOEIAP SubPanel is the favoured mechanism for approval (immunology IAP, neurology IAP, ENRAD MDT or full panel submission). ○ In the absence of a SubPanel, or where there is a risk of deterioration, an individual panel member may approve treatment (± panel pharmacist verification) providing there has been appropriate dialogue – written or verbal – between the requesting consultant and panel expert to assure the panel of the validity of the treatment request and need to use immunoglobulin over alternative treatments. However treatment decisions for Class II indications should involve at least 2 panel members where possible. • Treatment to be assessed against alternative treatment modalities and for long-term treatment plan. • Out of hours treatment is not permitted. • During shortages – use should be reviewed / modified in times of national shortage (eg dose reductions, alternative treatment). • Short-term/ long-term response to treatment must be assessed against criteria, documented and made available to EOEIAP as required.
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Class III Indications	Class III indications are commissioned and funded by NHS England providing there is clear and documented approval by the EoEIAP and where alternative therapy is not feasible or appropriate. Class III indications have LIMITED evidence for efficacy and access to treatment may be restricted during supply shortages. • Proposal to treat must originate from the treating consultant / consultant specialist in the field of medicine for the indication. • Out of hours treatment is not permitted. • IFR submission is not required if the EOEIAP have granted clinical approval for treatment. • During shortages – use should be reviewed/ modified in times of national shortage (eg dose reductions, alternative treatment). • Response to treatment (short- and long-term) must be assessed and reported to East of England IAP meetings. Failure to submit details for panel review may result in clinical approval being revoked. • Clinical criteria to monitor treatment efficacy are required (as agreed by EOEIAP).
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Class IV indications	• Indications that are not included in any version of national clinical guidelines (DH) or national commissioning guidelines (NHSE); i.e. ‘unlisted’ indications or indications formerly listed, but removed from the current NHS England commissioning guideline. • These indications are ‘not routinely commissioned’ • Proposal to treat must originate from the treating consultant/ consultant specialist in the field of medicine for the indication. A second opinion from a consultant within the same specialism is preferred where available. • These indications do not have specified eligibility criteria, dosing strategies or outcome criteria. These should be suggested by the treating clinician at the point of request for review by EOEIAP, subject to modification as necessary. Clinical approval from the EOEIAP is restricted to dosing and monitoring specified at the time of approval. Any treatments approved by the EOEIAP must have patient specific parameters agreed. This detail must be included in the subsequent IFR application. • Uncommissioned indications require both EOEIAP clinical approval and NHS England funding approval or internal funding arrangement prior to treatment* • It is the responsibility of the treating team to submit an IFR for uncommissioned indications. • Out of hours treatment is not permitted. • During shortages – use should be reviewed/ modified in times of national shortage (e.g. dose reductions, alternative treatment). • Response to treatment (short- and long-term) must be assessed and reported to East of England IAP meetings. Failure to submit details for panel review may result in clinical approval being revoked.
Class V indications	• These indications have good quality primary medical literature which confirm immunoglobulin therapy is not effective. • Applications automatically rejected • Not recommended for use

13 Indication specific guidelines

Immunology indications

For all immunodeficiency treatment (all indications for immunoreplacement therapy):

- Use ABW to guide initial dosing
- If using **IVIG**, premedication must be given before the first infusion
 - Antihistamine
 - Paracetamol
 - Plus, an 'as required' order for a corticosteroid
- If there is evidence of an infusion reaction during the first or subsequent doses, further premedication should be considered and the patient should be assessed by clinical immunology

Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Primary immunodeficiencies / Inborn errors of immunity (IEI) associated with significant antibody defects (excluding specific antibody deficiency) LONG TERM	A specific PID (IEI) diagnosis must be established by a clinical immunologist. In newly diagnosed patients with PID (IEI) and no significant burden of infection, the decision to commence Ig replacement should be recommended by immunology sub-panel / MDT.	No	Ig is the only definitive treatment for antibody deficiency	Initially: • 0.4-0.6 g/kg/month ABW; Dose requirements may increase or decrease within the range 0.2-0.8g/kg/month and should be based on clinical outcome. EOEIAP: Use ABW for initial dosing.	Raised: • Trough IgG level compared to baseline. Reduction in: • Number of infections • Days in hospital • Treatment courses with antibiotics	A single dose may be given at the discretion of the consultant immunologist prior to panel review. All patients must be discussed at Immunology MDT (panel

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						subgroup) at the start of maintenance treatment and for periodic review thereafter. Class II indication (non-emergency)
Haematopoietic stem cell transplant (HSCT) in primary immunodeficiencies (PID) / inborn errors of immunity (IEI) LONG TERM	PID patients undergoing HSCT	No	Ig is the only definitive treatment for antibody deficiency	Initially: • 0.4-0.6 g/kg/month; Dose requirements may increase or decrease and should be based on clinical outcome. Because of the possibility of B-cell reconstitution, evaluation of immune function (off Ig) is required at 2 years. EOEIAP: Use ABW for initial dosing.	• Raised trough IgG level compared to baseline.	All patients must be discussed at EOE Immunology MDT at the start of treatment and for periodic review thereafter. Class II indication (non-emergency)

Specific antibody deficiency LONG TERM	Diagnosis by a clinical immunologist - Severe, persistent, opportunistic or recurrent bacterial infections despite continuous oral antibiotic therapy for 6 months - Documented failure of serum antibody response to unconjugated pneumococcal or other polysaccharide vaccine challenge	None, but see comments in column of position of immunoglobulin	Many patients with specific antibody deficiency will achieve protection from bacterial infections with prolonged antibiotic prophylaxis. Ig is reserved for those patients in whom antibiotic prophylaxis proves to be ineffective.	Initially: 0.4-0.6 g/kg/month for a period of 6 to 12 months; Long-term maintenance treatment should be based on clear evidence of benefit from this trial and requires EOEIAP approval. Dose requirements may increase and should be based on clinical outcome. EOEIAP: Use ABW for initial dosing.	6 monthly reviews (compared to baseline) Raised: - Trough IgG level compared to baseline. Reduction in: - number of infections - days in hospital - treatment courses with antibiotics Database parameters will include entry of number of infections and days in hospital pre-treatment and 6 monthly thereafter.	All patients must be discussed at EOE Immunology MDT at the start of treatment and for periodic review Class II indication (non-emergency)
Secondary antibody deficiency LONG TERM	- Underlying cause of hypogammaglobinaemia cannot be reversed or reversal is contra-indicated; OR: - Hypogammaglobinaemia associated with drugs including emerging bispecifics, therapeutic monoclonals targeted at B cells and plasma cells (rituximab and other anti-CD20, CD19 agents,	None, but see comments in column of position of immunoglobulin	Many patients with specific antibody deficiency will achieve protection from bacterial infections with prolonged antibiotic prophylaxis. Ig is reserved for those patients in whom antibiotic prophylaxis proves to be ineffective. Since infection susceptibility in patients with haematological	Initially: 0.4-0.6 g/kg/month; Dose should be modified to achieve an IgG trough level of at least the lower limit of the age-specific serum IgG reference range. EOEIAP: Use ABW for initial dosing.	6 monthly reviews (compared to baseline) Raised: - Trough IgG level compared to baseline. Reduction in: - number of infections - days in hospital - treatment with antibiotic courses	All patients must be discussed at EOE Immunology MDT at the start of treatment and for periodic review Class II indication (non-emergency)

	daratumumab etc.) post-HSCT, NHL, CLL, MM or other relevant B-cell malignancy confirmed by a haematologist; AND: a) Recurrent or severe bacterial infection despite continuous oral antibiotic therapy for 6 months b) IgG <4g/L* (excluding paraprotein) c) Documented failure of serum antibody response to unconjugated pneumococcal or other polysaccharide vaccine challenge. NOTE: It is recognised that vaccine challenge may be of limited value in patients with very low serum IgG (<3g/L). In these circumstances vaccine challenge may be omitted if it is considered inappropriate clinically. *It is acknowledged that not all of the above criteria (a-c) will need to be fulfilled for an individual patient.		malignancies is frequently multifactorial, the reduction in overall burden of infections with long term Ig replacement therapy may be variable. For this reason biannual reviews of treatment are recommended. In patients with seasonal preponderance of infections, it may be appropriate to consider temporary cessation of Ig in the summer.		Database parameters will include entry of number of infections and days in hospital pre-treatment and 6 monthly thereafter.	
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	*IgG <4g/L – not specific for paediatric patients. In patients developing hypogammaglobinaemia associated with B-cell aplasia as a consequence of Chimeric Antigen Receptor – T-cell therapy (CAR-T cells) targeted against B cell or plasma cell antigens, the prophylactic use of Ig in the absence of a burden of severe infections and vaccine challenge may be appropriate. • Use of Ig post-CAR-T therapy in B-cell acute lymphoblastic leukaemia (B-ALL) Because of the severity of B-cell aplasia and the longer time required for reconstitution, it is anticipated that virtually all patients (children and adults) with B-ALL will initially require Ig replacement following CAR-T cell therapy. As with the use of Ig post-CAR-T therapy in B-cell lymphoma, continued use of IgG					
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	replacement therapy should be reviewed at regular intervals based on B-cell recovery, serum immunoglobulins and burden of infection. • Use of Ig post-CAR-T cell therapy in B-cell lymphoma The need for immunoglobulin replacement in patients receiving CAR-T cell therapy for B-cell lymphoma is variable ranging between 31% to 64% in published studies⁶ highlighting faster B-cell recovery in this group in contrast to patients with B-cell acute lymphoblastic leukaemia. • Use of Ig at inception of bi-specific antibody treatment in patients with myeloma and B-cell lymphoma Many patients in these disease groups will have a low serum IgG at baseline due to previous chemo-immunotherapy, including CD20- and CD38 depleting agents.					
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	The prophylactic use of Ig would be appropriate in patients with a serum IgG <4g/L at the time of commencement of a bi-specific antibody. *There is variable practice regarding Ig replacement in adult patients with hypogammaglobinaemia post-HSCT for haematological malignancy. The American Society for Blood and Marrow Transplantation and the Canadian Blood and Marrow Transplantation group have jointly stated: 'Do not routinely give Ig replacement to adult HSCT patients in the absence of infection regardless of the Ig level'. It is possible that patients with recurrent sino-pulmonary infections on a background of chronic pulmonary GVHD and hypogammaglobinaemia may benefit from Ig replacement therapy if they fulfil the criteria for secondary antibody deficiency.					
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Thymoma with immunodeficiency LONG TERM	- Profound B cell depletion AND / OR - Significant antibody deficiency	None	Ig is the only definitive treatment for antibody deficiency	Initially: • 0.4-0.6 g/kg/month; Dose requirements may increase and should be based on clinical outcome. EOEIAP: Use ABW for initial dosing.	Raised: • Trough IgG level compared to baseline. Reduction in: • Number of infections, • Treatment courses of antibiotics, • Days in hospital	All patients must be discussed at EOE Immunology MDT at the start of treatment and for periodic review Class II indication (non-emergency)
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*There is controversy regarding Ig replacement in adult patients with hypogammaglobinaemia post-HSCT for haematological malignancy. The American Society for Blood and Marrow transplantation and the Canadian Blood and Marrow Transplant group have recently states as follows:

“Don’t routinely give Ig replacement to adult HSCT recipients in the absence of recurrent infections regardless of the IgG level”
(Bhella et al. Choosing Wisely BMT. *Biol Blood Marrow Transplant* 2018; 24: 909-913.

It is possible that patients with recurrent sino-pulmonary infections on a background of chronic pulmonary GvHD and hypogammaglobinaemia may benefit if they fulfil the criteria for secondary antibody deficiency.

Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Haematological indications						
Acquired red cell aplasia associated with chronic parvovirus B19 infection SHORT TERM	Parvovirus B19 infection: - Parvovirus B19 infection confirmed by PCR, AND - Evidence of high viral load, usually above 109 IU/ml In cases of foetal hydrops: - Likely to be associated with parvovirus B19	Infection other than parvovirus B19	Immunoglobulin is an adjunct to transfusion. Chronic parvovirus infection generally occurs on a background of immunosuppressive therapy, primary or HIV-related immunodeficiency and may resolve with a reduction in immunosuppression. Acute parvovirus infection associated with transient aplastic crisis requires urgent transfusion rather than immunoglobulin.	1g/kg to 1.2g/kg in divided doses. This may be repeated on relapse and for a 2 nd relapse. EOEIAP: Use DDW for dosing.	- Rise in haemoglobin - Rise in reticulocyte count - Transfusion independence	Apply to EOEIAP Out of hours No. Class II indication
Alloimmune thrombocytopenia - Foetal-maternal (FMAIT)	<u>Prevention or treatment of foetal thrombocytopenia or haemorrhage:</u> Clinical suspicion of FMAIT in the antenatal setting based on clinical and laboratory features: Unexplained previous foetal death, haemorrhage,	None	FMAIT Immunoglobulin is the primary treatment and sometimes combined with steroids.	Maternal: The dose of IVIG and the gestation at which to start treatment should be tailored according to the history of NAIT in earlier pregnancies. A patient with a low-risk obstetric history (where the	Successful outcome of pregnancy – i.e. no severe haemorrhage such as intracranial haemorrhage Platelet count above $50 \times 10^9/L$ at time of delivery.	FMAIT – apply to EOEIAP Class II indication Out of hours No

	hydrocephalus or thrombocytopenia or known affected sibling, AND The presence of maternal platelet-specific alloantibodies directed against current paternal antigens (most commonly HPA-1a or HPA-5b).			previous infant had thrombocytopenia but no intracranial haemorrhage) should be commenced on 0.5g-1.0g/kg/week from 20 weeks gestation. In high-risk pregnancies, treatment should commence from as early as 12 weeks' gestation with a dose of 1g/kg/week (where the previous foetus or neonate had intracranial haemorrhage after 28 weeks gestation), or 2g/kg/week (where the previous foetus or neonate had intracranial haemorrhage before 28 weeks). ⁸⁻¹² Monitor for IVIG-associated haemolysis in all patients but especially those with the blood groups: A, AB or B EOEIAP: Use DDW based on 'booking weight' for dose calculations in the	Increment in neonatal platelet count.	
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				treatment of pregnant patients.		
Alloimmune thrombocytopenia - Neonatal (NAIT)	<u>Prevention or treatment of neonatal thrombocytopenia or haemorrhage:</u> Clinical suspicion of NAIT in the neonatal setting based on clinical features suggestive of bleeding e.g. • Purpura AND/OR • Bruising AND/OR • More serious bleeding AND • Low platelet count.		NAIT First line treatment is with HPA-1a/5b – negative platelets which covers 95% of HPA incompatibilities responsible for NAIT. Platelet transfusion is effective immediately. In contrast, immunoglobulin is a second-line treatment and works in approximately 75% of cases. It has a delayed effect over 24-48 hours. Immunoglobulin may be of value if there is a prolonged thrombocytopenia with the aim of minimising the need for platelet transfusions.	Neonatal: Use ABW dosing in line with specialist paediatric advice. 1g/kg; a 2 nd dose may be required if thrombocytopenia persists. In the rare event of retreatment after the 2 nd dose, seek approval from EOEIAP.		Consultant may approve up to TWO treatments Class I indication Subsequent doses – Class II indication Out of hours Neonatal treatment only
Autoimmune haemolytic anaemia (AHA) including Evans syndrome SHORT TERM	AHA – including Evans syndrome • Symptomatic or severe anaemia, except in patients with co-morbidities, AND	None	Immunoglobulin is reserved for patients unresponsive to steroids or where steroids are contraindicated.	1-2g/kg divided over two to five days. This may be repeated on relapse and for a 2 nd relapse. EOEIAP:	Rise in haemoglobin Transfusion independence Reduction in haemolysis	Consultant may approve – for treatment of acute episodes

	• Refractory to conventional treatment with corticosteroids OR • Corticosteroids contraindicated, OR • As a temporising measure prior to splenectomy AHA in pregnancy: • Pregnant women / patients with warm AHA refractory to corticosteroid OR with evidence of foetal anaemia • Neonates of mothers with AHA who have evidence of haemolysis AND rising bilirubin despite intensive phototherapy.			Use DDW for dosing in adults, ABW in infants or DDW based on booking weight in pregnancy.	markers (bilirubin, lactate dehydrogenase)	Apply to EOEIAP for repeat courses Out of hours No – unless emergency First dose Class I indication Subsequent doses – Class II indication
Coagulation factor inhibitors* (alloantibodies and autoantibodies) Including Acquired von Willebrand disease (vWD) SHORT TERM	• Life- or limb-threatening haemorrhage, AND • Failure to respond to other treatments, AND/OR • Prior invasive procedure Treatment is directed by the haemophilia centre at which the patients is registered	Acquired VWD associated with IgM monoclonal gammopathy	Immunoglobulin is a therapeutic option in acquired VWD, particularly in cases associated with an IgG monoclonal gammopathy alongside other therapies – plasmapheresis, desmopressin, VWF containing concentrates and recombinant Factor VII.	Either: 0.4g/kg/day for 5 days OR 1g/kg/day for 2 days EOEIAP: Use DDW for dosing.	Rise in factor level Resolution of bleeding Reduction in number of bleeding episodes	Apply to EOEIAP. If life-threatening, can commence treatment while panel decision pending. Out of hours

						No Class II indication
Haemolytic disease of the newborn SHORT TERM	Adjunct to continuous multiple phototherapy in cases of Rhesus haemolytic disease, or ABO haemolytic disease: • Rising bilirubin despite intensive phototherapy (see NICE CG98¹³) • Prevention of foetal haemolytic disease in women / patients with a previous history of this and confirmed red cell antibodies to current paternal or foetal antigens, to delay the need for intrauterine transfusions.	None	Immunoglobulin is an adjunct to phototherapy Also see NICE CG98 guidance ¹³	0.5g/kg over 4 hours EOEIAP: Use ABW for dosing paediatrics	Reduction in bilirubin level Reduced need for exchange transfusion Long-term morbidity	Consultant may approve Out of hours Permitted Class I indication
Haemophagocytic syndrome (Haemophagocytic lymphohistiocytosis or HLH) SHORT TERM	Diagnosis by a consultant haematologist or rheumatologist based on H-score* including: • pyrexia • organomegaly • multiple lineage cytopenias • triglycerides • fibrinogen • ferritin • serum aspartate aminotransferase • haemophagocytosis on	None	Other therapies include IL-1 inhibition (anakinra). Please refer to NHS England policy ¹⁴ . Depending on the underlying cause (e.g. EBV reactivation or HIV) alternative management following initial treatment with IVIG and corticosteroid may be appropriate.	Initially 2g/kg in divided doses over two to five days with corticosteroid (dexamethasone) as per HLH protocol. This may be repeated on relapse and for a 2 nd relapse, where alternative therapies are not indicated or are contraindicated.	Improvement of cytopenias Survival Improvement of HLH markers – Ferritin / soluble CD25.	Apply to EOEIAP Out of hours No Class II indication

	bone marrow biopsy • long-term pharmacological immunosuppression (*H-score >169 is 93% sensitive and 86% specific for HLH)		Primary HLH may have additional management strategy to prepare for bone marrow transplant.	EOEIAP: Use DDW for dosing. CUH operates an HLH panel. Referrals to the EOE panel for HLH may be triaged for specialist input and management.		
Immune Thrombocytopenic Purpura (ITP) SHORT TERM	Immunoglobulin generally used in only FOUR situations in ITP: 1) Life-threatening bleeding 2) Where an immediate increase in platelet count is required e.g. before emergency surgery or other procedure (see table for target platelet counts) 3) Where the patient is refractory to all other treatment to maintain the platelet count at a level to prevent haemorrhage. It may need to be given every 2-3 weeks during a period where other second line treatments are being tried. 4) Moderate severity bleeding in patient with higher risk of subsequent	None	Thrombopoietin mimetics may be useful substitutes in some patients (e.g. in situation #3) or as an adjunct in other situations. Relevant NICE CG/TA: Romiplostim TA221 Eltrombopag TA293 Fostamatinib TA835 Avatrombopag TA853 Other therapy listed by NICE for later treatments for ITP management include: • Rituximab (not licensed) • Splenectomy • Azathioprine, mycophenolate, ciclosporin, dapsone, danazol.	Acute ITP: 0.8g/kg as a single infusion; not exceeding 1g/kg. EOEIAP: Use DDW for dosing. A 2 nd infusion may be required after 24-48 hours if severe or life-threatening bleeding: e.g. intracranial bleed or pulmonary haemorrhage. Otherwise if a haemostatically adequate platelet count is not achieved, a second dose may be considered at day 5-7 Persistent ITP: While establishing a second line treatment, 0.8g/kg as a single	Increase in platelet count Resolution of bleeding Reduction in number of bleeding complications	Consultant haematologist may approve 1 st dose for acute ITP; the use of a 2 nd dose should be discussed with the EOEIAP Apply to EOEIAP – for maintenance treatment Out of hours Permitted for first acute treatment Repeat courses require EOEIAP application

	severe bleed. Patients with mucosal bleeding or bleeding from multiple sites or a previous history of severe bleeding are at higher risk of a subsequent severe bleed. These eligibility criteria are also applicable when considering the short-term use of Ig in patients with Chronic ITP experiencing acute bleeding or requiring invasive procedures. Bleeding severity is defined by the “Updated international consensus report on the investigation and management of primary immune thrombocytopenia 2019”¹⁵ Target platelet counts for surgery* <table><tr><td>Procedure</td><td>Platelet count</td></tr><tr><td>Dentistry</td><td>>20</td></tr><tr><td>Simple dental extraction</td><td>>30</td></tr><tr><td>Complex dental extraction</td><td>>50</td></tr><tr><td>Regional dental</td><td>>30</td></tr></table>	Procedure	Platelet count	Dentistry	>20	Simple dental extraction	>30	Complex dental extraction	>50	Regional dental	>30		Refer to specialist regional ITP services for specific guidance regarding chronic management.	infusion every 2-3 weeks (depending on response)		First dose Class I indication 2nd dose for subsequent relapse (<3 months) or dosing while establishing 2nd agent Class II indication Long-term dosing as sole agent Class IV indication
Procedure	Platelet count															
Dentistry	>20															
Simple dental extraction	>30															
Complex dental extraction	>50															
Regional dental	>30															

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	block						
	Minor surgery	>50					
	Major surgery	>80					
	Major neurosurgery	>100					
	PLT units x 10 ⁹ per litre.						
	ITP in pregnancy: Maintenance treatment with Ig may be required antenatally to maintain platelets to maintain platelets above 20x 10⁹/L and/or to increase platelets to over 50x10⁹/L for delivery in women / patients with symptomatic persistent or chronic ITP where other treatments have failed. *There is controversy regarding the target platelet count for epidural anaesthesia¹⁶. There are no data to support a minimum platelet count and each case must be carefully considered. In the absence of bruising, bleeding history, anticoagulation and if the INR, APTT and fibrinogen levels are normal, a small consensus of obstetric anaesthetists agree no changes to normal practice						

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	are needed until the platelet count drops below $50 \times 10^9/L$.					
Covid vaccine-induced thrombosis and thrombocytopenia (VITT) OR A syndrome of anti-PF4 (platelet factor 4) associated immune-mediated thrombosis and thrombocytopenia. SHORT TERM	Confirmed or probably diagnosis of VITT made by a haematologist conforming to the up-to-date guidance from the Expert Haematology Panel – see British Society for Haematology website for details. Also see NICE NG200 ¹⁷ Acute thrombosis or new onset thrombocytopenia within 28 days of receiving Covid-19 vaccination Also follow Expert Haematologist Panel advice, including investigation of: - FBC: check PLT - Coagulation screen: check fibrinogen and D dimer It is recommended that the online yellow card is completed and this will trigger a request from MHRA for further details. https://coronavirus-yellowcard.mhra.gov.uk/	If >28 days from vaccination, seek advice from EOEIAP Isolated thrombocytopenia or thrombosis: • Reduced PLT count without thrombosis with D dimer at or near normal and normal fibrinogen. • Thrombosis with normal PLT and D dimer.	Treat with intravenous Ig irrespective of the degree of thrombocytopenia urgently, as this is the treatment most likely to influence the disease process. A repeat course of IVIg may be required depending on the clinical course. AVOID platelet transfusion AVOID heparin AVOID thrombopoeitin receptor antagonists unless specifically authorised through the haematology MDT CONSIDER corticosteroid and ANTICOAGULATE with non-heparin based therapy either therapeutically or prophylactically (if no overt thrombosis but thrombocytopenia with raised D dimer) based on advice from the local	Adults and children: 0.8g/kg as a single infusion over 1-2 days; total dose not exceeding 1g/kg. EOEIAP: Use DDW for dosing. A 2nd infusion may be required (e.g. after 24-48 hours) depending on the clinical course.	Increase in platelet count Resolution of bleeding Number of bleeding complications Survival	Consultant haematologist may approve 1st dose. The use of a 2nd dose should be discussed with the EOEIAP before treatment. Out of hours Permitted for first acute treatment Repeat courses require EOEIAP application First dose: Class I indication Subsequent dose(s): Class II indication

			specialist haemostasis team.			
Post-transfusion hyperhaemolysis SHORT TERM	Treatment of acute post-transfusion hyperhaemolysis: Symptomatic or severe anaemia (Hb <60g/L, with evidence of ongoing intravascular haemolysis due to a delayed haemolytic transfusion / hyperhaemolysis). It is recognised that some patients with an Hb >60g/L may require treatment.	None	In combination with steroids, Ig is used as first-line treatment.	2g/kg over 2-5 days (usually over two days) given with IV methylprednisolone EOEIAP: Use DDW for dosing.	Rise in haemoglobin Reduction in haemolysis markers (bilirubin, lactate dehydrogenase) Transfusion independence No haemolysis Maintenance of post-transfusion Hb and 1-3 weeks Avoidance of need for repeated transfusion	Consultant may approve – for treatment of acute episodes Out of hours Yes Treatment - Class I indication
Prevention of haemolysis in patients with a history of transfusion-associated hyperhaemolysis Prevention of delayed haemolytic transfusion reaction SHORT TERM	Symptomatic or severe anaemia (Hb <60g/L, with evidence of ongoing intravascular haemolysis due to a delayed haemolytic transfusion / hyperhaemolysis). It is recognised that some patients with an Hb >60g/L may require treatment. Prevention of haemolysis in those with a history of	See position for Ig therapy	Eculizumab is commissioned as a 2 nd line treatment where 1 st line has failed; Rituximab is recommended as a 3 rd line treatment ¹⁸	1-2g/kg over two to five days given with steroids (usually IV methylprednisolone)		Apply to EOEIAP – for prevention unless emergency Out of hours Yes Prevention - Class I indication

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	transfusion-associated hyperhaemolysis / haemolytic transfusion reaction: Patients who have had previously delayed haemolytic transfusion reactions / post-transfusion hyperhaemolysis OR Who have single or multiple allo-antibodies AND Who may require a blood transfusion.					
Post-transfusion purpura SHORT TERM	- Sudden severe thrombocytopenia 5 to 10 days post-transfusion of blood products, AND - Active bleeding (typically occurs in Caucasian HPA-1a antigen negative females previously exposed to HPA-1a antigen in pregnancy or transfusion)	None	There are now very few cases in UK following the implementation of universal leucocyte-reduction of blood components in 1999.	1-2g/kg in divided doses over two to five days. EOEIAP: Use DDW for dosing.	Increase in platelet count Resolution of bleeding Reduction in number of bleeding complications	Haematology consultant may approve Out of hours Yes Class I indication

Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Neurology indications						
Acute idiopathic/autoimmune dysautonomia/ganglionopathy	- Acute onset autonomic failure with presence of ganglionic (alpha-3) acetylcholine receptor antibodies OR - Acute onset autonomic failure with clinical pattern consistent with above including pupillary involvement but without identifiable antibodies AND - Authorised by specialist autonomic unit	Non-immune causes of autonomic failure (for example primary autonomic failure (PAF) without pupillary involvement, MSA multisystem atrophy, diabetes mellitus).	IVIG may be required to obtain rapid control, but may be substituted for by prednisolone, MMF, plasma exchange or other immunosuppressants which are preferable in the longer term	2g/kg over 5 days initially repeated at 6 weeks then titrated to optimal interval and minimum dose to achieve stability Annual reassessment with IVIG suspension as necessary EOEIAP: Use DDW for dosing.	- Postural BP drop reduction with improved activities of daily living - Increase in time to significant postural BP drop - Reduction numbers of syncopal and pre-syncopal episodes - Reduced oral dryness score - Reduced diarrhoea and constipation frequency	Apply to EOEIAP Out of hours No Class II indication
Autoimmune encephalitides (AIE) (antibody associated) OR Autoimmune encephalitides (no known antibody defined)	<u>Antibody associated:</u> Non-infective encephalitis, with or without underlying teratoma or malignancy with known encephalitis associated antibody (e.g. LGI1, Caspr2, NMDAR, GAD GlycineR, DPPX, AMPA,	Infective encephalitis or other non-inflammatory cause of encephalopathy or seizures	Search for underlying malignancy and treat as appropriate Prednisolone (or methylprednisolone) is first line, with or without Plasma	2g/kg over 5 days initially repeated at 3 to 6 weeks. Repeat course 3 times if necessary. If repeated	AIE outcomes for all types (except Ab titre where antibody is undefined) Antibody titre (if relevant and measurable)	Apply to EOEIAP Out of hours No Class III indication

	GABAb and others) AND • Functional disability caused by seizures, encephalopathy, stiffness, cognitive dysfunction or other relevant neurological sequelae <u>No known antibody defined:</u> • Non-infective encephalitis, with or without underlying teratoma or malignancy without known encephalitis associated antibody AND • Functional disability caused by seizures, encephalopathy, stiffness, cognitive dysfunction or other relevant neurological sequelae AND • Evidence of inflammatory CNS disorder including active CSF, EEG defined seizures, MRI changes consistent with AIE, known antibodies etc in the absence of infection.		Exchange (where this is available) Ongoing treatment with IVIG may be necessary where long-term oral immunosuppression, tumour removal and definitive strategies to reduce antibody levels (e.g. cyclophosphamide / rituximab) are ineffective or contra-indicated NB: Please note the Enceph-19 study is available ¹⁹. Consider recruitment for eligible patients.	courses are required, consider institution of alternative longer-term strategy immediately EOEIAP: Use DDW for dosing.	• Modified Rankin Score • Reduction in seizure frequency or severity • Improvement on one or more validated tests of memory or executive tasks • Resolution of MR signal change (where present) • Resolution of hyponatraemia where present	
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Chronic inflammatory demyelinating polyradiculopathy (CIDP) - including IgG or IgA associated paraprotein associated demyelinating neuropathy	• Probable or definite diagnosis of CIDP by a neurologist according to the EAN/International Peripheral Nerve Society criteria; AND • Significant functional impairment inhibiting normal daily activities. All patients should have an initial documented assessment after induction dosing and a further assessment after 2-3 doses to demonstrate meaningful functional improvement. Annual withdrawal / clinical reviews should be performed to document continuing need.	No specific exclusion criteria but see general comments regarding prothrombotic risks of Ig	IVIg should not always be considered first line treatment for CIDP, although it may be where steroids are contra-indicated and plasma exchange is not available. Where steroids, IVIg and plasma exchange are all available, IVIg would be considered preferable in patients with motor predominant CIDP, rapidly progressive disease where rapid response is required (particularly patients requiring admission to hospital) or where steroids or plasma exchange are contra-indicated. Strong consideration should be given to the early use of steroids or plasma exchange in other circumstances.	An initial regimen of a maximum 4g/kg divided into at least two courses of 1-2g/kg each, and given over a 4 to 8 week period, with assessment at the end of the period. Regimens to establish response might include: • 2g/kg given over 2 to 5 days and repeated after 6 weeks¹⁹ • 2g/kg initially followed by 1g/kg after 3 weeks and a further 1g/kg 3 weeks later²⁰ For maintenance dose optimisation see general note at end of section. EOEIAP: Use DDW for dosing.	Efficacy outcomes should be used to measure response after the chosen initial regimen and therefore when assessing for dose optimisation. Clinically meaningful improvement in any three of the following pre-specified measures per patient: • MRC score (7 pairs of muscles in upper and lower limb scored 0-5, maximum 70) • INCAT sensory sum score • ONLS (Overall Neuropathy Limitation Score) • Hand dynamometry • Inflammation RODS score • 10-m walk (in seconds) • Berg Balance scale • Other validated disability score	Short-term initiation treatment to assess Ig responsiveness Neurology consultant may approve with retrospective application to EOEIAP Long-term treatment following initial assessment period Apply to EOEIAP Out of hours No Class II indication
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Guillain-Barre syndrome (GBS) -includes Bickerstaff's brain stem encephalitis and other GBS variants	• Diagnosis of GBS (or variant) in hospital, AND • Significant disability (Hughes Grade 4); OR • Disease progression toward intubation and ventilation OR • mEGRIS score ≥ 3 OR • Poor prognosis mEGROS ≥ 4 Potential cases of drug-induced GBS should be discussed with a neurologist to confirm diagnosis and guide treatment. • Many drugs have been associated with drug-induced GBS, including PD-1 and CTLA-4 immune checkpoint inhibitors (ICI) and others ⁴⁷	Patients with mild and/or non-progressive disease not requiring intubation.	Patients with Miller-Fisher Syndrome do not usually require IVIg and, unless associated with GBS overlap with weakness, will recover normally. Plasma exchange is equally efficacious as IVIg in GBS and should be preferentially considered where it is clinically appropriate and easily accessible. For those disease indications in children and young adults where IVIg and plasma exchange (PLEX) are equally efficacious, IVIg may be preferentially considered if poor peripheral venous access or challenges in service delivery preclude the use of PLEX.	2g/kg given over 5 days - Administration over a shorter time frame not recommended because of fluid overload with associated autonomic problems, and protein overload with pro-coagulation risks; EOEIAP: Use DDW for dosing. IVIg is unlikely to be effective if given more than 4 weeks after the onset of symptoms. Second doses of IVIg are rarely effective and may be associated with harm²¹. Plasma exchange may be considered if	None	Neurology consultant may approve first course. Out of hours Permitted unless mild / non-progressive Class I indication 2nd dose: Class II indication Apply to EOEIAP
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				deterioration following clear improvement after the first dose.		
IgM paraprotein- associated demyelinating neuropathy	• Diagnosis by a neurologist AND • Significant functional impairment inhibiting normal daily activities AND • Other therapies have failed, are contra-indicated or undesirable	Mild disease with non-progressive sensory loss and imbalance does not require treatment.	IVIg is seldom significantly effective and response should be reviewed at least every 6 months if there is an initial functional improvement. Alternative underlying haematological diagnoses should be considered which may direct treatment, or other therapies such as single agent rituximab (or biosimilars) should be considered. Rituximab is recommended in IgM paraproteinaemic demyelinating peripheral neuropathy in adults in line with NHS England policy²³	An initial regimen of a maximum 4g/kg divided into at least two courses of 1-2g/kg each, and given over a 4 to 8 week period, with assessment at the end of the period. Regimens to establish response might include: • 2g/kg given over 2 to 5 days and repeated after 6 weeks¹⁹ • 2g/kg initially followed by 1g/kg after 3 weeks and a further 1g/kg 3 weeks later²⁰ For maintenance dose adjustment see general note	Efficacy outcomes should be used to measure response after the chosen initial regimen and therefore when assessing for the dose optimisation. Clinically meaningful improvement in any three of the following prespecified measures per patient: • MRC score (7 pairs of muscles in upper and lower limb scored 0-5, maximum 70) • INCAT sensory sum score • ONLS (Overall Neuropathy Limitation Score) • Hand dynamometry • Inflammation RODS	Apply to EOEIAP Out of hours No Class II indication

				at end of section. EOEIAP: Use DDW for dosing.	score • 10-m walk (in seconds) • Berg Balance scale • Other validated disability score	
Inflammatory myopathies Including Dermatomyositis (DM) Juvenile dermatomyositis (JDM) Polymyositis (PM) Other inflammatory myopathies*	• Diagnosis of myositis by a neurologist, rheumatologist, dermatologist or immunologist AND EITHER • Patients who have significant muscle weakness OR • Dysphagia and has not responded to corticosteroid and other immuno-suppressive agents OR • DM with refractory skin involvement	No specific exclusion criteria but see general comments regarding prothrombotic risks of IVIg	Where progression is not rapid and in the absence of contra-indications, steroids should be considered first. In adult patients (and post-pubescent children through NHS England and NHS Improvement Medicines for Children policy²⁴) with refractory disease associated with myositis-specific antibodies, rituximab (or biosimilar) has been approved as a second-line treatment by NHS England²⁵. Abatacept is recommended in refractory idiopathic inflammatory myopathies (adults	An initiation course of a maximum 4g/kg divided into at least two courses of 1-2 g/kg each, and given over a 4 to 8-week period, with assessment after dosing. Regimens to establish response might include: 2g/kg given over 2 to 5 days and repeated after 6 weeks For maintenance dose optimisation see general note at end of section. The need for maintenance treatment in	Clinically meaningful improvement in three pre-defined measures from the list below; DM functional / disability scores (ADLs): • semi-quantitative muscle scores (MRC sum score) • other quantitative muscle strength (e.g. MMT8) • up and go 10-m walk (in secs) • CDASI • CAT or DAS • FVC • CHAQ (to include the childhood score) PM and other inflammatory myopathies functional / disability scores (ADLs):	Apply to EOEIAP Consider prospective applications for deteriorating patients. Out of hours No Class II indication

			and children aged 2 and over) as a third-line treatment by NHS England²⁶. IVIg is fourth-line treatment. IVIg is seldom effective in isolation and is best used as an adjunct to immunosuppressive therapy. Maintenance treatment with IVIg for a prolonged period (usually <12 months) may be required in a small minority of patients with inflammatory myositis, as third line treatment after consideration of rituximab (see comments under position of immunoglobulin). In such cases, every effort should be made to establish the minimum clinically effective dose by either reduction of	resistant juvenile dermatomyositis should be determined on an individual basis. Cessation trials should be attempted at least annually to establish ongoing need for treatment. EOEIAP: Use DDW for dosing.	• semi-quantitative muscle scores (MRC sum score) • other quantitative muscle strength (e.g. MMT8) • up and go 10-m walk (in secs) • HAQ • FVC For juvenile dermatomyositis (JDM): • MMT-8 • CMAS score • CK for baseline and assess how a patient has improved after each infusion or at least 3 infusions • PGALs is used to assess how many inflamed or swollen joints a patient has. Efficacy outcomes should be recorded after the initiation course and regularly reassessed and recorded thereafter.	
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			dose or lengthening the intervals between infusions. Attempt cessation at least annually.			
Multifocal Motor Neuropathy (MMN)	• Diagnosis by a neurologist of MMN with or without persistent conduction block; AND • Significant functional impairment inhibiting normal daily activities	No specific exclusion criteria but see general comments regarding prothrombotic risks of IVIg	No alternative treatments known	An initial regimen of a maximum 4g/kg divided into at least two courses of 1-2g/kg each, and given over a 4 to 8 week period, with assessment at the end of the period. Regimens to establish response might include: • 2g/kg given over 2 to 5 days and repeated after 6 weeks¹⁹ • 2g/kg initially followed by 1g/kg after 3 weeks and a further 1g/kg 3 weeks later²⁰ Refer to dose optimisation	Clinically meaningful improvement in three pre-defined measures from the list below; • MRC score • Power score from 7 pre-defined pairs of muscles including 4 most affected muscle groups neuro-physiologically • RODS for MMN • Hand dynamometry • ONLS • 10-m walk (in secs) • Any other validated MMN disability measure	Short-term treatment to assess Ig responsiveness Neurology consultant may approve Long-term treatment Apply to EOEIAP Out of hours No Class II indication

				section below for maintenance dosing; If no significant measurable and functionally meaningful improvement in abilities has been achieved after 3 doses, IVIg should be stopped. EOEIAP: Use DDW for dosing.		
Myasthenia Gravis (MG) includes Lambert-Eaton Myasthenic Syndrome (LEMS)	• Diagnosis of MG or LEMS by a neurologist AND EITHER • Acute exacerbation (myasthenic crisis); OR • Weakness requires hospital admission – for instance, deteriorated mobility, unable to walk unaided; OR Prior to surgery and/or thymectomy	No specific exclusion criteria but see general comments regarding prothrombotic risks of IVIg	All patients requiring urgent inpatient treatment should receive plasma exchange first if available, including considering transfer to an appropriate neuroscience centre. IVIg could follow plasma exchange if required. Where plasma exchange is not available, IVIg may be appropriate.	In acute exacerbation use plasma exchange first where available. Patients admitted to hospital should receive 1g/kg in the first instance, only receiving a further 1g/kg if there is further deterioration or no response (e.g. over 2-5 days).	Clinically meaningful improvement in variation of myasthenic muscular strength and fatigue measures by the QMGs MG composite score. Additional efficacy may be monitored using: • Forward arm abduction time (up to 5 min) • Quantitative	Myasthenic crisis – Consultant may approve Class I if myasthenic crisis Long-term treatment Apply to EOEIAP Out of hours If crisis;

			In rare circumstances where a patient has failed all standard treatments (including steroids and immunosuppression) and where authorised by a specialist in MG from a centre with a specialist neuromuscular service, maintenance therapy may be considered. A rituximab biosimilar agent is likely to be an equally effective alternative therapy and has been approved by NHS England²⁷ for this group of patients with resistant myasthenia.	Patients with life-threatening disease (e.g. in intensive care) with respiratory and/or bulbar failure) should receive 2g/kg over 2-5 days. Refer to dose optimisation section for maintenance. EOEIAP: Use DDW for dosing.	Myasthenia Gravis Score (Duke) • Respiratory function, e.g. forced vital capacity (FVC) • Variation of another myasthenic muscular score • Dysphasia score • Dysarthria 1-50 counting • Diplopia or ptosis measurement	Respiratory or bulbar failure Otherwise Class II indication
Neuromyotonia (Isaacs syndrome)	• Neuromyotonia from peripheral nerve hyperexcitability associated with significant disability AND • Supported by diagnostic electrophysiological changes with or without	Non autoimmune myotonia syndromes	Anticonvulsants should be tried first from phenytoin, carbamazepine, sodium valproate and lamotrigine. <u>Immunomodulation:</u> • Prednisolone +/-	2g/kg over 5 days initially repeated at 6 weeks then titrated to optimal interval and minimum dose to stability EOEIAP:	Clinically meaningful improvement in • Timed up and go walk • Functional measure: e.g. Myotonia Behaviour Scale (MBS), Rivermead	Apply to EOEIAP Out of hours No Class II indication

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	antibodies to the VGKCh complex (Caspr) and resistant to alternative agents.		azathioprine or oral immunosuppressant • Plasma exchange	Use DDW for dosing.	Mobility Index, or Brief Pain Inventory • Neurophysiological myotonia assessment	
Non-MS CNS inflammatory disease covering the clinical phenotype of Aquaporin-4 antibodies (AQP4 ab) disease, Neuromyelitis Optica Spectrum Disorder (NMOSD), Acute Disseminated Encephalomyelitis (ADEM) (with or without encephalopathy, including brainstem attacks), Myelin Oligodendrocyte Antibody Disease (MOGAD) disease, Transverse Myelitis (TM) and Optic Neuritis (ON)						
	All sub-types, refer also to <u>Further Information</u> section below for information on attack and relapse clarification					
Non-MS CNS inflammatory disease <u>Acute Disease: Short term use</u>	- Acute disease attack* not responding to IV methylprednisolone (5g-7g or equivalent in children) and PLEX. When PLEX is not available or delayed or contra-indicated, IVIG can be used before PLEX (see exclusions) - Consider patient transfer to specialist centre with PLEX availability AND - Evidence of ongoing inflammation AND - Within 6 weeks unless evidence of active inflammation	Mild relapses without: new neurological signs OR reduced activities of daily living OR other inflammatory disease diagnoses (e.g. MS Sarcoid, Behçet's etc.)	Refractory to IV methylprednisolone OR PLEX not available or contraindicated OR refractory to PLEX in cases of severe disability and ongoing inflammation (usually within 6 weeks)	2g/kg over 2-5 days EOEIAP: Use DDW for dosing.	To be determined by disease features including 3 of: - Modified Rankin score 10m walk 9-hole peg test - Validated neuropsychometric testing - Improvement of other relevant validated scale - Objective relevant imaging improvement If ON - clinical improvement of visual acuity.	Apply to EOEIAP Consider prospective applications for deteriorating patients. Out of hours No Class II indication Class I if preceding weekend or bank holiday and panel decision may

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					If TM – clinically meaningful improvement in either 1. EDMUS OR 2. ASIA	take >24 hours.
Non-MS CNS inflammatory disease <u>Chronic relapse prevention:</u> MOGAD (Myelin Oligodendrocyte Glycoprotein Antibody Disease)	MOGAD - refractory to (relapse* breakthrough) at least two treatments; one must be prednisolone and an immunosuppressant (any of mycophenolate / rituximab / azathioprine / methotrexate) OR serious side effects with prednisolone (adequate dose and length of time)	Pseudo relapse OR MS (may have low positive MOGAbs)	Failed 2 first line therapies	1g/kg daily over 2 days then 1g/kg monthly for first year (titrate to 2g/kg if relapses occur despite regular steroid and IVIg at 1g/kg) Annual reviews for dose optimisation EOEIAP: Use DDW for dosing.	Suppression of further relapses* Treatment Failure – defined as objective evidence of true relapse* on treatment	Apply to EOEIAP Out of hours No Class II indication
Non-MS CNS inflammatory disease <u>Chronic relapse prevention:</u> AQP4 NMOSD (Aquaporin 4 Neuromyelitis)	AQP4 NMOSD - Failed or intolerant to 3 or more 'usual treatments' resulting in relapse*, including at least prednisolone (unless severe prednisolone side effects from adequate dose and time) PLUS	Pseudo relapse	As per selection criteria	1g/kg monthly for first year; if relapse despite regular steroid and IVIg at 1g/kg, titrate up to 2g/kg	Suppression of further relapses* Treatment Failure – defined as objective evidence of true relapse* on	Apply to EOEIAP Out of hours No Class II

Optica Spectrum Disorder)	immunosuppressant (azathioprine / rituximab / mycophenolate / methotrexate / ciclosporin or tacrolimus / PLEX or new RCT treatment if available)			Review annually EOEIAP: Use DDW for dosing.	treatment	indication
Non-MS CNS inflammatory disease <u>Chronic relapse prevention:</u> Ab negative phenotypes	Failed or intolerant to 3 or more 'usual treatments' resulting in relapse* including at least prednisolone (unless severe prednisolone side effects from adequate dose and time) PLUS immunosuppressant (azathioprine / rituximab / mycophenolate / methotrexate / ciclosporin or tacrolimus / PLEX or new RCT treatment if available)	Pseudo relapse OR Other inflammatory disease diagnoses (e.g. MS Sarcoid, Behçet's etc.)	As per selection criteria	1g/kg over 2 days then monthly for first year Review at one year try reducing interval /dose with alternative options EOEIAP: Use DDW for dosing.	Suppression of further relapses* Failure – defined as objective evidence of true relapse* on treatment	Apply to EOEIAP Out of hours No Class II indication
<u>Further information</u> Non-MS CNS inflammatory disease	*Attack or Relapse is a new or extended neurological symptom with signs that reflects the anatomical location of the inflammatory lesion (note a minority of early MOGAD TM may be difficult to visualise) that is not a fluctuating residual symptom of an old lesion and that usually persists for at least one week. However, acute treatment should not be delayed. Contrast enhancement is present in the majority during the acute phase.					
Opsoclonus-myoclonus syndrome - paediatric or adult non paraneoplastic	- Paediatric OMS diagnosed by a paediatric neurologist OR - OMS in an adult with no evidence of neoplasm, anti-neuronal antibodies, or focal structural or	Structural disease. Multiple sclerosis / other inflammatory lesions associated with	Corticosteroids should be tried first Consider other anti-inflammatory strategies including oral	2g/kg over 5 days initially repeated at 6 weeks then titrated to optimal interval and minimum dose to achieve	Improvement in OMS score	Apply to EOEIAP Out of hours No

	inflammatory alternative diagnosis	defined diagnoses where the primary treatment of that disease is not Ig	immunosuppressants, rituximab or cyclophosphamide as appropriate	stability EOEIAP: Use DDW for dosing.		Class II indication
Paraneoplastic neurological syndromes (PNS) without evidence of autoantibodies	- Defined paraneoplastic syndrome (for example limbic encephalitis, sensory ganglionopathy, cerebellar degeneration etc.) AND - Evidence of a PNS associated tumour (e.g. small cell lung, ovarian or testicular, breast, thymoma etc.)	See eligibility criteria	Treatment of primary tumour Consider steroids and plasma exchange	2g/kg over 5 days initially repeated at 6 weeks. If beneficial then titrated to optimal interval and minimum dose to achieve stability. Discontinue if not objectively effective after 2 doses. EOEIAP: Use DDW for dosing.	- Modified Rankin Scale 10m walk - Any validated relevant disability measure appropriate to the condition	Apply to EOEIAP Out of hours No Class II indication
Rasmussen's Encephalitis	When other therapies (such as steroids) have failed.	No specific exclusion criteria but see general comments regarding prothrombotic risks of IVIg	Ig is reserved for patients unresponsive to steroids and other therapies.	2g/kg divided over two to five days, and repeated monthly for three months for initial trial. EOEIAP:	Seizure frequency with expected reduction of 30% to continue therapy.	Apply to EOEIAP Out of hours No Class II indication

				Use DDW for dosing.		
Stiff person syndrome (SPS) or variant	Diagnosis of SPS or a variant (stiff limb, PERM, etc.) by a consultant neurologist Supportive criteria; • Demonstration of auto-antibodies to GAD, Glycine receptor, DPPX, amphiphysin, gephyrin or other stiff person associated antibodies AND/OR • Continuous motor unit activity at rest on EMG testing in paraspinal or affected limb musculature	No specific exclusion criteria but see general comments regarding prothrombotic risks of IVIg	Consider plasma exchange as initial treatment. Rituximab is likely to be equally effective but is not commissioned for this indication.	An initiation regimen of a maximum 4g/kg divided into at least two courses of 1-2g/kg each, and given over a 4 to 8 week period, with assessment at the end of the period. Regimens to establish response might include: 2g/kg given over 2 to 5 days and repeated after 6 weeks¹⁹ 2g/kg initially followed by 1g/kg after 3 weeks and a further 1g/kg 3 weeks later²⁰ If no significant measurable and functionally meaningful	Clinically meaningful improvement in at least two of the measures below: • Reduction in stiffness • Up and go 10-m walk (in secs) • BRIT score • Number of spasms per day • Validated measure of functional disabilities	Apply to EOEIAP Out of hours No Class II indication

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				improved in abilities had been achieved after 3 doses IVIG should be stopped EOEIAP: Use DDW for dosing.		
Immune effector cell-associated neurotoxicity syndrome (ICANS)	Grade 3 or 4 (see reference below for criteria) or refractory to standard care.	Patient must be reviewed by a neurologist and CAR-T specialist	Most centres are using corticosteroids as first-line therapy for isolated ICANS, with tocilizumab plus corticosteroids given for ICANS that develops concurrently with CRS, although therapy remains largely empirical and there are no clinical trial data yet comparing the various approaches. Different corticosteroids are used depending on institutional standards, although dexamethasone use is most common	2g/kg Repeat as necessary with specialist advice EOEIAP: Use DDW for dosing. Submit IFR to NHSE	Seizure resolution Improved ADL Resolution of cerebral oedema Improved level of consciousness Improved dysphasia, tremor, headache or disorientation.	Apply to EOEIAP Out of hours No Class IV indication

			because it has excellent CNS penetration and improves the integrity of the blood–brain barrier. High pulse-dose methylprednisolone is used in the more severe cases of ICANS based on experience with fulminant neuroinflammatory disorders. Immunoglobulin should be reserved for cases that are more severe (higher grade) or refractory to standard care.			
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Dosing optimisation for maintenance – general notes:

An ongoing issue for diseases that require long-term immunoglobulin treatment is that once significant and functional responsiveness to intravenous immunoglobulin (IVIg) is demonstrated for a patient using standard immunomodulatory dosing, the ‘maintenance’ dosing required to maintain the therapeutic response is not well characterised. In this update, the dosing recommendations for some neurological indications include ‘time to relapse’ as the interval between doses. 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. In view of the uncertainty of both remission and disease progression in CIDP and MMN, The Oxford Programme

reviewed the dose and infusion frequency of patients on a regular basis and showed that increasing the infusion interval proved successful in some patients and resulted in treatment discontinuation²⁸.

An alternative approach based on establishing the 'time to relapse' following the first or second dose followed by dose reduction has also been proposed and is equally feasible¹⁹. This ensures patients who need no more than 1 or 2 doses are not exposed to unnecessary doses and those with ongoing needs are optimised to a minimal dose.

Based on evidence from randomised trials, it is likely that up to 40% of patients with CIDP may be able to discontinue treatment²⁹ after 6-12 months, although a significant proportion may relapse and require retreatment. For this reason, periodic trials of cessation of treatment are recommended, especially in patients who appear to be stable even if optimally treated. 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-term dependence and further withdrawals are highly unlikely to be effective. Referral to a specialist neurology centre is recommended as early as possible.

In inflammatory myositis, maintenance treatment with IVIg for a prolonged period (usually less than 12 months) may be required in a small minority of patients. In these cases, every effort should be made to establish the minimum clinically effective dose by either reduction of dose or lengthening the intervals between infusions. Cessation trials should be attempted at least annually to establish continuing need for treatment³⁰.

Specific exclusion criteria against the use of immunoglobulin have not been listed, but it is important to carry out benefit-risk analyses in certain patient groups: patients at high risk of thromboembolism (hypertension, diabetes, smoking, hypercoagulable states) should be counselled regarding the prothrombotic risks of immunoglobulin. IgA deficiency is no longer considered a contra-indication to the use of immunoglobulin and should not be withheld because of theoretical concerns of adverse reactions. The role of anti-IgA antibodies in causing reactions is controversial and measurement of anti-IgA antibodies prior to undertaking treatment is not warranted.

ICANS grading criteria available [here](#)

Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Infectious Disease indications						
Hepatitis A	Immunoglobulin is recommended in addition to hepatitis A vaccine for contacts of hepatitis A who are less able to respond to vaccine, ie. - those aged 60 or over, OR - those with immunosuppression and those with a CD4 count <200 cell per microliter, OR - those at risk of severe complications (those with chronic liver disease including chronic hepatitis B or C infection)	See eligibility criteria	Hepatitis A vaccine is recommended in addition to immunoglobulin Vaccine should be administered within 2 weeks of exposure. Use of commercial stock should be recorded in the National Immunoglobulin Database. UKHSA immunoglobulin stocks are issued nationally and distributed locally. Hospitals should keep records of all instances of use of UKHSA-provided stocks (e.g. in patient records).	Use commercial stock for any patient treated in hospital. UKHSA-provided SCIG for community-based treatment; available from nearest UKHSA depot (HPA team to advise). Use IVIG preferentially for hospital patients, in particular if thrombocytopaenic. Hospital treatment: Commercial stock of IVIG (as per local formulary) <10 years – 500mg >10 years – 1000mg If IV cannulation impractical, consider SCIG via IM route: <10 years – 500mg >10 years – 1000mg	Outcome measures not routinely recorded on surveillance database.	Permission required from UKHSA health protection team* Notification of treatment to EOEIAP only if commercial stock used (this is the expected route). Find local protection team here: https://www.gov.uk/health-protection-team Out of hours Permitted with ID consultant approval only if pressing need –

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				Given with vaccine in those at high risk, within 2 weeks of exposure in those less able to respond to vaccination and those at risk of severe complications. 1st line – equivalent dose of Cutaquig 16.5% by IM route 2nd line – seek advice from EOEIAP Community treatment: UKHSA-provided product, if available.. <10 years – 500mg >10 years – 1000mg For those exposure between 2-4 weeks ago, immunoglobulin may also be offered to modify disease in those at risk of severe complications (i.e. chronic liver disease including chronic hepatitis B or C infection), <i>See notes at the end of this section</i>		e.g. treating at risk contacts who will not be available later Class I indication Use UKHSA provided stock only for patients treated in the community.
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Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Measles (immunosuppressed individuals) Further info: Think measles	Immunosuppressed individuals (Group A and Group B based on the level of immunosuppression³¹) who have had a significant exposure to measles and are known to be susceptible (based on vaccine history and/or IgG testing). Advice is available at: National measles guidelines - https://www.gov.uk/government/publications/national-measles-guidelines All patients are to be reviewed in the context of the additional detail contained in the UKHSA guideline. HNIg is assumed to contain at least 80 IU/g, with 11 IU/Kg required to provide protection from measles.	Patients who are known to be measles IgG positive following immunosuppressive treatment are unlikely to require IVIG. Group A patients who have Hx of measles infection or vaccination are unlikely to require IVIG.	Eligibility is stratified by Group A and Group B risk groups as defined on pages 27-31 of the National Measles Guideline 2024. Immunoglobulin is mainstay management for PEP in: • Pregnant contacts • Infant contacts below 6 months • Group B contacts who are not already receiving IVIG replacement therapy • Immunosuppressed contacts Contacts already receiving Ig replacement therapy do not require additional IVIG if last dose of Ig within previous 3 weeks (IVIG) or previous week (SCIG).	Use commercial IVIG stock all patients. • 0.15g/kg IVIG (to provide 11 IU/kg of measles antibody) within 6 days of exposure – though ideally within 72 hours. Where exposure recognised late or found to be antibody negative between 6 and 18 days after exposure, IVIg may be considered following discussion with specialist clinician. EOEIAP: Use DDW for dosing in adults, ABW in infants or DDW based on booking weight in pregnancy.	Prevention of measles	Permission required from UKHSA health protection team Notification of treatment to EOEIAP Out of hours With UKHSA approval Class I indication Use hospital stocks Find local protection team here: https://www.gov.uk/health-protection-team

Dosing of IVIG in immunosuppressed individuals following a significant exposure to measles:

Weight (Kg)	Dose (g)	Weight (Kg)	Dose (g)
<20	2.5g	71-90	12.5g
20-35	5g	91-105	15g
36-54	7.5g	106-116	17.5g
55-70	10g	116-133	20g

- IVIG is available in 2.5g, 5g, 10g and 20g vial sizes.

Measles (in pregnancy and in infants) Further info: Think measles	Pregnant women / patients who have been identified as susceptible based on vaccine history and/or antibody testing who have had a significant exposure to measles. Neonates born to mothers who develop a measles rash 6 days before to 6 days after delivery. Infants under 9 months of age with a significant exposure to measles. Advice is available at: National measles guidelines - https://www.gov.uk/government/publications/national-measles-guidelines All patients are to be reviewed in the context of the	See eligibility criteria	For pregnant patients and infants who are immunosuppressed contacts, immunoglobulin is mainstay management. For infants aged between 6-8 months, MMR vaccine can be offered if exposure occurred outside household setting AND ideally should be given within 72 hours Use of commercial stock should be recorded in the National Immunoglobulin Database. UKHSA immunoglobulin stocks are issued	Use commercial stock for any patient treated in hospital. UKHSA-provided SCIG for community-based treatment; available from nearest UKHSA depot (HPA team to advise). Use IVIG preferentially for hospital patients, in particular if thrombocytopenic. • Pregnant patients: approximately 3000mg (round up to 5g if using IVIG) • Infants 100mg/kg up to a maximum of 1000mg.	Prevention of measles.	Permission required from UKHSA health protection team* Notification of treatment to EOEIAP only if commercial stock used. Find local protection team here: https://www.gov.uk/health-protection-team Out of hours Give in working hours if possible within 72 hour window
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	additional detail contained in the UKHSA guideline. Further advice in viral illness in pregnancy: Guidance on the investigation, diagnosis and management of viral illness (plus syphilis), or exposure to viral rash illness, in pregnancy.		nationally and distributed locally. Hospitals should keep records of all instances of use of UKHSA-provided stocks (e.g. in patient records).	Hospital treatment: Commercial stock of IVIG (as per local formulary) If IV cannulation impractical, consider SCIG via IM route: 1st line – Cutaquig 16.5% • 3g ≈ 20ml of 16.5% in pregnancy • 0.6ml/kg up to 1g for infants 2nd line – Seek advice from EOEIAP; if using 20% product • 3g ≈ 15ml of 20% in pregnancy • 0.5ml/kg up to 1g for infants Community treatment: UKHSA-provided product, if available. Several SCIG products are contraindicated by IM injection. For other brands and dosing, liaise with EOEIAP or UKHSA directly.		Class I indication Use UKHSA provided stock only for patients treated in the community.
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				EOEIAP: Use DDW for dosing in adults, ABW in infants or DDW based on booking weight in pregnancy. See notes at the end of this section		
Polio	To prevent or attenuate an attack: • An immunocompromised person inadvertently given live polio vaccine, OR • An immunocompromised person whose contacts are inadvertently given live polio vaccine	See eligibility criteria	Immunoglobulin represents first-line treatment. Use of commercial stock should be recorded in the National Immunoglobulin Database. UKHSA immunoglobulin stocks are issued nationally and distributed locally. Hospitals should keep records of all instances of use of UKHSA-provided stocks (e.g. in patient records).	Use commercial stock for any patient treated in hospital. UKHSA-provided SCIG for community-based treatment; available from nearest UKHSA depot (HPA team to advise). • <1 year: 250mg • 1 – 2 years: 500mg • >3 years: 750mg Use IVIG preferentially for hospital patients, in particular if thrombocytopaenic. Hospital treatment: Commercial stock of IVIG (as per local formulary)	Either: • Prevention of infection OR • Resolution of infection	Permission required from UKHSA health protection team* Notification of treatment to EOEIAP only if commercial stock used. Find local protection team here: https://www.gov.uk/health-protection-team Out of hours With UKHSA approval Class I indication

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				If IV cannulation impractical, consider SCIG via IM route: 1st line – equivalent dose of Cutaquig 16.5% by IM route 2nd line – Seek advice from EOEIAP Community treatment: UKHSA-provided product, if available. Stool samples from the immunosuppressed individual must be obtained one week apart. If poliovirus is grown from either sample, repeat immunoglobulin at 3 weeks. Continue weekly stool collection and administration of immunoglobulin three weekly until immunocompromised individual's stool is negative for poliovirus on two consecutive occasions.		Use UKHSA provided stock only for patients treated in the community.
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				<i>See notes at the end of this section</i>		
Severe or recurrent Clostridium difficile infection (CDI) colitis - short term use	- Severe cases (WCC >15 and/or, acutely rising creatinine and/or signs/symptoms of colitis) not responding to routine 1st line vancomycin and metronidazole OR - If multiple recurrences, especially with evidence of malnutrition.	See comments under position of Ig	For fulminant or recurrent CDI unresponsive to appropriate antibiotics (see under selection criteria) consider IV tigecycline or IVIg³² Faecal microbiota transplantation is approved by NICE for patients with recurrent CDI unresponsive to antibiotics and is likely to be an effective alternative³³.	0.4 g/kg IVIG, one dose, and consider repeating once EOEIAP: Use DDW for dosing.	- Clearance of C. diff. - Duration of hospital in-patient stay	Apply to EOEIAP [or ID consultant where delay could be detrimental] Out of hours No Class II indication
Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Staphylococcal (including PVL-associated sepsis) or streptococcal toxic shock syndrome (TSS)	Diagnosis of streptococcal or staphylococcal TSS, preferably with isolation of organism,	See comments under position of Ig	IVIg is reserved for patients with life-threatening disease who fail to achieve rapid improvement	Total dose of 2g/kg, because of uncertainty regarding the timing and optimal dose of IVIg, it is recommended that	- Improvement of FBC, ALK, CPK, and acute phase markers - Reduction in hospital inpatient stay	Consultant may approve Ideally, prior approval is

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- short term use	AND - Failure to achieve rapid improvement with antibiotic therapy and other supportive measures, AND - Life-threatening		with antibiotic therapy. However, for streptococcal TSS, it should be noted that there has been significant controversy regarding the benefits of IVIg treatment prompting the Infectious Diseases Society of America (IDSA) not to recommend its use in patients with necrotising Group A streptococcal infections³⁴. Since then a systematic review and meta-analysis of IVIg in clindamycin-treated patients with streptococcal TSS suggests a reduction in mortality from 33.7% to 15.7%, though this finding may be confounded by differences in baseline characteristics between patients receiving IVIg and	patients are reviewed after an initial dose of 1g/kg. Should there be no evidence of improvement at 24 hours, a further 1g/kg may be considered. EOEIAP: Use DDW for dosing.	Survival	recommended but if this is not possible, treatment should proceed, and retrospective approval should be sought. Out of hours Permitted Class I indication
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			those who didn't ³⁵ . Based on the results of this meta-analysis, the use of IVIg as adjunctive therapy is supported by Stevens DL ³⁶ .			
Tetanus prone injury (IM-TIg or SCIg via IM route)	Tetanus specific immunoglobulin (TIG) has limited stock and is recommended for susceptible individuals sustaining high risk tetanus prone injuries as defined in guidance ³⁷ (https://www.gov.uk/government/publications/tetanus-advice-for-health-professionals)	See eligibility criteria	• Thorough cleaning of wound is essential, including debridement of devitalised tissue if necessary • Immunoglobulin for Prophylaxis • Booster of tetanus-containing vaccine for long term protection Use of commercial stock should be recorded in the National Immunoglobulin Database.	<u>TIG:</u> • 250 IU for most uses • 500 IU if more than 24 hours have elapsed or there is a risk of heavy contamination or following burns The dose is the same for adults and children. <u>Immunoglobulin:</u> If TIG (for intramuscular use) cannot be sourced, immunoglobulin for subcutaneous or intramuscular use may be given as an alternative. Based on testing for the presence of anti-tetanus antibodies in commercial immunoglobulin products, the dose of HNIg required to achieve the	Prevention of tetanus infection	Consultant may approve Out of hours Permitted with ID consultant approval Class I indication

				recommended dose of 250IU anti-tetanus Ig is approximately 1g. Hospital treatment: Commercial stock of SCIG via IM route (as per local formulary) SCIG via IM route: • 250IU TIg ≈ 1000mg • 500IU TIg ≈ 2000mg 1st line – equivalent dose of Cutaquig 16.5% by IM route 2nd line – seek advice from EOEIAP. Doses for other brands are contained in the table at the end of this section. Although no time frame is specified in the guidance, IM-TIG /immunoglobulin following a tetanus prone wound is only likely to confer benefit when given within incubation period of		
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				tetanus (10-21 days).		
Suspected tetanus case (IVIg)	Person with clinical symptoms suggestive of localised or generalised tetanus ("in the absence of a more likely diagnosis, an acute illness with muscle spasms or hypertonia AND diagnosis of tetanus by a health care provider")	--	• Wound debridement • Antimicrobials • IVIG based on weight • Supportive care Vaccination with tetanus toxoid following recovery	Dosage based on equivalent dose of anti-tetanus antibodies of 5000 IU for individuals < 50kg and 10000 IU for individuals > 50kg See table below* If Tlg is not available, or the patient cannot tolerate the volume of Tlg IM, the EOEIAP recommend (where available): Gamunex 10%: 20g IV stat ≈ 5,000IU Tlg 40g IV stat ≈ 10,000IU Tlg Other IVIG brands have published anti-tetanus activity. Testing varies by company with either standard ranges or batch-specific results. See further information at the end of this table.	Resolution of tetanus infection	Consultant may approve Out of hours Permitted with ID consultant approval Class I indication
Varicella zoster (VZ)	Individuals for whom oral antivirals are contraindicated due to malabsorption or some	Unless contra-indicated,	Oral / enteral antivirals are the recommended first-line for post-	0.2g IVIG per kg body weight (i.e. 4ml/kg for a 5% solution)	Prevention of chicken pox infection	Permission required from UKHSA.

	cases of renal toxicity. Ig is indicated for those individuals who fulfil all the following criteria: - Significant exposure to chickenpox (varicella) or shingles (zoster) during the infectious period. - At increased risk of severe chickenpox i.e. immunosuppressed individuals, neonates and in pregnancy. - No antibodies to varicella-zoster virus (based on VZV antibody testing) - Unable to take oral antivirals due to malabsorption or renal toxicity. Updated guidance on post exposure prophylaxis has been published in January 2025. Advice is available at: https://www.gov.uk/government/publications/post-exposure-prophylaxis-for-chickenpox-and-shingles Immunosuppressed Neonates of mothers who	oral antivirals would be considered first-line. Mildly immunocompromised whose level of immunosuppression does not meet the criteria for either Group A or Group B do not require VZIG e.g. children on doses of prednisolone less than 2mg/kg/day, patients on doses of methotrexate 25mg/week or less. A further	exposure prophylaxis for all at risk groups including pregnant women, immunosuppressed individuals and susceptible neonates. For those patients fulfilling eligibility criteria, there are no alternatives to IVIg. Varitect CP (VZIG) is not available in the UK after 30th Sept 2024 [UKHSA briefing 2024/043]. Where immunoglobulin is indicated and HPT cannot supply VZIG, normal human IVIG should be used.	Brands have not been specified as no formal testing of products has been undertaken. IVIg should be administered ideally within 7 days of exposure in eligible individuals. Where the exposure has been identified beyond 7 days, IVIg can be offered up to 14 days after exposure. <i>Beyond this time for patients in both groups A and B, a discussion with the specialist caring for the individual should take place and IVIg (0.2g per kg body weight) may be considered in susceptible individuals for up to 21 days to attenuate infection</i> EOEIAP: Use DDW for dosing.	Prevention of severe chicken pox	Notification of treatment to EOEIAP. Find local protection team here: https://www.gov.uk/health-protection-team Out of hours No Class II indication Refer to UKHSA Guidelines on post exposure prophylaxis (PEP) for varicella or shingles Sept 2024
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	have developed chickenpox within 7 days of birth (either before or after delivery and who cannot obtain Varitect (Varicella-zoster immunoglobulin) in a timely manner. Immunosuppressed individuals are assessed at time of exposure into Group A & Group B based on likely level of immunosuppression	dose of IVIg is not required if a new exposure occurs within 3 weeks of administration of VZIG or IVIG				
Viral pneumonitis following HSCT or solid organ transplant	Definitive diagnosis of viral pneumonitis – Varicella Zoster Virus (VZV), Respiratory Syncytial Virus (RSV), Human Parainfluenza Virus (HPIV)	VZV – see comments under position of Ig. RSV, HPIV – patients with mild disease confined to the upper respiratory tract.	VZV – IVIg is reserved for disseminated disease. For guidance on treatment of patients with significant exposure to chicken pox or herpes zoster, please see the use of Ig in Varicella zoster (above). RSV, HPIV – patients with lower respiratory tract infections. In RSV, Ig would be used as an adjunct to ribavirin. RSV, HPIV, patients with RSV and HPIV upper respiratory tract infections post-HSCT,	1-2g/kg IVIG in divided doses EOEIAP: Use DDW for dosing.	• Radiological improvement • Length of stay in hospital • Survival	Apply to EOEIAP Out of hours No Class II indication

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			consider Ig in the presence of some or all of the following risk factors ³⁸ : • Older age • GvHD • Lymphopaenia <0.2 x 10⁹/L • Neutropenia • Mismatched / unrelated donor • Immediate aftermath of HSCT (<1 month)			
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* Please note SPC currently indicates subcutaneous route of administration only (although previously indicate both SC and IM routes), UKHSA guidance recommends intramuscular administration for post exposure prophylaxis with Subgam.

* Dose of immunoglobulin in suspected tetanus cases:

IVIg Products tested for anti-tetanus antibodies	Volume required (in ml)	
	Individuals less than 50kg	Individuals ≥50kg
Intratect 5%, Flebogamma DIF 5%, Octagam 5%	400ml	800ml
Gamunex 10%, Intratect 10%, Panzyga 10%, Privigen 10%,	200ml	400ml

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Indications	IM-TIG	Cutaquig 16.5%	20% SCIG
For most uses	250 IU	6ml	4.5ml
If more than 24 hours have elapsed or there is risk of heavy contamination or following burns	500 IU	12ml	9ml

*Note that IM administration of Hizentra and Cuvitru is included in the product contra-indications.

NHS Trusts should source supplies of immunoglobulin for the management of tetanus-prone wounds directly from the manufacturer.

Further information on the use of immunoglobulins in the Management of Suspected Tetanus Cases and on the Assessment and Management of Tetanus-prone Wounds is available in the Public Health England guidelines;

- <https://www.gov.uk/government/publications/tetanus-advice-for-health-professionals/guidance-on-the-management-of-suspected-tetanus-cases-and-the-assessment-and-management-of-tetanus-prone-wounds>

UK Health Security Agency (UKHSA) supply stocks of Subgam for the treatment of hepatitis A, measles, rubella[†] and polio to NHS Trusts. This stock is free of charge to the end user Trust and supplies must be maintained by each organisation through UKHSA channels. Where UKHSA stocks are not available, Subgam may be provided through normal routes and if used in line with the measures described in this guideline, NHS England will reimburse Trusts for this use. This mechanism is however secondary to the established route of supply through UK Health Security Agency.

[†]Treatment of rubella is not contained in this guideline. The UK Health Security Agency guidelines can be found at the following website:

<https://www.gov.uk/government/publications/immunoglobulin-when-to-use>

[National measles guidelines October 2023 \(publishing.service.gov.uk\)](https://www.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/115555/national-measles-guidelines-october-2023.pdf)

[PHE National Polio Guidelines - Local and regional services \(publishing.service.gov.uk\)](https://www.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/115555/phe-national-polio-guidelines-local-and-regional-services.pdf)

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Where Subgam stock from the UKHSA is not available (or not available in a timely manner) or where intravenous immunoglobulin is indicated **and** where there is written instruction from UKHSA or local Health Protection Team (HPT), it is permissible to use commercial stocks of immunoglobulin (human normal) for infection prophylaxis after a significant exposure to measles, hepatitis A, rubella, varicella zoster or polio. Specific clinical approval from the sub-regional IAP is not required for these indications in addition to UKHSA or HPT written instruction.

- GPs are not permitted to prescribe or direct the supply of immunoglobulins.

Cases requiring intramuscular administration of immunoglobulin should use UKHSA provided stock of Subgam where available. Where this is not available, or not available in a timely manner, hospitals should consider purchasing a suitable alternative to store in pharmacy in case of need, or enter into a mutual aid agreement with a local hospital that does hold stock. It is important to note that manufacturers have different recommendations for the use of 'subcutaneous' immunoglobulins given by the intramuscular route.

Product	Concentration	License in relation to IM use
<u>Cutaquig</u>	16.5% w/v	It must "not be administered intramuscularly in case of severe thrombocytopenia and in other disorders of haemostasis" [4.3]
<u>Cuvitru</u>	20% w/v	"Cuvitru must not be given intravascularly or intramuscularly" [4.3]
<u>Gammanorm</u>	16.5% w/v	<i>Not commercially available.</i> From 1 st April 2025, not included in the NHS Framework for supply.
<u>Hizentra</u>	20% w/v	For subcutaneous use only [4.2]. From 1 st April 2025, not included in the NHS Framework for supply.
<u>Subgam</u>	16% w/v	"Subgam must not be administered intramuscularly in cases of severe thrombocytopenia and in other disorders of haemostasis" [4.3]. From 1 st April 2025, not included in the NHS Framework for supply.
<u>Xembify</u>	20% w/v	Xembify must not be given intravascularly or intramuscularly.

*SmPC checked 05th Nov 2025

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Immunoglobulin Assessment Panel
(EOEIAP)

In the absence of Subgam and Gammanorm, the preferred commercial immunoglobulin for intramuscular administration is **Cutaquig 16.5%** (Octapharma). In the East of England, stocks of Cutaquig are held for this purpose at Cambridge University Hospitals and mutual aid can be arranged for EOE panel affiliated Trusts through Pharmacy Procurement, the pharmacy immunoglobulin team (add-tr.iap-eastofengland@nhs.net) or the on-call pharmacist out of hours.

In cases requiring intravenous immunoglobulin, local commercial stock should be used.

Relevant anti-toxin titres for Cutaquig are published in Gupta S, Kobayashi RH, Litzman J *et al.* Subcutaneous immunoglobulin 16.5% for the treatment of pediatric patients with primary antibody immunodeficiency. *Expert Review of Clinical Immunology* 2023; 19(1): 7-17 [<https://doi.org/10.1080/1744666X.2023.2144836>] and are republished below.

Antibody titres for subcutaneous immunoglobulin 16.5% (Cutaquig) from 8 batches:

Antibody	Units	Mean $\pm$ SD
Hepatitis A virus	IU/mL	26.7 $\pm$ 6.6
Hepatitis A virus surface antigen	IU/mL of IgG	70.9 $\pm$ 17.2
Parvovirus B19	IU/mL	547 $\pm$ 35.1
Poliovirus	Relative to NIH176	1.1 $\pm$ 0.6
Measles virus	Relative to NIH176	0.8 $\pm$ 0.2
Diphtheria virus	IU/mL	16.5 $\pm$ 4.8
Rubella virus	IU/mL	694 $\pm$ 131
Tetanus toxin	IU/mL	48.5 $\pm$ 14.5
Varicella zoster virus	mIU/mL	19,100 $\pm$ 8955

Indication	Selection criteria	Exclusion criteria	Position of immunoglobulin, taking into account alternative therapies	Recommended dose	Clinical outcomes	Prior panel approval required
Use of immunoglobulin in other indications						
Allo-immune neonatal haemochromatosis or gestational allo-immune liver disease (GALD)	- Pregnant mothers with a previous adverse pregnancy outcome and clear post-mortem evidence of foetal haemochromatosis, OR - Women / patients who have had an offspring with neonatal liver failure confirmed to be allo-immune neonatal haemochromatosis OR - Affected neonates Decision to treat with Ig made by a consultant obstetrician with input from a liver unit specialist	No	For those patients fulfilling eligibility criteria, there are no alternatives to IVIg. For further information please refer to the NHS England Clinical Commissioning Policy: Maternal intravenous immunoglobulin (IVIg) for the prevention of alloimmune foetal and neonatal haemochromatosis³⁸.	Maternal dose: Immunoglobulin is administered by intravenous infusion at a dose of 1g/kg (dose capped at 60g 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. Neonatal dose: 1g/kg ± repeat. The need for repeat doses, which may exceptionally be required, should be based on clinical need and local policy. EOEIAP: Use DDW based on booking weight. Use ABW for neonates.	- Foetal loss (including gestation) - Gestation at delivery - Neonatal outcomes	Apply to EOEIAP (including retrospectively if emergency out of hours) Consultant obstetrician may approve out of hours in lieu of formal panel decision if both 1) clinically urgent, 2) liver unit specialist recommends treatment. Out of hours No, unless emergency (see above). Class II indication

						For further information please see; NHSE Clinical Commissioning Policy: Maternal intravenous immunoglobulin (IVIg) for the prevention of allo-immune fetal and neonatal haemochromatosis
ANCA-associated systemic vasculitides (AAV)	- Patients with refractory/relapsing AAV in whom conventional immunosuppressive therapy is contra-indicated e.g. presence of severe infection or in pregnancy as bridging therapy - The role of IVIg in the treatment of ANCA-negative small vessel vasculitis is unclear and each case will need to be assessed on individual grounds.	No specific exclusion criteria – see comments under selection criteria	IVIg is reserved as adjunctive or very rarely as sole therapy for the minority of patients in whom conventional immunosuppressive therapy is contra-indicated. A single 2g/kg over 5 days treatment may be commenced as an emergency with panel application to be submitted retrospectively in the rare event of all of the following being true: Panel will not be available on the following day (e.g. on a Fri/Sat), and	Total dose of 2g/kg over 2 – 5 days every 4 weeks. The optimal duration of therapy is not known though most patients are likely to achieve remission after 3 months. IVIg should be discontinued after 3 months in the absence of clinical improvement. EOEIAP: Use DDW for dosing. See also statement relating to critical care admission.	- Improvement in Birmingham Vasculitis Activity Score (BVAS)/PVAS – to capture paediatric assessment tool. - Fall in inflammatory markers - Improvement in organ function	Apply to EOEIAP. Consider prospective applications for deteriorating patients. Out of hours No Class III indication See also statement relating to critical care admission.

			• A prospective application has not been submitted, and • Significant disease associated with a critical care admission, where other immune suppression is contra-indicated, and • IVIG recommended by a consultant nephrologist or rheumatologist, or specialist MDT.			
(Prevention of) Autoimmune congenital heart block (anti-Ro) SHORT TERM	Prophylactic IVIg therapy has previously been given during pregnancy when: • There is a history of autoimmune congenital heart block in at least one previous pregnancy, AND • Maternal anti-Ro and/or anti-La antibodies are present. More recent evidence has cast doubt on the beneficial effects of IVIg, with hydroxychloroquine being regarded as first line therapy – see comments under	See comments under position of Ig	Hydroxychloroquine is regarded as the treatment of choice IVIg may be considered in exceptional cases refractory to hydroxychloroquine or if the patient is unable to tolerate hydroxychloroquine, or there is uncertainty regarding its efficacy. At a dose of 0.4 g/kg every 3 weeks administered from weeks 12 through to week 24 of gestation, IVIg was ineffective in	Two infusions of 1g/kg/day, the first at 14 weeks and the second at 18 weeks of gestation EOEIAP: Use DDW based on mother's booking weight for dosing.	• Improvement in the degree of heart block at birth	Apply to EOEIAP Out of hours No Class II indication

	position of Immunoglobulin		preventing the development of CHB in neonates in two prospective open-label trials. Based on a case series a higher dose (1g/kg) alongside high dose oral prednisolone may possibly be effective.			
Autoimmune uveitis SHORT TERM	Severe aggressive sight-threatening disease unresponsive to conventional immunosuppressive treatment (topical and systemic steroids and oral or injectable immunosuppressants)	See comments under position of Ig	IVIg is reserved for exceptional cases where anti-TNF agents are contra-indicated or ineffective or associated with intolerable adverse effects, especially in the context of autoimmune retinopathy. Adalimumab is regarded as the treatment of choice for other forms of severe, refractory uveitis and is routinely commissioned by NHS England (NICE TA 460) for this indication ⁴⁰.	1.0 - 1.5 g/kg/month – two to three infusions given 6 – 8 weeks apart to assess benefit EOEIAP: Use DDW for dosing.	• Clinically meaningful improvement or stabilisation in visual acuity • Imaging endpoints • Electrodiagnostic studies	Apply to EOEIAP Out of hours No Class III indication
Capillary Leak Syndrome – systemic (SCLS) (AKA Clarkson's syndrome)	Patients are eligible for preventative treatment after an acute episode of SCLS if all of the following criteria are met: • Diagnosis of idiopathic SCLS made by a relevant	Exclusions include patients who have not had an acute episode of	IVIg is considered first-line preventative treatment with a strong indication for improved survival. Acute episodes often require ICU admission to stabilise	Initially 2g/kg over 3-5 days, repeated initially 4 weekly, then every 4-6 weeks to assess benefit. Range for long-term therapy 1-2g/kg every 4-	• Reduction in frequency of acute flares • Reduction in severity of acute flares • Number of hospital admissions for SCLS.	Apply to EOEIAP Out of hours No Class III Indication

	specialist or specialists, which may include: immunology, rheumatology, nephrology or haematology. • Patient has been discussed by an MDT with relevant specialist involvement Acutely: • Hypovolaemia • Interstitial oedema • Haemoconcentration (HCT or Hb exceeding normal values for age / gender, or >20% of the last patient reference value). • Monoclonal gammopathy Diagnosis relies on recurrent acute flares associated with monoclonal gammopathy (>85% of patients).	SCLS during which blood biochemist ry shows haemo-concentrat ion or patients where SCLS is secondary to a document ed cause as assessed by a specialist MDT (for example, medication -induced capillary leak).	fluid balance and manage blood pressure. [NHSE CCP 2270, Dec 25]	8 weeks. Aim to slowly reduce dose or dosing interval as able without relapse. Use DDW for dosing. Cases to be reviewed at regional EOEIAP meetings at 3 months, 6 months and then at least annually. A complete clinical response is defined as a year without any acute episode and without any associated hospital admissions. Patients with a complete clinical response should be reviewed for a potential trial off therapy.	• Number of intensive care admissions for SCLS • Survival Severity is judged on the presence of any of the following (though other criteria may also be appropriate): • SBP <80mmHg, • MAP <65mmHg, • LOC, • admission to an ICU.	
Catastrophic antiphospholipid syndrome (CAPS) SHORT TERM	Diagnosis of definite or probable CAPS: • Thromboses in 3 or more organs, systems and/ or tissues simultaneously in	Chronic recurrent thrombosis due to other	Steroids, anticoagulant and plasma exchange (PLEX) represents optimal therapy.	2g/kg over 4-5 days EOEIAP: Use DDW for dosing.	• Clinically meaningful improvement • Reduction in anti-phospholipid antibody levels	Apply to EOEIAP Out of hours No

	less than a week. • Histological evidence of microthrombosis (small vessel occlusion) in at least one organ or tissue • Persistent antiphospholipid antibody positivity (lupus anticoagulant and / or anticardiolipin antibody / Anti-β2GPI of IgG or IgM isotype) Definite CAPS: all 4 criteria Probable CAPS: • All 4 criteria, except only two organs, systems or tissues involved. • All 4 criteria, except unable to confirm antiphospholipid antibody persistence owing to new diagnosis. • Development of a third event in >1 week but < 1 month despite anticoagulation. • Absence of histological confirmation of small vessel occlusion.	causes Thrombosis associated with stable anti-phospholipid syndrome in the context of other disorders	IVIg is likely to be beneficial in selected cases associated with severe thrombocytopenia where PLEX is either unavailable or contra-indicated or in the event of deterioration following PLEX. IVIg may be less suitable in elderly patients and patients with renal insufficiency owing to an increased risk of adverse renal effects.		It may also be appropriate to monitor for: • Survival • Prevention of permanent organ dysfunction	Class III indication In life-threatening disease ONLY: Apply to EOEIAP If PLEX unavailable & patient cannot be transferred to a centre offering PLEX or thrombocytopenia prevents PLEX AND if panel decision is not communicated on same day as application, Trusts may commence treatment over 5 days pending panel decision. Pharmacy supply sufficient IVIG to last until next working day while panel decision pending.
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Immunobullous diseases	- Severely affected AND - Conventional corticosteroid treatment with adjuvant immunosuppressive agents has failed or is inappropriate	See comments under position of Ig	IVIg is reserved as adjunctive therapy for patients with severe disease refractory to conventional immunosuppressive therapy. Rituximab is increasingly supplanting IVIg as the preferred treatment for resistant disease and is approved by NHS England⁴¹. In such patients it is listed as a 3rd line treatment alongside IVIg. However, rituximab should be favoured over IVIG, given the stronger evidence base supporting its use.	1-2g/kg over 2-5 days. There may be a need for maintenance therapy in exceptional patients unresponsive or intolerant of rituximab. In such cases every attempt should be made to define the minimum effective dose of Ig by undertaking periodic dose reduction and /or lengthening the intervals between treatments. EOEIAP: Use DDW for dosing.	- Reduction in recurrence of disease/relapse - Dose reduction / discontinuation of other immunosuppressive therapy - Improved quality of life - Resolution of blisters / healing of affected skin - Resolution of pruritis	Apply to EOEIAP Out of hours No Class III indication
Kawasaki disease SHORT TERM Paediatric Inflammatory Multisystem Syndrome temporally	Clinical diagnosis in a <u>paediatric patient</u> by a paediatrician, paediatric infectious disease consultant or paediatric immunologist of: Kawasaki disease (fulfilling full or partial criteria for Kawasaki disease)	None	Kawasaki IVIg in combination with anti-inflammatory doses of aspirin is the treatment of choice Consider steroids as first-line therapy while	2g/kg single dose – given over 8-12 hours, in conjunction with high dose aspirin, a second dose may be given if no response, or if relapse within 48 hours.	- Resolution of fever - Improvement in acute phase markers	Consultant may approve Out of hours Permitted Class I indication

associated with Covid-19 (PIMS-TS) SHORT TERM	OR • PIMS-TS Clinical diagnosis in an <u>adult</u> of PIMS-TS (also known as MIS-A or AIMS-TS) by a consultant in infection or immunologist or appropriate specialist MDT Because of the similarities between PIMS and Kawasaki disease, the use of IVIg is approved for any child fulfilling diagnostic criteria for PIMS [Royal College of Paediatrics and Child Health guideline 'Paediatric multisystem inflammatory syndrome temporally associated with Covid-19']. https://www.rcpch.ac.uk – <i>document withdrawn</i>. More recent data suggests that steroids should be first-line therapy, especially for children 6 years or over without symptoms of Kawasaki disease – see comments under position of immunoglobulin.		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-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. There were no significant differences	Consider slowing the rate of administration if there are features of heart failure (disproportionate tachycardia, gallop rhythm, liver enlargement, breathlessness)^{46,47} EOEIAP: Use ABW for dosing. Risk factors for IVIG resistance – age <1 year, PLT <100, liver derangement - ALT >100).		
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			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 the groups.			
Scleromyxedema (adults) As per NHS England clinical commissioning policy 2271 [Nov 2024] - Refer to NHS England CCP for further information including scoring systems and patient pathway	Patient will be eligible for Ig treatment if they fulfil ALL of the following criteria: - Diagnosis, following biopsy, of scleromyxedema by a joint rheumatology and dermatology MDT within a rheumatology or dermatology specialist centre with expertise in autoimmune connective tissue disease. AND - Diagnosis, as per Rongioletti and Reborna 2001, should include ANY three of the following criteria: - Generalised, papular and sclerodermoid eruption - Presence of monoclonal	Patients with contra-indications to therapy with human normal immune-globulin are not eligible for treatment.	As per NHSE CCP 2271, IVIG may be used at any stage of therapy alone or combined with other treatments. Clonal plasma cell is a key feature of scleromyxoedema. Consider plasma cell-directed therapies (anti-CD38, proteasome inhibitors, lenalidomide and its analogues) as an alternative to Ig. Stopping criteria are: - Worsening of disease activity - Worsening of extra-cutaneous manifestations	Initial treatment as IVIG 1-2g/kg over 2-5 days, then repeat 1-2g/kg every 4 weeks, or as equivalent SC dose. Dose adjustment should be considered at 3, 6 and 12 months after starting treatment. The dose can be reduced, providing the condition is clinically stable by: - Increasing the interval between treatments (typically not less than 6 weekly). OR - Reduce the dose with each infusion	Review for clinical response at 3 months, 6 months and every 12 months at specialist joint rheumatology and dermatology clinic with outcomes reported to EOEIAP. Criteria for assessment must include: - Absence or presence of systemic involvement, including progression to dermatoneuro syndrome as a marker of neurological involvement. - Hospital admissions per year relating to scleromyxedema.	Apply to EOEIAP Out of hours No Class III indication

	gammopathy • Absence of thyroid disease • Historical triad of mucin deposition, fibroblast proliferation and fibrosis as confirmed by biopsy.		• Worsening health-related QoL • No treatment response after at least 6 months of therapy.	(from 2g/kg). Dose to achieve minimum effective dose (reduce from 2g/kg) The minimum effective clinical dose to maintain remission should be established for each individual patient. EOEIAP: Use DDW for dosing.	• Modified Rodnan skin score • Level of paraprotein. Criteria for assessment should also include some or all of: • Disease severity (e.g. progression to dermatoneuro syndrome) • Papule involvement (e.g. papule count in fixed 2x2cm² area using a photographic record with the same views taken at intervals) • Itch visual analogue score (VAS) • Patient Global Assessment (VAS) • Physician Global Assessment (VAS) • Nutritional status	
Toxic epidermal necrolysis, Stevens Johnson Syndrome Indication excluded	Diagnosis by a dermatologist or consultant in a specialist burns unit; AND Involved body surface area	Mild / moderate disease or any level amenable	No therapy with unequivocal benefit for SJS/TEN exists ³⁵ . The immunological basis has led to the use of	2g/kg, usually divided as 1g/kg over 2 days. EOEIAP: Use DDW for dosing.	Resolution of the disease Survival	Apply to EOEIAP (<u>no treatment</u> without panel approval)

Pharmacy

Division B

On behalf of the East of England
Immunoglobulin Assessment Panel
(EOEIAP)

from NHS England commissioning guidance (from Aug 2021) SHORT TERM (if approved)	>10% AND When other treatments are contraindicated AND The condition is life-threatening	to supportive care ± steroid / ciclosporin See general comments regarding prothrombotic risks of IVIg	immunomodulation; the best studied of which are IVIg, corticosteroid and ciclosporin. In meta-analysis, there is no robust evidence that IVIg improves overall survival vs. supportive care alone, nor is there a benefit demonstrated (with or without corticosteroid) that IVIg improves ocular, oral or urogenital outcomes versus corticosteroid alone³⁵.			Consider prospective applications for deteriorating patients. Out of hours No Class IV indication
Transplant (solid organ) SHORT TERM	Antibody Incompatible Transplant (AIT) Patients in whom renal, heart liver or lung transplant is prevented because of antibodies. Blood group incompatibility renal transplant only.	See comments under position of Ig See comments under position of Ig	While IVIg is included in many protocols, there is a paucity of high-quality evidence to support its use. A systemic review of AMR in kidney transplant recipients categorised the evidence supporting IVIg as 'very low'⁴². Where IVIg is used in combination with PLEX, any beneficial effects of Ig	Renal transplant blood group incompatible transplant (renal desensitisation): 100mg/kg IVIG for 8 - 12 doses. AIT: Up to 2 g/kg to be repeated as per DSA; EOEIAP: Use DDW for dosing.	AIT and AMR: <u>Renal:</u> • Type of renal transplant • HLA class DSA (where available) • Rejection episodes • Patient survival • Graft survival • Renal function = eGFR	Apply to EOEIAP Consider prospective applications for deteriorating patients. Out of hours No Class II

			are likely negated by subsequent PLEX. For this reason, the use of Ig immediately prior to PLEX is not supported. The addition of rituximab to IVIg appears to be of benefit in lowering HLA antibody titres.		(MDRD)	indication
	Antibody Mediated Rejection (AMR) Patients experiencing steroid resistant rejection or where other therapies are contra-indicated after renal, heart, liver and/or lung transplant. e.g. Renal transplant Especially in the known presence of donor reactive anti-HLA antibody (DSA) pre-transplantation. Diagnosis based on: - Graft dysfunction (oliguria, rise in serum creatinine) - Rising DSA level - High level of association with T-Cell mediated rejection		Following a significant positive DSA finding in HLA-antibody screening, commence plasma exchange where available for this indication (min. 5 sessions in 7 days) with pulsed IV corticosteroid (given after PLEX on days of PLEX. Then refer to “recommended dose” in these guidelines for immunoglobulins.	Renal transplant: If DSA levels have fallen following 5th course of PLEX therapy, commence 2g/kg over 4-5 days. If DSA levels remain high, continue PLEX on alternative days followed on the same day as PLEX by 10g of IVIG or 100mg/kg IVIG (whichever is the greater). Round up to the nearest 5g. EOEIAP: Use DDW for dosing.	<u>Cardiothoracic:</u> • DSA • Length of ITU and hospital stay Resolution / improvement in objective measures of graft dysfunction: Renal transplant If DSA levels remain high or graft dysfunction persists, then a further transplant biopsy is indicated. Liver transplant Liver function Clotting indices Lung transplant Spirometry Heart transplant Ejection fraction	

14 IFR applications

IFR form and more information on IFRs in general, can be here:

<https://www.england.nhs.uk/contact-us/privacy-notice/how-we-use-your-information/our-services/individual-requests-for-funding/>

NHS England will monitor use of Ig in Class III and IV indications via the MDSAS database and provide SRIAPs and commissioners with data relating to use in uncommissioned, unlisted indications and indications with less evidence.

- See main body for Class I to III indications.
- See paragraph 12 for a list of Class IV and V indications.

15 Class I, Class II, Class III (commissioned, lower ranking), Class IV (unlisted / formerly listed) and Class V (automatically rejected) indications

NHS England classify indications as commissioned or not commissioned. Commissioned indications are further classified into those which require panel approval before treatment, and those with Group Prior Approval (GPA) which can commence without panel approval (Class I indications).

- Class I treatment must be notified to panel for tracking, audit, billing and retrospective review of eligibility.
- Class II indications require **prospective panel authorisation**. This may be given by a single panel member who is specialist in the condition to be treated.
- Class III indications require **prospective panel consensus**. This is given where there are three or more panel members in support of the treatment with no panel member who objects.
- Class IV indications are those which are not listed in the guidelines including new clinical entities, or those which have formerly been listed in the clinical guidelines (NHSE commissioning guideline or DH clinical guideline). Class IV indications require **prospective panel consensus** and **funding approval**.

No Class II to IV indication treatment may commence without approval from the East of England Immunoglobulin Assessment Panel (EOEIAP). www.cuh.nhs.uk

- Only electronic applications are accepted by the EOEIAP. Class III and IV indications must have presumed immune-mediated disorders with some evidence of efficacy or a presumed mechanism immune-mediation.
- Class I, II and III indications are funded as a commissioned treatment provided treatment is approved by the EOEIAP and used with the stipulation of the clinical approval.
- Class IV indications require IFR submission following clinical panel approval (if granted). that indication. The EOEIAP will advise following a request for treatment.

Class IV - Not routinely commissioned indications / indications that are no longer routinely commissioned (those with limited or no evidence for efficacy).

Class V [where started] – Not commissioned

Acquired red cell aplasia NOT due to parvovirus B19	
Acute disseminated encephalomyelitis (if high dose steroids have failed)	
Acute idiopathic dysautonomia	
Adrenoleukodystrophy	(Class V)
Alzheimer's disease	(Class V)
Amyotrophic lateral sclerosis	(Class V)
Aplastic anaemia / pancytopenia NOT due to parvovirus infection	
Asthma	(Class V)
Atopic dermatitis / eczema	
Autoimmune neutropenia	
Autologous BMT	(Class V)
Cerebral infarction with antiphospholipid antibodies	
Chronic facial pain	
Chronic fatigue syndrome	(Class V)
Chronic idiopathic urticaria	(Class V)
Chronic immune thrombocytopenia (ITP); as monotherapy	
Chronic regional pain syndrome	
CNS vasculitis	

Critical illness neuropathy	
Diabetic proximal neuropathy	
Graves' ophthalmopathy	(Class V)
Haemolytic uraemic syndrome	
Immunodeficiency secondary to paediatric HIV infection	(Class V)
Inclusion body myositis	
Intractable childhood epilepsy	
IVF failure	(Class V)
Multiple sclerosis	(Class V)
Neonatal sepsis (treatment) – IgM-enriched HNIg (Pentaglobulin) may be used.	
EOEIAP support use of Pentaglobulin as part of a continuing service evaluation using defined criteria for overwhelming neonatal sepsis.	
Opsoclonus-myoelonus syndrome – adult carcinoma related	
Paediatric myocarditis	
PANS/PANDAS	
Paraneoplastic disorders that are known not to be B-cell or T-cell mediated	
POEMS	
Pyoderma gangrenosum	
Recurrent spontaneous pregnancy loss	(Class V)
Rheumatoid arthritis	(Class V)
Sepsis in the intensive care unit not related to specific toxins or C Difficile	(Class V)
SLE without secondary immunocytopenias (including juvenile)	
Systemic juvenile idiopathic arthritis	
Toxic Epidermal Necrolysis (TEN) or Stevens Johnson Syndrome (SJS)	
Urticaria (severe, intractable)	
ANY INDICATION NOT LISTED BY NAME IN THIS DOCUMENT is considered to be CLASS IV	

All indications that are classified as **Class V indications** are not recommended and are **automatically rejected** by the EOEIAP.

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18 Associated documents

The [NHS England clinical commissioning policy for the use of therapeutic immunoglobulin \(Ig\)](#) England (2025)

The [Immunoglobulin Policy and Procedure](#) (CUH users only)

The immunoglobulin [eReferral application webpage](#) (NIgD)

The [Immunoglobulin Treatment Authorisation Form](#) (Immunomodulation)

The [Immunoglobulin Treatment Authorisation Form](#) (Immunodeficiency)

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Appendix 1:

List of guideline amendments by date:

July 2026 Version 7.5	New: • New requirement to specifically seek neurologist advice for the management of potential drug-induced GBS. Many of the medicines associated with drug-induced GBS also have associations with similar side effects such as peripheral neuropathy.
March 2026 Version 7.4	New: • NHS England clinical commissioning policy 2270 incorporated into the clinical Ig guideline: "Human normal immunoglobulin for preventative treatment of idiopathic systemic capillary leak syndrome following an acute episode (adults)".
December 2025 Version 7.3	New: • Acceptance of a single emergency treatment for ANCA vasculitides in an acutely deteriorating patient, admitted to critical care, with appropriate local review to commence, provided retrospective approval from panel is sought.
November 2025 Version 7.2	New: • Advice to 'consider prospective application to the EOEIAP for a patient who is deteriorating' for five indications: systemic vasculitides, inflammatory myopathy, Non-MS CNS inflammatory disease, AIT/AMR following solid organ transplant and TEN/SJS. • Concession to permit consultant obstetrician to approve commencement of treatment for haemochromatosis out of hours in emergency circumstances (risk to life or limb) where a specialist liver unit has recommended immunoglobulin treatment. Retrospective panel approval remains mandatory. • Review of URL links. Publication as a protected ODT.
June 2025 Version 7.1	New: • Infusion rate advice in Kawasaki disease
March 2025 Version 7	New: • New modified to reflect March 2025 NHS England Clinical Commissioning Policy for immunoglobulins. • Review of Class IV and Class V indications. • Removal of Subgam • First line SCIG for IM injection – Cutaquig. All others require advice from panel.
November 2024 Version 6.04	New: • New commissioned indication for the treatment of scleromyxedema with human normal immunoglobulin as per NHS England clinical commissioning policy 2271 • eReferral link • Dosing review – all indications (quality check)
October 2024 Version 6.03	New: • Updated information for the treatment of varicella zoster exposure in at risk groups, including neonates and in

		pregnancy. In line with UKHSA briefing 2024/043 and UKHSA Guidelines on post exposure prophylaxis (PEP) for varicella or shingles (September 2024)
July 2024 Version 6.02	New:	Updated NICE TA referencing in ITP
June 2024 Version 6.01	New:	Clarification in measles advice
April 2024 Version 6.01	New:	Amended in line with the publication of updated national commissioning policy
Apr 2024 Version 5.13	New:	- Updated advice on antibody-incompatible transplant and antibody mediated rejection (of a transplant) - Updated advice for use of commercial vs. UKHSA supplied immunoglobulin in post-exposure prophylaxis (viral).
Mar 2024 Version 5.12	New:	- Link to UKHSA viral illness in pregnancy. - Dosing advice for neonates after maternal exposure to measles.
Feb 2024 Version 5.11	New:	Updated dosing advice following exposure to measles.
Feb 2024 Version 5.10	New:	Updated link to the revised National Measles Guideline
Jan 2024 Version 5.9	New:	Update to unify units used for Hb (g/L)
Dec 2023 Version 5.8	New:	Update on the use of HNIg in viral exposure
Oct 2023 Version 5.7	New:	Updated advice on the management of catastrophic antiphospholipid syndrome published
Sept 2023 Version 5.6	Minor edit	
July 2022 Version 5.5	New:	- Updated with NICE CG information in ITP - Immunobullous diseases update - Addition of autoimmune neutropenia to Class IV
June 2022 Version 5.4	Review of document: New:	- Revised Class I information - Information including re: place of Ig therapy for chronic ITP - Clarification re: dosing in children - References reviewed and corrected, DOI hyperlinks - Autoimmune encephalitis with known or without known antibody information combined
Feb 2022	Further update reflecting NHS England revised commissioning	
July 2021	Further update on classification structure.	
	Indications are classified as Class I to V as before:	- Class IIIa becomes Class III - Class IIIb joins unlisted indications in Class IV

	References to Red, Blue, Grey and Black are removed. Updated advice re: IFR applications
June 2021	Updates in line with revised NHSE commissioning guidelines: New: - Secondary antibody deficiency – CAR-T specific information - Acute idiopathic / autoimmune dysautonomia / ganglionopathy - Opsoclonus myoclonus - Paraneoplastic neurological syndromes - Neuromyotonia - Non-MS CNS inflammatory syndromes Revised: - Coagulation factor antibodies - Autoimmune encephalitis - GBS outcome criteria - Inflammatory myopathies - Catastrophic antiphospholipid syndrome - Severe or recurrent Clostridium difficile colitis - Immunobullous diseases - Autoimmune uveitis - ANCA associated systemic vasculitides - Antibody incompatible transplant / Antibody mediated rejection - Class IV indications
Apr 2021	Thrombosis and Thrombocytopenia following Covid-19 vaccination Preliminary advice in line with MHRA and NHSE guidance covering an emerging and commissioned indication for IVIG. Consult in line with the Expert Haematology Panel (working in conjunction with the MHRA) advice from March 2021 and will be reviewed as new information comes to light. Measles exposure: Update to reflect UKHSA guidance
Dec 2020	Haemophagocytic syndrome: update to clinical treatment and monitoring criteria
Dec 2020	Toxic epidermal necrolysis: update to permit regional burns unit to commence treatment
Oct 2020	Toxic epidermal necrolysis: Change to OOH permissions for TEN
Oct 2020	General document: Modification to document title
Aug 2020	Tetanus treatment and prophylaxis: Revised “recommended dose” information for NAIT / Foeto-maternal alloimmune thrombocytopenia, in line with revised
Aug 2020	Foeto-maternal alloimmune thrombocytopenia / NAIT: Revised recommended dose information.
Aug 2020	Commissioning status for former GREY / Class III indications: Clinical approval from a Sub-Regional Immunoglobulin Assessment Panel is now sufficient to commence treatment for all former grey / Class III indications. All “little to no evidence for efficacy” indications now therefore become Class IIIb. Class IV indications are now any indication which is not listed in national commissioning documents