Immunoglobulin (IV or SC) Usage - Full Clinical Guideline

Reference No.: CG-T/2012/108

For Paediatric Immunoglobulin request please refer to relevant trust guideline

Aim

To ensure that Immunoglobulin prescribing in the Trust complies with the directives from the Department of Health's Demand Management Programme for Immunoglobulin.

Purpose

To ensure that all medical staff in all clinical areas has easy access to guidelines and are informed of the procedure when prescribing immunoglobulin within the Trust. The guideline is to be used in conjunction with the Department of Health clinical guidelines and demand management plan documents.

Introduction

Therapeutic immunoglobulin is a blood product which is used to treat patients with a wide range of diseases. Due to global shortages and UK specific issues, there has been concern about the availability of immunoglobulin to the NHS.

In May 2008, the Department of Health introduced a national Demand Management Programme (DMP) to provide guidance on appropriate use of immunoglobulin, to manage demand through more appropriate and consistent prescribing and to ensure that supply is maintained for patients for whom immunoglobulin is life-saving, regardless of geographical location. In 2011, this guidance was updated with new dosing information and drug classification.

The national DMP incorporates a demand management plan and clinical guidelines for immunoglobulin use, as well as an immunoglobulin treatment database. All documents can be accessed via www.igd.nhs.uk. The programme also incorporates immunoglobulin referral forms, requirements for a Trust Immunoglobulin Assessment Panel (IAP), and close liaison with commissioners.

Indications for treatment

1. Refer to the clinical guidelines and demand management plan on the website above to clarify the indication priority (red (high), blue (medium), grey & unlisted (low) and black (not recommended)).

Clinical guidelines – although a large document, there is a clear contents page which is useful for directing you to the different conditions where immunoglobulin is used in each speciality. There is a summary table which indicates the colour coding for your indication and also further information stating the evidence and recommendations for the listed conditions.

Demand management plan – a smaller document outlining the programme's background, objectives, definitions of colour coding, approval process, need for immunoglobulin assessment panel, commissioning & funding.

2. The table of indications, as described by the Demand Management Plan can be found in Appendix 1

3. Each indication is assigned a priority as follows:
    - **Red**-high priority. Available at all times because of risk to life without treatment.
    - **Blue**- medium priority. Alternative treatments may be available. At times of shortage restrict use in this group.
    - **Grey**-low priority. Use to be considered on case-by-case basis by the IAP
    - **Black**-not recommended/not commissioned

4. Conditions not listed in the table, for which immunoglobulin treatment may be considered, should be treated as grey indications.

5. For further details on the indications and associated evidence base, please refer to the DH document, Clinical Guidelines for Immunoglobulin Use and the Second Edition Update Clinical Guidelines for Immunoglobulin Use.

6. Duration of treatment:

    - Short term treatment is classed as up to three doses of up to 2g/kg at appropriate intervals, with total treatment duration of no greater than three months.
    - Long term treatment is any treatment with duration of longer than three months.

Immunoglobulin Panel

1. The Immunoglobulin Assessment Panel (IAP) review and approve all immunoglobulin use. The Panel's decision whether or not to approve immunoglobulin therapy will be based on the information provided on the Immunoglobulin Request form, the National Clinical Guidelines, expert knowledge of the condition, and a knowledge of locally available supplies of immunoglobulin products. The Panel consists of consultants from relevant specialities, clinical pharmacists and Commissioners or their representatives.
2. The Panel will review all new requests for IVIg as a standing agenda item.

3. **Red** and **Blue** indications will be reviewed retrospectively. Treatment may be commenced in advance of the Panel meeting. The Pharmacist for IVIG will compile the list of new patients and indications for each Panel meeting.

4. **Grey** indications include two categories:

- Conditions with limited evidence of efficacy- the Immunoglobulin Panel must approve the request before treatment is commenced. See appendix 3 for the application form. Final agreement for funding for these indications will also need to be sought from the Area Team at NHS England.
- Conditions with little or no evidence of efficacy- an Individual Funding Request (IFR) to NHS England is required before treatment is commenced.

5. **Black** indications require an IFR to NHS England before treatment is commenced.

6. If treatment is required urgently before the Panel is due to meet, the application form must be sent by email for approval by the IAP. The Panel will review this request on an ad-hoc basis.

7. Patients who receive IVIG for any indication should have a follow up outcome form completed and returned to pharmacy for uploading to the national database

8. For patients on long-term immunoglobulins for any indication, the follow up form is required every year the patient is receiving treatment. The IAP should review this information at each meeting. It is the responsibility of the IAP to identify any missing follow up forms and ensure this is completed by the treating clinician.

Prescribing of immunoglobulins

1. Prior to prescribing, the requesting clinician should complete the immunoglobulin request form found in appendix two and send this over the either the ward pharmacist in hours or the out of hours pharmacist. ***All sections of the request form (including patient weight) must be completed prior to supply being made.***

2. The pharmacist should review the request form ensuring the accuracy of the information recorded. The pharmacist should ensure the indication is approved for use prior to supplying any immunoglobulins. Any red or blue indications can be supplied automatically. Any indications listed as grey, black or not listed on the guideline should be referred to the IAP before a supply is made.

3. For inpatient areas using EPMA, IVIG should be prescribed on EPMA with a reference to ‘see infusion protocol’. The indication has to be completed on EPMA prior to prescribing.

4. For outpatient/day case areas, IVIG will be prescribed using the usual outpatient paper drug charts.

Dosing of immunoglobulins

1. The standard immunomodulatory dose is 2g/kg. This is usually divided into 5 daily infusions of 0.4g/kg.

2. Some physicians prefer to use two daily doses of 1g/kg each.

3. For specific dosing information for each indication, please refer to the tables within the DH Second Edition Update Clinical Guidelines for Immunoglobulin Use.

4. For patients with BMI ≥30 kg/m2 or if actual weight >20% more than IBW, prescribers should consider using adjusted-bodyweight dosing of immunoglobulin.

5. In patients on long term immunomodulatory doses, reasonable attempts should be made to reduce the dose, by increasing the dose interval or by using a reduced dose, or both.

6. To minimize the amount of IVIG used in individual treatments, rounding down IVIG dose to the nearest whole vial (adults) is recommended. Where the dose would be less than one vial in children, IVIG dose should be rounded up to a whole vial of the most appropriate size.

IVIG Preparations

1. The preparations in use at DTHFT are Iqymune (1st line), Octagam and Intratect. Other product may be available but discussions must be had with pharmacy prior to prescribing.

2. For patients on long term treatment, the same brand must be maintained throughout treatment.

3. Switching IVIg products should only be done with the clinician's approval. Patients established on one preparation may need to be changed to another during periods of non-availability of their usual brand. This is unavoidable. However, caution should be exercised when patients are switched from one IVIG preparation to another, as there may be an increased risk of adverse reactions. If an alternative product must be given to a patient on chronic therapy, it is usually prudent to use slow infusion rates and monitor the patient closely. Also, if side effects occur, a reduction in the infusion rate may minimise side effects

4. For patients commencing new therapy the brand of IVIG will be dispensed by pharmacy according to stock availability and acquisition cost. Where possible the 10% strength will be issued. Once a patient has started treatment they will be maintained on that brand. Patients who are transferred from other hospitals established on a brand will be maintained on that brand.

Administration of IVIG

1. Prior to administration of IVIG, assess that the patient is fit to proceed with treatment and perform baseline observations of:
    - Temperature
    - Pulse
    - Respiration rate
    - Blood Pressure
    - Weight

2. Cannulate the patient as per DTHFT policy.

3. IVIG can be administered peripherally or centrally. It should be infused via a separate line and should not be mixed with other IV fluids or medication.

4. Check that the named product to be used corresponds to that on the prescription and the bottle and is the correct brand for the patient.

5. Check the product, dose, batch number and expiry date of the product. Ensure the product is homogeneous. Do not use if a non-homogeneous solution, or a deposit can be seen.

6. Ensure that if pre-medication is required, it is prescribed and administered (only usually required if there has been a previous adverse reaction)

7. Ensure the product is at room temperature. If the product is stored in the fridge, ensure it is removed from the fridge at least 30 minutes prior to administration.

8. Pharmacy will supply an infusion chart which each supply of IVIG Ensure the patient name and details are correct on the infusion chart prior to starting administration. At each rate change ensure appropriate documentation has been completed.

9. Infuse product from its container. No further reconstitution is required.

10. It is recommended that administration should begin immediately after piercing the cap.

11. Flush line with either sodium chloride 0.9% or glucose 5% after use

Management of adverse reactions

1. Adverse reactions to IVIG are uncommon.

2. Acute reactions occur during the infusion or shortly after

3. Delayed reactions occur 24 – 48 hours after the infusion

4. Most common causes of adverse reactions are due to administering IVIG when there is an untreated bacterial infection and infusion at the incorrect rate

5. Risk of adverse reactions can be minimised by adhering to the prescribed rate

6. Rarely IVIG may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration

7. If a reaction does occur, refer to the following advice:

Symptoms	**Action**
MILD reaction Headache Light headedness Fever, shivers or sweating Nausea, vomiting Generalised aches and pains Irritability	 Slow or stop infusion Give paracetamol for fever/headaches Restart infusion as per protocol when symptoms have resolved If symptoms persist, stop the infusion and seek medical advice
MODERATE/SEVERE reaction Severe headache Nausea and vomiting Wheezing/difficulty breathing Chest/loin pain Itching, nettle rash, hives Loss of consciousness	 Stop infusion Call for medical help Inform senior nurse If necessary, administer supportive drugs Hydrocortisone IV Chlorphenamine IV Salbutamol Anaphylaxis/Crash box should be available

Request for Immunoglobulin (Ig)
Refer to immunoglobulin procedure on Trust Intranet and immunoglobulin clinical guidelines on the website www.igd.nhs.uk

⇩

What is the colour code for the indication?

⇦ Indication is **GREY** or **BLACK** in the Clinical Guidelines

⇩

Complete an **Ig request form**

Discuss with divisional lead pharmacist. Requesting consultant to discuss with chair of immunoglobulin assessment panel.

Request to be reviewed by immunoglobulin assessment panel.

⇨

Panel Decision

↙ **Not Approved**

Clinician informed
Pharmacy informed
Decision logged on the National Database

⇩ **Panel Approved**

Clinician Informed
Pharmacy Informed
Decision logged on the National Database
Refer to NHSE for approval

⇩

Approved by NHS E.
Prescribe Ig. Contact pharmacy for supply.

⇨

Give completed forms to divisional lead pharmacist within 48hr.
Patients consultant to complete immunoglobulin efficacy form.

⇨ Indication is **RED** or BLUE in the Clinical Guidelines

⇩

Complete an **Ig request form**
Prescribe immunoglobulin.
Contact pharmacy for supply.
Give IVIG.

⇩

Give completed forms to a ward pharmacist within 48hr.
Patients consultant to complete immunoglobulin efficacy form.

⇨ **Not approved by NHS E**

Clinician Informed
Pharmacy Informed
Decision logged on Database

<u>All patients are required to have an outcome and a follow up form completed after receiving treatment with IVIg</u>

References

Available via website: www.igd.nhs.uk

- DH Second Edition Update Clinical Guidelines for Immunoglobulin Use

Keywords Immunoglobulin, IVIG

Documentation Control

Development of Guideline:	Advanced Pharmacist – Specialist medicine Immunoglobulin Assessment Panel
Consultation with:	Chief Pharmacist Deputy Chief Pharmacist Divisional Lead Pharmacist Drugs & Therapeutics Committee
Approved By:	August 2017 - Derby Immunoglobulin Panel September 2017 - Drugs & Therapeutics Committee 11/12/17 - Integrated Care Division
Review Date:	September 2020
Key Contact:	Advanced Pharmacist – Specialist medicine

Appendix 1: Indications for Treatment -Adapted from DH Second Edition Update Clinical Guidelines for Immunoglobulin Use

Red
High priority

Conditions	Short term	Long term
Alloimmune Thrombocytopenia (Foeto - Maternal/Neonatal)		
Chronic inflammatory demyelinating polyradiculoneuropathy		
Gullian-Barre Syndrome		
Haemolytic disease for the newborn		
HSCT in primary immunodeficiencies		
Immune thrombocytopenic pupura (acute and persistent, excluding chronic*)		
Kawasaki disease		
Paraprotein - associated demyelinating neuropathy (IgM, IgG or IgA)		
Primary immunodeficiences		
Specific antibody deficiency		
Thymoma with immunodeficiency		
Toxic epidermal necrolysis, stevens Johnson syndrome		

*Updated February 2016

Blue
Medium priority

Conditions	Short term	Long term
Acquired red cell aplasia		
Autoimmune congential heart block		
Autoimmune haemolytic anaemia		
Autoimmune uveitis		
Coagulation factor inhibitors (allonatibodies and autoantibodies)		
Haemophagocytic syndrome		
Immunobullous disease		
Inflammatory myopathies		
Multifocal motor neuropathy		
Myasthenia gravis (including Lambert - Eaton myasthenic syndrome)		
Necrotising (PVL - associated) staphylococcal sepsis		
Post - transfusion purpora		
Rasmussen syndrome		
Secondary antibody deficiency (any cause)		
Severe or recurrent clostridium difficile colitis		
Staphylococcalor Streptococcal toxic shock syndrome		
Stiff person syndrome		
Transplantation (solid organ)		

Grey
Low Priority

Conditions	
Immune-mediated disorders with limited evidence of immunoglobulin efficiency	Presumed immune-mediated disorders with little or no evidence of efficiency
Acute disseminated encephalomyelitis (If high dose steroids have failed)	Acquired red cell aplasia not due to parvovirus B19
Autoimmune encephalitis (including NMDA and VGKC antibodies, among others) Catastrophic antiphospholipid syndrome	Acute idiopathic dysautonomia
Cerebral infection with antiphospholipid antibodies	Aplastic anaemia/pancytopenia
Chronic ITP	Atopic dermatitis/eczema
CNS Vasculitis	Autoimmune neutropenia
Complex regional pain syndrome	Chronic facial pain
Neuromyotonia	Diabetic proximal neuropathy
Intractable childhood epilepsy	Haemolytic uraemic syndrome
Opsoclonus Myoclonus	PANDAS
Post exposure prophylaxis for viral or pathogenic infection if intramuscular infections is contraindicated, or treatment when hyper-immune	Paraneoplastic disorders that are know not to be B- or T-cell mediated
Immunoglobulins are unavailable	POEMS
Pyoderma gangrenosum	SLE without secondary immunocytopenias (Including juvenile)
Systemic juvenile idiopathic arthritis	
Systemic vasculitides and ANCA disorders	
Urticaria (Severe, intractable)	

Black

Conditions
Immunodeficiency secondary to paediatric HIV infection
Autologous BMT
Adrenoleukodystrophy
Alzheimer's disease
Amyotrophic lateral sclerosis
Critical illness neuropathy
Multiple sclerosis
Rheumatoid arthritis
Neonatal sepsis (prevention or treatment)
Sepsis in the intensive care unit not related to specific toxins or C. difficile
Asthma
Graves ophthalmopathy IVF failure
Recurrent spontaneous pregnancy loss

Version .2.

Appendix 2: immunoglobulin request form

Immunoglobulin - Request Form

Ver. 5.416

Has this patient met the Selection Criteria as prescribed in the Clinical Guidelines Second Edition Update:

* Fields marked with an asterisk are mandatory for the upload feature
** Fields marked with a double asterisk are mandatory for a subsequent panel review
*** For Scottish Centres the CHI number is required and the Trust Id is not mandatory

Registration Details:

Patient Name:			
Trust Id (Hospital Number): *		Date First Seen: (dd/mm/yy)	
		Treatment Episode Start Date:	
Date of Birth: * (dd/mm/yyyy)		Gender: *	
NHS / CHI Number: ***			
GP Postcode:		or GP Practice Code:	
Height (m):		Weight (kg):	
Patient Transferred from other trust:		Date Transferred: (dd/mm/yy)	
If yes which trust:			

Panel Details:

Panel Decision: **		Panel Date: ** (dd/mm/yy)	
If rejected give details:			
Panel Colour:		Term:	
Efficacy Tracking Method:			
Name of Panel Member: **			
Next Panel Review Date: (dd/mm/yy)			
Administrative Category:			

Clinical Details:

Care Speciality: *			
Consultant/Registrar Name:		Bleep No. (If known):	
Diagnosis: *			
if Other please specify:			
Confidence in diagnosis:			
Comments, including additional justification for use:			
Secondary Diagnosis:			
Was Plasma Exchange Considered?			
Alternative Tried Before Ig:			
if Other please specify:			
Current Treatment:			
if Other please specify:			
Place of Treatment:		Stage of Treatment:	
Has The Patient Been Offered Home Care: **		Patient received Training from a UK PIN accredited centre: **	
Treatment Route:		Proposed Treatment Regime: *	
Dosage Type:			
Proposed Dose:		grams	
	every		Day(s)
	for		Day(s)
Proposed Treatment Date:			
Preferred Product:			
Additional Comments:			
Completed By:		Date: (dd/mm/yy)	

Appendix 3: Application to Immunoglobulins Panel for Grey Indications with limited evidence (not IFR)

Patient Name	
Hospital/NHS number	
Date of Birth	
Indication for Treatment	
Intended dose and schedule	
Intended duration of treatment	
Reason for request (why alternative treatment is not appropriate)	
Intended monitoring process (NB annual efficacy monitoring must be entered into the immunoglobulin	
Requesting Consultant	
Urgency of request	

Request to be submitted to the Trust Immunoglobulins Panel

Approved by Immunoglobulins Panel Yes/No Date…….

Approved by Area Team Yes/No Date……..