APPENDIX – PAEDIATRIC AND ADULT PATIENT DRUG OVERVIEW – Lifetime Management of Kawasaki Disease

PAEDIATRIC DRUG DOSES

Patient Group	Therapy	Drug	Dose	Daily Max Dose	Formulations	Notes- According to current best practice.
All patients with CAA persisting > 6 weeks	**Antiplatelet therapy**	Aspirin	Maintenance dose of 2-5mg/kg daily	75mg daily	75mg dispersible tablet Some hospitals round the dose to the nearest quarter tablet.	Patients who have CAA persisting after 6 weeks, even if these remodel, should remain on long term aspirin Omit if high fever due to intercurrent disease, such as chickenpox to reduce risk of Reye's syndrome Best practice is to dissolve known dose in water, rather than dissolve 75mg tablet in water – when the amount given per unit volume is unknown
		Clopidogrel (second line)	Maintenance dose of 0.2-1 mg/kg daily (not in BNF-C, unlicensed)	75mg daily	75 mg tablet 25mg/5ml suspension	Consider clopidogrel (or alternative antagonist of ADP-mediated platelet aggregation). Add ranitidine if both therapies used. Lanzoprazole can be used
Those with giant CAA - Older children	**Add in Anticoagulant therapy**	Warfarin **OR**	Initially 200 micrograms/kg (max. per dose 10 mg) for 1 dose on day 1, then reduced to 100 micrograms/kg once daily (max. per dose 5 mg) for the following 3 days, subsequent doses adjusted according to INR levels, induction dose may need to be altered according to condition (e.g. abnormal liver function tests, cardiac failure), concomitant interacting drugs, and if baseline INR above 1.3.	Maintain the international normalised ratio (INR) at 2.5-3.5	Liquid 1mg/ml Tablets 0.5mg/1mg/3mg/ 5mg	Combined anti-coagulation and anti-platelet therapy are recommended for all KD patients with a coronary artery Z score ≥ 10 Check Appendix 1 of BNF-C for interactions
- Infants		Heparin (low molecular weight subcutaneous (LMWH))	Titrate to LMWH anti-Xa level (dose depending on which LMWH being used, as per BNF-C)	Keep LMWH anti-Xa activity at 0.5-1.0 IU/mL	Subcutaneous injection solution, using graduated pre-filled syringes (rounding dose for ease) Dose/monitoring depends on proprietary version	

Additional comments:

- It is recommended that the drug doses are checked against the BNF and BNFC for updated guidance and to ensure correct dosing.
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- Aspirin does not easily disperse https://ejhp.bmj.com/content/early/2019/06/11/ejhpharm-2019-001903
  https://www.researchgate.net/publication/312446743_Dose_uniformity_of_samples_prepared_from_dispersible_aspirin_tablets_for_paediatric_use
- For administration to use MEDUSA monographs (http://www.injguide.nhs.uk)
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  *a guideline which may be useful http://nww.avon.nhs.uk/dms/download.aspx?did=19365

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APPENDIX – PAEDIATRIC AND ADULT PATIENT DRUG OVERVIEW – Lifetime Management of Kawasaki Disease

Patient Group	Therapy	Drug	Dose	Daily Max Dose	Formulations	Notes
Children presenting with acute thrombosis	**Thrombolysis**	tPA (Tissue plasminogen activator) (alteplase) **AND**	By intravenous infusion: **neonate**: 100-500 micrograms per kilogram per hour for 3 to 6 hours; use ultrasound (echocardiography) to monitor effect before considering a 2nd course of treatment **child**: 100 to 500 micrograms per kilogram per hour for 3 to 6 hours, use ultrasound assessment to monitor effect before considering a 2nd course of treatment If using systemically, then the dose is 10 x than if by catheter directed local delivery	Maximum 100mg daily	Actilyse 10mg or 20mg powder and solvent for solution for injection – 1mg in 1ml. Draw up 1mg, make up to 5ml in normal saline 1ml=200mcg 10mg, 20mg, 50mg powder and solvent (administer via a dedicated line **not** with heparin)	Include monitoring of full blood count, clotting, fibrinogen and anti-Xa activity daily. Keep fibrinogen >100mg/dl and platelets >50,000/mm^3
		Concurrent Heparin (Unfractionated heparin UFH)	10 units/kg/hr IV maintenance (no bolus when running with alteplase)	Max 500 units/hr. To achieve APTT 1.5-2.5 or Activated clotting time of 200-250 or Unfractionated anti-Xa activity 0.35-0.7 IU/mL	Intravenous solution	
		Heparin (UFH) only	75units/kg bolus IV Then 20 units/kg/hr IV maintenance			
	Chest pain	Glyceryl trinitrate (use BNF-C)	Initially 0.2-0.5microgram/kg/minute IV adjusted according to response Then: 1-3micrograms/kg/minute	Max 10 micrograms /kg/minute	Intravenous solution	
With stent insertion	**IIb/IIIa platelet inhibitor**	Abciximab **OR**	250 microgram/kg as IV bolus over 1 min then 125 nanograms/kg/min infusion every 12 hours	Max 10 micrograms /minute	Dilute required dose in infusion fluid	**Not commonly used in paediatrics, doses are those for adults**
		Eptifibatide	180 microgram/kg IV bolus, then 2 microgram/kg/min infusion for 12 hours Often combine with heparin		Solution for injection/ solution for infusion	**Not commonly used in paediatrics, doses are those for adults** Measure baseline prothrombin time, APTT, platelet count, Hb and creatinine Monitor again at 6 hours then daily
	Anti-Inflammatory	Atorvastatin	Child 10-17 years 10mg daily	20mg/daily	10mg, 20mg chewable tablets	Potential anti-inflammatory benefit

Additional comments:

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APPENDIX – PAEDIATRIC AND ADULT PATIENT DRUG OVERVIEW – Lifetime Management of Kawasaki Disease

ADULT DRUG DOSES

Patient Group	Therapy	Drug	Dose	Daily Max Dose	Formulations	Notes
All patients with history of CAA	**Antiplatelet therapy**	Aspirin **AND/OR**	Maintenance dose 75mg daily	75mg daily	75mg dispersible tablet	Patients who have CAA persisting after 6 weeks, even if these remodel, should remain on long term aspirin.
		Clopidogrel	Maintenance dose of 75mg daily	75mg daily	75mg tablets	Consider alternative or addition of an antagonist of ADP-mediated activation platelet aggregation such as clopidogrel short term dual therapy
	PLUS Gastric protection if dual antiplatelet therapy	Lansoprazole	30mg daily	30mg daily	30mg capsule 30mg orodispersible tablets	Lansoprazole or Ranitidine
		Ranitidine	150mg twice daily	300mg twice daily	150mg tablets 150mg effervescent tablets	Lansoprazole or Ranitidine
Those with giant CAA	**Add in Anticoagulant therapy**	Warfarin **OR** Direct oral anticoagulant if warfarin not tolerated or contraindicated	Titrate to target international normalised ratio (INR)	Maintain the international normalised ratio (INR) at 2.5-3.5	Tablets 0.5/1/3/5mg	Combined anti-coagulation and anti-platelet therapy are recommended for all KD patients with a coronary artery Z score ≥ 10 Initial therapy to be covered with heparin to avoid paradoxical thrombosis at sub-therapeutic INR
		Apixaban	5mg twice daily. Reduce dose to 2.5mg twice daily in patients with at least two of the following: Age over 80 years, bodyweight <61kg, or serum creatinine 133micromol/L or more	10mg twice daily	Tablets 2.5mg/5mg	
		Rivaroxaban	2.5mg twice daily	20mg daily	Tablets 2.5mg/5mg /15mg/20mg	

Additional comments:

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Patient Group	Therapy	Drug	Dose	Daily Max Dose	Formulations	Notes
Adults presenting with acute thrombosis	**Thrombolysis**	tPA (Alteplase)	**For adults up to 65Kg** give: 15mg initially (within 6 hours of event) Followed by 0.75mg/kg over 30 minutes, Then by 0.5mg/kg over 60 minutes **For adults over 65Kg** give: 15mg initially (within 6 hours of event) Followed by 50mg over 30 minutes, Then by 35mg over 60 minutes	Intravenous infusion Maximum dose 100mg over 90 minutes	Actilyse 10mg or 20mg powder and solvent for solution for injection – 1mg in 1ml. Draw up 1mg and make up to 10ml with normal saline (1ml=100mcg) 10mg, 20mg, 50mg powder and solvent	Can also be given intracoronary- consult advice for dose. Include monitoring of full blood count, clotting, fibrinogen and anti-Xa activity
With stent insertion	**IIb/IIIa platelet inhibitor (or Tirofiban*)**	Abciximab **OR**	250 microgram/kg as IV bolus over 1 minute then immediately followed by an infusion of 125 nanograms/kg/min for 12 hours (started 10-60 minutes after PCI)	Max 10 micrograms/minute infusion	Solution for injection	Measure baseline prothrombin time, APTT, platelet count, Hb, and creatinine Monitor again at 6 hours then daily
		Eptifibatide	180 microgram/kg IV bolus, then 2 microgram/kg/min infusion for up to 72 hours (up to 96 hours if PCI during treatment see BNF)		Solution for injection/solution for infusion	
	Anti-Inflammatory	Atorvastatin	20mg/daily	Max 80mg daily	20mg Tablets	Potential anti-inflammatory benefit

Good practice in prescribing and managing medicines and devices (2013)

https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/prescribing-and-managing-medicines-and-devices/prescribing-unlicensed-medicines

Additional comments:

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