Prescription Chart: Cyclophosphamide & Rituximab Regimen for Systemic Vasculitis

Including Juvenile Dermatomyositis, Wegner's Granulomatosis, Microscopic Polyarteritis, Polyarteritis Nodosa, Unclassified Vasculitis, Scleroderma

Patients Name:

Date of birth:

Diagnosis:
Allergies: **Consultant:**

Regimen

1. Methylprednisolone infusion 15mg/kg (max300mg) in 100ml over at least 60mins
2. Ondansetron 5mg/m^2 IV (Max 8mg) prior to Cyclophosphamide infusion (Metoclopramide 100micrograms/kg (Max 10mg) tds prn for 3 days for persistent nausea).
3. Mesna 3mg/kg oral or IV prior to Cyclophosphamide infusion.
4. Chlorphenamine oral - Dose as per CBNF
5. **Cyclophosphamide 15mg/kg (max1g) slow infusion over 30 minutes.**
6. Mesna 7.5mg/kg (Max 500mg) oral or IV. Given whilst cyclophosphamide running (T =15).
7. Oral paracetamol 15mg/kg (Max 1g)
8. IV fluids - hyperhydration rate = 125ml/m^2/hr for 1 hour of Dextrose 2.5% / Sodium Chloride 0.45%
9. **Rituximab 750mg/m²** (rounded to nearest 100mg, **max dose 1g**) Infused as per prescription.
10. Oral Mesna 7.5mg/kg (Max 500mg) oral or IV. Oral can be given whilst Rituximab running or IV given when Rituximab has finished, due to incompatibility.
11. IV flush of Sodium Chloride 0.9% at rate of last infusion.
12. Repeat cyclophosphamide & Rituximab 2 weeks later. Further doses of cyclophosphamide on its own may be given for a further 4 doses.
13. Request form to be given for GP to arrange blood test 2-3 days before the 2nd infusion. Results will be chased by the paediatric rheumatology team & Kamrans ward informed.

***Investigations*—**

Baseline bloods prior to each infusion. FBC, ESR, U&E's, LFT's. CRP, lymphocyte subsets CD19 or CD20 & Immunoglobulins (G,A & M)

Special Precautions for Cyclophosphamide: Cyclophosphamide is a human carcinogen. Contraception (regardless of gender) is advised during and for at least 3 months after therapy. No live vaccines should be given during treatment.

***Special Precautions for Rituximab*:** Contraception (regardless of gender) is advised during and for at least 12 months after therapy, Vaccines (live & non-live) should be completed at least 4 weeks prior to commencing a course of Rituximab. It is not known whether patients may need re-immunisation of previous non-live vaccines following rituximab. Once immunoglobulin's back to normal, check specific antibodies (Tetanus, Hib, Polio etc) from previous immunisations and if low, re-immunise and recheck levels. If patient has a contaminated wound (has received rituximab within the last 6 months) and there is any doubt about the patient's tetanus status, then a tetanus immunoglobulin should be administered.

Contraindications for Cyclophosphamide: Pregnancy, lactation, hypersensitivity, haemorrhagic cystitis and porphyria.

Contraindications for Rituximab: Pregnancy, lactation, Previous TB (unless treated), hypersensitivity. Active severe infections. Severe uncontrolled cardiac disease.

Name (sticker): **Kamran ward**
Date of birth:

GENERIC PROTOCOL

Must be completed before treatment starts

To be completed by treating Physician

Patient counselled on the following benefits of treatment?		N/A
Reduced mortality	☐	
Disease control	☐	
Prevention of premature organ failure	☐	
Patient counselled on the following risks of treatment?		
Need for adequate contraception during treatment and for 3 months afterwards	☐	
Infection	☐	
Reduced fertility – current guidelines	☐	☐
Malignancy	☐	
Adverse reactions		
e.g. nausea, hair thinning, diarrhoea, mouth ulcers	☐	
Risk of developing or worsening diabetes (due to steroid therapy)	☐	
Transient steroid side effects	☐	
Haemorrhagic cystitis (bleeding from an irritated bladder)	☐	
Pre screening checklist		
Blood tests taken within last 7 days; FBC, U&E, LFT, CRP lymphocyte subsets CD19 or CD20 & Immunoglobulins (G,A & M)	☐	
Chest x-ray within the last 3 months prior to 1st pulse in each cycle of treatment	☐	
Copy of this policy explained to patient	☐	
Give patient – information sheet plus AR-UK sheet	☐	

Complete CHAQ
Peds Qol
If time available PVAS, BILAG, SLICC

Date	
Counselled by (name and signature)	
Patient name and signature	

Special Precautions: Cyclophosphamide is a human carcinogen. Contraception in both sexes is advised during and for at least 3 months after therapy.

Contraindications: Pregnancy, lactation, hypersensitivity haemorrhagic cystitis and porphyria

Patient given PIL? YES/NO

Name (sticker): **Kamran ward**
Date of birth:

Delay of treatment / Dose Modifications.

Neutropenia - delay treatment until >1.5x10^9/L Discuss with consultant (cyclophosphamide can be reduced by 25%).

Thrombocytopenia – if <150 x 10/L discuss with consultant

Renal impairment-	creatinine	97-150 μmol/l	25% CYC reduction (& discuss with consultant)
		> 150 μmol/l	50-75% reduction (see GFR)
	GFR	50-80ml/min/1.73m^2	25% CYC reduction
		15-49 ml/min/1.73m^2	50% CYC reduction
		<15ml/ min/1.73m^2	75% CYC reduction
Hepatic impairment	ALT / AST	>200 iu/l consider reducing dose and discuss with consultant	

No dose reduction of steroid in term of neutropenia or renal impairment.

Dose Calculations and modifications
Patient weight =
Initial dose of cyclophosphamide = weight x 15mg
Subsequent dose = initial dose x percentage reduction (see above)

Repeat bloods day 12-13. FBC, ESR, U&E's, LFT's. CRP, lymphocyte subsets CD19 or CD20 & Immunoglobulins (G,A & M) If neutrophil <1.5x10/L or platelet <150x10/L discuss with consultant

Date		
HB		
Platelets		
Neutrophil		
Creatinine		
Bilirubin		
ALT		
BP		
others		

TTO: Please prescribe
Metoclopramide 100micrograms / kg (Max 10mg) orally tds prn for 3 days for persistent nausea.
Reduce Prednisolone maintenance dose if the patient is on it, but do not stop.

Nuffield Orthopaedic Centre and Children's Hospital Oxford

Oxford University Hospitals NHS
NHS Trust

For use in Juvenile Dermatomyositis, Vasculitis, JSLE and other organ threatening autoimmune disorders **Cyclophosphamide Dose – 15mg/kg for cycle 1 then review as per protocol** Contact Rheumatology team if concerned (Dr Nick Wilkinson 07944 723273, Joel David via NOC Switchboard or secretary ext 38049) **TTOs: prescribe Metoclopramide 100mcg/kg (Max 10mg) oral TDS PRN for 3 days**	**PAEDIATRIC CHEMOTHERAPY PRESCRIPTION KAMRAN'S WARD** CYCLOPHOSPHAMIDE and RITUXIMAB for PAEDIATRIC RHEUMATOLOGY PATIENTS Cycle_____ **TREATMENT INDICATION:_____** **CONSULTANT:_____** **PCT funding approved for Rituximab? Y/N (Pharmacy must have a copy of approval in writing for records)** **Number doses approved:_____**	Date Prescribed	
		Weight(kg) /Date taken	
		Surface Area (m^2)	
		TARGET DATE	

N.B. Always consult the full protocol

Admin Day/ Date	Admin Time	Drug	Dose	Route	Frequency / Duration	Administration Details	Prescriber Signature	Pharmacist Signature	ON HOLD Y/N	Dispensed From	**Admin Record** Date	Start time	Sign .nurse
DAY 1 or 15 (circle correct)	T= -1 hour	Methylprednisolone 15mg/kg up to a max of 300mg	mg	IVI	1 hour	Dilute in sodium chloride 0.9% 100ml				JR PHARM			
	T= 0 hours	Ondansetron 5mg/m^2	mg	IV	Bolus					Ward Stock			
	T= 0 hours	Chlorphenamine Dose as per CBNF	mg	Oral	Stat					Ward Stock			
	T= 0 hours	MESNA 3mg/kg	mg	Oral/ IV	Slow Bolus	Dose 1 Injection can be given orally				Ward Stock			
	T= 0 hours	Paracetamol 15mg/kg	mg	Oral	stat	Max dose 1g				Ward Stock			
	T= 0 hours	**CYCLOPHOSPHAMIDE** ☐ **15mg/kg** **or** ☐ **_____mg/kg**	mg	IVI	30 mins	In Sodium Chloride 0.9% 100ml bag			Y	BAXTER			
	T= +15 minutes	MESNA 7.5mg/kg	mg	Oral/ IV	Slow Bolus (if IV)	Dose 2 Injection can be given orally during Cyclophosphamide infusion				Ward Stock			
	T= +30mins	2.5% Glucose + 0.45% Sodium chloride	125ml/m^2/hour	IVI	1 hour	*1 hour post hydration then proceed to Rituximab infusion*				Ward Stock			

 Produced by Nick Wilkinson, Rhoda Welsh, Eunice Kendall and Emma Inness based on protocol of Connie Kon and Raashid Luqmani, Nuffield Orthopaedic Centre Date. Agreed July 2012. Version 2.0

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PAEDIATRIC CHEMOTHERAPY PRESCRIPTION
Cyclo/Ritux for Paed Rheumatology

Admin Record

Admin Day and Date	Admin Time	Drug	Dose	Route	Frequency/ Duration	Administration Details	Prescriber Signature	Pharmacist Signature	ON HOLD Y/N	Dispensed From	Date	Start time	Sign Nurse
DAY 1/15 **CONTINUED**	T= +1.5 hours	**RITUXIMAB**	mg	IVI	As per variable infusion rates opposite	**RECONSTITUTION – withdraw ____ml from a ____ml Sodium Chloride 0.9% bag (Remember to account for overage) Add ____ml (____mg) Rituximab to give a final concentration of 2 mg/ml and mix by inverting bag gently. Do not shake. Inspect for particles and administer immediately.** **INITIAL INFUSION** – start at 50mg/hr, increasing by 50mg/hr every 30 minutes to max 400mg/hr **SECOND and SUBSEQUENT INFUSIONS** – can start at 100mg/hr, increasing by 100mg/hr every 30 minutes to max 400mg/hr				JR PHARM			
		750mg/m^2 (Max 1g) (Round to nearest 100mg)				**Time (mins) / Rate (mg/hr) / Rate (ml/hr) / Set vol to be infused** **0-30** 50 25 12.5 **30-60** 100 50 25 **60-90** 150 75 37.5 **90-120** 200 100 50 **120-150** 250 125 62.5 **150-180** 300 150 75 **180-210** 350 175 87.5 **210 until completion** 400 200 150						
	T= + 2 hours	MESNA 7.5mg/kg	mg	Oral/ IV	Slow bolus (if IV)	Dose 3 Injection can be given orally during Rituximab infusion , otherwise give IV after Rituximab has finished due to incompatibility				Ward Stock			

- Monitor patient's vital signs (BP, pulse, respiration, temperature) every 15 minutes for the first hour, then hourly until one hour post infusion, or two hours post infusion if complications arise
- Have adrenaline, antihistamines and resuscitation equipment at bedside in case of anaphylactic reaction
- In the event of an infusion related reaction reduce infusion rate to half the current rate
- In the event of a moderate to severe reaction, stop infusion immediately, administer symptomatic treatment and restart at half the previous infusion rate when symptoms have resolved.
- Contact Rheumatology team if concerned (Dr Nick Wilkinson 07944 723273, Joel David via NOC Switchboard or secretary ext 38049)

Paediatric Rheumatology Cyclophosphamide Protocol

Name (sticker): **Kamran ward**
Date of birth:

ASSESSMENT OF RESPONSE
Patient assessed by consultant/SpR at baseline and following final pulse. Please refer to out-patient notes for details

Date	Assessment eg BVAS, BILAG, SLEDAI, SLAM

TOXICITY: document any toxicity experienced.
E.g.Nausea, vomiting, diarrhoea, alopecia, haematological, stomatitis etc.

Date	Assessment

Reference: [1] Adu D, Pall A, Luqmani RA, Richards NT, Howie AJ, Emery P, Michael J, Savage CO, Bacon PA.Controlled trial of pulse versus continuous prednisolone and cyclophosphamide in the treatment of systemic vasculitis. QJM. 1997 Jun;90(6):401-9.

Date	**Pulse 1**	**Pulse 2**
Next Blood Test		
Next Clinic Visit		
Assessed by Dr:		