Clinical Guideline

WARFARIN MANAGEMENT FOR PAEDIATRIC CARDIAC PATIENTS

SETTING Cardiac Unit Bristol Royal Hospital for Children and Regional Network

FOR STAFF Medical and Nursing staff

PATIENTS Children and Young People with cardiac conditions requiring warfarin

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Disclaimer:
This has been produced as a guide; each individual patient should be considered whether treatment is clinically appropriate. If needed, please discuss further with specialist teams.

GUIDELINE CONTENT

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INDICATIONS FOR WARFARIN

Warfarin is indicated for anticoagulation in children and young people who have a prosthetic mechanical valve or Fontan circulation (total cavo-pulmonary connection[TCPC]).It may also be indicated in children where there has been extensive pulmonary artery reconstruction or stent implantation associated with a venous shunt (Glenn shunt). Additional indications where warfarin may be required include children with cardiomyopathy, Kawasaki disease or thrombo-embolic problems. For long term anti-coagulation, neonates and infants, up to 6 months of age, subcutaneous heparin should be considered as an alternative due to the problems of managing warfarin in this age group. After 6 months changing to warfarin should be considered.

TARGET INTERNATIONAL NORMALISED RATIO (INR) RANGE

Indication for Anticoagulation	INR range
TPCP/Fontan circuit	2-3
Mechanical mitral valve* replacement	2.5-3.5
Mechanical aortic valve* replacement	2-3
Other e.g. Cardiomyopathy, arrhythmias Kawasaki, pulmonary valves	2-3
Individualised patient protocols on warfarin and low molecular weight heparin	As suggested & documented in the medical notes
On discussion with the cardiac surgeon and Cardiologist	As suggested & documented in the medical notes

Note: these are guide ranges and depend on the individual patient.
* Higher INR range may be appropriate in infants with small mechanical valve. Any deviation from this should be documented in the patient's medical notes.

DRUG INFORMATION

Class of drug
Anticoagulant- Coumadin (vitamin K antagonist)

Available preparations
1mg/ml sugar free oral solution
1mg (brown coloured) & 3mg (blue coloured) tablets (tablets available in UHBristol)

Note: 0.5mg & 5mg tablets not stocked in UHBristol due to risk of dosing errors.

Administration
The tablets can be crushed and dispersed in a small volume of water and the dose can be taken from this solution. New tablets should be used for each dose.

Method of action
Warfarin acts on secondary haemostasis by interfering with hepatic synthesis of Vitamin K dependent clotting factors. Factors II (prothrombin), VII, IX and X require Vitamin K for synthesis in the liver. Warfarin antagonises vitamin K by inhibiting the enzyme 'Vitamin K epoxide reductase'. In the absence of vitamin K the coagulation cascade is depleted and fibrin generation is inadequate to form the mesh, reducing the chance of clots developing.

Side effects
Main side effect is bleeding (long nose bleeds/bleeding from a graze that does not stop after 10 minutes/bruising/black tarry faeces/blood in urine). Other side effects include rash, headache, diarrhoea).

Relative Contra-indications
Gastrointestinal ulceration, severe hypertension, bacterial endocarditis.

Cautions
In severe renal and hepatic impairment (especially if prothrombin time is already prolonged). Use under consultant specialist advice only. Head injury in this patient population should be taken seriously due to risk of bleeding).

Drug Interactions
Warfarin interacts with many drugs. Homeopathic medicines do not interact with warfarin but herbal medication can. Please refer to NICE guidelines or discuss with ward pharmacist.
https://bnf.org.uk/interaction/warfarin.html

INITIATING WARFARIN

When a patient is started on warfarin, the following information should be documented in the patient's medical notes. Relevant information should also be documented on their drug chart;

- Start date of warfarin
- Diagnosis/indication
- Target International normalised ratio (INR) range
- Duration of treatment
- The team monitoring treatment e.g. G.P., community team or cardiac nurse specialist
- Documentation that verbal & written information has been given

Most patients commencing warfarin will have initially been commenced on intra-venous anti-coagulation (refer to anticoagulation guidelines).

Venous Monitoring prior to Commencement of Warfarin
Full clotting screen, U&Es, LFTs & FBC within 48 hours prior to commencing warfarin.

Loading

Day 1 200-300micrograms/kg (0.2mg/kg) [max 10 mg] once a day orally, depending on medical indication

[Note: a lower dose of 100 micrograms/kg can be used initially if required e.g. if coagulation already abnormal, liver dysfunction, severe renal dysfunction or at consultant discretion]

Day 2-4 Dose relative to the INR result

INR < 1.4	Repeat day one dose
INR 1.4-1.9	50% of day one dose
INR 2-3	25% of day one dose
INR>3	stop until INR <3 and restart at 50% of previous dose

Loading period is usually 3 - 5 days until stable INR obtained.

Note: the prescribing doctor must check the INR result from that day prior to prescribing the next dose

Timing of Dose

Warfarin should be given as near as possible at the same time every day.

VENOUS & FINGERPRICK INR SAMPLING

For in-patients on a loading regime and IV unfractionated heparin, INR must be checked with venous samples. For out-patients & inpatients on maintenance dose warfarin, use Coaguchek® machine.

Coaguchek® machine is not accurate if the INR is high, in this case a venous sample is required. Coaguchek® should not be used if also on unfractionated heparin or if the haematocrit is high (>0.55).

Patient and carers are instructed how to use the Coaguchek®, using manufacturer guidelines. Information will be given about lifestyle, diet, drug interactions (See “Changes in INR” section).

A member of the cardiac specialist nurse team will see the patient and carer 6 monthly- yearly to assess competency and correlate Coaguchek® against either a venous sample or by an externally controlled machine using UK National External Quality Assessment Schemes (NEQAS). The patient’s GP and cardiology consultant will receive letters informing them of these results.

MAINTENANCE DOSES (See Table 1)

Use Table 1 to decide how many incremental changes (if any) are needed and then calculate the warfarin dose using the dosage table (see Appendix 1).

INR Result	Warfarin Dose
>1 below target range	Increase dose by 3 increments
>0.5 – 1.0 below target range	Increase dose by 2 increments
0.2 – 0.5 below target range	Increase dose by 1 increment
Target range	No change in dose
<0.2 above target range	No change (depending on trend)
0.2 – 1.0 above target	Reduce dose by 1 decrement
1.01 – 1.5 above target range	Reduce dose by 2 decrements
>1.5 above target range	Halve dose, discuss with consultant; repeat INR next day; restart with dose reduced by 1 decrement.

TABLE 1. WARFARIN DOSAGE TABLE (dose in mg)

10	5
9.5 / 10 / 10	4.5 / 5 / 5
9.5 / 10	4.5 / 5
9.5 / 9.5 / 10	4.5 / 4.5 / 5
9.5	4.5
9 / 9.5 / 9.5	4 / 4.5 / 4.5
9 / 9.5	4 / 4.5
9 / 9 / 9.5	4 / 4 / 4.5
9	4
8.5 / 9 / 9	3.5 / 4 / 4
8.5 / 9	3.5 / 4
8.5 / 8.5 / 9	3.5 / 3.5 / 4
8.5	3.5
8 / 8.5 / 8.5	3 / 3.5 / 3.5
8 / 8.5	3 / 3.5
8 / 8 / 8.5	3 / 3 / 3.5
8	3
7.5 / 8 / 8	2.5 / 3 / 3
7.5 / 8	2.5 / 3
7.5 / 7.5 / 8	2.5 / 2.5 / 3
7.5	2.5
7 / 7.5 / 7.5	2 / 2.5 / 2.5
7 / 7.5	2 / 2.5
7 / 7 / 7.5	2 / 2 / 2.5
7	2
6.5 / 7 / 7	1.5 / 2 / 2
6.5 / 7	1.5 / 2
6.5 / 6.5 / 7	1.5 / 1.5 / 2
6.5	1.5
6 / 6.5 / 6.5	1 / 1.5 / 1.5
6 / 6.5	1 / 1.5
6 / 6 / 6.5	1 / 1 / 1.5
6	1
5.5 / 6 / 6	0.5 / 1 / 1
5.5 / 6	0.5 / 1
5.5 / 5.5 / 6	0.5
5.5	0 / 0.5 / 0.5
5 / 5.5 / 5.5	0 / 0.5
5 / 5.5	0 / 0 / 0.5
5 / 5 / 5.5	

Reducing by one increment

Increase by one increment (example 2)

Reduce by 1 increment (example 1)

Increasing by one increment

Example dose; 5 / 5 / 5.5 means give 5 mg on Day 1, 5 mg on Day 2 and 5.5 mg on Day 3; then repeat the cycle.

Example1 : Patient range 1.8-2.5 usual dose 3/3.5/3.5, has an INR of 3.4. Above range 0.9 therefore reduce dose by 1 place making dose 3/3.5 then re-check INR.
Example 2: Patient range 3-4 usual dose 4/4.5, has INR of 2.5. Below range 0.5 therefore

increase by 1 place 4.5/4.5/4 then recheck INR.

MONITORING INR FOR OPD ON WARFARIN (near point testing)

INR is:	Recheck
Stable and within range	Every 2 weeks
Dose changed 1 place up or down	Weekly (depending on trend)
Dose changed >1 place up or down	Within 3 days (depending on trend)
Half dose or re-load	Daily

Note: parents or carers of patients on warfarin should contact the cardiac nurse specialist team or on call cardiology registrar (out of hours) if child is unwell. Firstly, consider checking the INR if there has been any changes in diet or drug therapy or any other changes that could affect their INR.

OUT OF RANGE INR OR UNUSUAL BLEEDING

INR	Action/Comment
<1.5 TCPC valve Cardiomyopathy Kawasaki disease <1.8 Aortic Valve <2 Mitral Valve	Discuss with medical team and alter dose as per protocol Consult with Consultant cardiologist/Senior Registrar .Consider admission for heparinisation in patients with a prosthetic valve. Patients with other indications for anticoagulation may need increased dose or limited re-load, but this can often be overseen as an outpatient.
INR >6	Confirm INR reading with venous sample. If venous INR > 6 discuss with consultant on call. High INR levels may require hospital admission. If venous INR is <6 with no active bleeding, alter dose management and check INR next day
INR >10	Hospital admission. Stop warfarin. May require treatment. Rx should only be initiated after discussion with the consultant cardiologist on call.
INR>6 with active bleeding PR/PU/Gums/ Haemoptysis	Urgent discussion with senior medical staff. Confirm with venous INR sample. Arrange for admission to hospital with consideration for Vitamin K or prothrombin complex concentrate* (OctAplex-dose based on weight and INR) INR should be repeated if Vitamin K or prothrombin complex concentrate given
Normal INR with unusual or new bleeding	Discussed with the Cardiac Nurse Specialist team and/or senior medical staff if required

*available in hours via paediatric haematology team or out of hours via clinical site team (Bristol Hospital for Children).

REVERSAL OF WARFARIN

If, after discussion with the consultant cardiologist, partial reversal of warfarin is needed, stop warfarin and consider giving a small dose of vitamin K (not weight based dose), which competes with warfarin for the enzyme 'vitamin K epoxide reductase'.

Give initial single dose of vitamin K (Phytomenanadione) 0.1mg IV,

which after review by senior medical staff in discussion with consultant can be repeated in increments of 0.1mg up to a total maximum of 1mg.

[Note: this is lower than the dose stated in the BNF-C. For complete reversal of warfarin, seek advice from consultant cardiologist].

Vitamin K should be diluted with sodium chloride 0.9% or glucose 5% to 10ml and given over 5-10 minutes. IV injection may cause peripheral vascular collapse, cyanosis, sweating and flushing if given too rapidly.

If immediate reversal is required then discuss with a Paediatric Consultant Haematologist, with the possibility of using Prothrombin Complex Concentrate.

Note: large doses of vitamin K will make re-warfarinisation difficult for several weeks and should be avoided and compromise mechanical prosthetic valve function if INR drops rapidly. Small doses should therefore be used to bring INR back into range. If there is bleeding, administration of prothrombin complex* if available or FFP may be considered but can precipitate mechanical valve dysfunction.

INVASIVE PROCEDURES , CARDIAC CATHETERS OR SURGERY

If a patient is coming into hospital for a cardiac catheter or surgery that has a mechanical valve:

- Their warfarin is stopped by the cardiac specialist nurse team 3 days prior to catheter or surgery
- They should be admitted to hospital 2 days before cardiac catheter or surgery and venous INR checked on admission. The INR should be less than 2.
- Once INR is less than 2, initiate unfractionated heparin at the age appropriate flow rate as shown in the non-cardiac procedure (prosthetic valves) section below.

If a patient is coming into hospital for surgery (excluding patients with mechanical valves):

- Their warfarin should be stopped 3 days prior to surgery by the cardiac nurse specialist.
- They should be admitted to hospital the day before surgery when their venous INR is checked. The INR should be less than 2.

If a patient is coming into hospital for a cardiac catheter (excluding patients with mechanical valves):

- Their warfarin should be stopped 3 days, by the cardiac nurse specialist, prior to cardiac catheter
- They should be admitted to hospital either the day before the catheter when the INR should be checked by finger prick on arrival or if patient arrives on the morning of the cardiac catheter, the INR should be checked at home 24 hours prior to the catheter. The INR should be less than 2.

Prosthetic valves

NON CARDIAC PROCEDURE: treated on a case by case basis on discussion with the Cardiac Nurse Specialist team in discussion with senior medical staff if required.

If anticoagulation is necessary an unfractionated heparin infusion will need to be initiated:

- < 1 year old 28 units/kg/hour
- >1year old 20 units/kg/hour (up to a maximum of 1000 units/hour)

IMPORTANT PATIENT INFORMATION

Counselling the Family
Why warfarin is needed?
Action of warfarin
Monitoring of INR
Different tablet strengths
What to do if you miss a dose?
What to do if you take the wrong dose?
What to do if medication is added/stopped or changed?
Dietary advice-no binge dieting
Lifestyle advice- pregnancy/no contact sports

Supply yellow anticoagulant treatment pack with warfarin alert card

FACTORS INFLUENCING INR CONTROL

Changes in diet, intercurrent illness, drug therapy & alcohol intake can affect anticoagulation control.

Patient Factors

Enhanced anticoagulation can occur with intercurrent illness, weight loss, liver disease, renal failure and heart failure. Reduced anticoagulant effect can occur with weight gain and diarrhoea & vomiting.

Dietary

Foods high in vitamin K will antagonise the effects of warfarin (decrease INR) e.g. green leafy vegetables so the patient should be advised not to change the level of consumption of these foods. Infant formula is supplemented with vitamin K, which makes formula fed infants more resistant to warfarin whereas breast milk contains low concentrations of vitamin K making breast fed infants more sensitive to warfarin.

Medication

There are various drug-warfarin interactions which can increase the rate of metabolism of warfarin, decrease the rate of metabolism of warfarin, reduce the absorption of warfarin from the gut, displace warfarin from protein binding sites, antagonise the mechanism of action of warfarin or increase the risk of bleeding without affecting INR. BNF-C Appendix 1.

Alcohol

Although this may not apply to the majority of children, it is relevant to transition patients. Heavy, regular intake of alcohol may reduce the anticoagulant effect. Acute intake may enhance anticoagulant effect.

PROBLEM SOLVING

Consider the following if there are changes in INR

- New medicine added
- A medicine has been stopped
- A change in dose of medication
- Over the counter/ herbal medicines
- Change in diet
- Compliance issues

IMMUNISATIONS

Some immunisations can be given subcutaneously rather than intra- muscularly, check with the ward pharmacist regarding administration.

ANNUAL AUDIT

An annual audit of the safety indicators outlined in the National Patient Safety Alert (NPSA) 18; 'Actions that make anticoagulants safer', which includes those patients newly started and those patients on maintenance therapy. The results should be collated and feedback to the cardiac governance group at least annually by the cardiac nurse specialist team.

Table A

REFERENCES	BNF-C 2017-18 NPSA ALERT 18 Children's Heart Unit for Wales Clinical Guidelines
RELATED DOCUMENTS AND PAGES	Warfarin leaflet http://nww.avon.nhs.uk/dms/download.aspx?did=21441 Anticoagulation guideline-PICU/Cardiac: http://nww.avon.nhs.uk/dms/Download.aspx?r=1&did=16300&f=AnticoagulationOnPicuAndWard32-3.pdf
AUTHORISING BODY	Paediatric Cardiac Governance Group
SAFETY	If there are unusual or unexpected safety concerns (to staff or patients) which you would wish to draw users' attention to, add them here.
QUERIES AND CONTACT	This is for whomever might be best placed to answer a query, not necessarily the author of the document. A department telephone or bleep can be placed here.