1. Introduction

This guideline provides information on the use of Thymoglobuline® (rabbit anti-human thymocyte immunoglobulin or r-ATG) in the Leicester transplant unit for the treatment of steroid resistant graft rejection in renal transplantation.

2. Scope

This guideline has been developed for use by registered nurses, pharmacists and doctors to prescribe, order and administer r-ATG to kidney transplant patients. Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt consult a senior colleague or expert.

3. Guideline Standards and Procedures

3.1. Supply and Storage

- r-ATG must always be kept refrigerated (between 2 and 8°C). Once reconstituted, r-ATG has an expiry of 24 hours and should be administered within that time limit (including the infusion time).

3.2. Prescribing and administration

- r-ATG must be prescribed on the r-ATG prescription and monitoring chart (see Appendix 1) AND in the patient's Nervecentre Medication chart .
- The treatment dose of r-ATG is 1.5 mg/kg/day (rounded to the nearest 25 mg vial) given for a total of 10-14 days. Most patients will receive r-ATG every 2-4 days depending on their clinical condition and WBC, platelet and lymphocyte counts.
- Dose adjustments:
    - Reduce r-ATG dose by 50% if the total platelet count < 80 x 10 /L or the total WCC is < 2.5 x 10/L
    - Do not administer r-ATG if the total platelet count < 50 x 10 /L, or the WCC < 1.5 x 10 /L or the total lymphocyte count < 0.05 x 10 /L
- All patients will receive the following pre-medication 1 hour before each dose of r-ATG – they need prescribing on NerveCentre:
    - Paracetamol 1g PO
    - Chlorphenamine 4mg PO
    - Hydrocortisone 100mg IV
- r-ATG is diluted in 500mL of sodium chloride 0.9% and infused via a central line over at least 6 hours.
- Severe r-ATG associated cytokine release syndrome (CRS) can lead to fatal pulmonary oedema. All patients must have a fluid assessment before receiving r-ATG. This will be done by a senior clinician to ensure patients are not fluid overloaded.
- r-ATG must be given during core working hours and life support measures are readily available due to its side- effect profile (including severe anaphylaxis). Subsequent doses will also be given during core working hours unless instructed otherwise by the leading clinician on duty. Patients being treated with r-ATG must have all other

immunosuppression stopped (prednisolone is usually continued but this is the only exception). Oral immunosuppression therapy (calcineurin inhibitors and antiproliferative agents) should be re-started 48 hours before the last dose of r-ATG and levels monitored and acted upon.

3.3. Adverse Effects

- In rare instances, serious immune-mediated reactions have been reported with the use of r-ATG and consist of anaphylaxis (could be fatal) or CRS, which has been associated with cardiorespiratory dysfunction (including hypotension, ARDS, pulmonary oedema, myocardial infarction, tachycardia, and/or death).
- Severe, acute infusion-associated reactions (IARs) are consistent with CRS which is attributed to the release of cytokines by activated monocytes and lymphocytes. IARs may occur following the administration of r-ATG. Such reactions may occur as soon as the first or second dose. Clinical manifestations of IARs have included some of the following signs and symptoms: fever, chills/rigors, dyspnoea, nausea/vomiting, diarrhoea, hypotension or hypertension, malaise, rash, and/or headache.
- r-ATG must be used only under strict medical and nursing supervision (see r-ATG chart for more details) in an area with readily available life support equipment. If an anaphylactic or acute infusion reaction occurs, the infusion should be stopped immediately and appropriate emergency treatment should be initiated.

3.4. CMV prophylaxis

- Patients that have been treated with r-ATG may need prophylaxis against CMV and PJP infections.
- A 3 month course of oral valganciclovir is given to all patients treated with r-ATG unless BOTH the donor and recipient are CMV IgG negative. Valganciclovir doses are adjusted according to the patient's creatinine clearance – using the Cockcroft and Gault formula .
- All patients will receive a 6 month course of oral co-trimoxazole (480 mg daily). If they are allergic to either trimethroprim or sulfamethoxazole, patients will receive a 6 month course of oral atovaquone (750 mg bd). PJP prophylaxis must be prescribed on discharge to minimise the risk of myelosuppression if given concomitantly with r-ATG.
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4. Education and Training

None

5. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency
Number of patients treated with r-ATG per year	JAC report, medical notes review	Amy Page	Annually
Number of patients that received CMV prophylaxis after r-ATG	JAC report, medical notes review	Amy Page	Annually

6. Supporting References (maximum of 3)

Thymoglobuline® 25 mg powder for solution for infusion - Summary of Product Characteristics. Genzyme. Last revision: 3 May 2015. Available on the electronic medicines compendium (eMC) at www.medicines.org.uk. Accessed on 31/03/2016.

7. Key Words

ATG, thymoglobuline, rejection, kidney transplant

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Jorge Jesus-Silva HoS Nephrology	**Executive Lead** Atul Bagul HoS Transplant
Details of Changes made during review: April 2022 – Added r-ATG administration and monitoring chart, removed aseptic preparation at LRI pharmacy laboratory to reflect preparation and administration on the transplant ward. November 2024 – Minor amedments of style and form, but contents remain unchanged	

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THYMOGLOBULINE (r-ATG) CHART

Appendix 1 - PRESCRIBING, ADMINISTRATION AND MONITORING

Patient's details

Patient name
Hospital number
Date of birth
Address

Drug Sensitivities

Date recorded	Drug(s)	Reaction

The treatment dose of r-ATG is **1.5 mg/kg/day** (rounded to the nearest 25 mg vial) given for a total of **10-14 days** based on WBC, platelet and lymphocyte counts. See dose adjustments below:

- **Reduce r-ATG dose by 50%** if the total platelet count < 80 x 10^9/L or the total WBC is < 2.5 x 10^9/L
- **Do not administer r-ATG** if the total platelet count < 50 x 10^9/L, or the WBC < 1.5 x 10^9/L or the total lymphocyte count < 0.05 x 10^9/L

Patient's weight

Date										
Weight (Kg)										

Date										
Weight (Kg)										

Blood results

Date	Cr	K	Hb	WBC	Platelet count	Lymphocyte count		

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THYMOGLOBULINE (r-ATG) CHART

Patient's details

Patient name
Hospital number
Date of birth
Address

Indication for the use of r-ATG *(please include biopsy findings and other relevant clinical details)*

Concurrent therapies for the treatment of graft rejection *(please add details below)*

Patient's name:	**S number:**	**Date of birth:**

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THYMOGLOBULINE (r-ATG) CHART

1st THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

2nd THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

3rd THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

4th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

5th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

6th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

7th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

8th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

9th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations

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THYMOGLOBULINE (r-ATG) CHART

Patient's name:	S number:	Date of birth:

10th THYMOGLOBULINE (r-ATG) INFUSION

Date	Time	Premedication drugs	Route	Dose	Signature/ print name	Time Given	Given by/Checked by Sign/Print name	
		Paracetamol	oral	1g				
		Chlorphenamine	oral	4mg				
		Hydrocortisone	iv	100mg				
Start ATG 1 hour after administration of premedication drugs								
		r-ATG in 500mls of sodium chloride 0.9%*	iv					

* Infuse over at least 6 hours via central line. r-ATG must be administered during **core working hours** and life support measures are readily available due to its side-effect profile (including severe anaphylaxis).

	Start r-ATG	15 min	30 min	45 min	1 h	75 min	1.5 h	105 min	2 h
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

	2.5 h	3 h	3.5 h	4 h	5 h	6 h	7 h	8 h	9 h **
Time									
BP									
Pulse									
Respiratory rate									
Temp (°C)									
Oxygen saturation (%)									

**Follow EWS chart recommendations for further observations frequency.

Any other patient observations