Whittington Health NHS

Intravenous Immunoglobulin Use

Subject:	Intravenous Immunoglobulin Use
Policy Number	N/A
Ratified By:	Clinical Guidelines Committee
Date Ratified:	July 2008. Review, Dec 2010, June 2011, Nov 2015
Version:	4.0
Policy Executive Owner:	Clinical Director, Medicine, Frailty and Networked Service ICSU
Designation of Author:	Consultant Haematologist
Name of Assurance Committee:	As above
Date Issued:	November 2015
Review Date:	November 2018 (3 years hence)
Target Audience:	Trust wide
Key Words:	Immunoglobulin, IVIg

Revision Chronology:		
Version Number	***Effective date***	***Reason for Change***
2	***1st December 2010***	***Change of brand from Octagam to Vigam (Priyal Shah)***
3	***30th June 2011***	***Change of brand from Vigam to Privigen – IV administration guide (Ian Man)***
4	***11 November 2015***	***Updated indications from DOH***

➢ Criteria for use

Patients being considered for treatment with intravenous immunoglobulin.

➢ Background

Therapeutic intravenous immunoglobulin (IVIg) is a blood product used in a number of clinical situations. However in recent years there have been concerns over the availability of IVIg to the NHS due to global shortages.

Therefore in 2007 (updated guidelines 2011) the Department of Health (DoH) instigated an initiative to ensure that IVIg is used appropriately particularly at times of shortage and to introduce consistency in usage.

The key features of the new DoH initiative are:

- clinical guidelines for the indications for the use of IVIG
- requirement for approval by the hospital IVIg assessment panel
- registration of patients receiving IVIg on national database

As a result, IVIg can only be used in specified situations and use will need to be approved prior to being prescribed.

➢ Indications for IVIg

Table 1 summarises the common indications for IVIg. For other indications and more detailed information please refer to the DoH clinical guidelines:

http://www.ivig.nhs.uk/documents/dh_129666.pdf

For use in the **infectious diseases** setting, which are not covered by the guidelines, please discuss with a Microbiology consultant.

Definitions of recommendations in guidelines

Red indications: *are of the highest priority and absence of treatment is life threatening. These do not require IvIg lead consultant approval and IvIg should be prioritised for these patients in times of shortage.*

Blue indication: *are indications where these is evidence to support use of IvIg but require approval from the immunoglobin approval lead (haematology consultant)*

Grey indications *are now listed as immune-mediated disorders with limited evidence of immunoglobulin efficacy, or presumed immune-mediated disorders with little or no evidence of efficacy*

Table 1 Summary of indications for IVIg (see also Table 2)

Condition	Short duration <3months	long duration 3 months	dose
Primary and secondary antibody deficiency states			
Primary immunodeficiencies		●	0.4-0.6g/kg/month
Thymoma with immunodeficiency		●	0.4-0.6 g/kg/month
HSCT in primary immunodeficiencies		●	0.4-0.6g/kg/month
HSCT in primary immunodeficienc		●	0.4-0.6g/kg/month
Specific antibody deficiency		●	0.4-0.6g/kg/month
Secondary antibody deficiency (any cause		●	0.4g/kg/month
Haematology			
Acquired red cell aplasia	●		2g/kg in 2 to 5 divided doses
Alloimmune thrombocytopenia (foeto-maternal/neonatal		●	Maternal: 1g/kg/week throughout pregnancy

			Fetal: 1g/kg occasionally more than one dose required
Autoimmune haemolytic anaemia including hyperhaemolysis	●		Up to 2g /kg as a single or divided doses
Coagulation factor inhibitors (alloantibodies and autoantibodies)	●		0.4g/kg for 5 days or 1g/kg 2 days
Haemolytic disease of the newborn	●		0.5g/kg over 4 hours
Haemophagocytic syndrome	●		Up to 2g/kg as single or divided dose
Immune thrombocytopenic purpura (acute and persistent, excluding chronic*)	●		1g/kg as a single infusion 0.8-1g/kg in children
Post-transfusion purpura	●		2g/kg in divided doses over 2 to 5 days
Neurology			
Chronic inflammatory demyelinating polyradiculoneuropathy**	●	●	2g/kg in divided doses repeated after 6 weeks
Guillain-Barré syndrome	●		2g/kg given over 5 days
inflammatory myopathies		●	2g/kg in divided doses repeated after 6 weeks
Myasthenia gravis (including Lambert-Eaton myasthenic syndrome)	●		2g/kg over 2 to 5 days
Multifocal motor neuropathy		●	2g/kg in divided doses repeated after 6 weeks
Paraprotein-associated demyelinating neuropathy (IgM, IgG or IgA)	●	●	2g/kg in divided doses repeated after 6 weeks
Rasmussen syndrome		●	2g/kg in divided doses repeated after 6 weeks
Stiff person syndrome		●	2g/kg in divided doses repeated after 6 weeks
Others			
Autoimmune congenital heart block	●		0.4g/kg every 3 weeks for 5 treatments week 12 to 24 gestation
Autoimmune uveitis	●		1.5g/kg/month for 3 months

Immunobullous diseases		●	2g/kg over 2 to 5 days
Kawasaki disease	●		2g/kg single dose over 12 hours with high dose aspirin, repeat after 48 hrs if relapse or no response
Necrotising (PVL-associated) staphylococcal sepsis	●		2g/kg single dose
Severe or recurrent Clostridium difficile colitis	●		0.4g/kg one dose, consider repeating
Staphylococcal or streptococcal toxic shock syndrome	●		2g/kg single dose
Toxic epidermal necrolysis, Stevens Johnson syndrome	●		2g/kg as single or divided dose
Transplantation (solid organ)	●		Variable dose dependant on indication refer to DOH guidance.

Chronic immune thrombocytopenic purpura is a grey indication
*** The disease should be life-threatening to allow database entry as red*

Table 2 Grey Indications

Immune-mediated disorders with limited evidence of immunoglobulin efficacy	Presumed immune-mediated disorders with little or no evidence of efficacy
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)	Acute idiopathic dysautonomia
Catastrophic antiphospholipid syndrome	Aplastic anaemia/pancytopenia
Cerebral infarction with antiphospholipid antibodies	Atopic dermatitis/eczema
Chronic ITP	Autoimmune neutropenia
Complex regional pain syndrome	Chronic facial pain
CNS vasculitis	Diabetic proximal neuropathy
Intractable childhood epilepsy	Haemolytic uraemic syndrome
Neuromyotonia	PANDAS
Opsoclonus Myoclonus	Paraneoplastic disorders that are known not to be B- or T-cell mediated
Post-exposure prophylaxis for viral or pathogenic infection if intramuscular injection is contraindicated, or treatment when hyper-immune immunoglobulins are unavailable	POEMS
Pyoderma gangrenosum	SLE without secondary immunocytopenias (including juvenile)
Systemic juvenile idiopathic arthritis	
Systemic vasculitides and ANCA disorders	
Urticaria (severe, intractable)	

Table 3 Indications for which IVIg is not recommended:

• Immunodeficiency secondary to paediatric HIV infection • Autologous BMT • Adrenoleukodystrophy • Alzheimer's disease • Amyotrophic lateral sclerosis • Chronic fatigue syndrome • 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

➢ Obtaining approval for use of IVIg

For approval for use during weekdays (Monday to Friday 9am to 5pm) please contact Dr Shah or one of the other Haematology Consultants.

Out-of-hours, please contact the on-call Haematologist (SpR or Consultant) via the hospital switchboard.

For approval in infectious conditions, please discuss with Consultant Microbiologist.

IVIg use will be formally approved at the Hospital Immunoglobulin Assessment Panel meetings.

The Transfusion Practitioner or Haematology Consultant or Registrar will register patients receiving IVIg on the database.

➢ Preparations available

Privigen® 10% (100 mg/ml) normal immunoglobulin in 2.5g, 5g, 10g and 20g vials.
Privigen® should be stored at room temperature. Do not store above 25^{o}C.
Do not freeze.
Keep the vial in the outer carton in order to protect from light.

➢ Prescribing IVIg

- Obtain patient's weight in kilograms
- For obese patients (>20% above ideal body weight), **calculate dose determining weight** (see appendix 1). There is no maximum total dose.
- Patients on maintenance with IVIg should be reviewed regularly and a trough level measured to adjust dosage and dosing interval
- Order IVIg from pharmacy

➢ Administration of IVIg

Ensure patient is well hydrated prior to infusion and avoid concomitant use of loop diuretics

loop diuretics

• Monitor serum creatinine and urine output

• IVIg should be infused at:

- An initial rate (test dose) of 0.3ml/kg/hour for 30 minutes.

- If well tolerated, the rate of administration may be increased to 0.6ml/kg/hour for a further 30 minutes.

- Subsequent increases could be to 1.2ml/kg/hour and so on, up to the maximum approved rate.

- The maximum approved rate is 4.8ml/kg/hour.

- In PID patients, who have tolerated the infusion rate of 4.8ml/kg/hour well, the rate may be further increased gradually to 7.2ml/kg/hour

• Patients should be closely observed for symptoms of adverse reactions during the infusion and for 60 minutes afterwards

➢ Contraindications to IVIg

- Hypersensitivity to any components of product
- Known IgA deficiency with anti-IgA antibodies
- Caution in patients with pre-existing risk factors for arterial or venous thromboembolic disease (use minimum dose and rate of infusion practicable)
- Caution in patients at risk of acute renal failure (use minimum dose and rate of infusion practicable)

➢ Adverse effects of IVIg

Common adverse effects

- hypotension
- allergic and hypersensitivity type of reactions
- headache
- chills, back pain, chest pain
- fever, hot flushes
- cutaneous reactions
- fatigue

- nausea

Severe adverse effects (usually related to rate of infusion)

- anaphylaxis
- circulatory shock
- acute renal failure
- arterial and venous thromboembolism
- transfusion transmitted infection

Interactions

- may impair response to **live attenuated vaccines** for up to 3 months. In particular, patients receiving measles vaccine up to one year after IVIg should have antibody levels checked.
- may cause false positive results in **serological assays**, in particular direct antiglobulin test
- may interfere with some **blood glucose monitoring** systems, if maltose in IVIg is measured as glucose, resulting in falsely high glucose levels. Check with glucose monitoring equipment information or manufacturer

➢ Contacts

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Consultant Haematologist
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Mr Abdul Adamu
Transfusion Practitioner
Ext 5192 bleep 2953

DrAli Rismani
Consultant Haematologist
Ext 5437

Dr B Davis
Consultant Haematologist
Ext 5035

Dr M Kelsey
Consultant Microbiologist
Ext 5082

Dr J Andrews
Consultant Microbiologist
Ext 3894

Haematology SpRs
Bleep 3060 or 3070

On-call Haematologist
(out-of-hours) via switchboard

➢ References

DoH Clinical Guidelines for the Use of Intravenous Immunoglobulin 2011

DoH Demand Management Plan for Immunoglobulin Use 2007

Vigam®Liquid liquid 5% normal immunoglobulin, Summary of Product Characteristics, BPL (Bio Products Laboratory), text revised December 2007

➢ Appendix 1

Ideal body weight (IBW) (kg):
IBW for males = 50 + (2.3 x (height in inches - 60))
IBW for female = 45.5 + (2.3 x(height in inches - 60))

Dose determining weight (DDW) (kg):
DDW = IBW + 0.4 (actual bodyweight (kg) - IBW)

➢ Compliance with this guideline

Audit: compliance with the guidelines will be monitored and discussed annually at the thrombosis committee.

Appendix A

Plan for Dissemination and implementation plan of new Procedural Documents

To be completed and attached to any document which guides practice when submitted to the appropriate committee for consideration and approval.

Acknowledgement: University Hospitals of Leicester NHS Trust

Title of document:	**Intravenous Immunoglobulin Use**		
Date finalised:	**December 2010, re-issued Nov 2015**	**Dissemination lead: Print name and contact details**	**Dr Shah**
Previous document already being used?	**Yes** **(Please delete as appropriate)**		
If yes, in what format and where?	**electronic**		
Proposed action to retrieve out-of-date copies of the document:	**To remove document from intranet guidelines page and replace with this version.**		
To be disseminated to:	**How will it be disseminated/implemented, who will do it and when?**	**Paper or Electronic**	**Comments**
All trust surgical SPR and ST/FY trainees	**via intranet**	**electronic**	
All orthopaedic consultants	**As above**	**electronic**	
Pharmacy staff	**As above**	**electronic**	
Is a training programme required?	**no**		
Who is responsible for the training programme?			

Appendix B

Equality Impact Assessment Tool

To be completed and attached to any procedural document when submitted to the appropriate committee for consideration and approval.

Impact (= relevance) **1 Low** **2 Medium** **3 High**	**Evidence for impact assessment (monitoring, statistics, consultation, research, etc)**	**Evidential gaps (what info do you need but don't have)**	**Action to take to fill evidential gap**	**Other issues**
Race **1**	No mention of race			
Disability **1**	No mention of disability			
Gender **1**	No mention of gender			
Age **1**	Dose adjusted for age>75			
Sexual Orientation **1**	No mention of sexual orientation			
Religion and belief **1**	No mention of religion			

Once the initial screening has been completed, a full assessment is only required if:

- The impact is potentially discriminatory under equality or anti-discrimination legislation
- Any of the key equality groups are identified as being potentially disadvantaged or negatively impacted by the policy or service
- The impact is assessed to be of high significance.

If you have identified a potential discriminatory impact of this procedural document, please refer it to relevant Head of Department, together with any suggestions as to the action required to avoid/reduce this impact.